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Methods to decrease blood loss during liver resection: a network meta-analysis (Review)

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[Intervention Review]

Methods to decrease blood loss during liver resection: a network meta-analysis

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ABSTRACT

Background

Liver resection is a major surgery with significant mortality and morbidity. Specialists have tested various methods in attempts to limit blood loss, transfusion requirements, and morbidity during elective liver resection. These methods include different approaches (anterior versus conventional approach), use of autologous blood donation, cardiopulmonary interventions such as hypoventilation, low central venous pressure, different methods of parenchymal transection, different methods of management of the raw surface of the liver, different methods of vascular occlusion, and different pharmacological interventions. A surgeon typically uses only one of the methods from each of these seven categories. The optimal method to decrease blood loss and transfusion requirements in people undergoing liver resection is unknown.

Objectives

To assess the effects of different interventions for decreasing blood loss and blood transfusion requirements during elective liver resection.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, and Science Citation Index Expanded to September 2015 to identify randomised clinical trials. We also searched trial registers and handsearched the references lists of identified trials.

Selection criteria

We included only randomised clinical trials (irrespective of language, blinding, or publication status) comparing different methods of decreasing blood loss and blood transfusion requirements in people undergoing liver resection.

Data collection and analysis

Two review authors independently identified trials and collected data. We assessed the risk of bias using Cochrane domains. We conducted a Bayesian network meta-analysis using the Markov chain Monte Carlo method in WinBUGS 1.4, following the guidelines of the National Institute for Health and Care Excellence Decision Support Unit guidance documents. We calculated the odds ratios (OR) with 95% credible intervals (CrI) for the binary outcomes, mean differences (MD) with 95% CrI for continuous outcomes, and rate ratios with 95% CrI for count outcomes, using a fixed-effect model or random-effects model according to model-fit. We assessed the evidence with GRADE.

Main results

We identified 67 randomised clinical trials involving a total of 6197 participants. All the trials were at high risk of bias. A total of 5771 participants from 64 trials provided data for one or more outcomes included in this review. There was no evidence of differences in most of the comparisons, and where there was, these differences were in single trials, mostly of small sample size. We summarise only the evidence that was available in more than one trial below. Of the primary outcomes, the only one with evidence of a difference from more than one trial under the pair-wise comparison was in the number of adverse events (complications), which was higher with radiofrequency dissecting sealer than with the clamp-crush method (rate ratio 1.85, 95% CrI 1.07 to 3.26; 250 participants; 3 studies; very low-quality evidence). Among the secondary outcomes, the only differences we found from more than one trial under the pair-wise comparison were the following: blood transfusion (proportion) was higher in the low central venous pressure group than in the acute normovolemic haemodilution plus low central venous pressure group (OR 3.19, 95% CrI 1.56 to 6.95; 208 participants; 2 studies; low-quality evidence); blood transfusion quantity (red blood cells) was lower in the fibrin sealant group than in the control (MD −0.53 units, 95% CrI −1.00 to −0.07; 122 participants; 2; very low-quality evidence); blood transfusion quantity (fresh frozen plasma) was higher in the oxidised cellulose group than in the fibrin sealant group (MD 0.53 units, 95% CrI 0.36 to 0.71; 80 participants; 2 studies; very low-quality evidence); blood loss (MD −0.34 L, 95% CrI −0.46 to −0.22; 237 participants; 4 studies; very low-quality evidence), total hospital stay (MD −2.42 days, 95% CrI −3.91 to −0.94; 197 participants; 3 studies; very low-quality evidence), and operating time (MD −15.32 minutes, 95% CrI −29.03 to −1.69; 192 participants; 4 studies; very low-quality evidence) were lower with low central venous pressure than with control. For the other comparisons, the evidence for difference was either based on single small trials or there was no evidence of differences. None of the trials reported health-related quality of life or time needed to return to work.

Authors' conclusions

Paucity of data meant that we could not assess transitivity assumptions and inconsistency for most analyses. When direct and indirect comparisons were available, network meta-analysis provided additional effect estimates for comparisons where there were no direct comparisons. However, the paucity of data decreases the confidence in the results of the network meta-analysis. Low-quality evidence suggests that liver resection using a radiofrequency dissecting sealer may be associated with more adverse events than with the clamp-crush method. Low-quality evidence also suggests that the proportion of people requiring a blood transfusion is higher with low central venous pressure than with acute normovolemic haemodilution plus low central venous pressure; very low-quality evidence suggests that blood transfusion quantity (red blood cells) was lower with fibrin sealant than control; blood transfusion quantity (fresh frozen plasma) was higher with oxidised cellulose than with fibrin sealant; and blood loss, total hospital stay, and operating time were lower with low central venous pressure than with control. There is no evidence to suggest that using special equipment for liver resection is of any benefit in decreasing the mortality, morbidity, or blood transfusion requirements (very low-quality evidence). Radiofrequency dissecting sealer should not be used outside the clinical trial setting since there is low-quality evidence for increased harm without any evidence of benefits. In addition, it should be noted that the sample size was small and the credible intervals were wide, and we cannot rule out considerable benefit or harm with a specific method of liver resection.

PLAIN LANGUAGE SUMMARY

Surgical methods to decrease blood loss during liver surgery

Background

Many cancerous and non-cancerous growths that develop in the liver are treated by removing part of the liver (liver resection), which is major surgery with high risk of complications, including blood loss during division of the liver tissue. Specialists have tested several methods to decrease blood loss during liver resection. These include lowering the pressure in the liver veins (low central venous

pressure) or decreasing the amount of air that enters and leaves the lungs (hypoventilation), again aimed at decreasing central venous pressure; different ways of cutting the liver, for example, without any special equipment or using ultrasound waves or high-frequency (radiofrequency); applying glue to decrease bleeding from the cut surface; blocking the blood supply to the liver during the operation, a process known as vascular occlusion, which could be performed continuously or intermittently. In addition, medical treatments that improve clotting of blood can be given to decrease blood loss. A surgeon typically uses one or more methods to decrease blood loss during liver surgery. The optimal method is unknown. We sought to identify the best methods of decreasing blood loss during liver surgery by performing a literature search that included all studies reported until September 2015. We used special statistical methods, so-called network meta-analyses. to compare the different treatments simultaneously as compared to the traditional Cochrane method of comparing two treatments at a time as there are multiple treatment strategies.

Study characteristics

We identified 67 randomised clinical trials involving a total of 6197 participants that met our inclusion criteria. However, we were only able to include 5771 participants from 64 trials since investigators either did not include the remaining participants in the analysis or did not report any outcomes of interest.

Source of funding: 24 trials (35.8%) were funded by parties with no financial interest in obtaining positive results for the treatment being evaluated. The remaining trials received funding from either parties who would gain financially from the results of the study or did not report the funding.

Quality of evidence

All the trials were at high risk of bias, that is, investigators may have overestimated the benefits or underestimated the harms of one method or the other because of the way that the studies were conducted. Many trials included few participants, and there was a good chance of arriving at the wrong conclusions because of this. The overall quality of evidence was low or very low.

Key results

There was no evidence of differences in most of the comparisons, and where there was, these differences were in single trials, mostly of small sample size. Such evidence is unreliable. So, we mention only the evidence that was available in more than one trial. Of the primary outcomes, the only one where there was evidence of difference was in the number of adverse events, which was higher with radiofrequency dissecting sealer than with clamp-crush method. Among the secondary outcomes, the only evidence of difference was in the following:

Blood transfusion (percentage): higher in the low central venous pressure group than in the acute normovolemic haemodilution (diluting the blood by giving fluids during operation) plus low central venous pressure group.

Blood transfusion amount: lower in the fibrin sealant group (a type of glue applied to the cut surface of the liver) than in the control.

Blood transfusion (fresh frozen plasma — a component of blood): higher in the oxidised cellulose (another type of glue applied to the cut surface of the liver) group than in the fibrin sealant group.

Blood loss, total hospital stay, and operating time: lower with the low central venous pressure group than control.

For other comparisons, the evidence for difference was based on single small trials, or there was no evidence of differences. None of the trials reported health-related quality of life or time needed to return to work. There is no evidence to suggest that using special equipment for liver resection is of any benefit.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Methods to decrease blood loss during liver resection: a network meta-analysis. Primary outcomes

Patient or population: people undergoing liver resection
Settings: secondary or tertiary setting
Intervention and control: various treatments
Follow-up: until discharge or 1 month (except for mortality (long-term follow-up) which was reported at 1 year

Outcomes	Anterior approach versus conventional approach	Autologous blood donation versus control	Cardiopulmonary interventions	Methods of parenchymal transection	Methods of dealing with cut surface	Methods of vascular occlusion	Pharmacological interventions
Treatments The first treatment listed is the control. The remaining are interventions	1. Conventional approach 2. Anterior approach	1. Control 2. Autologous blood donation	1. Control 2. Acute normovolemic haemodilution plus low central venous pressure 3. Hypoventilation 4. Low central venous pressure	1. Clamp-crush method 2. Cavitron ultrasonic surgical aspirator 3. Hydrojet 4. Radiofrequency dissecting sealer 5. Sharp transection method 6. Stapler	1. Control 2. Argon beam 3. Collagen 4. Cyanoacrylate 5. Fibrin sealant 6. Fibrin sealant plus collagen 7. Oxidised cellulose 8. Plasmajet	1. Control 2. Continuous hepatic vascular exclusion 3. Continuous portal triad clamping 4. Continuous selective hepatic vascular exclusion 5. Continuous selective portal triad clamping 6. Intermittent portal triad clamping 7. Intermittent selective portal triad clamping	1. Control 2. Anti-thrombin III 3. Recombinant factor VIIa 4. Tranexamic acid
Link for detailed 'Summary of Findings tables'	Table 14	Table 15	Table 16	Table 17	Table 18	Table 19	Table 20

Mortality (perioperative)	There was no evidence of differences in perioperative mortality between the 2 groups Quality of evidence = very low[1,2,3].	There was no evidence of differences in perioperative mortality between the two groups Quality of evidence = very low[1,2,3].	There was no evidence of differences in perioperative mortality for any of the comparisons Quality of evidence = very low[1,2,3].	There was no evidence of differences in perioperative mortality for any of the comparisons Quality of evidence = very low[1,2,3].	There was no evidence of differences in perioperative mortality for any of the comparisons Quality of evidence = very low[1,2,3].	There was no evidence of differences in perioperative mortality for any of the comparisons Quality of evidence = very low[1,2,3].	There was no evidence of differences in perioperative mortality for any of the comparisons Quality of evidence = very low[1,2,3].
Mortality (longest follow-up)	None of the trials reported this outcome.	There was no evidence of differences in mortality at 1 year between the 2 groups. Quality of evidence = very low)[1,2,3].	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.
Serious adverse events (proportion)	There was no evidence of differences in the proportion of participants experiencing serious adverse events between the 2 groups Quality of evidence = very low[1,2,3].	None of the trials reported this outcome.	There was no evidence of differences in the proportion of participants experiencing serious adverse events (for any of the comparisons Quality of evidence = very low[1,2,3].	There was no evidence of differences in the proportion of participants experiencing serious adverse events for any of the comparisons Quality of evidence = very low[1,2,3].	There was no evidence of differences in the proportion of participants experiencing serious adverse events for any of the comparisons Quality of evidence = very low[1,2,3].	The proportion of participants experiencing serious adverse events[a] was lower in continuous selective portal triad clamping than continuous portal triad clamping • Proportion with serious adverse events in continuous portal triad clamping: 367 per 1000 • Proportion with serious adverse events in continuous	There was no evidence of differences in the proportion of participants experiencing serious adverse events for any of the comparisons Quality of evidence = very low[1,2,3].

						selective portal triad clamping: 154 per 1000 (66 to 352) • Relative effect: OR 0.42, 95% CrI 0. 18 to 0.96 • 120 participants; 1 study. • Quality of evidence = very low [1,2,3]. There was no evidence of differences in other comparisons. Quality of evidence = very low [1,2,3]	
Serious adverse events (number)	None of the trials reported this outcome.	None of the trials reported this outcome.	There was no evidence of differences in the number of serious adverse events for any of the comparisons Quality of evidence = very low [1,2,3].	The number of serious adverse events was higher in radiofrequency dissecting sealer than clamp-crush method • Serious adverse rate in clamp-crush method: 53 per 1000 • Serious adverse rate in radiofrequency dissecting sealer: 193 per 1000 (66 to 740)	The number of serious adverse events was higher in fibrin sealant than argon beam • Serious adverse event rate in argon beam: 65 per 1000 • Serious adverse event rate in fibrin sealant: 313 per 1000 (112 to 1138) • Relative effect: rate ratio 4.81, 95% CrI 1.73 to 17.5.	The number of serious adverse events was lower in intermittent portal triad clamping than continuous portal triad clamping • Serious adverse event rate in continuous portal triad clamping: 136 per 1000 • Serious adverse event rate in intermittent portal triad clamping: 12 per	There was no evidence of differences in the number of serious adverse events for any of the comparisons Quality of evidence = very low [1,2,3].

				• Relative effect: rate ratio 3.64, 95% CrI 1.25 to 13.97. • 130 participants; 2 studies. • Quality of evidence = low[1,2]. There was no evidence of differences in other comparisons. Quality of evidence = very low[1,2,3].	• 121 participants; 1 study. • Quality of evidence = low[1,2]. There was no evidence of differences in other comparisons. Quality of evidence = very low[1,2,3].	1000 (0 to 76) • Relative effect: rate ratio 0.09, 95% CrI 0.00 to 0.56 • 86 participants; 1 study. • Quality of evidence = low[1,2]. There was no evidence of differences in other comparisons Quality of evidence = very low[1,2,3].	
Health-related quality of life	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome at any time point.	None of the trials reported this outcome at any time point.	None of the trials reported this outcome at any time point.	None of the trials reported this outcome at any time point.	None of the trials reported this outcome at any time point.

CrI: credible intervals; **OR**: odds ratio.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).
[2] Sample size was low (total number of participants fewer than 400 for continuous outcomes and fewer than 300 events in total in both groups for other outcomes) (downgraded by 1 point).
[3] Credible intervals spanned no effect and clinically significant effect (20% relative risk reduction for binary outcomes; standardised mean difference of 0.5 for health-related quality of life) (downgraded by 1 point).
[a] Network meta-analysis was performed for this outcome because of the availability of direct and indirect comparisons in the network. The remaining outcomes were analysed by direct comparisons.

BACKGROUND

Description of the condition

Liver resection refers to removal of part of the liver. Every year, an average of 2400 people undergo liver resections in England (HSCIC 2015), 11,000 in the USA (Asiyanbola 2008), and 7200 in France (Farges 2012). In the West, the main indication for liver resection is colorectal liver metastases. Colorectal cancer is the third most common cancer in the world. Approximately 1.36 million people develop colorectal cancer each year (IARC 2012), and 50% to 60% will have colorectal liver metastases (Garden 2006). Liver resection, the only curative option for people with colorectal liver metastases, is indicated in 20% to 30% of people in whom the metastasis is confined to the liver (Garden 2006). Five-year survival for people with colorectal liver metastases who undergo liver resection is about 45% (Garden 2006; Nordlinger 2013).

The second most common reason for liver resection is hepatocellular carcinoma. Hepatocellular carcinoma is one of the most common cancers, with a worldwide annual incidence of 780,000 people (IARC 2012). Most hepatocellular carcinomas develop in cirrhotic livers (Llovet 2005). Liver resection and liver transplantation are the main curative treatments (Llovet 2005; Taefi 2013). Of people who present with hepatocellular carcinoma, about 5% are candidates for liver resection (Chen 2006). Survival after surgery depends on the stage of cancer and the severity of the underlying chronic liver disease. People with early-stage disease (cancers smaller than 5 cm) have a five-year survival of about 50%, whereas people with more advanced disease have a five-year survival of about 30% (Chen 2006; Navadgi 2016). Screening programmes in theory should lead to a diagnosis at an earlier stage, when surgery is feasible and associated with better outcomes.

Liver resection may also be performed for benign liver tumours (Belghiti 1993).

The liver can be subdivided into eight segments (Couinaud 1999), which can be removed individually or by right hemi-hepatectomy (Couinaud segments 5 to 8), left hemi-hepatectomy (segments 2 to 4), right trisectionectomy (segments 4 to 8), or left trisectionectomy (segments 2 to 5 and 8 ± 1) (Strasberg 2000). Although every liver resection is considered major surgery, only resection of three or more segments is considered a major liver resection (Belghiti 1993).

Blood loss during liver resection is an important factor affecting complications and mortality in people undergoing liver resection (Shimada 1998; Yoshimura 2004; Ibrahim 2006). Estimates of blood loss have ranged from 200 mL to 2 L per patient (Gurusamy 2009a). Major blood loss during surgery or in the immediate postoperative period may result in death of the patient. Major blood loss can be defined based on the Advanced Trauma Life Support (ATLS definition of class 3 or class 4 shock, where there is a loss of 30% or more of blood volume) (ATLS 2008). During liver resection, the liver parenchyma is transected at the plane of resection. The blood vessels and the bile duct branches in the plane of resection (cut surface) are then sealed by different methods to prevent blood or bile leakage.

Description of the intervention

Specialists have tested various interventions in attempts to decrease blood loss during liver resection. These interventions include anterior approach as compared to the standard (conventional) surgical approach (Capussotti 2012); autologous blood donation with an aim of decreasing the use of others' blood (heterologous blood transfusion) (Kajikawa 1994), various cardiopulmonary interventions such as acute normovolemic haemodilution (ANH), low central venous pressure (central venous pressure), and hypoventilation that can be used either alone or in combination to decrease blood loss (Gurusamy 2012; Table 1); different methods of liver parenchymal transection (the way that the liver parenchyma is divided), such as the clamp-crush method, the cavitron ultrasonic surgical aspirator, or the radiofrequency dissecting sealer (Gurusamy 2009b; Table 2); different methods of management of the cut surface of the liver (the way that the resection plane of the remnant liver is managed), such as use of fibrin sealant, argon beamer, or electrocautery and suture material (Frilling 2005; Table 3); temporary occlusion of the blood vessels that supply the liver (Gurusamy 2009a; Table 4); and various pharmacological interventions such as recombinant factor VIIa, antithrombin III, and tranexamic acid (Gurusamy 2009c).

Interventions selected to decrease blood loss can be used alone or in various combinations. Usually surgeons at different centres follow their own protocol for decreasing blood loss. The finger-fracture and clamp-crush techniques do not involve specialist equipment. The minimum and standard method of managing the cut surface involves electrocautery for sealing small vessels and suturing larger vessels. Altogether, the goal of these interventions is to decrease blood loss and the associated morbidity and mortality.

How the intervention might work

Temporarily occluding the vessels that supply blood to the liver may reduce the blood loss from the cut vessels. Different methods of liver transection are used to identify major vessels and allow them to be sutured and divided. This might result in clear visualisation of the blood vessels, which can be clamped and then divided. Different topical methods of managing the cut surface attempt to seal the blood vessels on the resection plane, preventing blood loss. Cardiopulmonary interventions decrease the amount of blood lost by dilution of blood or reducing the pressure in the hepatic veins (low central venous pressure). Autologous blood donation involves venesection of the patient prior to surgery and storage of blood

which can be replaced if required during or after surgery with the aim of reducing homologous blood transfusion. Pharmacological interventions work by increasing the clotting of blood with a view to decreasing the blood loss. The anterior approach is a surgical technique that involves occluding the inflow and outflow vessels and performing parenchymal transection prior to mobilisation of the right liver (Liu 2006). The potential advantage of anterior approach over the conventional approach, in which liver is mobilised first, is that inadvertent injury to the blood vessels and the resulting bleeding can be avoided since the blood vessels are occluded before liver mobilisation in the anterior approach. Blood vessels may also be occluded first in conventional approach if one of the methods of vascular occlusion is used.

Why it is important to do this review

Liver resection is a major surgical procedure with significant mortality (estimated at 3.5%) and morbidity (estimated around 40%) (Finch 2007; Reissfelder 2011). Interventions that decrease blood loss may improve outcomes of liver resection. Previous systematic reviews have assessed some of the categories of interventions (Gurusamy 2009a; Gurusamy 2009b; Gurusamy 2009c; Gurusamy 2012). We also performed a network meta-analysis assessing the combination of a method of vascular occlusion, parenchymal transection, and method of dealing with raw surface as a package (Simillis 2014). However, in that review, we found that most authors did not report the different aspects of the method of liver resection other than the factor being randomised or allowed surgeons to choose how to deal with the other factors according to their preference. Since that review excluded such trials, reviewers could only include a few studies. In this updated review, we have covered all the different aspects of the methods to decrease blood loss and blood transfusion requirements during liver resection. We included trials where at least one of the methods to decrease blood loss and blood transfusion requirements during liver resection was included in a randomised comparison with the other aspects either not reported or allowed to vary according to surgeons' preference. This systematic review is intended as a useful guide for patients and healthcare providers as they seek to understand the role of different methods in decreasing blood loss and blood transfusion requirements in people undergoing elective liver resection.

OBJECTIVES

To assess the effects of different interventions for decreasing blood loss and blood transfusion requirements during elective liver resection.

METHODS

Criteria for considering studies for this review

Types of studies

We considered only randomised clinical trials for this network meta-analysis. We excluded studies of other designs.

Types of participants

We included randomised clinical trials in which participants underwent elective liver resection using different types of vascular occlusion or no vascular occlusion, irrespective of the method of vascular occlusion or the nature of the background liver (i.e. normal or cirrhotic), different types of parenchymal transection, different types of management of cut surface, or whether pharmacological interventions were used. We excluded randomised clinical trials in which participants underwent liver resection combined with other major surgical procedures (e.g. one-stage liver and bowel resection for synchronous metastases from colorectal tumours).

Types of interventions

We included randomised clinical trials that assessed one or more of the following interventions in this review.

1. Anterior approach versus conventional approach.
2. Autologous blood donation versus control.
3. Cardiopulmonary interventions.
4. Methods of liver parenchymal transection.
5. Methods of management of the raw surface (resection plane) of the liver.
6. Methods of vascular occlusion (including no vascular occlusion).
7. Pharmacological interventions.

The surgeon (and hence the trialists) may use a particular combination of each of the above. For example, one surgeon may perform liver resection using intermittent vascular occlusion, clamp-crush technique as the method of liver parenchymal transection, and a fibrin sealant on the cut surface, while another surgeon may perform liver resection without using any method of vascular occlusion, with the cavitron ultrasonic surgical aspirator as the method of liver parenchymal transection, without any fibrin sealant on the cut surface, or any additional pharmacological intervention.

Commonly used surgical techniques under each of the above categories are listed in Table 1, Table 2, Table 3, and Table 4. In practice, surgeons can use any intervention in Table 1 in combination with an intervention from Table 2, Table 3, or Table 4. Any intervention in Table 2 can be used in combination with an intervention from Table 3 or Table 4. Any intervention in Table 3 can be used in combination with an intervention in Table 4. Any of these combinations can be used in combination with anterior or conventional approach, with autologous blood donation, and with or without a pharmacological intervention.

Types of outcome measures

We assessed the comparative effectiveness of available treatment strategies that aimed to decrease blood loss during liver resection for the following outcomes.

Primary outcomes

1. Mortality.
   i) Peri-operative (30-day mortality or postoperative mortality). We used in-hospital mortality as defined in the included trials.
   ii) Long-term (at longest follow-up).
2. Adverse events. We defined an adverse event as any untoward medical occurrence not necessarily having a causal relationship with the treatment but resulting in a dose reduction or discontinuation of treatment (ICH-GCP 1997). We considered a serious adverse event to be any event that would increase mortality; was life-threatening; required inpatient hospitalisation; resulted in persistent or significant disability; might have jeopardised the person; or required intervention to prevent it. Serious adverse events correspond approximately to grade III or above of the Clavien-Dindo classification - the only validated system for classifying postoperative complications (Dindo 2004; Clavien 2009;Table 5). In cases where the authors did not classify the severity of adverse events, we followed the criteria provided in Table 5 to classify the severity. We analysed the following information.
   i) Proportion of participants experiencing serious adverse events.
   ii) Number of serious adverse events.
   iii) Proportion of participants experiencing adverse events.
   iv) Number of adverse events.
3. Quality of life as defined in the included trials.
   i) Short-term (30 days, three months).
   ii) Long-term (longest follow-up).

Secondary outcomes

1. Blood transfusion requirements.
   i) Number of participants who required red blood cells or whole blood heterologous blood transfusion.
   ii) Quantity of blood transfusion (heterologous red blood cells or whole blood product, platelet, or fresh frozen plasma).
   iii) Total operative blood loss.
   iv) Number of participants who had major operative blood loss.
2. Hospital stay.
   i) Length of total hospital stay (including re-admissions).
   ii) Intensive therapy unit stay.
3. Operating time.
4. Time needed to return to work.

Search methods for identification of studies

Electronic searches

We aimed to identify all relevant randomised clinical trials regardless of language or publication status (published, unpublished, in press, or in progress) (Royle 2003).
We searched the following databases up to 23 September 2015.

- The Cochrane Central Register of Controlled Trials (CENTRAL; 2015, Issue 9) in the Cochrane Library.
- MEDLINE via PubMed (from 1947).
- EMBASE via Ovid SP (from 1974).
- Science Citation Index Expanded via Web of Science (from 1975).

We also searched the World Health Organization International Clinical Trials Registry Platform search portal (www.who.int/ictrp), which searches various trial registers, including ISRCTN and ClinicalTrials.gov, to identify further trials (searched 23 September 2015). Because existing Cochrane systematic reviews have comprehensively assessed subsets of all available interventions on this topic, we also used these reviews as a way to identify trials(Gurusamy 2009a; Gurusamy 2009b). We present full search strategies in Appendix 1.

Searching other resources

We searched the references of the identified trials for additional trials eligible for inclusion.

Data collection and analysis

Selection of studies

Two review authors (EM and KG) independently screened the titles and abstracts of all records retrieved. We sought full text for any references that at least one of the authors identified as potentially eligible. We assessed the full text for inclusion and listed the reasons for the excluding trials in the Characteristics of excluded studies tables. We listed any ongoing trials in Characteristics of ongoing studies for further follow-up in updates of the reviews. We resolved discrepancies through discussion.

Data extraction and management

Two review authors (KG and EM) independently extracted the following data.

1. Year and language of publication.
2. Country in which investigators recruited the participants.
3. Year(s) in which the trial took place.
4. Inclusion and exclusion criteria.

5. Participant characteristics such as age, sex, underlying disease, comorbidity, number and proportion of participants with cirrhosis, and number and proportion of participants undergoing major versus minor liver resection.

6. Details of the intervention and treatment strategy that aimed to decrease blood loss and blood transfusion requirements (e.g. surgical technique, procedure and co-intervention, concurrent surgery, and medications).

7. Outcomes (Primary outcomes; Secondary outcomes).

8. Follow-up time points.

9. Risk of bias (Assessment of risk of bias in included studies).

We sought unclear or missing information by contacting the authors of the individual trials. If there had been any doubt whether trials shared the same participants - completely or partially (by identifying common authors and centres) - we would have contacted the authors of the trials to clarify whether the trial report was duplicated. We resolved any differences in opinion through discussion.

Assessment of risk of bias in included studies

We followed the guidance in the *Cochrane Handbook for Systematic Reviews of Intervention* and those described in the Cochrane Hepato-Biliary Group Module to assess the risk of bias in included studies (Higgins 2011; Gluud 2013). Specifically, we assessed the risk of bias in included trials for the following domains (Schulz 1995; Moher 1998; Kjaergard 2001; Wood 2008; Lundh 2012; Savovic 2012a; Savovic 2012b).

Allocation sequence generation

- Low risk of bias: sequence generation was achieved using computer random number generation or a random number table. Drawing lots, tossing a coin, shuffling cards, and throwing dice were adequate if an independent adjudicator performed them.
- Uncertain risk of bias: authors described the trial as randomised but did not specify the method of sequence generation.
- High risk of bias: the sequence generation method was not, or may not have been, random. Quasi-randomised studies (those using dates, names, or admittance numbers to allocate participants) were inadequate, and we excluded them for the assessment of benefits butof harms.

Allocation concealment

- Low risk of bias: allocation was controlled by a central and independent randomisation unit and involved sequentially numbered, opaque, sealed envelopes, or something similar, so that neither participants nor investigators could have foreseen intervention allocations in advance of or during enrolment.
- Uncertain risk of bias: authors described the trial as randomised but did not describe the method used to conceal the allocation, so participants or operators may have been able to foresee intervention allocations in advance of, or during, enrolment.
- High risk of bias: the investigators who assigned participants were aware of the allocation sequence, or the study was quasi-randomised. We excluded quasi-randomised studies for assessment of benefits but not of harms.

Blinding of participants and personnel

- Low risk of bias: blinding was performed adequately, or the outcome measurement was not likely to be influenced by lack of blinding.
- Uncertain risk of bias: information was insufficient to allow assessment of whether the type of blinding used was likely to induce bias on the estimate of effect.
- High risk of bias: no blinding or incomplete blinding and the outcome or the outcome measurements were likely to be influenced by lack of blinding.

Blinding of outcome assessors

- Low risk of bias: blinding was performed adequately, or the outcome measurement was not likely to be influenced by lack of blinding.
- Uncertain risk of bias: information was insufficient to allow assessment of whether the type of blinding used was likely to induce bias on the estimate of effect.
- High risk of bias: no blinding or incomplete blinding and the outcome or the outcome measurements were likely to be influenced by lack of blinding.

Incomplete outcome data

- Low risk of bias: the underlying reasons for missing data were unlikely to make treatment effects depart from plausible values, or proper methods were employed to handle missing data.
- Uncertain risk of bias: information was insufficient to allow assessment of whether the missing data mechanism in combination with the method used to handle missing data was likely to induce bias on the estimate of effect.
- High risk of bias: the crude estimate of effects (e.g. complete case estimate) were clearly biased because of the underlying reasons for missing data, and the methods used to handle missing data were unsatisfactory.

Selective outcome reporting

- Low risk of bias: authors reported pre-defined or clinically relevant and reasonably expected outcomes (mortality and serious adverse events).
- Uncertain risk of bias: authors did not fully report all pre-defined or clinically relevant and reasonably expected outcomes,

or it was unclear whether authors recorded data on these outcomes.

- High risk of bias: authors failed to report one or more clinically relevant and reasonably expected outcomes; data on these outcomes were likely to have been recorded.

Vested interest bias

- Low risk of bias: a party with no vested interests in the outcome (i.e. a party that would not benefit from the results of the trial) conducted the trial.
- Uncertain risk of bias: it was not clear if those conducting the trial had a vested interest in its outcome.
- High risk of bias: a party with vested interests in the outcome of the trial (such as a drug manufacturer) conducted the trial.

We considered a trial to be at low risk of bias if we assessed it as being at low risk of bias for all domains. We considered a trial at low risk of bias for an outcome if we assessed it as being at low risk of bias for all study level domains, as well as for outcome-specific domains (e.g. blinding, incomplete outcome data). Otherwise, we considered trials with uncertain or high risk of bias regarding one or more domains to be trials at high risk of bias.

Measures of treatment effect

For dichotomous variables (short-term mortality, serious adverse events, participants requiring blood transfusion), we calculated the odds ratio (OR) with 95% credible interval (CrI). For continuous variables, such as quantity of blood transfused, blood loss, hospital stay, and operating time, we calculated the mean difference (MD) with 95% CrI. When trials reported the blood transfusion as mL or L rather than units, we converted these into units by considering that each unit of whole blood or red blood cell transfusion was 400 mL and each unit of fresh frozen plasma was 250 mL. We planned to use MD and 95% CrI for time needed to return to work, but we did not use this because none of the included trials reported this outcome. We planned to use standardised mean difference (SMD) with 95% CrI for quality of life if trials used different scales, but we did not plan to combine the quality of life at different time points. For time-to-event data, such as long-term survival, we planned to use the hazard ratio (HR) with 95% CrI.

Relative ranking

We estimated the probabilities for each intervention of being at each possible rank. Then we obtained a treatment hierarchy using the probability of each intervention being the best treatment by using the surface under the cumulative ranking curve (SUCRA) (Salanti 2011).

Unit of analysis issues

The unit of analysis was the person undergoing elective liver resection according to the intervention group to which they were randomly assigned.

Dealing with missing data

We performed an intention-to-treat analysis whenever possible (Newell 1992). Otherwise, we used data that were available to us (e.g. a trial may have reported only per protocol analysis results). As per protocol analyses may be biased, we planned to conduct best-worst case scenario and worst-best case scenario analyses as sensitivity analyses, if there was a possibility that authors could have judged a treatment as effective because of attrition bias.
For continuous outcomes, we imputed the standard deviation from P values according to guidance in the *Cochrane Handbook for Systematic Reviews of Intervention* (Higgins 2011). If the data were likely to be normally distributed and the mean was not available, we used the median for meta-analysis. If it was not possible to calculate the standard deviation from the P value or the confidence intervals, we imputed the standard deviation using the largest standard deviation in other trials for that outcome. This form of imputation may decrease the weight of the study for calculation of mean differences and may bias the effect estimate to no effect for calculation of SMDs (Higgins 2011).

Assessment of heterogeneity

We assessed clinical and methodological heterogeneity by carefully examining the characteristics and design of included trials. Major sources of clinical heterogeneity included cirrhotic compared to non-cirrhotic livers and major compared to minor liver resections. In addition, we anticipated considerable heterogeneity in the way the intervention was performed. For example, surgeons may perform intermittent portal triad clamping with different time periods of occlusion and non-occlusion. In addition, they may use different doses of fibrin sealant. Different study design and risk of bias may contribute to methodological heterogeneity.
We used the residual deviance and Deviance Information Criteria (DIC) for assessing between-study heterogeneity as per the guidance from the National Institute for Health and Care Excellence (NICE) Decision Support Unit (DSU) Technical Support Documents (Dias 2012b; Dias 2013a). We also calculated the between-trial standard deviation and reported this if we used a random-effects model. See Data synthesis for further details regarding residual deviance, DIC, and choice of model.
If we identified substantial heterogeneity - clinical, methodological, or statistical - we planned to explore and address it in a subgroup analysis (see section on Subgroup analysis and investigation of heterogeneity).

Assessment of reporting biases

We planned to use visual asymmetry on a funnel plot to explore reporting bias in case at least 10 trials were included for the outcome (Egger 1997; Macaskill 2001). In the presence of heterogeneity that we could explain by subgroup analysis, we planned to perform the funnel plot for each subgroup in the presence of the adequate number of trials. We planned to perform the linear regression approach described by Egger 1997 to determine the funnel plot asymmetry in the presence of at least 10 trials for the direct comparison. However, we did not perform this because there were not enough trials.

We also considered selective reporting as evidence of reporting bias.

Data synthesis

We applied classifications described in Table 1, Table 2, Table 3, and Table 4 to categorise cardiopulmonary interventions, parenchymal transection methods, methods of dealing with cut surface, and different vascular occlusion methods. Each category in the table is broadly defined to encompass a relatively homogeneous group of interventions, although we noted variations in the way each method is carried out. For example, surgeons may perform intermittent portal triad clamping with different time periods of occlusion and non-occlusion. We categorised them under intermittent portal triad clamping regardless of the time intervals. Likewise, we did not distinguish different maximum periods for continuous vascular occlusion (Clavien 1996). These practice variations might be a source of heterogeneity; however, evidence was insufficient to suggest that they could affect the outcome. For the comparisons of anterior approach versus conventional approach and autologous blood donation versus control, there are only two treatments for each comparison. For pharmacological interventions, we treated each pharmacological treatment as a separate category.

In liver resection, a surgeon typically uses one item each from Table 1, Table 2, Table 3, and Table 4. Liver resection is usually performed using conventional approach without autologous blood donation or any pharmacological agent. Compared to the previous version of the review (Simillis 2014), where we considered a combination of one method each from Table 2, Table 3, and Table 4 as a treatment strategy, in this review, we considered each of these interventions (different methods of cardiopulmonary interventions, parenchymal transection methods, methods of dealing with raw surface, vascular occlusion methods, and pharmacological interventions) as separate networks. This approach was in response to the lack of information on the details of co-interventions in the trials and the design of the trials, which limited the number of trials included in the previous analysis. In many of the trials, the surgeons involved were allowed to choose their method of liver resection apart from the factor being randomised, based on the assumption that the factors are independent of each other (i.e. there is no interaction between the factors, or the choice of one factor is independent of the choice of other factors). There is no evidence to support or refute this assumption. However, if we had included only trials that reported all the intervention variables adequately, and none were left to the choice of the surgeons, this would have resulted in inclusion of fewer trials than the previous version, as we have now included all the interventions aimed at decreasing blood loss and blood transfusion requirements during liver resection.

Direct comparison

We performed pair-wise meta-analyses using WinBUGS by Bayesian analysis using the same codes and methods described immediately below in the network meta-analysis section (i.e. same burn-in, number of simulations, choice of initial values, and choice of models). In addition, we performed the meta-analysis using frequentist methods with Review Manager 5 (RevMan 2014), in accordance with recommendations of Higgins 2011 and those described in the Cochrane Hepato-Biliary Group Module (Gluud 2013). For frequentist analyses, we presented the results of the model that was used for Bayesian analysis (which was determined by the model fit).

Network meta-analysis

We conducted network meta-analyses to compare multiple interventions simultaneously for each of the outcomes listed in the Types of outcome measures section. Network meta-analysis combines direct evidence within trials and indirect evidence across trials (Mills 2012).

We obtained a network plot to ensure that the trials were connected by treatments using Stata/IC 11 (StataCorp LP). We performed a network meta-analysis only when it was possible to compare the direct and indirect estimates. This is because one cannot assess whether there is consistency between the direct and indirect estimates unless both are available. We planned to exclude any trials that were not connected to the network. We conducted a Bayesian network meta-analysis using the Markov chain Monte Carlo method in WinBUGS 1.4. We modelled the treatment contrast (e.g. log OR for binary outcomes, MD for continuous outcomes) for any two interventions ('functional parameters') as a function of comparisons between each individual intervention and an arbitrarily selected reference group ('basic parameters') (Lu 2006). We used inconsistency models to assess this consistency assumption (Dias 2013e). The reference groups selected for the different comparisons are as follows.

- Anterior approach versus conventional approach: conventional approach.
- Autologous blood donation versus control: inactive control.
- Cardiopulmonary interventions: inactive control.
- Methods of parenchymal transection: clamp-crush method.
- Methods of dealing with raw surface: inactive control.

- Methods of vascular occlusion: no vascular occlusion.
- Pharmacological interventions: inactive control.

We performed the network analysis as per the guidance from the NICE DSU documents (Dias 2013a; Dias 2013c). Further details of the codes used, the raw data, and the technical details of how we performed the analysis are in Appendix 2, Appendix 3, and Appendix 4. We tested the codes on simulated data (Appendix 5) using predetermined effect estimates with no inconsistency between direct and indirect comparisons. This simulation testing demonstrated that the codes produced similar effect estimates as the predetermined effect estimates (allowing for some variability because of simulation) and that the effect estimates obtained using these codes were almost identical to the effect estimates obtained by direct estimates using RevMan (Appendix 6).

The codes allow handling of trials with multiple arms to be dealt in the same way as two-armed trials, that is, one can enter the data from all the intervention arms in a trial as number of events and the number of people exposed to the event for binary outcomes; for continuous outcomes, one can enter the mean and standard error for all intervention arms in the trial. The choice between the fixed-effect model and random-effects model was based on the model fit as per the guidelines of the NICE TSU (a difference of three to five for deviance information criterion (DIC)) is important (Dias 2013a; Dias 2013c); we used a difference of three as important). We reported the treatment contrasts (i.e. log ORs for binary outcomes and MDs for continuous outcomes) of the different treatments in relation to the reference treatment, the deviance residuals, the number of effective parameters, and DIC for the fixed-effect model and random-effects model for each outcome. We also reported the parameters used to assess the model fit (i.e. deviance residuals, number of effective parameters, and DIC) for the inconsistency model in Table 6, Table 7, and Table 8.

We reported estimates of treatment effects (ORs for binary outcomes, MDs for continuous outcomes, and rate ratios for count outcomes). We calculated the 95% credible intervals of treatment effects (e.g. odd ratios for binary outcomes, mean differences for continuous outcomes, and so on) in the Bayesian meta-analysis and indicate that the average effect in the population lies within the credible intervals with 95% probability. We used the posterior median as the point estimate of treatment effect, the posterior 2.5 percentile as the lower bounds of its 95% credible interval, and the 97.5 percentile as the upper bounds, and we reported the effect estimates and associated 95% credible intervals for each pair-wise comparison in a table. We presented these in Table 9, Table 10, and Table 11. We also presented the cumulative probability of the treatment ranks (i.e. the probability that the treatment is within the top two, top three, etc.) in SUCRA graphs (Salanti 2011). We also plotted the probability of each rank for each treatment (rankograms), which are generally considered more informative (Salanti 2011; Dias 2012a; Dias 2013b).

Sample size calculations and imprecision

To control for the risk of random errors, we interpreted the information with caution when the accrued sample size in the meta-analysis was less than the required sample size (required information size). For calculation of the required information size, please see Appendix 7. We considered a 20% relative risk reduction as the minimal clinically important difference for binary outcomes and count outcomes. For continuous outcomes, we used or planned to use the following minimal clinically important differences: a standardised mean difference of 0.5 for health-related quality of life, a mean difference of one unit for blood transfusion quantity, a mean difference of 500 mL for blood loss, a mean difference of one day of hospital stay and time-to-return to activity, and a mean difference of 15 minutes for operating time.

Subgroup analysis and investigation of heterogeneity

We planned to assess the differences in the effect estimates between the following subgroups using meta-regression with the help of the WinBUGS code if we included a sufficient number of trials (Appendix 8). We planned to use study level co-variates for meta-regression.

1. Trials at low risk of bias compared to trials at
2. high risk of bias.
3. Participants with cirrhosis compared to those without cirrhosis.
4. Participants undergoing major liver resections compared to those undergoing minor liver resections.

We planned to calculate the interaction term (Dias 2012b; Dias 2013d). If the 95% credible intervals of the interaction term did not cross zero, we planned to consider this statistically significant. We did not perform any of the above because of the paucity of data.

Sensitivity analysis

We performed a sensitivity analysis when we imputed the mean, the standard deviation, or both.

Summary of findings table

We presented a 'Summary of findings' table, similar to the ones used in direct comparisons. We modified the table from the original format because of the presence of many comparisons and many outcomes. We presented only the comparisons in which there was evidence of differences with the illustrative examples. For other comparisons, we simply mentioned that there was no evidence of differences. This is to ensure that the most important information is available in the table. We provided links in the table to specific tables using more a traditional format.

In addition to this 'Summary of findings' table, we also provided the 'Summary of findings' table for network meta-analysis in a

graphical format (in the form of forest plots along with the quality of evidence), in which we used the methodology of grading the quality of evidence in network meta-analysis suggested by the GRADE Working group (Puhan 2014). The first step was to estimate the evidence from direct and indirect effect estimates. Further steps included rating the quality of evidence from direct and indirect effect estimates, presenting the estimate combined from the direct estimate and indirect estimate, and rating the quality of the network meta-analysis effect estimates (Puhan 2014). Although codes are available for node splitting, they resulted in numerical errors because of the data. So we calculated the direct estimates (including only the trials which compared the specific intervention and control) and indirect estimates (after removing the trials which compared the specific intervention and control).

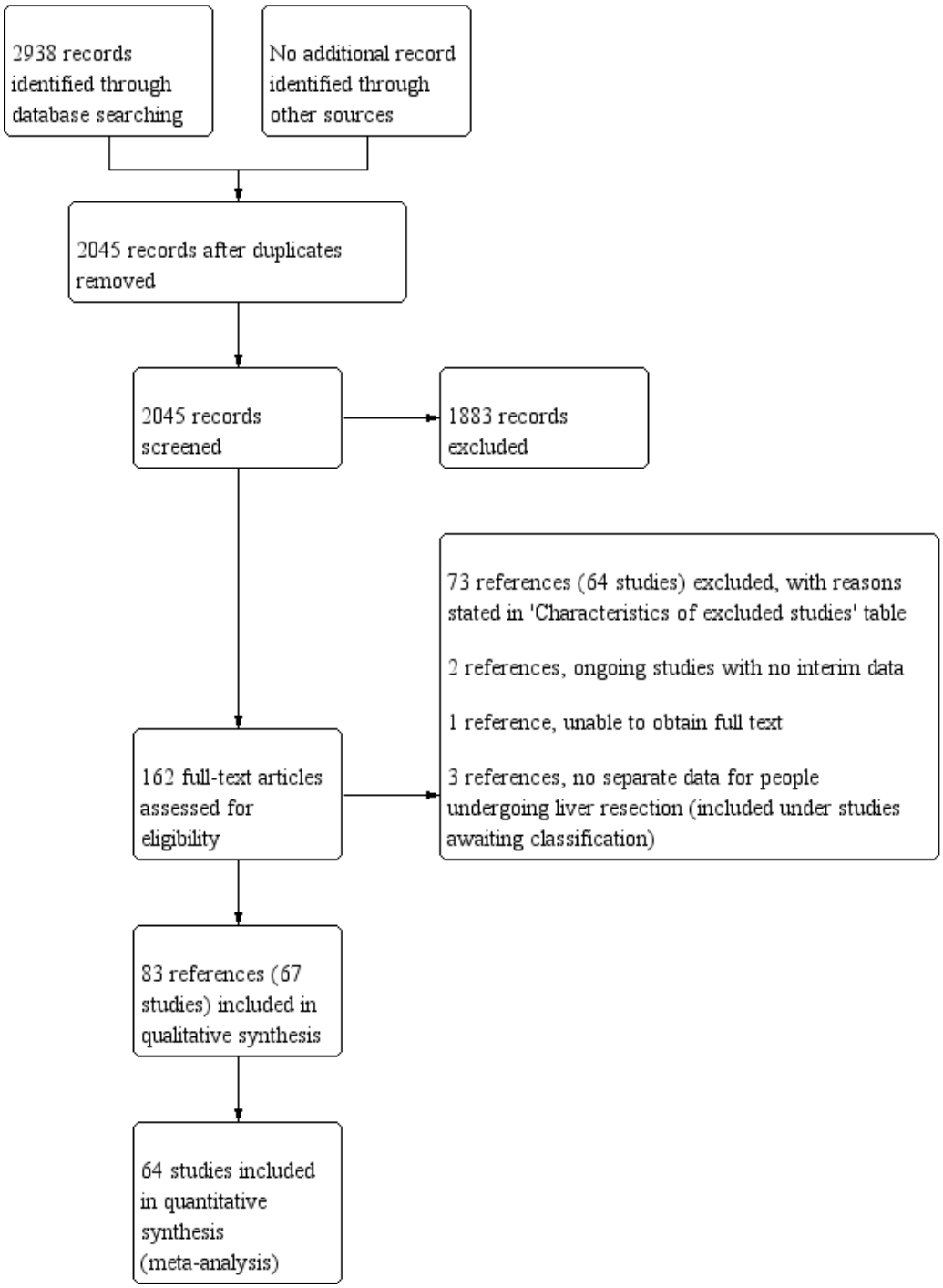
RESULTS

Description of studies

Results of the search

We identified 2938 references through electronic searches of CENTRAL (N = 342), MEDLINE (N = 1431), Embase (N = 445), Science Citation Index Expanded (N = 641), WHO ICTRP (N = 47), and ClinicalTrials.gov (N = 32). We excluded 893 duplicates and 1883 clearly irrelevant references through screening titles and reading abstracts. We retrieved 162 references for further assessment. We did not identify any references by scanning reference lists of the identified randomised trials. We excluded 76 references (67 studies) for the reasons listed in the Characteristics of excluded studies table. In total, 83 references for 67 completed randomised clinical trials met the inclusion criteria. Two references were for ongoing studies (Schmidt 2008; Chen 2015). We were unable to obtain one reference (Franceschi 2006). We included three studies under 'Studies awaiting classification' because there were no separate data for people who underwent liver resection, that is, the studies included a number of different surgical procedures, and information on people who underwent liver resection was not available (Chapman 2006; Bochicchio 2015; Wright 2015). This is summarised in the study flow diagram (Figure 1).

Figure 1. Study flow diagram.



Included studies

We describe the treatments used in the 67 randomised clinical trials in the Characteristics of included studies table and in Table 12.

Two trials compared anterior approach versus conventional approach (Liu 2006; Capussotti 2012). Two trials compared autologous blood donation versus control (Kajikawa 1994; Kostopanagiotou 2007). Ten trials compared different methods of cardiopulmonary interventions (Hasegawa 2002; Matot 2002; El-Kharboutly 2004; Wang 2006; Yao 2006; Choi 2007; Jarnagin 2008; Kato 2008; Guo 2013; Guo 2014). Twelve trials different compared methods of parenchymal transection (Takayama 2001; Rau 2001; Arita 2005; Koo 2005; Lesurtel 2005; Smyrniotis 2005; Lupo 2007; Ikeda 2009; Doklestic 2012; Savlid 2013; Muratore 2014; Rahbari 2014). Seventeen trials compared different methods of dealing with raw surface (Kohno 1992; Liu 1993; Noun 1996; Chapman 2000; Frilling 2005; Franceschi 2006; Figueras 2007; Fischer 2011; Gugenheim 2011; De Boer 2012; Porte 2012; Kakaei 2013; Koea 2013; Ollinger 2013; Bektas 2014; Genyk 2014; Moench 2014). Eighteen trials compared different methods of vascular occlusion (Belghiti 1996; Clavien 1996; Man 1997; Belghiti 1999; Wu 2002; Capussotti 2003; Man 2003; Chouker 2004; Figueras 2005; Capussotti 2006; Chen 2006; Liang 2009; Dayangac 2010; Pietsch 2010; Lee 2012; Park 2012; Ni 2013; Si-Yuan 2014). Six trials compared different pharmacological interventions (Shimada 1994; Lentschener 1997; Wong 2003; Lodge 2005; Shao 2006; Wu 2006).

All the trials assessed different methods of open liver resection. Four trials were three-armed trials (Yao 2006; Doklestic 2012; Kakaei 2013; Guo 2014), one trial was a four-armed trial of which we included three arms (Lesurtel 2005), and the remaining trials were two-armed trials. The 67 trials involved a total of 6197 participants. After exclusion of 133 participants after randomisation and 293 participants in three trials that did not provide any information about the outcomes included in this review (Franceschi 2006; Porte 2012; Koea 2013), we included 5771 participants who contributed to one or more outcomes of interest in this review.

Excluded studies

Of the 64 excluded studies, we excluded 6 because they were comments on included or excluded studies (Gonzalez 2009; Petras 2009; Schilling 2009; Strobel 2012; Strobel 2014; Hamady 2015); 19 because they were not randomised clinical trials (Le Treut 1995; Man 2002; Yin 2003; Azoulay 2005; Arru 2007; Kim 2008; Nagano 2009; Wang 2010; Wang 2011; Bellolio 2012; Beppu 2012; Narita 2012; NCT01651182; Palibrk 2012; Yang 2012; Dominioni 2014; Vlad 2014; Li 2015; Takatsuki 2015); 7 because of inadequate randomisation (Rau 1995; Smyrniotis 2002; Smyrniotis 2003a; Smyrniotis 2003b; Richter 2009; Obiekwe 2014; Shu 2014); 6 because they were comparisons of interventions that were not of interest to this review (Figueras 2003; Grobmyer 2009; Harimoto 2011; Levit 2012; Correa-Gallego 2015; Feldheiser 2015); 18 since they were trials comparing variations within the treatments included in this review (for example, different periods of intermittent vascular occlusion or different methods of achieving low central venous pressure) (Standl 1998; Esaki 2006; Saiura 2006; Chapman 2007; Hashimoto 2007; Kim 2007; Torzilli 2008; El-Moghazy 2009; Ryu 2010; Broek 2011; Rahbari 2011; Dello 2012; Zhu 2012; Frankel 2013; Kaibori 2013; Yang 2013; Saiura 2014; Zhang 2014); and 8 because the co-interventions were not used equally in the intervention and control (Schwartz 2004; Petrowsky 2006; Smyrniotis 2006; Si-Yuan 2011; Li 2013; Lu 2014; Gotohda 2015; Hanyong 2015).

Risk of bias in included studies

We summarise the risk of bias in the included trials in Figure 2 and Figure 3. Overall, we judged all trials to be at high risk of bias. The risk of bias according to the type of comparison is shown in Table 13.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

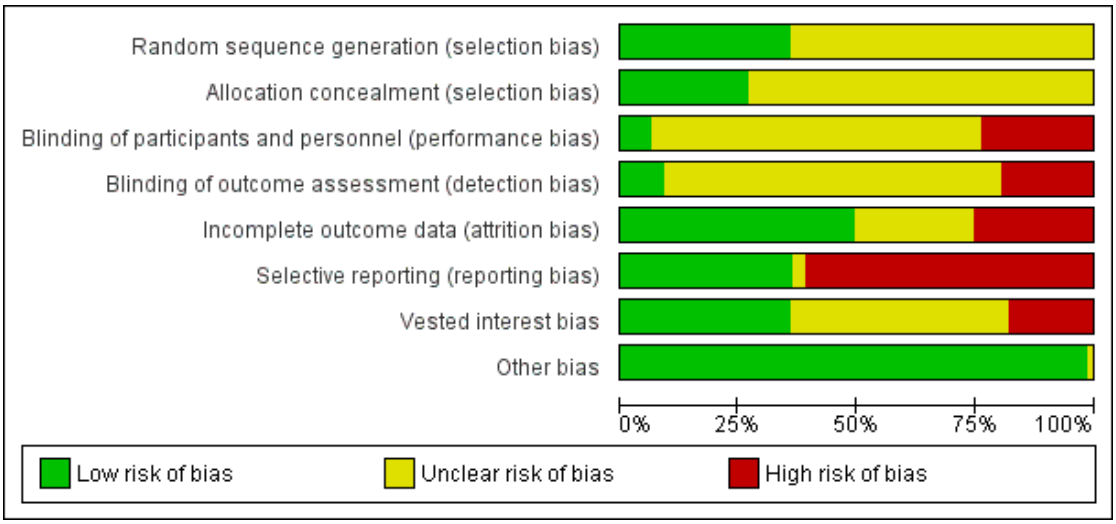
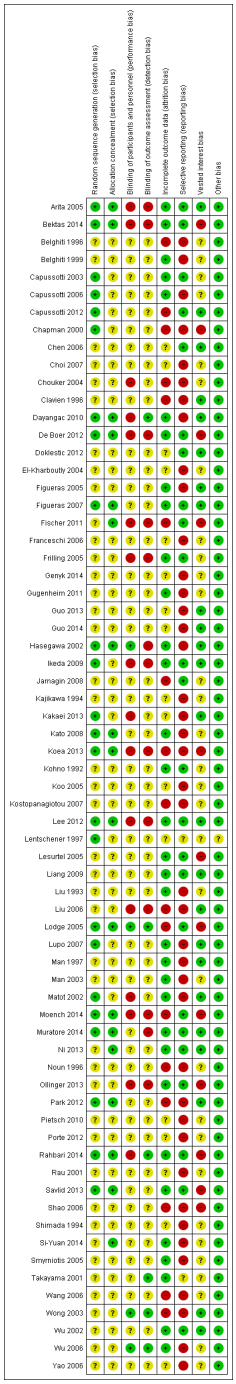


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Twenty-four trials (35.8%) were at low risk of bias in the 'sequence generation' domain (Lentschener 1997; Chapman 2000; Hasegawa 2002; Matot 2002; Capussotti 2003; Arita 2005; Lodge 2005; Capussotti 2006; Figueras 2007; Lupo 2007; Kato 2008; Ikeda 2009; Dayangac 2010; Capussotti 2012; De Boer 2012; Lee 2012; Park 2012; Kakaei 2013; Koea 2013; Savlid 2013; Bektas 2014; Moench 2014; Muratore 2014; Rahbari 2014). Eighteen trials (26.9%) were at low risk of bias in the 'allocation concealment' domain (Hasegawa 2002; Arita 2005; Lodge 2005; Figueras 2007; Kato 2008; Dayangac 2010; Fischer 2011; De Boer 2012; Lee 2012; Park 2012; Koea 2013; Ni 2013; Savlid 2013; Bektas 2014; Moench 2014; Muratore 2014; Rahbari 2014; Si-Yuan 2014). Fifteen trials (22.4%) were at low risk of bias in the 'both sequence generation and allocation concealment' domains and were free from selection bias (Hasegawa 2002; Arita 2005; Lodge 2005; Figueras 2007; Kato 2008; Dayangac 2010; De Boer 2012; Lee 2012; Park 2012; Koea 2013; Savlid 2013; Bektas 2014; Moench 2014; Muratore 2014; Rahbari 2014).

Blinding

Four trials (6.0%) were at low risk of bias in the 'blinding of participants and healthcare providers' domain (Hasegawa 2002; Wong 2003; Lodge 2005; Wu 2006). Six trials (9.0%) were at low risk of bias in the 'blinding of outcome assessors' domain (Lentschener 1997; Wong 2003; Lodge 2005; Wu 2006; Dayangac 2010; Rahbari 2014). Three trials (4.5%) were at low risk of bias in both the 'blinding of participants and healthcare providers' and 'blinding of outcome assessors' domains and were free from performance and detection bias (Wong 2003; Lodge 2005; Wu 2006).

Incomplete outcome data

Thirty-three trials (49.3%) were at low risk of bias in the 'missing outcome bias' domain (Kohno 1992; Liu 1993; Man 1997; Belghiti 1999; Takayama 2001; Hasegawa 2002; Matot 2002; Wu 2002; Capussotti 2003; Man 2003; Arita 2005; Figueras 2005; Frilling 2005; Lesurtel 2005; Smyrniotis 2005; Capussotti 2006; Wu 2006; Figueras 2007; Lupo 2007; Kato 2008; Ikeda 2009; Liang 2009; Dayangac 2010; Gugenheim 2011; De Boer 2012; Lee 2012; Ni 2013; Ollinger 2013; Savlid 2013; Bektas 2014; Muratore 2014; Rahbari 2014; Si-Yuan 2014).

Selective reporting

Twenty-five trials (37.3%) reported mortality and serious adverse events and hence were considered to be at low risk of bias in the 'selective reporting bias' domain (Kohno 1992; Takayama 2001; Wu 2002; Capussotti 2003; Arita 2005; Frilling 2005; Lesurtel 2005; Lodge 2005; Chen 2006; Figueras 2007; Jarnagin 2008; Ikeda 2009; Liang 2009; Fischer 2011; Capussotti 2012; De Boer 2012; Doklestic 2012; Lee 2012; Ni 2013; Ollinger 2013; Savlid 2013; Bektas 2014; Moench 2014; Muratore 2014; Rahbari 2014).

Other potential sources of bias

Twenty-four trials (35.8%) were at low risk of bias in the 'source of funding bias' domain (Clavien 1996; Man 1997; Hasegawa 2002; Matot 2002; Wu 2002; Wong 2003; Arita 2005; Figueras 2005; Chen 2006; Liu 2006; Figueras 2007; Lupo 2007; Ikeda 2009; Liang 2009; Dayangac 2010; Capussotti 2012; Doklestic 2012; Lee 2012; Park 2012; Guo 2013; Kakaei 2013; Ni 2013; Guo 2014; Muratore 2014).

We did not identify any other bias in the trials.

Effects of interventions

See: **Summary of findings for the main comparison**

We provide the data used in network meta-analysis in Appendix 3; the data used for direct comparisons in Data and analyses; and the overall results in Summary of findings for the main comparison, Appendix 9, and Appendix 10. We present the data in the following format for each comparison.

- Outcome.
    - Different methods of measuring the outcome.
        - Direct comparison.
        - Network meta-analysis (when applicable).
        - Differences between direct comparison and network meta-analysis (when applicable).
- Differences between Bayesian and frequentist meta-analysis.
- An overall summary for the comparison.

In addition, we also provide an overall summary for each outcome across all interventions at the end.

Anterior approach versus conventional approach

Two trials compared anterior approach versus conventional approach (Liu 2006; Capussotti 2012). Since this comparison only involved two treatments, we did not perform network meta-analysis.

Quality of evidence

The quality of evidence was very low for all the outcomes. This was because of high risk of bias in the trials (downgraded by one point), imprecision due to small sample size (downgraded by one point),

and wide credible intervals for all outcomes (downgraded by one point) as well as considerable heterogeneity for blood transfusion (proportion) and major blood loss (proportion) (downgraded by two points).

Mortality

Mortality (perioperative)

Two trials reported perioperative mortality (Liu 2006; Capussotti 2012). The unadjusted proportions of perioperative mortality are as follows.

- Conventional approach: 7/92 (7.6%).
- Anterior approach: 2/93 (2.2%).

Based on the DIC, we chose the fixed-effect model. There was no evidence of differences in perioperative mortality between the two groups (OR 0.23, 95% CrI 0.03 to 1.08; 185 participants; 2 studies).

Mortality (longest follow-up)

None of the trials reported this outcome.

Adverse events

Serious adverse events (proportion)

One trial reported serious adverse events as a proportion of participants who experienced one or more (Capussotti 2012). The unadjusted proportions of serious adverse events are as follows.

- Conventional approach: 4/32 (12.5%).
- Anterior approach: 5/33 (15.2%).

There was no evidence of differences in the proportion of participants experiencing serious adverse events between the two groups (OR 1.27, 95% CrI 0.29 to 5.89; 65 participants; 1 study).

Serious adverse events (number)

None of the trials reported this outcome.

Adverse events (proportion)

Two trials reported adverse events as a proportion (Liu 2006; Capussotti 2012). The unadjusted proportions of adverse events are as follows.

- Conventional approach: 33/92 (35.9%).
- Anterior approach: 31/93 (33.3%).

Based on the DIC, we chose the fixed-effect model. There was no evidence of differences in the proportion of participants experiencing adverse events between the two groups (OR 0.89, 95% CrI 0.48 to 1.64; 185 participants; 2 studies).

Adverse events (number)

One trial reported the number of adverse events (Capussotti 2012). The unadjusted rates of adverse events (number) are as follows.

- Conventional approach: 18/32 (56.3 per 100 participants).
- Anterior approach: 17/33 (51.5 per 100 participants).

There was no evidence of differences in the number of adverse events between the two groups (rate ratio 0.91, 95% CrI 0.47 to 1.78; 65 participants; 2 studies).

Health-related quality of life

None of the trials reported this outcome at any time point.

Blood transfusion requirements

Blood transfusion (proportion)

Two trials reported blood transfusion as a proportion of participants requiring one (Liu 2006; Capussotti 2012). The unadjusted proportions of participants receiving a blood transfusion are as follows.

- Conventional approach: 20/92 (21.7%).
- Anterior approach: 10/93 (10.8%).

Based on the DIC, we chose the random-effects model. The between-study standard deviation was 2.60. There was no evidence of differences in the proportion of participants receiving a blood transfusion between the two groups (OR 0.57, 95% CrI 0.01 to 50.91; 185 participants; 2 studies).

Blood transfusion (quantity)

None of the trials reported the quantity of blood transfusion in red blood cells, platelets, fresh frozen plasma, or cryoprecipitate.

Blood loss

Two trials reported blood loss (Liu 2006; Capussotti 2012). The median blood loss reported for each treatment in the two trials are as follows.

- Conventional approach: 0.5 L and 1 L.
- Anterior approach: 0.437 L and 0.8 L.

We did not perform meta-analysis since both trials reported the median blood loss rather than the mean and standard deviation of blood loss. There was no evidence of differences in blood loss in either trial (Liu 2006; Capussotti 2012).

Major blood loss (proportion)

Two trials reported major blood loss as a proportion of participants experiencing it (Liu 2006; Capussotti 2012). One trial defined major blood loss as more than one litre of blood loss (Capussotti 2012), while the other trial defined it as more than two litres (Liu 2006). The unadjusted proportions of major blood loss (proportion) are as follows.

- Conventional approach: 22/92 (23.9%).
- Anterior approach: 12/93 (12.9%).

Based on the DIC, we chose the random-effects model. The between-study standard deviation was 2.3. There was no evidence of differences in the proportion of participants experiencing major blood loss between the two groups (OR 0.54, 95% CrI 0.01 to 34.54; 185 participants; 2 studies).

Hospital stay

Total hospital stay

Two trials reported hospital stay (Liu 2006; Capussotti 2012). The median hospital stay reported for each treatment in the two trials are as follows.

- Conventional approach: 11.5 days (d) and 12.5 d.
- Anterior approach: 10 d and 11 d.

We did not perform meta-analysis since both trials reported the median hospital stay rather than the mean and standard deviation of hospital stay. There was no evidence of differences in hospital stay in either trial (Liu 2006; Capussotti 2012).

Intensive therapy unit (ITU) stay

One trial reported ITU stay (Liu 2006). The median ITU stay reported for each treatment is as follows.

- Conventional approach: 2 d.
- Anterior approach: 1.5 d.

We did not perform meta-analysis since the trial reported the median ITU stay rather than the mean and standard deviation of ITU stay. There was no evidence of differences in ITU stay in this trial (Liu 2006).

Operating time

Two trials reported operating time (Liu 2006; Capussotti 2012). The median operating times reported for each treatment are as follows.

- Conventional approach: 312.8 minutes (min) and 415 min.
- Anterior approach: 295.8 min and 420 min.

We did not perform meta-analysis since both trials reported the median operating time rather than the mean and standard deviation of operating time. There was no evidence of differences in operating time in either trial.

Time needed to return to work

None of the trials reported this outcome.

Difference between Bayesian and frequentist meta-analysis

The interpretation of information and conclusions did not alter by using the frequentist meta-analysis.

Overall summary

There was no evidence of differences between the anterior approach and conventional approach in any of the reported outcomes of interest for this review.

Autologous blood donation versus control

Two trials compared autologous blood donation versus control (Kajikawa 1994; Kostopanagiotou 2007). As this comparison only included two treatments, we did not perform network meta-analysis.

Quality of evidence

The quality of evidence was very low for all the outcomes and comparisons unless specifically indicated within the results. This was because of unclear or high risk of bias in the trials (downgraded by one point), imprecision due to small sample size (downgraded by one point), and wide credible intervals (downgraded by one point) for all outcomes with very low quality of evidence.

Mortality

Mortality (perioperative)

One trial (28 participants) reported perioperative mortality (Kostopanagiotou 2007); there was none in either group.

Mortality (longest follow-up)

One trial (28 participants) reported mortality at longest follow-up (Kostopanagiotou 2007). There was no mortality in either group after a follow-up period of one year.

Adverse events

Serious adverse events (proportion)

None of the trials reported this outcome.

Serious adverse events (number)

None of the trials reported this outcome.

Adverse events (proportion)

One trial reported adverse events as a proportion of participants experiencing at least one (Kostopanagiotou 2007). The unadjusted proportions of participants experiencing an adverse event are as follows.

- Control: 5/13 (38.5%).
- Autologous blood donation: 5/15 (33.3%).

There was no evidence of differences in the proportion of participants experiencing adverse events between groups (OR 0.79, 95% CrI 0.15 to 3.98; 28 participants; 1 study).

Adverse events (number)

None of the trials reported this outcome.

Health-related quality of life

None of the trials reported this outcome at any time point.

Blood transfusion requirements

Blood transfusion (proportion)

One trial reported the proportion of participants requiring a blood transfusion (Kajikawa 1994). The unadjusted proportions are as follows.

- Control: 13/21 (61.9%).
- Autologous blood donation: 5/21 (23.8%).

The proportion of participants requiring a blood transfusion was lower in the autologous blood donation group than in the control (OR 0.18, 95% CrI 0.04 to 0.66; 42 participants; 1 study; low-quality evidence: downgraded one point for unclear or high risk of bias and one point for small sample size).

Blood transfusion (red blood cells)

One trial reported blood transfusion quantity in red blood cells (Kostopanagiotou 2007). The mean blood transfusion quantities reported for each treatment are as follows.

- Control: 1.7 units.
- Autologous blood donation: 1.6 units.

There was no evidence of differences in blood transfusion quantity (red blood cells) between the groups (MD −0.10 units, 95% CrI −0.59 to 0.38; 28 participants; 1 study).

Blood transfusion (platelets)

None of the trials reported this outcome.

Blood transfusion (fresh frozen plasma)

None of the trials reported this outcome.

Blood transfusion (cryoprecipitate)

None of the trials reported this outcome.

Blood loss

Two trials reported blood loss (Kajikawa 1994; Kostopanagiotou 2007). The mean blood loss reported for each treatment are as follows.

- Control: 0.78 L and 1.193 L
- Autologous blood donation: 0.68 L and 1.272 L

Based on the DIC, we chose the fixed-effect model. There was no evidence of differences in blood loss between the groups (MD −0.02 L, 95% CrI −0.37 to 0.34; 70 participants; 2 studies).

Major blood loss (proportion)

One trial reported the proportion of participants experiencing major blood loss, defined as the loss of more than two litres (Kajikawa 1994). The unadjusted proportions of participants with major blood loss are as follows.

- Control: 2/21 (9.5%).
- Autologous blood donation: 4/21 (19.0%).

There was no evidence of differences in the proportion of participants experiencing major blood loss between the groups (OR 2.44, 95% CrI 0.39 to 21.5; 42 participants; 1 study).

Hospital stay

Total hospital stay

One trial reported total hospital stay (Kostopanagiotou 2007). The mean hospital stays reported for each treatment are as follows.

- Control: 10 d.
- Autologous blood donation: 11 d.

There was no evidence of differences in hospital stay between the groups (MD 0.99 d, 95% CrI −0.92 to 2.91; 28 participants; 1 study).

ITU stay

None of the trials reported this outcome.

Operating time

Two trials reported operating time (Kajikawa 1994; Kostopanagiotou 2007). The mean operating times reported for each treatment are as follows.

- Control: 190 min and 290 min.
- Autologous blood donation: 175 min and 318 min.

Based on the DIC, we chose the fixed-effect model. There was no evidence of differences in operating times between the groups (MD 1.78 min, 95% CrI −28.13 to 31.68; 70 participants; 2 studies).

Time needed to return to work

None of the trials reported this outcome.

Difference between Bayesian and frequentist meta-analysis

The interpretation of information and conclusions did not alter by using the frequentist meta-analysis.

Overall summary

There was no evidence of difference between autologous blood donation and control in any of the reported outcomes of interest for this review other than the proportion of people who required blood transfusion, which was lower in the autologous blood donation group than control (OR 0.18, 95% CrI 0.04 to 0.66; 42 participants; 1 study).

Cardiopulmonary interventions

Ten trials compared different methods of cardiopulmonary interventions (Hasegawa 2002; Matot 2002; El-Kharboutly 2004; Wang 2006; Yao 2006; Choi 2007; Jarnagin 2008; Kato 2008; Guo 2013; Guo 2014). We performed network meta-analysis only for blood transfusion quantity (red blood cells) and blood loss since direct comparison and indirect comparison effect estimates (which would enable assessment of inconsistency) were available only for these outcomes. We present only direct comparison results for other outcomes.

Quality of evidence

The quality of evidence was very low for all the outcomes and comparisons unless specifically indicated within the results. This was because of unclear or high risk of bias in the trials (downgraded by one point), imprecision due to small sample size (downgraded by one point), and wide credible intervals (downgraded by one point) for all outcomes with very low quality of evidence.

Mortality

Mortality (perioperative)

Four trials reported perioperative mortality (Hasegawa 2002; Matot 2002; Jarnagin 2008; Kato 2008). These studies used four treatments in 372 participants. The unadjusted proportions of perioperative mortality are as follows.

- Control: 0/81 (0.0%).
- Acute normovolemic haemodilution plus low central venous pressure: 1/102 (1.0%).
- Hypoventilation: 0/40 (0.0%).
- Low central venous pressure: 3/149 (2.0%).

There was no evidence of differences in perioperative mortality for any of the comparisons.

Mortality (longest follow-up)

None of the trials reported this outcome.

Adverse events

Serious adverse events (proportion)

Two trials reported the proportion of participants experiencing serious adverse events (Hasegawa 2002; Jarnagin 2008). A total of four treatments were used in a total of 209 participants in these studies. The unadjusted proportions of participants with serious adverse events are as follows.

- Control: 1/39 (2.6%).
- Acute normovolemic haemodilution plus low central venous pressure: 19/63 (30.2%).
- Hypoventilation: 2/40 (5.0%).
- Low central venous pressure: 19/67 (28.4%).

There was no evidence of differences in the proportion of participants experiencing serious adverse events for any of the comparisons.

Serious adverse events (number)

Two trials reported the total number of serious adverse events (Matot 2002; El-Kharboutly 2004). These studies used three treatments in 118 participants. The unadjusted rates of serious adverse events (number) are as follows.

- Control: 2/20 (10.0 per 100 participants).
- Acute normovolemic haemodilution plus low central venous pressure: 4/39 (10.3 per 100 participants).
- Low central venous pressure: 3/59 (5.1 per 100 participants).

There was no evidence of differences in the number of serious adverse events observed for any of the comparisons.

Adverse events (proportion)

Four trials reported the proportion of participants experiencing adverse events (Hasegawa 2002; Matot 2002; Wang 2006; Jarnagin 2008). These studies used four treatments in 337 participants. The unadjusted proportions of participants experiencing adverse events are as follows.

- Control: 19/64 (29.7%).
- Acute normovolemic haemodilution plus low central venous pressure: 37/102 (36.3%).
- Hypoventilation: 16/40 (40.0%).
- Low central venous pressure: 35/131 (26.7%).

There was no evidence of differences in the proportion of participants experiencing adverse events for any of the comparisons.

Adverse events (number)

Two trials reported adverse events (number) (Matot 2002; El-Kharboutly 2004). These studies used three treatments in 118 participants. The unadjusted rates of adverse events (number) are as follows.

- Control: 6/20 (30.0 per 100 participants).
- Acute normovolemic haemodilution plus low central venous pressure: 12/39 (30.8 per 100 participants).
- Low central venous pressure: 15/59 (25.4 per 100 participants).

There was no evidence of differences in adverse events (number) for any of the comparisons.

Health-related quality of life

None of the trials reported this outcome at any time point.

Blood transfusion requirements

Blood transfusion (proportion)

Six trials reported the proportion of participants requiring a blood transfusion (Hasegawa 2002; Matot 2002; El-Kharboutly 2004; Wang 2006; Jarnagin 2008; Kato 2008). These studies used four treatments in 462 participants. The unadjusted proportions of participants requiring a blood transfusion are as follows.

- Control: 29/126 (23.0%).
- Acute normovolemic haemodilution plus low central venous pressure: 12/102 (11.8%).
- Hypoventilation: 3/40 (7.5%).
- Low central venous pressure: 48/194 (24.7%).

Based on the DIC, we chose the fixed-effect model. The proportion of participants requiring a blood transfusion was higher in the low central venous pressure group than in the group receiving acute normovolemic haemodilution plus low central venous pressure (OR 3.19, 95% CrI 1.56 to 6.95; 208 participants; 2; low-quality evidence: downgraded by one point for unclear or high risk of bias in the trials and one more point for small sample size). There was no evidence of differences in other comparisons.

Blood transfusion (red blood cells)

Six trials reported blood transfusion quantity (as red blood cells) (Matot 2002; El-Kharboutly 2004; Wang 2006; Yao 2006; Jarnagin 2008; Guo 2013), testing five treatments in 358 participants. The median and range of the mean blood transfusion quantity (red blood cells) reported for each treatment are as follows.

- Control: 1.38 units (range 0.88 to 3.22).
- Acute normovolemic haemodilution: 0.17 units (range 0.17 to 0.17).
- Acute normovolemic haemodilution plus hypotension: 0.00 units (range 0.00 to 0.00).
- Acute normovolemic haemodilution plus low central venous pressure: 0.44 (range 0.00 to 1.15).
- Low central venous pressure: 0.61 (range 0.00 to 1.31).

Direct comparison

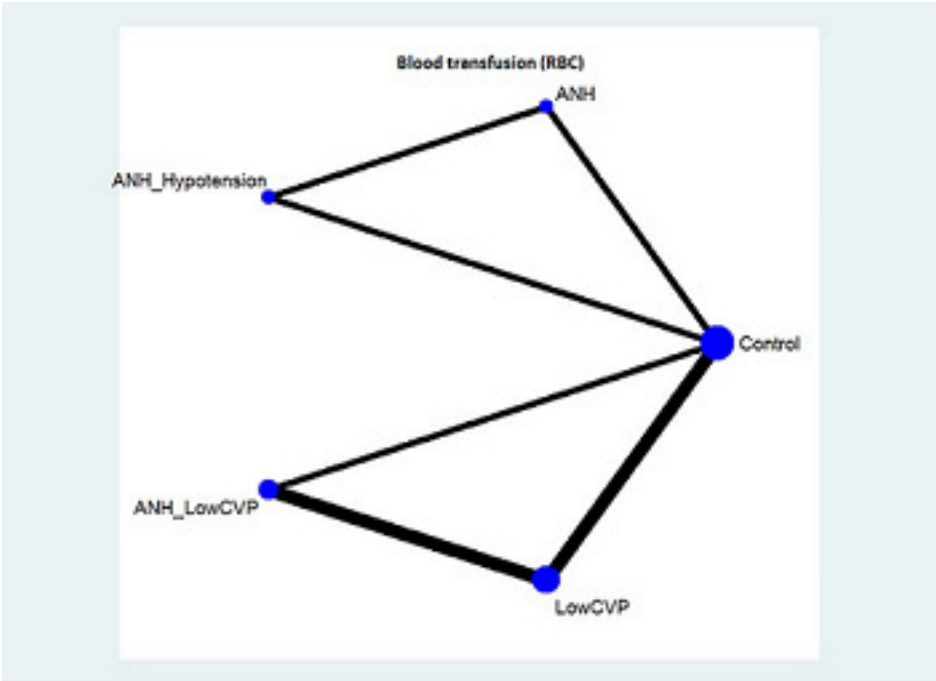
Based on the DIC, we chose the fixed-effect model. The blood transfusion quantity (in red blood cells) was lower in the group receiving acute normovolemic haemodilution (MD −1.25 units, 95% CrI −1.75 to −0.74; 20 participants; 1 study; low-quality evidence: downgraded by one point for unclear or high risk of bias in the trials and one more point for small sample size) and acute normovolemic haemodilution plus hypotension (MD −1.67 units, 95% CrI −2.06 to −1.32; 20 participants; 1 study; low-quality evidence: downgraded by one point for unclear or high risk of bias in the trials and one more point for small sample size) than control.The blood transfusion quantity (red blood cells) was higher inthe acute normovolemic haemodilution plus low central venous pressure group than in the control group (MD 0.27 units, 95% CrI 0.01 to 0.52; 30 participants; 1 study). There was no evidence of differences in other comparisons. We imputed either the mean or standard deviation in two trials (Matot 2002; Jarnagin 2008). Excluding these trials did not alter the conclusions.

Network meta-analysis

We present the network plots in Figure 4. Based on the DIC, we chose the random-effects model. There was no evidence of differences in blood transfusion quantity (red blood cells) for any of the comparisons. Excluding the trials in which we imputed

the mean or standard deviation (Matot 2002; Jarnagin 2008), we could not assess whether the direct and indirect evidence was consistent. We show the probability of each treatment being best, second best, third best, and so on in Figure 5 and the cumulative probability of a treatment being best in Figure 6.

Figure 4. The network plot showing the comparisons in the trials included in the comparison of cardiopulmonary interventions in which network meta-analysis was performed. The size of the node (circle) provides a measure of the number of trials in which the particular treatment was included as one of the arms. The thickness of the line provides a measure of the number of direct comparisons between two nodes (treatments).ANH: acute normovolemic haemodilution; CVP: central venous pressure; RBC: red blood cells.



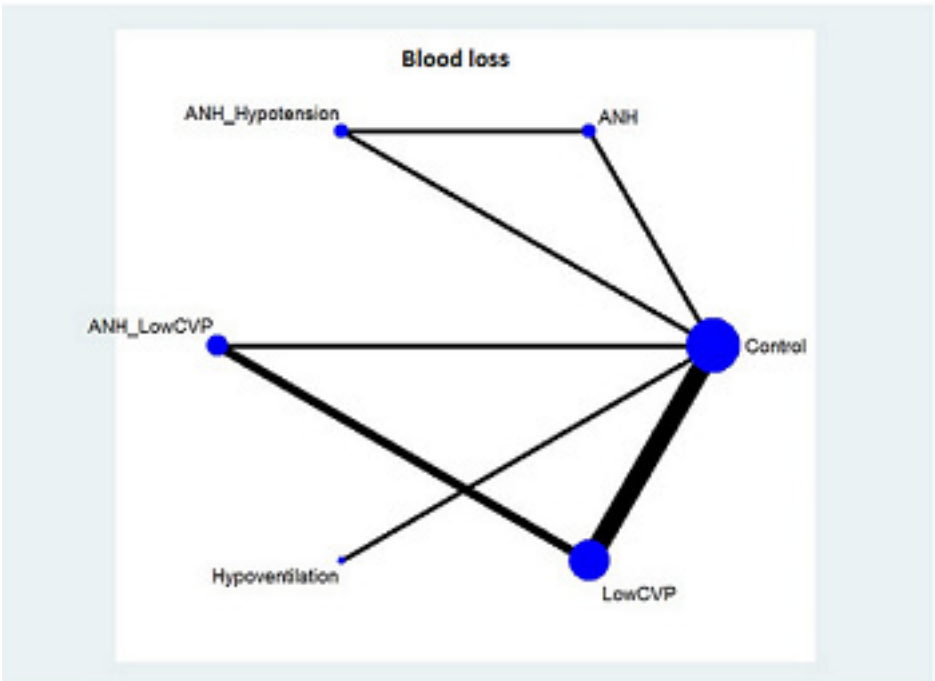


Figure 5. Probability of best treatment: probability of being best, second best, third best, etc. for each treatment for blood transfusion (red blood cells) (cardiopulmonary interventions). A probability of more than 90% is a reliable indicator that a treatment is best with regards to the specific outcome. A probability of less than 90% is less reliable. None of the treatments have a 90% probability of being best treatment.ANH: acute normovolemic haemodilution; CVP: central venous pressure; RBC: red blood cells.

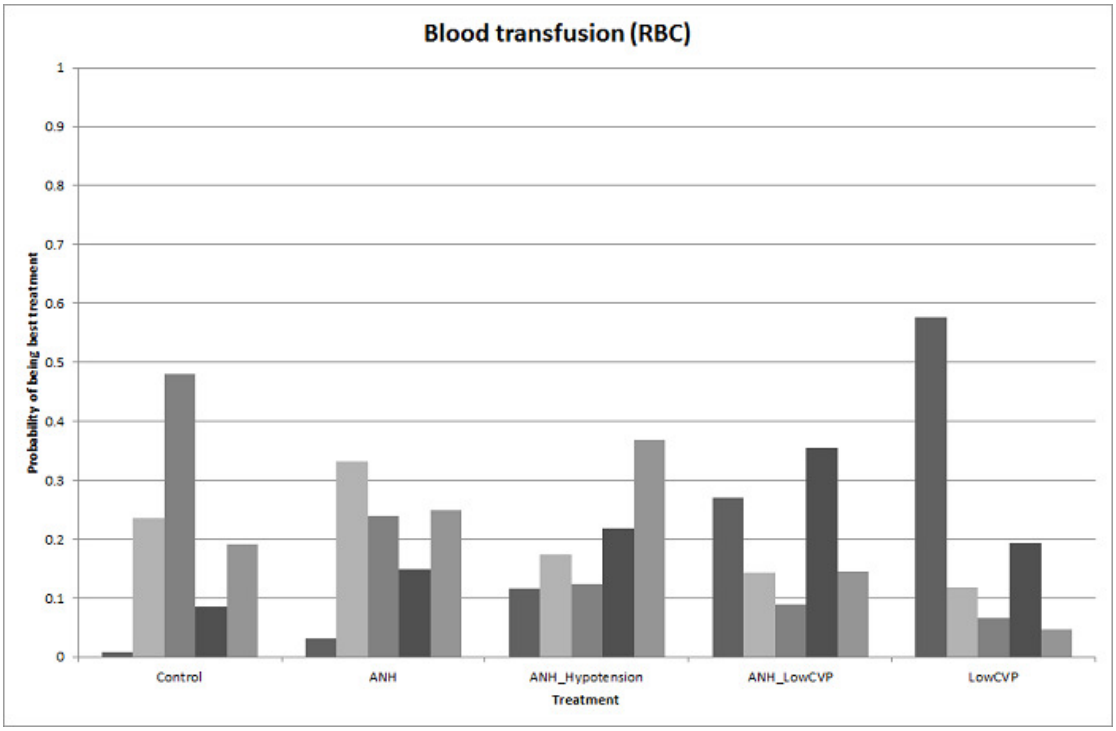
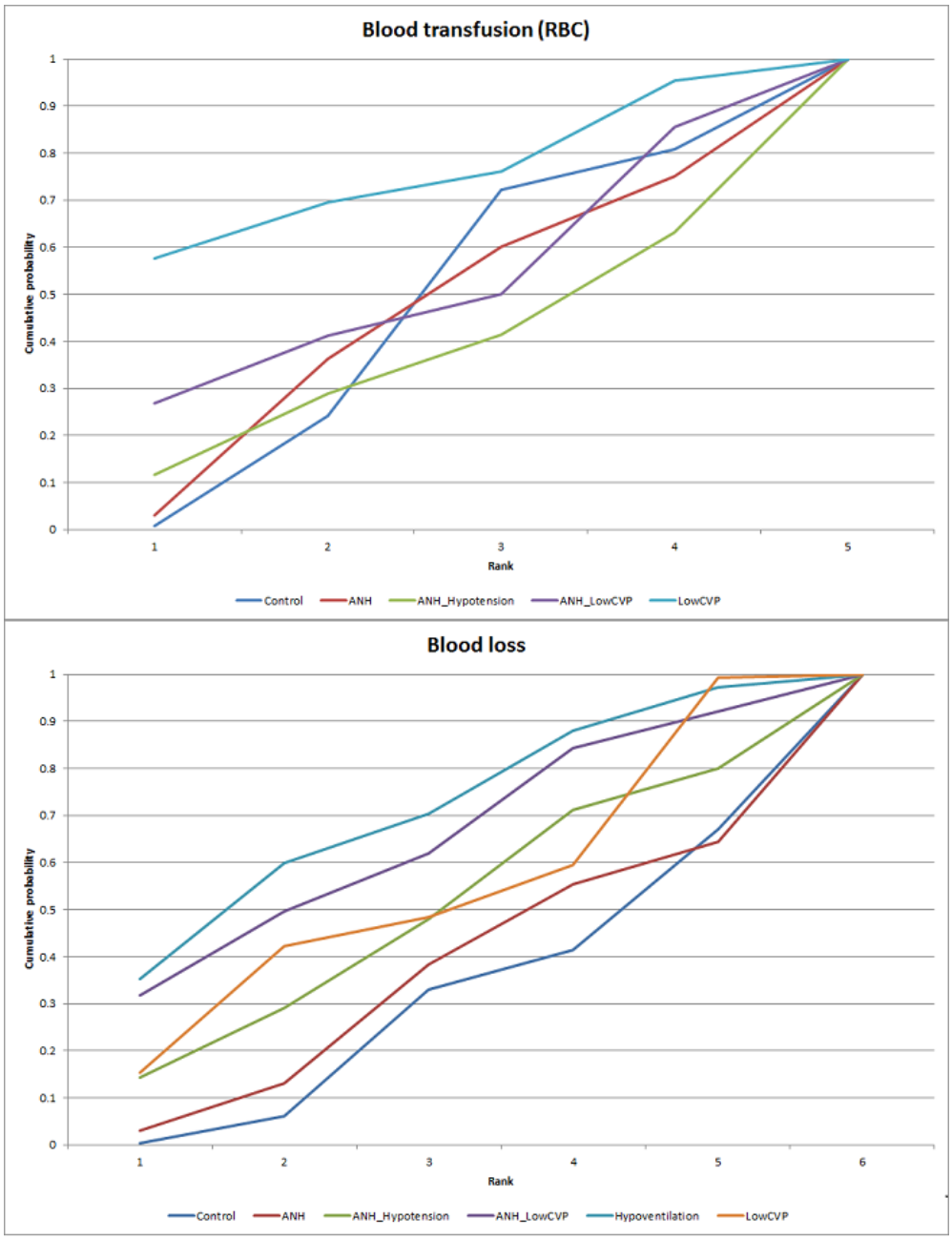


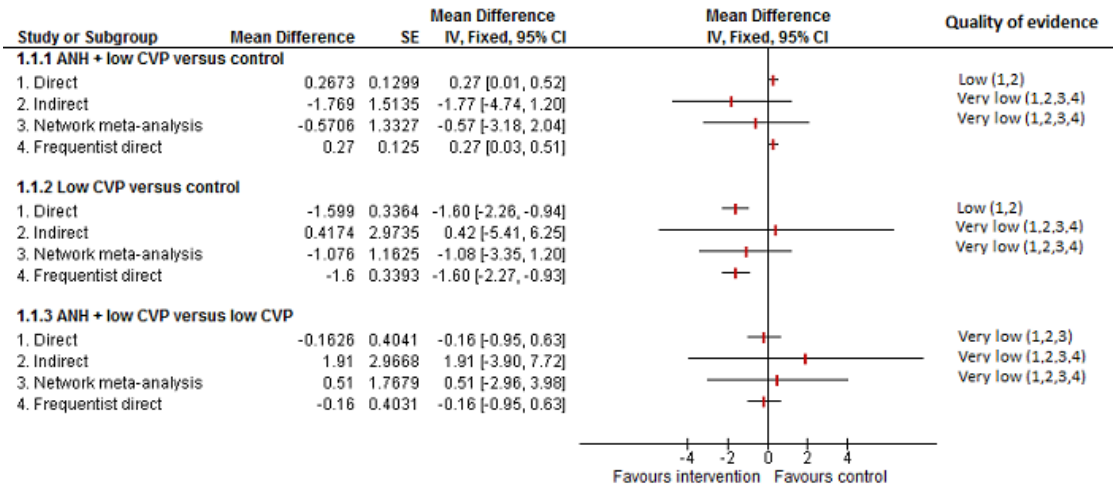
Figure 6. Cumulative probability of being best treatment: cumulative probability of being best for each treatment for cardiopulmonary interventions. Rank 1 indicates the probability that a treatment is best, rank 2 indicates the probability that a treatment is in the two best treatments, rank 3 indicates the probability that a treatment is in the three best treatments, and so on.ANH: acute normovolemic haemodilution; CVP: central venous pressure; RBC: red blood cells.



Direct evidence compared to network meta-analysis

We compare the information on direct evidence to network meta-analysis in Figure 7. The mean effect goes in opposite directions in the indirect and direct estimates, suggesting that there may be discrepancies (incongruence or inconsistency) between direct and indirect estimates. Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.

Figure 7. Cardiopulmonary intervention: blood transfusion (red blood cells) Forest plot of the comparisons in which direct and indirect estimates were available. The mean effect is in opposite directions in the indirect estimate and the direct estimates, thus suggesting that there may be discrepancies between direct and indirect estimates. Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.1 Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).2 Sample size was low (downgraded by 1 point).3Confidence intervals spanned no effect and clinically significant effect (downgraded by 1 point).4There was substantial or considerable heterogeneity (downgraded by 2 points).



Blood transfusion (platelets)

None of the trials reported this outcome.

Blood transfusion (fresh frozen plasma)

Two trials reported blood transfusion quantity (as fresh frozen plasma) (Wang 2006; Jarnagin 2008), testing three interventions in 180 participants. The mean blood transfusion quantities (fresh frozen plasma) reported for each treatment are as follows.

- Control: 4.23 units.
- Acute normovolemic haemodilution plus low central venous pressure: 0.17 units.
- Low central venous pressure: 0.28 and 1.75 units.

The blood transfusion quantity (fresh frozen plasma) was lower in the low central venous pressure group than the control group (MD −2.48 units, 95% CrI −3.58 to −1.37; 50 participants; 1 study; low-quality evidence: downgraded by one point for unclear or high risk of bias in the trials and one more point for small sample size). There was no evidence of differences in the other comparison (low central venous pressure versus acute normovolemic haemodilution

plus low central venous pressure) (MD 0.11 units, 95% CrI −0.79 to 1.01; 130 participants; 1 study). We imputed the standard deviation in one of the trials (Jarnagin 2008). Excluding this trial did not alter the outcome.

Blood transfusion (cryoprecipitate)

One trial reported blood transfusion quantity (cryoprecipitate) (Hasegawa 2002). The mean blood transfusion quantities (cryoprecipitate) are as follows.

- Control: 0.076 units.
- Hypoventilation: 0.052 units.

There was no evidence of differences in blood transfusion quantity (cryoprecipitate) between the groups (MD −0.02 units, 95% CrI −0.12 to 0.07; 79 participants; 1 study).

Blood loss

Nine trials reported blood loss (Hasegawa 2002; Matot 2002; El-Kharboutly 2004; Wang 2006; Yao 2006; Choi 2007; Jarnagin 2008; Kato 2008; Guo 2013),testing six interventions in 584 participants. The median and range of the mean blood loss reported for each treatment are as follows.

- Control: 0.711 L (range 0.584 to 2.329).
- Acute normovolemic haemodilution: 0.654 L (one trial only).
- Acute normovolemic haemodilution plus hypotension: 0.404 L (one trial only).
- Acute normovolemic haemodilution plus low central venous pressure: 0.75 L (range 0.735 to 0.8).
- Hypoventilation: 0.63 L (one trial only).
- Low central venous pressure: 0.6445 L (range 0.49 to 0.904).

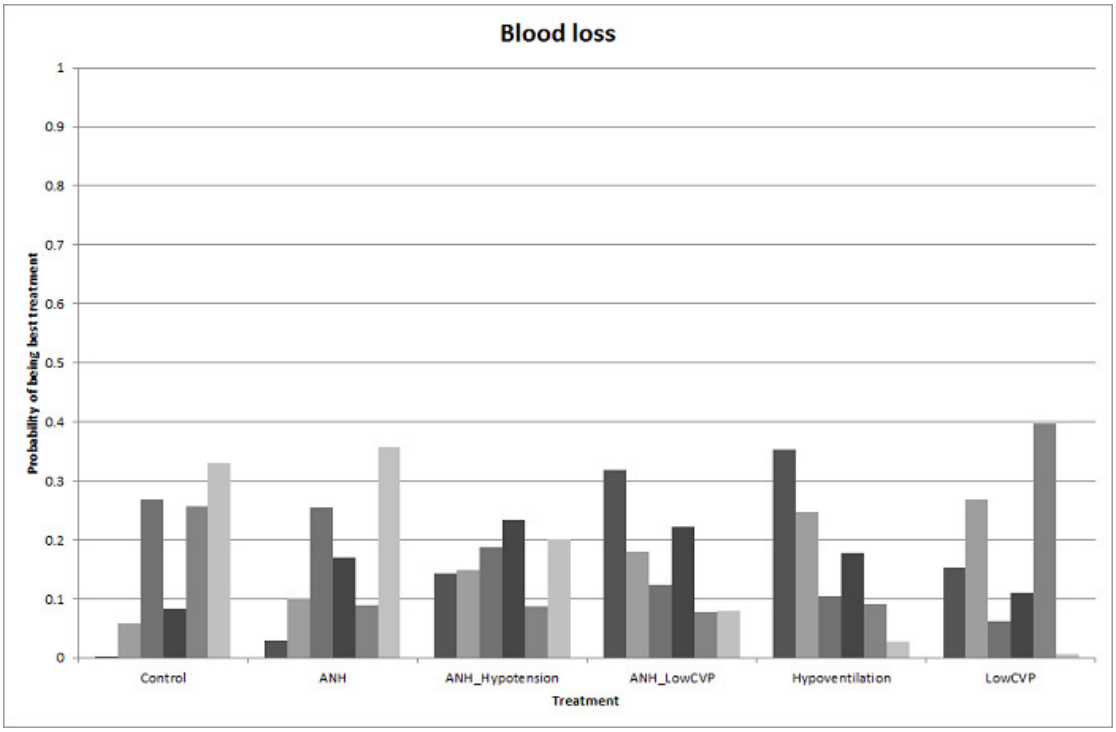
Direct comparison

Based on the DIC, we chose the fixed-effect model. The blood loss was lower in the acute normovolemic haemodilution plus hypotension group (MD −0.25 L; 95% CrI −0.37 to −0.13; 20 participants; 1 study) and the low central venous pressure group than in the control (MD −0.34 L, 95% CrI −0.46 to −0.22; 237 participants; 4 studies).The blood loss was lower for acute normovolemic haemodilution plus hypotension than for acute normovolemic haemodilution (MD −0.25 L; 95% CrI −0.40 to −0.10; 20 participants; 1 study). There was no evidence of differences in other comparisons. We imputed either the mean or standard deviation in four trials (Hasegawa 2002; Matot 2002; Jarnagin 2008; Kato 2008). Excluding these trials did not alter the conclusions.

Network meta-analysis

We present the network plots in Figure 4. Based on the DIC, we chose the random-effects model. There was no evidence of differences in blood loss for any of the comparisons. Excluding the trials in which we imputed the mean or standard deviation (Hasegawa 2002; Matot 2002; Jarnagin 2008; Kato 2008) meant that there would be no evidence from direct and indirect evidence, which would allow the assessment of whether the direct and indirect evidence was consistent. We show the probability of each treatment being the best, second best, third best, and so on in Figure 8. The cumulative probability of a treatment being best is shown in Figure 6.

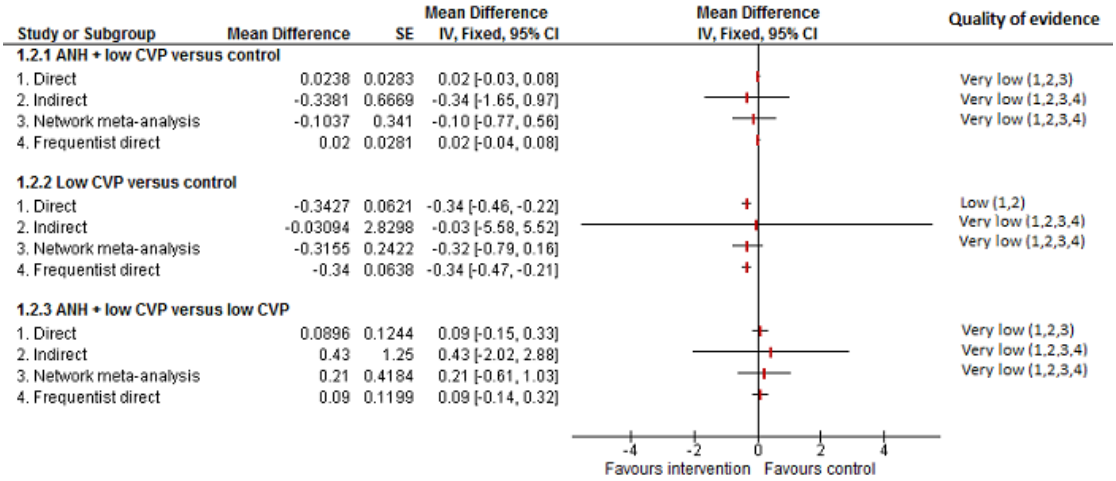
Figure 8. Probability of best treatment: probability of being best, second best, third best, etc. for each treatment for blood loss (cardiopulmonary interventions). A probability of more than 90% is a reliable indicator that a treatment is best with regards to the specific outcome. A probability of less than 90% is less reliable. None of the treatments have a 90% probability of being best treatment.ANH: acute normovolemic haemodilution; CVP: central venous pressure.



Direct evidence compared to network meta-analysis

We show the information on direct evidence compared to network meta-analysis in Figure 9. There does not appear to be any discrepancy between the direct and indirect estimates, although the indirect estimates have wide credible intervals. Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.

Figure 9. Cardiopulmonary intervention: blood loss Forest plot of the comparisons in which direct and indirect estimates were available. There does not appear to be any discrepancy between the direct and indirect estimates, although the indirect estimates have wide credible intervals.Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.ANH: acute normovolemic haemodilution; CVP: central venous pressure.1Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).2Sample size was low (downgraded by 1 point).3Confidence intervals spanned no effect and clinically significant effect (downgraded by 1 point).4There was substantial or considerable heterogeneity (downgraded by 2 points).



Major blood loss (proportion)

One trial reported the proportion of participants experiencing major blood loss (Jarnagin 2008), defined as more than 0.8 L. The unadjusted proportions of of participants experiencing major blood loss are as follows.

- Acute normovolemic haemodilution plus low central venous pressure: 33/63 (52.4%).
- Low central venous pressure: 29/67 (43.3%).

There was no evidence of differences in the proportion of participants experiencing major blood loss between the groups (OR 0.69, 95% CrI 0.34 to 1.38; 130 participants; 1 study).

Hospital stay

Total hospital stay

Five trials reported hospital stay (Hasegawa 2002; Wang 2006; Choi 2007; Jarnagin 2008; Kato 2008). They used four treatments in 406 participants. The median length and range of the mean or median hospital stay reported for each treatment are as follows.

- Control: 21 d (range 14 to 30).
- Acute normovolemic haemodilution plus low central venous pressure: 7 d (one trial only).
- Hypoventilation: 20 d (one trial only).
- Low central venous pressure: 15 d (range 7 to 26).

Based on the DIC, we chose the fixed-effect modelwhen there were two or more trials under the comparison. The total hospital stay was lower in the low central venous pressure group than in the control group (MD −2.42 d, 95% CrI −3.91 to −0.94; 197 participants; 3 studies). There was no evidence of differences in the remaining comparisons. In three trials, either the mean or the standard deviation was not available (Hasegawa 2002; Jarnagin 2008; Kato 2008), so we did not perform a meta-analysis. Exclusion of these three trials did not alter the conclusions.

ITU stay

None of the trials reported this outcome.

Operating time

Seven trials reported operating time (Hasegawa 2002; Matot 2002; El-Kharboutly 2004; Wang 2006; Choi 2007; Jarnagin 2008; Guo 2014). They used four treatments in 499 participants. The median and range of the mean operating times reported for each treatment are as follows.

- Control: 246 min (range 190 to 498).

- Acute normovolemic haemodilution plus low central venous pressure: 255 min (range 179 to 293).
- Hypoventilation: 498 min (one trial only).
- Low central venous pressure: 244 min (range 164 to 321).

Based on the DIC, we chose the fixed-effect model. The operating time was lower in the low central venous pressure group than in the control group (MD −15.32 min, 95% CrI −29.03 to −1.69; 192 participants; 4 studies). There was no evidence of differences in other comparisons. Two trials failed to report the mean, standard deviation, or both (Hasegawa 2002; Jarnagin 2008). Excluding these trials did not alter the conclusions.

Time needed to return to work

None of the trials reported this outcome.

Difference between Bayesian and frequentist meta-analysis

The interpretation of information and conclusions did not alter by using the frequentist meta-analysis.

Overall summary

There was no evidence of differences between different cardiopulmonary interventions in any of the reported outcomes of interest for this review other than the following.

- The proportion of participants requiring a blood transfusion was higher in those receiving low central venous pressure than in those receiving acute normovolemic haemodilution plus low central venous pressure (OR 3.19, 95% CrI 1.56 to 6.95; 208 participants; 2 studies).
- The blood transfusion quantity (red blood cells) was lower in the acute normovolemic haemodilution group (MD −1.25 units, 95% CrI −1.75 to −0.74; 20 participants; 1 study) and the acute normovolemic haemodilution plus hypotension group (MD −1.67 units, 95% CrI −2.06 to −1.32; 20 participants; 1 study) than in the control group. The blood transfusion quantity (red blood cells) was higher in the acute normovolemic haemodilution plus low central venous pressure group than in the control group (MD 0.27 units, 95% CrI 0.01 to 0.52; 30 participants; 1 study).
- The blood transfusion quantity (fresh frozen plasma) was lower for low central venous pressure than for control (MD −2.48 units, 95% CrI −3.58 to −1.37; 50 participants; 1 study).
- The blood loss was lower in the acute normovolemic haemodilution plus hypotension group (MD −0.25 L; 95% CrI −0.37 to −0.13; 20 participants; 1 study) and the low central venous pressure group than in the control (MD −0.34 L, 95% CrI −0.46 to −0.22; 237 participants; 4 studies). The blood loss was lower in the acute normovolemic haemodilution plus hypotension group than in the acute normovolemic haemodilution group (MD −0.25; 95% CrI −0.40 to −0.10; 20 participants; 1 study).
- The total hospital stay was lower in the low central venous pressure group than in the control (MD −2.42 d, 95% CrI −3.91 to −0.94; 197 participants; 3 studies).
- The operating time was lower in the low central venous pressure group than in the control (MD −15.32 min, 95% CrI −29.03 to −1.69; 192 participants; 4 studies).

Methods of parenchymal transection

Twelve trials compared different methods of parenchymal transection (Rau 2001; Takayama 2001; Arita 2005; Koo 2005; Lesurtel 2005; Smyrniotis 2005; Lupo 2007; Ikeda 2009; Doklestic 2012; Savlid 2013; Muratore 2014; Rahbari 2014). We performed network meta-analysis only for adverse events (proportion), adverse events (number), and proportion requiring blood transfusion, since direct comparison and indirect comparison effect estimates (which would enable assessment of inconsistency) were available only for these outcomes. We present only direct comparison results for other outcomes.

Quality of evidence

The quality of evidence was very low for all the outcomes and comparisons unless specifically indicated within the results. This was because of unclear or high risk of bias in the trials (downgraded by one point), imprecision due to small sample size (downgraded by one point), and wide credible intervals (downgraded by one point) for all outcomes with very low-quality of evidence. In addition, we downgraded the outcome of blood transfusion (proportion) by two points because of the presence of substantial or considerable heterogeneity in the pair-wise comparison or in the network.

Mortality

Mortality (perioperative)

Eleven trials reported perioperative mortality (Rau 2001; Takayama 2001; Arita 2005; Lesurtel 2005; Smyrniotis 2005; Lupo 2007; Ikeda 2009; Doklestic 2012; Savlid 2013; Muratore 2014; Rahbari 2014). They used six treatments in 990 participants. The unadjusted proportions of perioperative mortality are as follows.

- Clamp-crush method: 4/368 (1.1%).
- Cavitron ultrasonic surgical aspirator: 3/191 (1.6%).
- Hydrojet: 3/56 (5.4%).
- Radiofrequency dissecting sealer: 4/219 (1.8%).
- Sharp transection method: 0/41 (0.0%).
- Stapler: 4/115 (3.5%).

Based on the DIC, the fixed-effect model was chosen for all comparisons involving two or more trials. There was no evidence of differences in perioperative mortality for any of the comparisons.

Mortality (longest follow-up)

None of the trials reported this outcome.

Adverse events

Serious adverse events (proportion)

Seven trials reported the proportion of participants experiencing serious adverse events (Rau 2001; Takayama 2001; Arita 2005; Smyrniotis 2005; Ikeda 2009; Doklestic 2012; Rahbari 2014). They used six treatments in 665 participants. The unadjusted proportions of participants experiencing serious adverse events are as follows.

- Clamp-crush method: 28/292 (9.6%).
- Cavitron ultrasonic surgical aspirator: 6/116 (5.2%).
- Hydrojet: 2/31 (6.5%).
- Radiofrequency dissecting sealer: 6/120 (5.0%).
- Sharp transection method: 4/41 (9.8%).
- Stapler: 19/65 (29.2%).

Based on the DIC, we chose the fixed-effect model for all comparisons involving two or more trials. There was no evidence of differences in serious adverse events (proportion) for any of the comparisons.

Serious adverse events (number)

Five trials reported the number of serious adverse events (Takayama 2001; Arita 2005; Lesurtel 2005; Lupo 2007; Savlid 2013). They used five treatments in 437 participants. The unadjusted rates of serious adverse events (number) are as follows.

- Clamp-crush method: 7/132 (5.3 per 100 participants).
- Cavitron ultrasonic surgical aspirator: 13/141 (9.2 per 100 participants).
- Hydrojet: 3/25 (12.0 per 100 participants).
- Radiofrequency dissecting sealer: 16/89 (18.0 per 100 participants).
- Stapler: 12/50 (24.0 per 100 participants)..

Based on the DIC, we chose the fixed-effect model for all comparisons involving two or more trials. The number of serious adverse events was higher in the radiofrequency dissecting sealer group than in the clamp-crush method group (rate ratio 3.64, 95% CrI 1.25 to 13.97; 130 participants; 2 studies; low-quality evidence: downgraded by one point for unclear or high risk of bias in the trials and one more point for small sample size). There was no evidence of differences in other comparisons.

Adverse events (proportion)

Eight trials reported the proportion of participants experiencing adverse events (Rau 2001; Takayama 2001; Arita 2005; Koo 2005; Smyrniotis 2005; Doklestic 2012; Muratore 2014; Rahbari 2014). They used six treatments in 695 participants. The unadjusted proportions of participants experiencing adverse events are as follows.

- Clamp-crush method: 116/307 (37.8%).
- Cavitron ultrasonic surgical aspirator: 60/141 (42.6%).
- Hydrojet: 3/31 (9.7%).
- Radiofrequency dissecting sealer: 37/110 (33.6%).
- Sharp transection method: 17/41 (41.5%).
- Stapler: 31/65 (47.7%).

Direct comparison

Based on the DIC, we chose the fixed-effect model for all comparisons involving two or more trials. There was no evidence of differences in adverse events (proportion) for any of the comparisons.

Network meta-analysis

We show the network plots in Figure 10. Based on the DIC, we chose the random-effects model. The between-study standard deviation was 2.44. There was no evidence of differences in the proportion of participants experiencing adverse events for any of the comparisons. We show the probability of each treatment being best, second best, third best, and so on in Figure 11 and the cumulative probability of a treatment being best in Figure 12.

Figure 10. The network plot showing the comparisons in the trials included in the comparison of methods for parenchymal transection in which network meta-analysis was performed. The size of the node (circle) provides a measure of the number of trials in which the particular treatment was included as one of the arms. The thickness of the line provides a measure of the number of direct comparisons between two nodes (treatments).CUSA: cavitron ultrsonic surgical aspirator; RFDS: radiofrequency dissecting sealer.

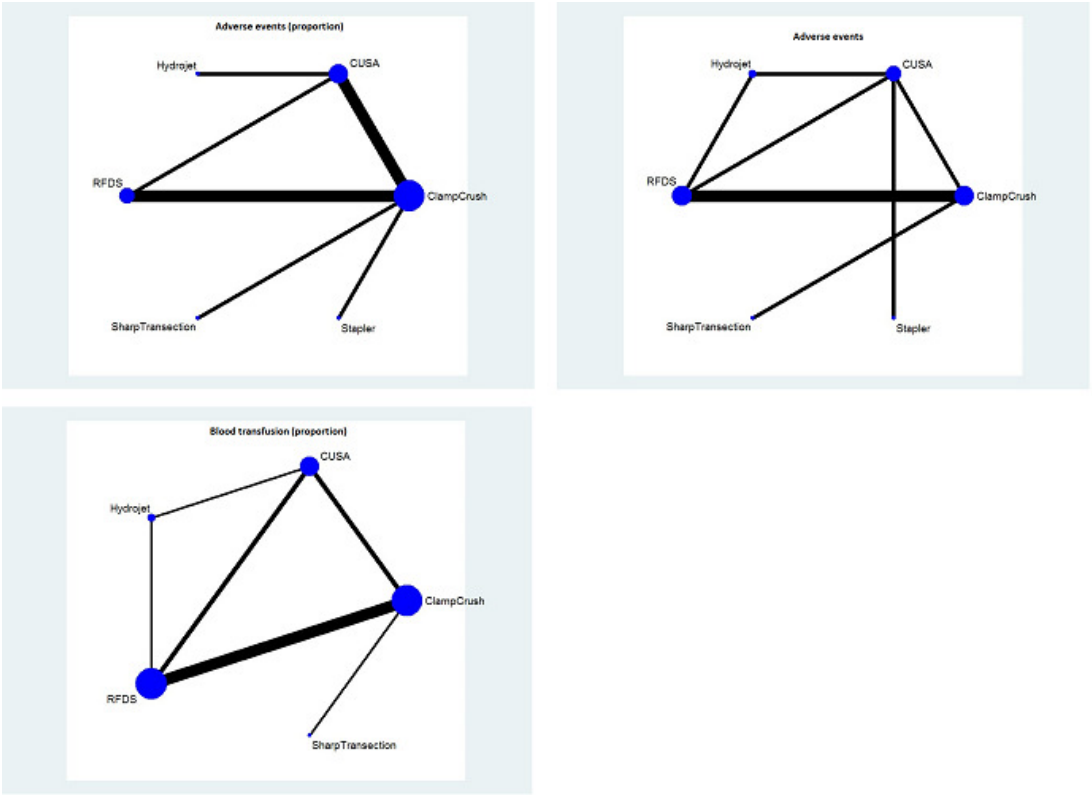


Figure 11. Probability of best treatment: probability of being best, second best, third best, etc. for each treatment for adverse events (proportion) (parenchymal transection methods). A probability of more than 90% is a reliable indicator that a treatment is best with regards to the specific outcome. A probability of less than 90% is less reliable. None of the treatments have a 90% probability of being best treatment.CUSA: cavitron ultrsonic surgical aspirator; RFDS: radiofrequency dissecting sealer.

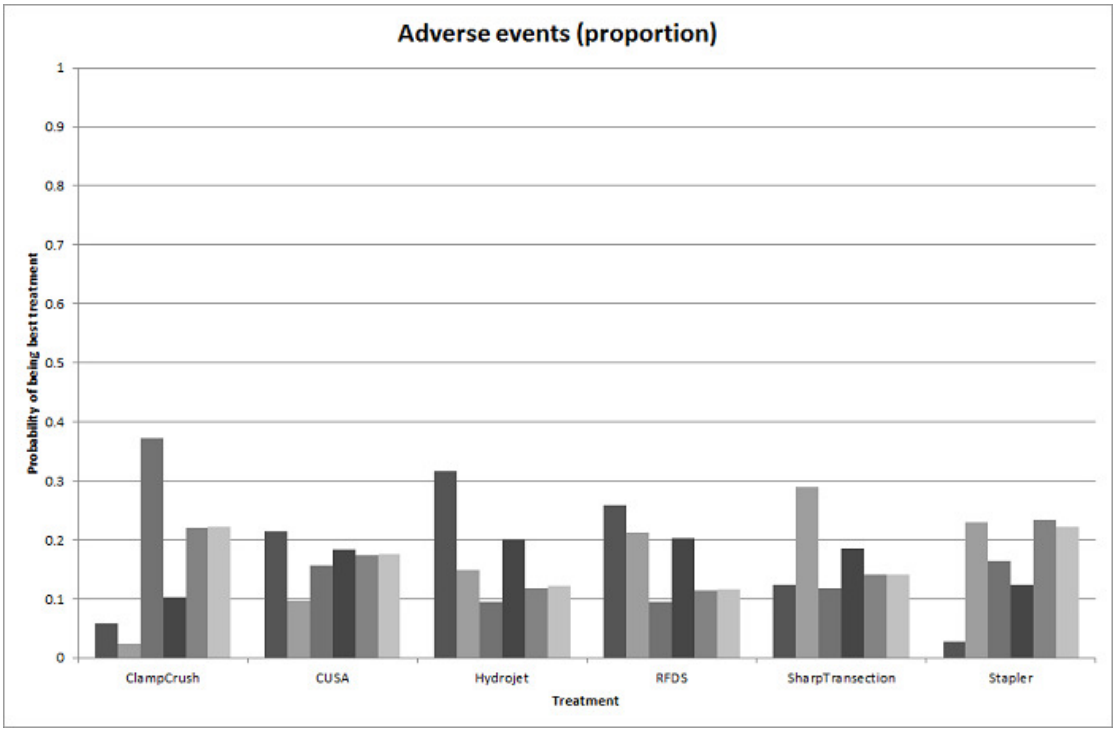
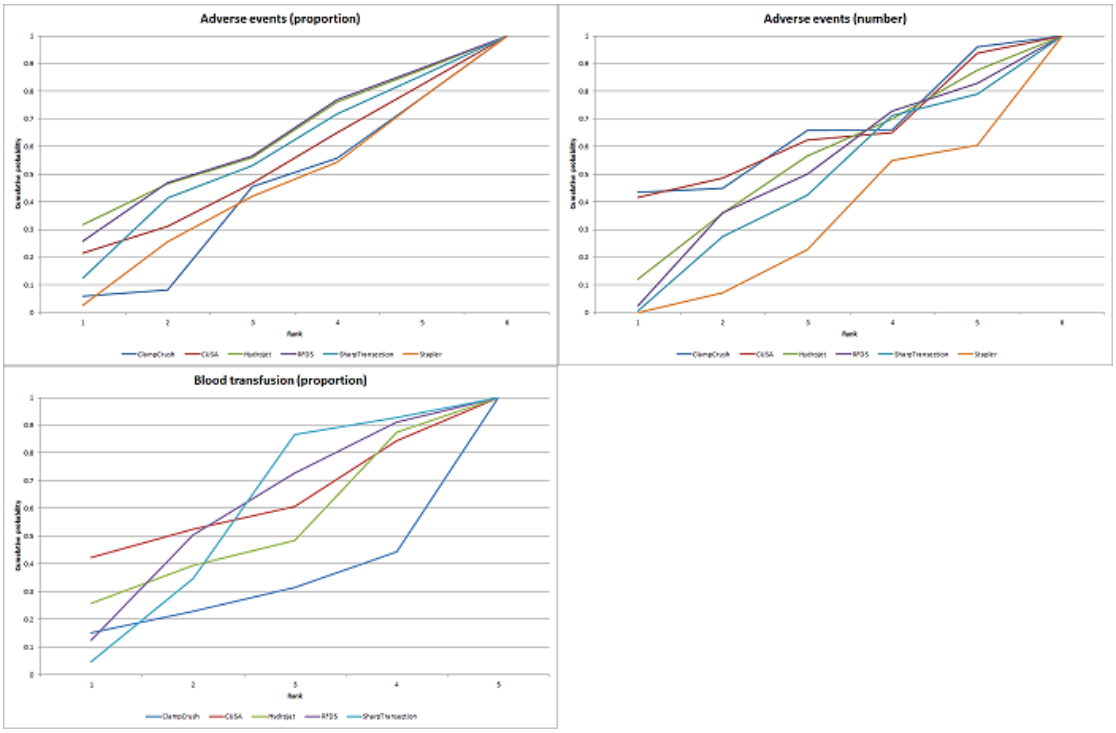


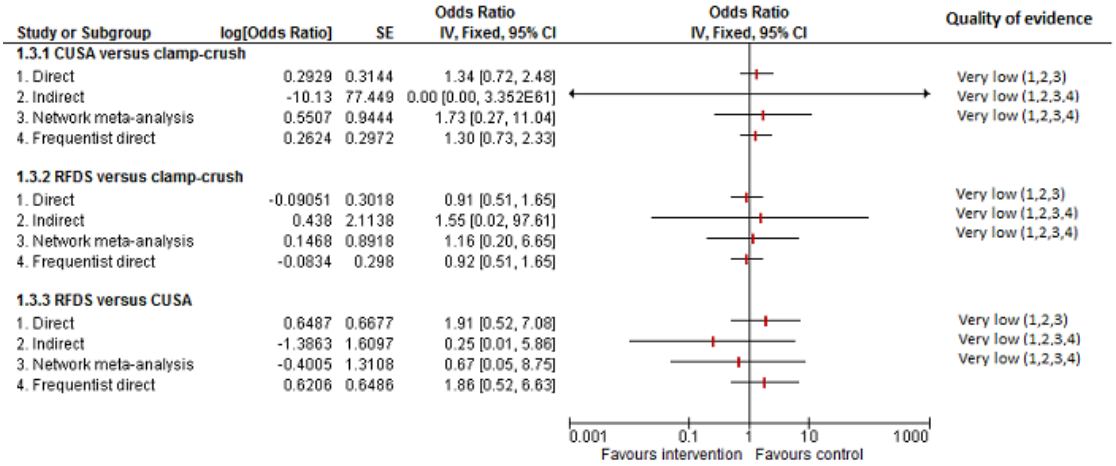
Figure 12. Cumulative probability of being best treatment: cumulative probability of being best for each treatment for parenchymal transection methods. Rank 1 indicates the probability that a treatment is best, rank 2 indicates the probability that a treatment is in the two best treatments, rank 3 indicates the probability that a treatment is in the three best treatments, and so on.CUSA: cavitron ultrsonic surgical aspirator; RFDS: radiofrequency dissecting sealer.



Direct evidence compared to network meta-analysis

Figure 13 shows the information on direct evidence compared to network meta-analysis. There does not appear to be any discrepancy between the direct and indirect estimates, although the indirect estimates have wide credible intervals. Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.

Figure 13. Parenchymal transection: adverse events (proportion) Forest plot of the comparisons in which direct and indirect estimates were available. There does not appear to be any discrepancy between the direct and indirect estimates, although the indirect estimates have wide credible intervals.Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.CUSA: cavitron ultrsonic surgical aspirator; RFDS: radiofrequency dissecting sealer.1Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).2Sample size was low (downgraded by 1 point).3Confidence intervals spanned no effect and clinically significant effect (downgraded by 1 point).4There was substantial or considerable heterogeneity (downgraded by 2 points).



Adverse events (number)

Seven trials reported the number of adverse events (Takayama 2001; Arita 2005; Lesurtel 2005; Smyrniotis 2005; Lupo 2007; Ikeda 2009; Savlid 2013). They used six treatments in 639 participants. The unadjusted rates of adverse events (number) are as follows.

- Clamp-crush method: 52/233 (22.3 per 100 participants).
- Cavitron ultrasonic surgical aspirator: 52/141 (36.9 per 100 participants).
- Hydrojet: 7/25 (28.0 per 100 participants).
- Radiofrequency dissecting sealer: 45/149 (30.2 per 100 participants).
- Sharp transection method: 18/41 (43.9 per 100 participants)
- Stapler: 22/50 (44.0 per 100 participants).

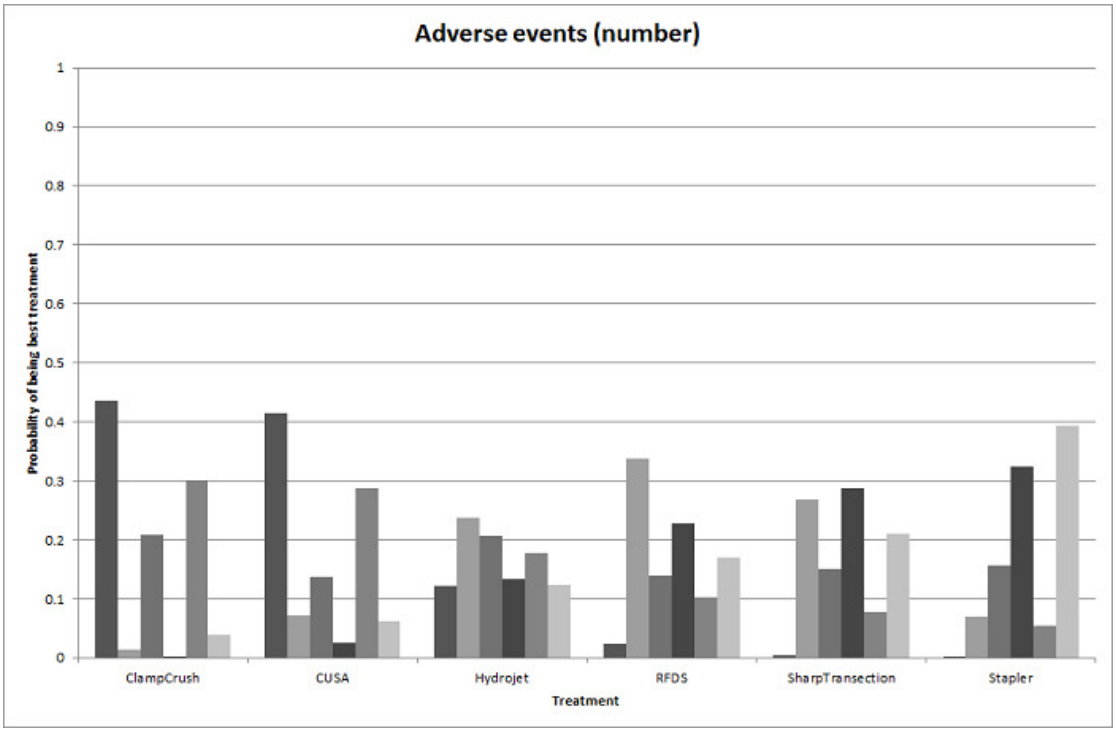
Direct comparison

Based on the DIC, we chose the fixed-effect model for all comparisons involving two or more trials. There was evidence for a higher adverse events (number) with radiofrequency dissecting sealer than with the clamp-crush method (rate ratio 1.85, 95% CrI 1.07 to 3.26; 250 participants; 3 studies). There was no evidence of differences in the number of adverse events for any of the comparisons.

Network meta-analysis

Figure 10 shows the network plots. Based on the DIC, we chose the fixed-effect model. There was evidence of more adverse events (number) with the radiofrequency dissecting sealer method than with the clamp-crush method (rate ratio 1.84, 95% CrI 1.13 to 3.06). There was no evidence of differences in other comparisons. Figure 14 shows the probability of each treatment being best, second best, third best, and so on, and Figure 12 shows the cumulative probability of a treatment being best.

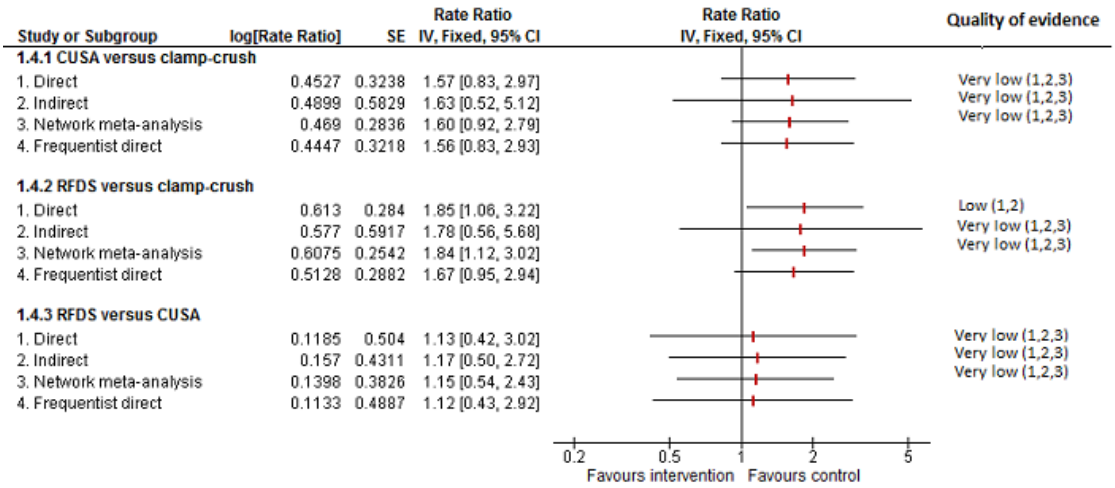
Figure 14. Probability of best treatment: probability of being best, second best, third best, etc. for each treatment for adverse events (number) (parenchymal transection methods). A probability of more than 90% is a reliable indicator that a treatment is best with regards to the specific outcome. A probability of less than 90% is less reliable. None of the treatments have a 90% probability of being best treatment.CUSA: cavitron ultrsonic surgical aspirator; RFDS: radiofrequency dissecting sealer.



Direct evidence compared to network meta-analysis

Figure 15 shows the information on direct evidence compared to network meta-analysis. There does not appear to be any discrepancy between the direct and indirect estimates. Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.

Figure 15. Parenchymal transection: adverse events (number) Forest plot of the comparisons in which direct and indirect estimates were available. There does not appear to be any discrepancy between the direct and indirect estimates.Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.CUSA: cavitron ultrsonic surgical aspirator; RFDS: radiofrequency dissecting sealer.1Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).2Sample size was low (downgraded by 1 point).3Confidence intervals spanned no effect and clinically significant effect (downgraded by 1 point).



Health-related quality of life

None of the trials reported this outcome at any time point.

Blood transfusion requirements

Blood transfusion (proportion)

Eight trials reported the proportion of participants requiring a blood transfusion (Takayama 2001; Arita 2005; Lesurtel 2005; Smyrniotis 2005; Lupo 2007; Ikeda 2009; Doklestic 2012; Muratore 2014). They used five treatments in 699 participants. The unadjusted proportions of blood transfusion (proportion) are as follows.

- Clamp-crush method: 46/303 (15.2%).
- Cavitron ultrasonic surgical aspirator: 12/111 (10.8%).
- Hydrojet: 8/25 (32.0%).
- Radiofrequency dissecting sealer: 37/219 (16.9%).
- Sharp transection method: 13/41 (31.7%).

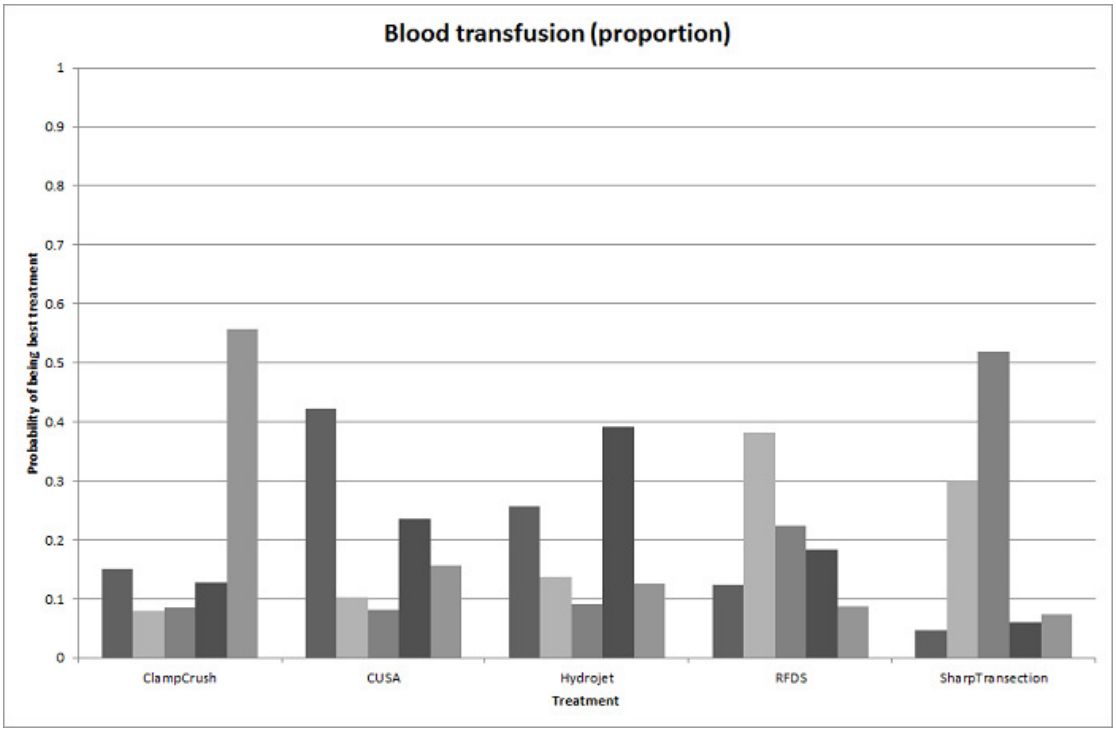
Direct comparison

Based on the DIC, we chose the fixed-effect model for comparisons involving two or more trials. There was no evidence of differences in the proportion of participants requiring a blood transfusion for any of the comparisons.

Network meta-analysis

Figure 10 shows the network plots. Based on the DIC, we chose the fixed-effect model. There was no evidence of differences in the proportion of participants requiring a blood transfusion for any of the comparisons. Figure 16 shows the probability of each treatment being best, second best, third best, and so on. Figure 12 shows the cumulative probability of a treatment being best.

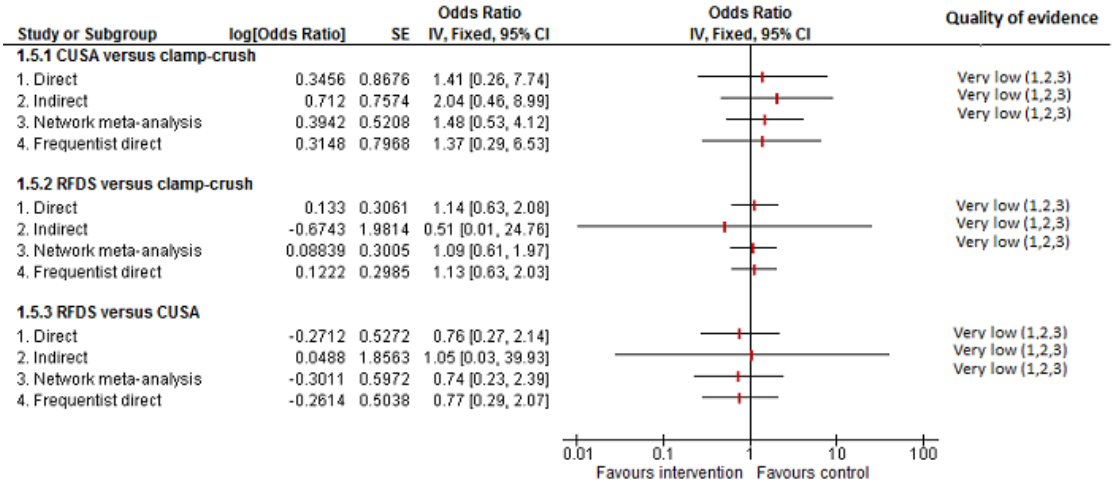
Figure 16. Probability of best treatment: probability of being best, second best, third best, etc. for each treatment for blood transfusion (proportion) (parenchymal transection methods). A probability of more than 90% is a reliable indicator that a treatment is best with regards to the specific outcome. A probability of less than 90% is less reliable. None of the treatments have a 90% probability of being best treatment.CUSA: cavitron ultrsonic surgical aspirator; RFDS: radiofrequency dissecting sealer.



Direct evidence compared to network meta-analysis

Figure 17 shows the information on direct evidence compared to network meta-analysis. There does not appear to be any discrepancy between the direct and indirect estimates, although the indirect estimates have wide credible intervals for some comparisons. There was little apparent difference in the quality of evidence between direct, indirect estimates, and network meta-analysis; so, we could not choose one estimate over the others based on the quality of evidence.

Figure 17. Parenchymal transection:blood transfusion (proportion) Forest plot of the comparisons in which direct and indirect estimates were available. There does not appear to be any discrepancy between the direct and indirect estimates, although the indirect estimates have wide credible intervals for some comparisons. There was little apparent difference in the quality of evidence between direct, indirect estimates, and network meta-analysis; so, we could not choose one estimate over the others based on the quality of evidence.CUSA: cavitron ultrsonic surgical aspirator; RFDS: radiofrequency dissecting sealer.1Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).2Sample size was low (downgraded by 1 point).3Confidence intervals spanned no effect and clinically significant effect (downgraded by 1 point).



Blood transfusion (red blood cells)

Four trials reported blood transfusion quantity (in red blood cells) (Rau 2001; Smyrniotis 2005; Savlid 2013; Rahbari 2014). They used five treatments in 373 participants. The median or mean blood transfusion quantity (red blood cells) reported for each treatment are as follows.

- Clamp-crush method: 0.00 and 1.20 units (two trials only).
- Cavitron ultrasonic surgical aspirator: 2.48 and 4.00 units (two trials only).
- Hydrojet: 1.50 units (one trial only).
- Sharp transection method: 0.00 units (one trial only).
- Stapler: 1.10 and 4.00 units (two trials only).

The blood transfusion quantity (red blood cells) was lower in the hydrojet group than in the cavitron ultrasonic surgical aspirator group (MD −0.98 units, 95% CrI −1.90 to −0.06; 61 participants; 1 study). There was no evidence of difference in blood transfusion quantity (red blood cells) in the remaining comparisons. Either mean or standard deviation or both were not available in two trials (Smyrniotis 2005; Savlid 2013). Excluding these two trials did not change the conclusion.

Blood transfusion (platelets)

None of the trials reported this outcome.

Blood transfusion (fresh frozen plasma)

One trial reported blood transfusion quantity (fresh frozen plasma) (Rahbari 2014). It used two treatments in 130 participants in these studies. The mean blood transfusion quantity (fresh frozen plasma) reported for each treatment are as follows.

- Clamp-crush method: 0.5 units.
- Stapler: 0.3 units.

There was no evidence of differences in blood transfusion quantity (fresh frozen plasma) between the groups (MD −0.20 units, 95% CrI −0.66 to 0.26; 130 participants;1 study).

Blood transfusion (cryoprecipitate)

None of the trials reported this outcome.

Blood loss

Ten trials reported blood loss (Rau 2001; Takayama 2001; Arita 2005; Koo 2005; Smyrniotis 2005; Ikeda 2009; Doklestic 2012; Savlid 2013; Muratore 2014; Rahbari 2014). They used six treatments in 915 participants. The median or mean blood loss reported for each treatment are as follows.

- Clamp-crush method: 0.56 L (range 0.2 to 1.05).

- Cavitron ultrasonic surgical aspirator: 0.875 L (range 0.15 to 1.797).
- Hydrojet: 1.479 L (range 1.479 to 1.479).
- Radiofrequency dissecting sealer: 0.47 L (range 0.15 to 0.665).
- Sharp transection method: 0.5 L (range 0.5 to 0.5).
- Stapler: 0.9625 L (range 0.925 to 1).

Of the 10 trials, 8 did not provide either the mean, the standard deviation or both (Takayama 2001; Arita 2005; Smyrniotis 2005; Ikeda 2009; Doklestic 2012; Savlid 2013; Muratore 2014; Rahbari 2014), so we performed the analysis only for two trials (Rau 2001; Koo 2005). There was no evidence of differences in blood loss for any of the comparisons.

Major blood loss (proportion)

None of the trials reported this outcome.

Hospital stay

Total hospital stay

Ten trials reported hospital stay (Doklestic 2012; Takayama 2001; Arita 2005; Lesurtel 2005; Smyrniotis 2005; Lupo 2007; Ikeda 2009; Savlid 2013; Muratore 2014; Rahbari 2014). They used six treatments in 929 participants. The mean and range of the mean hospital stays reported for each treatment are as follows.

- Clamp-crush method: 11 d (range 7 to 18).
- Cavitron ultrasonic surgical aspirator: 11.95 d (range 8.5 to 17).
- Hydrojet: 9 d (one trial only).
- Radiofrequency dissecting sealer: 10.5 d (range 8 to 16).
- Sharp transection method: 11 d (one trial only).
- Stapler: 10 to 14.9 d (two trials only).

All 10 trials failed to provide the mean, standard deviation or both. There was no evidence of differences in total hospital stay for any of the comparisons.

ITU stay

Four trials reported ITU stay (Lesurtel 2005; Smyrniotis 2005; Doklestic 2012; Rahbari 2014). They used six treatments in 347 participants. The median ITU stays reported for each treatment are as follows.

- Clamp-crush method: 1 d (range 0 to 1.5).
- Cavitron ultrasonic surgical aspirator: 0 and 1 d (two trials only).
- Hydrojet: 1 d (one trial only).
- Radiofrequency dissecting sealer: 1 d (two trials only).
- Sharp transection method: 1 d (one trial only).
- Stapler: 0 d (one trial only).

Either the mean, the standard deviation, or both were not available in all the four trials. There was no evidence of differences in ITU stay for any of the comparisons.

Operating time

Six trials reported operating time (Koo 2005; Smyrniotis 2005; Lupo 2007; Doklestic 2012; Savlid 2013; Rahbari 2014). They used five treatments in 472 participants. The median or mean operating time reported for each treatment are as follows.

- Clamp-crush method: 231 min (range 211 to 278).
- Cavitron ultrasonic surgical aspirator: 270 min (range 259 to 298).
- Radiofrequency dissecting sealer: 292 and 295 min (two trials only).
- Sharp transection method: 205 min (one trial only).
- Stapler: 190 and 272 min (two trials only).

Based on the DIC, we chose the fixed-effect model when there were two or more studies in a comparison. There was no evidence of differences in operating time in any of the comparisons. We imputed either the mean or the standard deviation in two trials (Lupo 2007; Doklestic 2012). Excluding this trial did not alter the results.

Time needed to return to work

None of the trials reported this outcome.

Difference between Bayesian and frequentist meta-analysis

The interpretation of information and conclusions did not change upon use of the frequentist meta-analysis except for the following.
Adverse events (number): the number of adverse events was higher in the radiofrequency dissecting sealer group than in the group receiving the clamp-crush method with Bayesian meta-analysis (rate ratio 1.85, 95% CrI 1.07 to 3.26; 250 participants; 3 studies), while there was no evidence of difference in adverse events (number) in any comparisons by frequentist meta-analysis (rate ratio 1.67, 95% CI 0.95 to 2.94; 250 participants; 3 studies).
Operating time: there was no evidence of difference in operating time in any comparisons by Bayesian meta-analysis (stapler resection versus clamp-crush method: MD −27.99 min, 95% CrI −56.91 to 1.02; 130 participants; 1 study), while the operating time was lower in stapler resection than clamp-crush method with frequentist meta-analysis (MD −31.00 min, 95% CI −60.40 to −1.60; 130 participants; 1 study).

Overall summary

There was no evidence of differences between different parenchymal transection methods in any of the reported outcomes of interest for this review other than the following.

- The adverse events (number) was higher with the radiofrequency dissecting sealer than with the clamp-crush method (rate ratio 1.85, 95% CrI 1.07 to 3.26; 250 participants; 3 studies) (Bayesian analysis only: both direct and network meta-analysis).
- The blood transfusion quantity (red blood cells) was lower in the hydrojet group than with the cavitron ultrasonic surgical aspirator group (MD −0.98 units, 95% CrI −1.90 to −0.06; 61 participants; 1 study).
- The operating time was lower with stapler resection than with the clamp-crush method with frequentist meta-analysis (MD −31.00 min, 95% CI −60.40 to −1.60; 130 participants; 1 study) (frequentist analysis only).

Methods of dealing with cut surface

Seventeen trials compared different methods of dealing with cut surface (Kohno 1992; Liu 1993; Noun 1996; Chapman 2000; Frilling 2005; Franceschi 2006; Figueras 2007; Fischer 2011; Gugenheim 2011; De Boer 2012; Porte 2012; Kakaei 2013; Koea 2013; Ollinger 2013; Bektas 2014; Genyk 2014; Moench 2014). We did not perform network meta-analysis since direct comparison and indirect comparison effect estimates (which would enable assessment of inconsistency) were not available for any of the outcomes.

Quality of evidence

The quality of evidence was very low for all the outcomes and comparisons unless specifically indicated within the results. This was because of unclear or high risk of bias in the trials (downgraded by one point), imprecision due to small sample size (downgraded by one point), and wide credible intervals (downgraded by one point) for all outcomes with very low quality of evidence. In addition, some of the pair-wise comparisons in blood transfusion proportion and blood transfusion (red blood cells) were downgraded by two points because of the presence of substantial or considerable heterogeneity.

Mortality

Mortality (perioperative)

Ten trials reported perioperative mortality (Kohno 1992; Chapman 2000; Frilling 2005; Figueras 2007; Fischer 2011; Gugenheim 2011; De Boer 2012; Ollinger 2013; Bektas 2014; Moench 2014). They used seven interventions in 1271 participants. The unadjusted proportions of perioperative mortality are as follows.

- Control: 4/339 (1.2%).
- Argon beam: 6/114 (5.3%).
- Collagen: 4/122 (3.3%).
- Fibrin sealant: 23/485 (4.7%).
- Fibrin sealant plus collagen: 6/150 (4.0%).
- Oxidised cellulose: 1/32 (3.1%).
- Plasmajet: 2/29 (6.9%).

Based on the DIC, we chose the fixed-effect model when there were two or more trials. There was no evidence of differences in perioperative mortality for any of the comparisons.

Mortality (longest follow-up)

None of the trials reported this outcome.

Adverse events

Serious adverse events (proportion)

Seven trials reported the proportion of participants experiencing serious adverse events (Noun 1996; Fischer 2011; Gugenheim 2011; De Boer 2012; Ollinger 2013; Bektas 2014; Moench 2014). They used six interventions in 798 participants. The unadjusted proportions of serious adverse events (proportion) are as follows.

- Control: 43/231 (18.6%).
- Argon beam: 14/52 (26.9%).
- Collagen: 16/62 (25.8%).
- Fibrin sealant: 90/392 (23.0%).
- Oxidised cellulose: 10/32 (31.3%).
- Plasmajet: 1/29 (3.4%).

Based on the DIC, we chose the fixed-effect model when there were two or more trials. There was no evidence of differences in serious adverse events (proportion) for any of the comparisons.

Serious adverse events (number)

Six trials reported the number of serious adverse events (Kohno 1992; Frilling 2005; Figueras 2007; Kakaei 2013; Bektas 2014; Moench 2014). They used seven interventions in 725 participants. The unadjusted rates of serious adverse events (number) are as follows.

- Control: 39/185 (21.1 per 100 participants).
- Argon beam: 4/62 (6.5 per 100 participants).
- Collagen: 30/93 (32.3 per 100 participants).
- Cyanoacrylate: 1/15 (6.7 per 100 participants).
- Fibrin sealant: 72/205 (35.1 per 100 participants).
- Fibrin sealant plus collagen: 29/150 (19.3 per 100 participants).
- Oxidised cellulose: 4/15 (26.7 per 100 participants).

Based on the DIC, we chose the fixed-effect model when there were two or more trials. The serious adverse events (number) was higher in the fibrin sealant group than in the argon beam group (rate ratio 4.81, 95% CrI 1.73 to 17.5; 121 participants; 1 study;

low-quality evidence: downgraded one point for unclear or high risk of bias in the trial and one more point for small sample size). There was no evidence of differences in other comparisons.

Adverse events (proportion)

Nine trials reported the proportion of participants experiencing adverse events (Noun 1996; Frilling 2005; Figueras 2007; Fischer 2011; De Boer 2012; Ollinger 2013; Bektas 2014; Genyk 2014; Moench 2014). They used six interventions in 1385 participants. The unadjusted proportions of adverse events (proportion) are as follows.

- Control: 166/381 (43.6%).
- Argon beam: 52/114 (45.6%).
- Collagen: 38/62 (61.3%).
- Fibrin sealant: 227/536 (42.4%).
- Fibrin sealant plus collagen: 35/150 (23.3%).
- Oxidised cellulose: 27/142 (19.0%).

Based on the DIC, we chose the fixed-effect model when there were two or more trials. There was no evidence of differences in adverse events (proportion) for any of the comparisons.

Adverse events (number)

Five trials reported the number of adverse events (Kohno 1992; Frilling 2005; Kakaei 2013; Bektas 2014; Moench 2014). They used six interventions in 425 participants. The unadjusted rates of adverse events (number) are as follows.

- Control: 89/35 (254.3 per 100 participants).
- Argon beam: 47/62 (75.8 per 100 participants).
- Collagen: 135/93 (145.2 per 100 participants).
- Cyanoacrylate: 2/15 (13.3 per 100 participants).
- Fibrin sealant: 302/205 (147.3 per 100 participants).
- Oxidised cellulose: 7/15 (46.7 per 100 participants).

Based on the DIC, we chose the fixed-effect model when there were two or more trials. There was no evidence of differences in adverse events (number) for any of the comparisons.

Health-related quality of life

None of the trials reported this outcome at any time point.

Blood transfusion requirements

Blood transfusion (proportion)

Four trials reported the proportion of participants requiring a blood transfusion (Noun 1996; Figueras 2007; De Boer 2012; Kakaei 2013). They used five interventions in 737 participants. The unadjusted proportions of participants requiring a blood transfusion are as follows.

- Control: 62/348 (17.8%).
- Cyanoacrylate: 2/15 (13.3%).
- Fibrin sealant: 38/209 (18.2%).
- Fibrin sealant plus collagen: 40/150 (26.7%).
- Oxidised cellulose: 4/15 (26.7%).

Based on the DIC, we chose the fixed-effect model when there were two or more trials. There was no evidence of differences in blood transfusion (proportion) for any of the comparisons.

Blood transfusion (red blood cells)

Five trials reported blood transfusion (red blood cells) (Liu 1993; Noun 1996; Figueras 2007; Kakaei 2013; Ollinger 2013). They used five interventions in 517 participants. The median and range of the mean blood transfusion (red blood cells) reported for each treatment are as follows.

- Control: 3.50 units (range 0.31 to 8.13).
- Cyanoacrylate: 2.13 units (one trial only).
- Fibrin sealant: 4.30 units (range 3.00 to 5.94).
- Fibrin sealant plus collagen: 0.30 units (one trial only).
- Oxidised cellulose: 1.86 and 4.35 units (two trials only).

Based on the DIC, we chose the fixed-effect model for the comparison of fibrin sealant versus control and the random-effects model for the comparison of oxidised cellulose versus fibrin sealant. The remaining comparisons had only one trial. The blood transfusion quantity (red blood cells) was lower in the fibrin sealant group than in the control (MD −0.53 units, 95% CrI −1.00 to −0.07; 122 participants; 2 studies). The blood transfusion quantity (red blood cells) was higher in the fibrin sealant group than the cyanoacrylate group (MD 2.20 units; 95% CrI 1.59 to 2.81; 30 participants; 1 study; low-quality evidence: downgraded one point for unclear or high risk of bias in the trial and one more point for small sample size). There was no evidence of differences in other comparisons.

Blood transfusion (platelets)

None of the trials reported this outcome.

Blood transfusion (fresh frozen plasma)

Two trials reported blood transfusion quantity (fresh frozen plasma) (Kakaei 2013; Ollinger 2013). They used three treatments in 95 participants. The median blood transfusion quantities (fresh frozen plasma) reported for each treatment are as follows.

- Cyanoacrylate: 0.80 units (one trial only).
- Fibrin sealant: 0.00 and 17.64 units (two trials only).
- Oxidised cellulose: 0.53 and 20.12 units (two trials only).

Based on the DIC, we chose the fixed-effect model when there were two or more trials. The blood transfusion quantity (fresh frozen plasma) was lower in the fibrin sealant group than in the cyanoacrylate group (MD −0.81 units, 95% CrI −1.04 to −0.62;

30 participants; 1 study). The blood transfusion quantity (fresh frozen plasma) was higher with oxidised cellulose than with fibrin sealant (MD 0.53 units, 95% CrI 0.36 to 0.71; 80 participants; 2 studies). There was no evidence of differences in other comparisons.

Blood transfusion (cryoprecipitate)

None of the trials reported this outcome.

Blood loss

Five trials reported blood loss (Kohno 1992; Liu 1993; Figueras 2007; De Boer 2012; Kakaei 2013). They usedsix interventions in 757 participants. The median and range of the mean blood loss reported for each treatment are as follows.

- Control: 0.82 L (range 0.55 to 4.052).
- Collagen: 1.027 L (one trial only).
- Cyanoacrylate: 0.653 L (one trial only).
- Fibrin sealant: 0.9325 L (range 0.675 to 3.047).
- Fibrin sealant plus collagen: 0.884 L (one trial only).
- Oxidised cellulose: 0.573 L (one trial only).

Based on the DIC, we chose the fixed-effect model when there were two or more trials. There was no evidence of differences in blood loss for any of the comparisons. Excluding the trial for which the mean and standard deviation were not available did not alter the conclusions (De Boer 2012).

Major blood loss (proportion)

None of the trials reported this outcome.

Hospital stay

Total hospital stay

Four trials reported hospital stay (Noun 1996; Figueras 2007; Kakaei 2013; Ollinger 2013). They used five interventions in 477 participants. The median and range of the mean hospital stay reported for each treatment are as follows.

- Control: 11.3 d and 12.6 d (two trials only).
- Cyanoacrylate: 8.8 d (one trial only).
- Fibrin sealant: 10.8 d (range 7.5 to 18.5).
- Fibrin sealant plus collagen: 13.3 d (one trial only).
- Oxidised cellulose: 8.1 d, 15.2 d (two trials only).

Based on the DIC, we chose the fixed-effect model when there were two or more trials. There was no evidence of differences in hospital stay for any of the comparisons.

ITU stay

One trial (50 participants) reported ITU stay (Ollinger 2013). The median ITU stay reported for each treatment are as follows.

- Fibrin sealant: 2.2 d (one trial only).
- Oxidised cellulose: 2.8 d (one trial only).

There was no evidence of differences in ITU stay for any of the comparisons.

Operating time

Five trials reported operating time (Kohno 1992; Liu 1993; Noun 1996; Figueras 2007; Ollinger 2013). They used five interventions in 534 participants. The median and range of the mean operating time reported for each treatment are as follows.

- Control: 263 min (range 258 to 343).
- Collagen: 169 min (one trial only).
- Fibrin sealant: 245 min (range 165 to 295).
- Fibrin sealant plus collagen: 282 min (one trial only).
- Oxidised cellulose: 253 min (one trial only).

Based on the DIC, we chose the fixed-effect model when there were two or more trials. The operating time was higher in the group receiving fibrin sealant and collagen than in the control group (MD 19.72 min, 95% CrI 2.93 to 36.57; 300 participants; 1 study). There was no evidence of differences in other comparisons.

Time needed to return to work

None of the trials reported this outcome.

Difference between Bayesian and frequentist meta-analysis

The interpretation of information and conclusions did not alter by using the frequentist meta-analysis.

Overall summary

There was no evidence of differences between different methods of dealing with cut surface in any of the reported outcomes of interest for this review other than the following.

- The serious adverse events (number) was higher in the fibrin sealant group than in the argon beam group (rate ratio 4.81, 95% CrI 1.73 to 17.5; 121 participants; 1 study).
- The blood transfusion quantity (red blood cells) was lower in the fibrin sealant group than in the control (MD −0.53 units, 95% CrI −1.00 to −0.07; 122 participants; 2 studies). The blood transfusion quantity (red blood cells) was higher in fibrin sealant than cyanoacrylate (MD 2.20 units; 95% CrI 1.59 to 2.81; 30 participants; 1 study).
- The blood transfusion quantity (fresh frozen plasma) was lower with fibrin sealant than with cyanoacrylate (MD −0.81 units, 95% CrI −1.04 to −0.62; 30 participants; 1 study). The

blood transfusion quantity (fresh frozen plasma) was higher with oxidised cellulose than with fibrin sealant (MD 0.53 units, 95% CrI 0.36 to 0.71; 80 participants; 2 studies).

- The operating time was higher with fibrin sealant and collagen than with control (MD 19.72 min, 95% CrI 2.93 to 36.57; 300 participants; 1 study).

Methods of vascular occlusion

Eighteen trials compared different methods of vascular occlusion (Belghiti 1996; Clavien 1996; Man 1997; Belghiti 1999; Wu 2002; Capussotti 2003; Man 2003; Chouker 2004; Figueras 2005; Capussotti 2006; Chen 2006; Liang 2009; Dayangac 2010; Pietsch 2010; Lee 2012; Park 2012; Ni 2013; Si-Yuan 2014). We performed network meta-analysis only for serious adverse events (proportion), adverse events (proportion), blood transfusion (proportion), and blood transfusion quantity (red blood cells) since direct comparison and indirect comparison effect estimates (which would enable assessment of inconsistency) were not available for the other outcomes. We present only direct comparison results for other outcomes.

Quality of evidence

The quality of evidence was very low for all the outcomes and comparisons unless specifically indicated within the results. This was because of unclear or high risk of bias in the trials (downgraded by one point), imprecision due to small sample size (downgraded by one point), and wide credible intervals (downgraded by one point) for all outcomes with very low quality of evidence. In addition, we downgraded the evidence for blood transfusion quantity (red blood cells), blood loss, and operating time by two points because of the presence of substantial or considerable heterogeneity in the pair-wise comparison or in the network.

Mortality

Mortality (perioperative)

Fourteen trials reported perioperative mortality (Belghiti 1996; Clavien 1996; Man 1997; Belghiti 1999; Wu 2002; Capussotti 2003; Man 2003; Figueras 2005; Capussotti 2006; Chen 2006; Liang 2009; Lee 2012; Ni 2013; Si-Yuan 2014). They used seven treatments in 1196 participants. The unadjusted proportions of perioperative mortality are as follows.

- Control: 5/203 (2.5%).
- Continuous hepatic vascular exclusion: 0/88 (0.0%).
- Continuous portal triad clamping: 6/290 (2.1%).
- Continuous selective hepatic vascular exclusion: 0/80 (0.0%).
- Continuous selective portal triad clamping: 0/100 (0.0%).
- Intermittent portal triad clamping: 3/364 (0.8%).
- Intermittent selective portal triad clamping: 1/71 (1.4%).

Based on the DIC, we chose the fixed-effect model for all comparisons with two or more trials. There was no evidence of differences in perioperative mortality for any of the comparisons.

Mortality (longest follow-up)

None of the trials reported this outcome.

Adverse events

Serious adverse events (proportion)

Eight trials reported the proportion of participants experiencing serious adverse events (Capussotti 2003; Capussotti 2006; Chen 2006; Liang 2009; Lee 2012; Park 2012; Ni 2013; Si-Yuan 2014). They used six treatments in 815 participants. The unadjusted proportions of participants experiencing serious adverse events are as follows.

- Control: 15/151 (9.9%).
- Continuous hepatic vascular exclusion: 3/60 (5.0%).
- Continuous portal triad clamping: 30/216 (13.9%).
- Continuous selective hepatic vascular exclusion: 0/80 (0.0%).
- Continuous selective portal triad clamping: 13/100 (13.0%).
- Intermittent portal triad clamping: 23/208 (11.1%).

Direct comparison

Based on the DIC, we chose the fixed-effect model for all comparisons with two or more trials. The serious adverse events (proportion) was lower in the group receiving continuous selective portal triad clamping than in the continuous portal triad clamping group (OR 0.42, 95% CrI 0.18 to 0.96; 120 participants; 1 study). There was no evidence of differences in other comparisons.

Network meta-analysis

The network plots are shown in Figure 18. Based on the DIC, we chose the fixed-effect model. There was no evidence of differences in adverse events (proportion) for any of the comparisons. Figure 19 shows the probability of each treatment being best, second best, third best, and so on. Figure 20 shows the cumulative probability of a treatment being best.

Figure 18. The network plot showing the comparisons in the trials included in the comparison of methods for vascular occlusion in which network meta-analysis was performed. The size of the node (circle) provides a measure of the number of trials in which the particular treatment was included as one of the arms. The thickness of the line provides a measure of the number of direct comparisons between two nodes (treatments).Con: continuous; Int: intermittent; HVE: hepatic vascular exclusion; PTC: portal triad clamping; RBC: red blood cells.

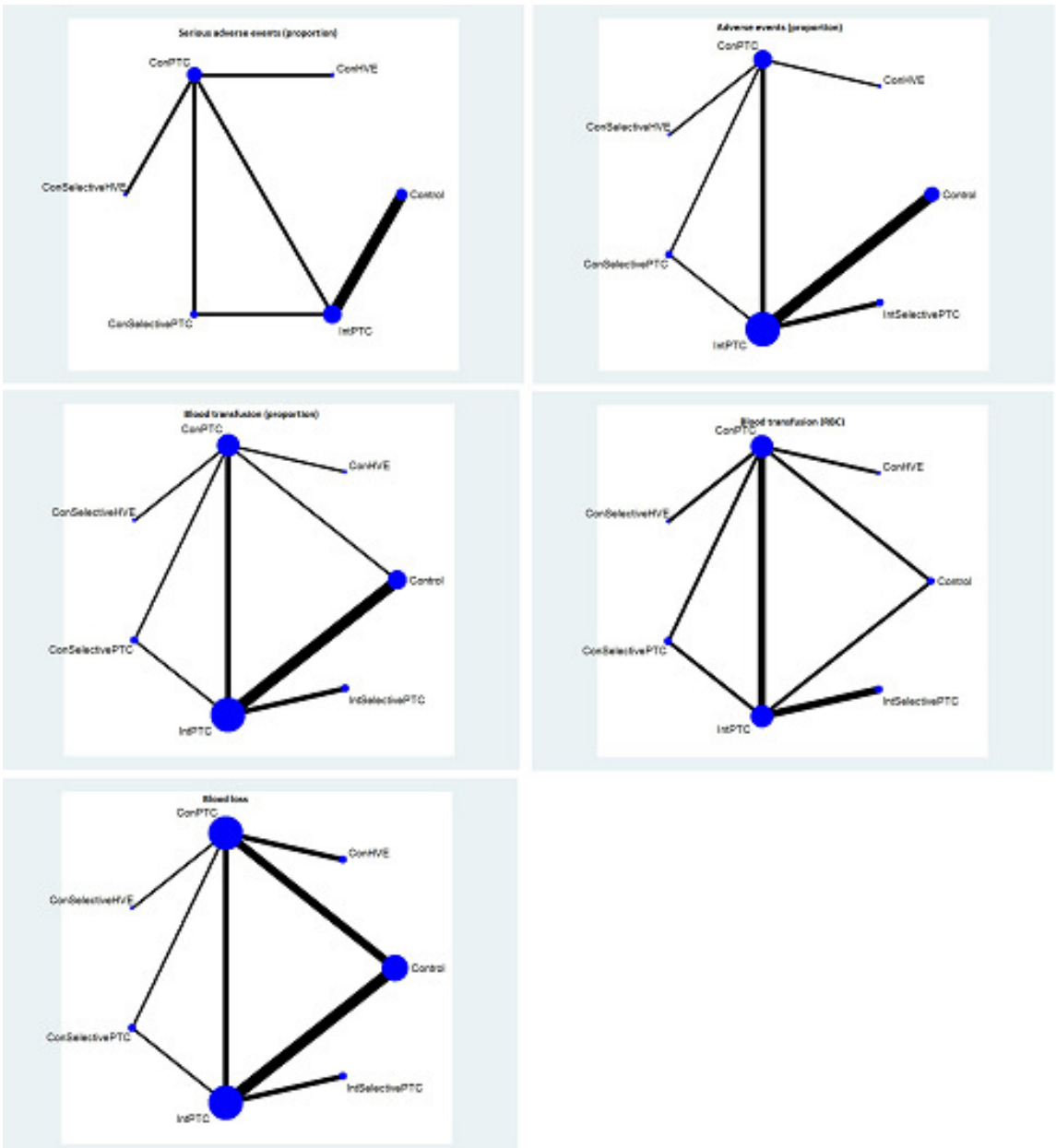


Figure 19. Probability of best treatment: probability of being best, second best, third best, etc. for each treatment for serious adverse events (proportion) (vascular occlusion methods). A probability of more than 90% is a reliable indicator that a treatment is best with regards to the specific outcome. A probability of less than 90% is less reliable. None of the treatments have a 90% probability of being best treatment.Con: continuous; Int: intermittent; HVE: hepatic vascular exclusion; PTC: portal triad clamping.

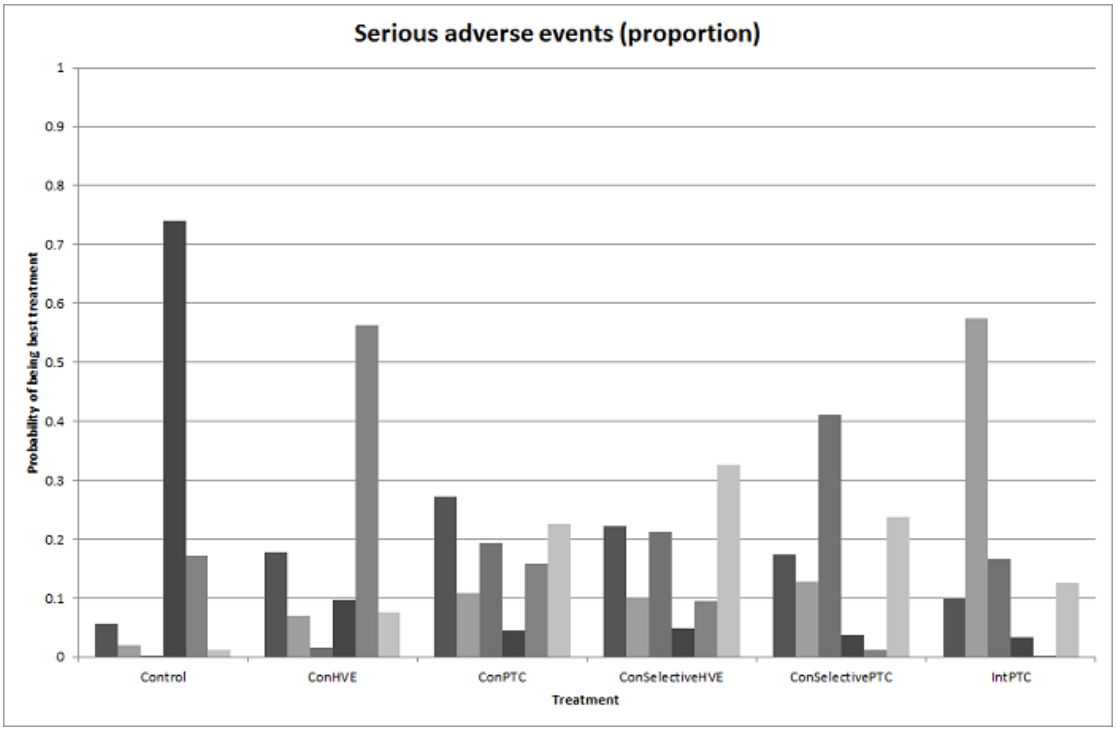
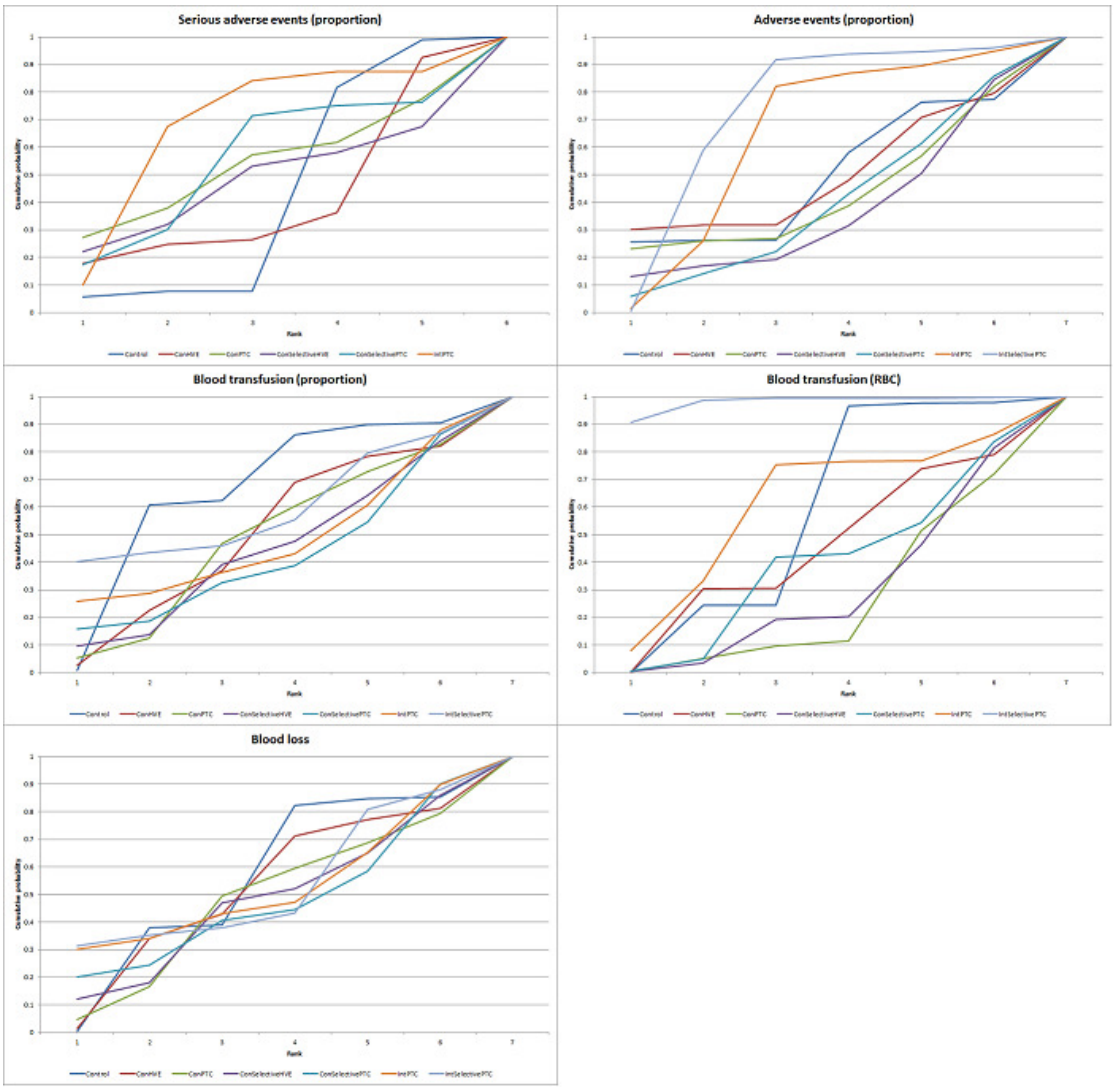


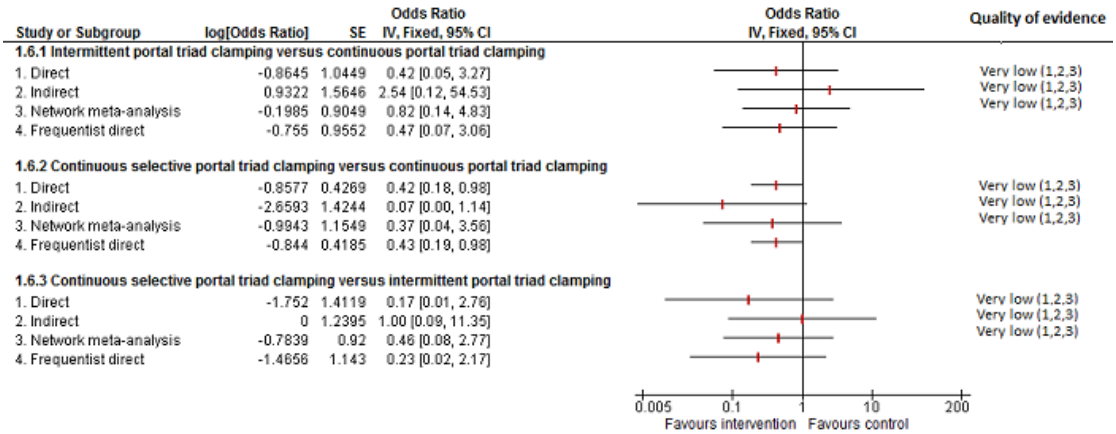
Figure 20. Cumulative probability of being best treatment: cumulative probability of being best for each treatment for vascular occlusion methods. Rank 1 indicates the probability that a treatment is best, rank 2 indicates the probability that a treatment is in the two best treatments, rank 3 indicates the probability that a treatment is in the three best treatments, and so on.Con: continuous; Int: intermittent; HVE:hepatic vascular exclusion; PTC: portal triad clamping.



Direct evidence compared to network meta-analysis

Figure 21 shows the information on direct evidence compared to network meta-analysis. Although there is overlap of credible intervals, the mean indirect estimate seems to be quite different from the direct estimate (sometimes suggesting an opposite effect), thus suggesting that there may be discrepancies between direct and indirect estimates. There was little apparent difference in the quality of evidence between direct, indirect estimates, and network meta-analysis; so, we could not choose one estimate over the others based on the quality of evidence.

Figure 21. Methods of vascular occlusion: serious adverse events (proportion) Forest plot of the comparisons in which direct and indirect estimates were available. Although there is overlap of confidence intervals, the mean indirect estimate seems to be quite different from the direct estimate (sometimes, suggesting an opposite effect), thus suggesting that there may be discrepancies between direct and indirect estimates.There was little apparent difference in the quality of evidence between direct, indirect estimates, and network meta-analysis; so, we could not choose one estimate over the others based on the quality of evidence.1Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).2Sample size was low (downgraded by 1 point).3Confidence intervals spanned no effect and clinically significant effect (downgraded by 1 point).



Serious adverse events (number)

Five trials reported the number of serious adverse events (Belghiti 1996; Man 1997; Belghiti 1999; Wu 2002; Figueras 2005). They used five treatments in 376 participants. The unadjusted rates of serious adverse events (number) are as follows.

- Control: 4/50 (8.0 per 100 participants).
- Continuous hepatic vascular exclusion: 5/28 (17.9 per 100 participants).
- Continuous portal triad clamping: 9/66 (13.6 per 100 participants).
- Intermittent portal triad clamping: 16/161 (9.9 per 100 participants).
- Intermittent selective portal triad clamping: 12/71 (16.9 per 100 participants).

Based on the DIC, we chose the fixed-effect model for all comparisons with two or more trials. The number of serious adverse events

was lower in the intermittent portal triad clamping group than in the continuous portal triad clamping group (rate ratio 0.09, 95% CrI 0.00 to 0.56; 86 participants; 1 study; low-quality evidence: downgraded one point for unclear or high risk of bias in trial and one more point for small sample size). There was no evidence of differences in other comparisons.

Adverse events (proportion)

Twelve trials reported the proportion of participants experiencing adverse events (Man 1997; Belghiti 1999; Wu 2002; Capussotti 2003; Man 2003; Figueras 2005; Capussotti 2006; Chen 2006; Liang 2009; Lee 2012; Ni 2013; Si-Yuan 2014). They used seven treatments in 1129 participants. The unadjusted proportions of adverse events (proportion) are as follows.

- Control: 55/196 (28.1%).
- Continuous hepatic vascular exclusion: 19/60 (31.7%).
- Continuous portal triad clamping: 75/258 (29.1%).
- Continuous selective hepatic vascular exclusion: 9/80 (11.3%).
- Continuous selective portal triad clamping: 22/100 (22.0%).
- Intermittent portal triad clamping: 109/364 (29.9%).
- Intermittent selective portal triad clamping: 22/71 (31.0%).

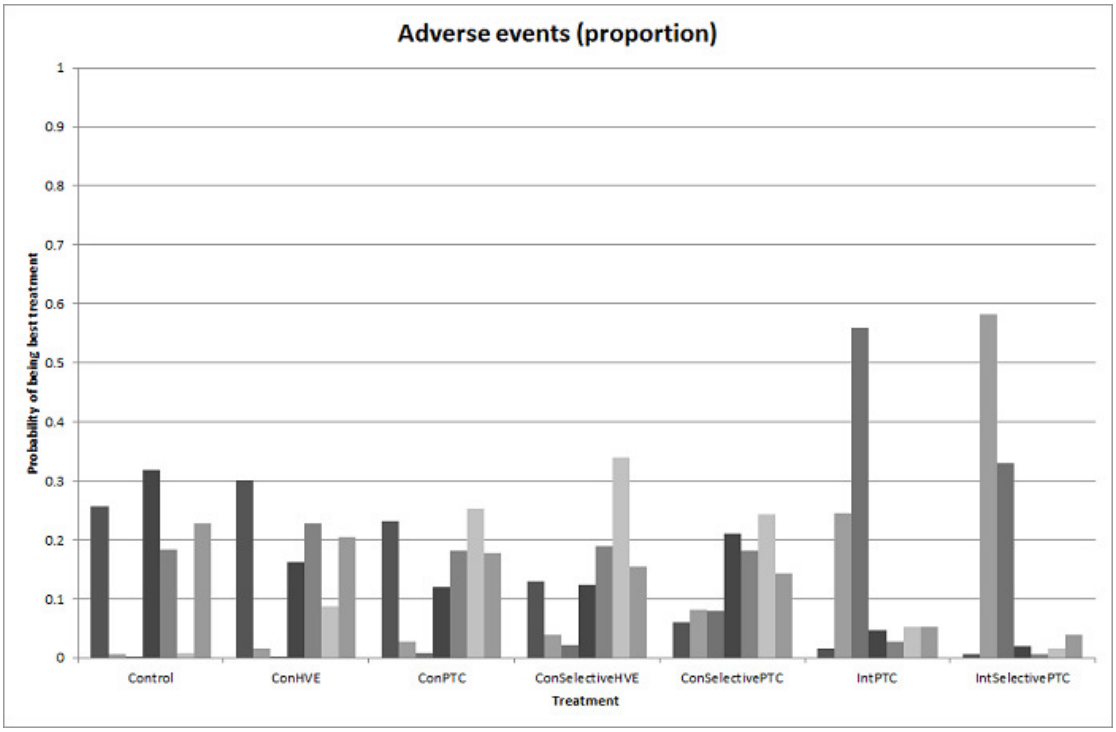
Direct comparison

Based on the DIC, we chose the fixed-effect model for comparisons with two or more studies. The proportion of participants experiencing adverse events was lower in the continuous selective portal triad clamping group than in the continuous portal triad clamping group (OR 0.41, 95% CrI 0.18 to 0.90; 120 participants; 1 study). There was no evidence of differences in other comparisons.

Network meta-analysis

Figure 18 shows the network plots. Based on the DIC, we chose the fixed-effect model. There was no evidence of differences in the proportion of participants experiencing adverse events for any of the comparisons. Figure 22 shows the probability of each treatment being best, second best, third best, and so on. Figure 20 shows the cumulative probability of a treatment being best.

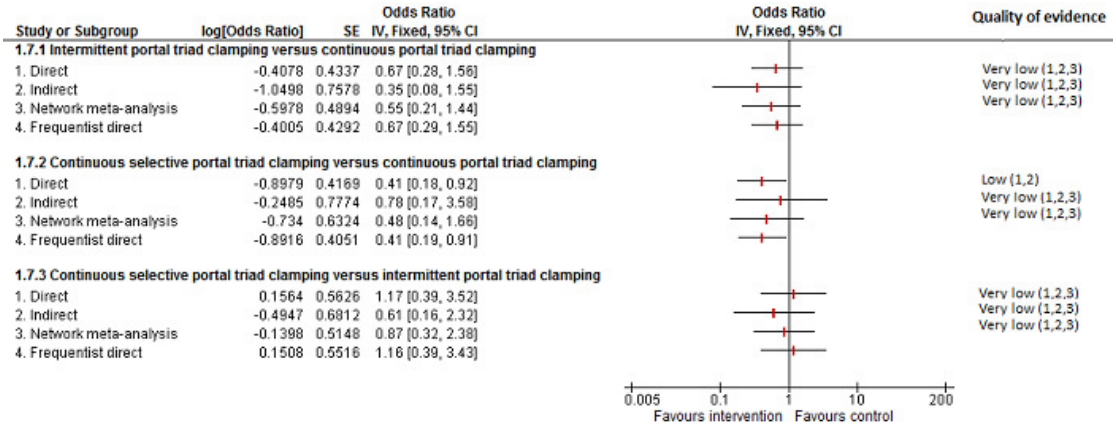
Figure 22. Probability of best treatment: probability of being best, second best, third best, etc. for each treatment for adverse events (proportion) (vascular occlusion methods). A probability of more than 90% is a reliable indicator that a treatment is best with regards to the specific outcome. A probability of less than 90% is less reliable. None of the treatments have a 90% probability of being best treatment.Con: continuous; Int: intermittent; HVE: hepatic vascular exclusion; PTC: portal triad clamping.



Direct evidence compared to network meta-analysis

Figure 23 shows the information on direct evidence compared to network meta-analysis. There do not appear to be any discrepancies between direct and indirect estimates. Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.

Figure 23. Methods of vascular occlusion: adverse events (proportion) Forest plot of the comparisons in which direct and indirect estimates were available. There does not appear to be any discrepancies between direct and indirect estimates. Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.1Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).2Sample size was low (downgraded by 1 point).3Confidence intervals spanned no effect and clinically significant effect (downgraded by 1 point).



Adverse events (number)

Six trials reported the number of adverse events (Belghiti 1996; Man 1997; Belghiti 1999; Wu 2002; Figueras 2005; Lee 2012). They used five in 502 participants. The unadjusted rates of adverse events (number) are as follows.

- Control: 47/113 (41.6 per 100 participants).
- Continuous hepatic vascular exclusion: 19/28 (67.9 per 100 participants).
- Continuous portal triad clamping: 28/66 (42.4 per 100 participants).
- Intermittent portal triad clamping: 97/224 (43.3 per 100 participants).
- Intermittent selective portal triad clamping: 36/71 (50.7 per 100 participants).

Based on the DIC, we chose the fixed-effect model for comparisons with two or more studies. There was no evidence of differences in adverse events (number) for any of the comparisons.

Health-related quality of life

None of the trials reported this outcome at any time point.

Blood transfusion requirements

Blood transfusion (proportion)

Thirteen trials reported the proportion of participants requiring a blood transfusion (Man 1997; Belghiti 1999; Wu 2002; Capussotti 2003; Man 2003; Chouker 2004; Figueras 2005; Capussotti 2006; Chen 2006; Liang 2009; Lee 2012; Ni 2013; Si-Yuan 2014). They used seven treatments in 1163 participants. The unadjusted proportions of participants requiring a blood transfusion are as follows.

- Control: 64/211 (30.3%).
- Continuous hepatic vascular exclusion: 8/60 (13.3%).
- Continuous portal triad clamping: 71/277 (25.6%).
- Continuous selective hepatic vascular exclusion: 13/80 (16.3%).
- Continuous selective portal triad clamping: 21/100 (21.0%).
- Intermittent portal triad clamping: 101/364 (27.7%).
- Intermittent selective portal triad clamping: 11/71 (15.5%).

Direct comparison

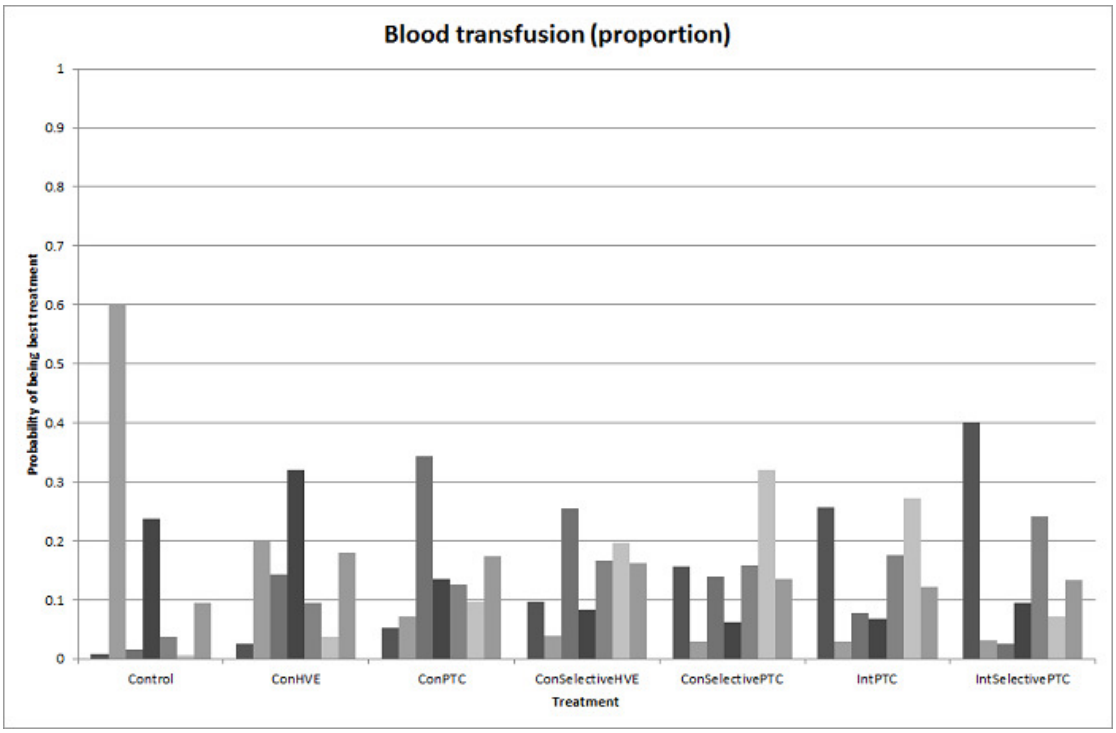
Based on the DIC, we used the random-effects model for comparisons with two or more studies for intermittent portal triad clamping versus continuous portal triad clamping and the fixed-effect model for the remaining comparisons with two or more studies. The proportion of participants requiring a blood transfusion was lower in the continuous portal triad clamping group than in the control (OR 0.06, 95% CrI 0.00 to 0.49; 34 participants; 1 study; low-quality evidence: downgraded one point for unclear or high

risk of bias in trial and one more point for small sample size). The blood transfusion (proportion) was higher in continuous portal triad clamping than continuous hepatic vascular exclusion (OR 5.90, 95% CrI 2.45 to 15.58; 118 participants; 1 study; low-quality evidence: downgraded one point for unclear or high risk of bias in trial and one more point for small sample size). There was no evidence of differences in other comparisons.

Network meta-analysis

Figure 18 shows the network plots. Based on the DIC, we chose the random-effects model. There was no evidence of differences in the proportion of participants requiring a blood transfusion for any of the comparisons. Figure 24 shows the probability of each treatment being best, second best, third best, and so on. Figure 20 shows the cumulative probability of a treatment being the best.

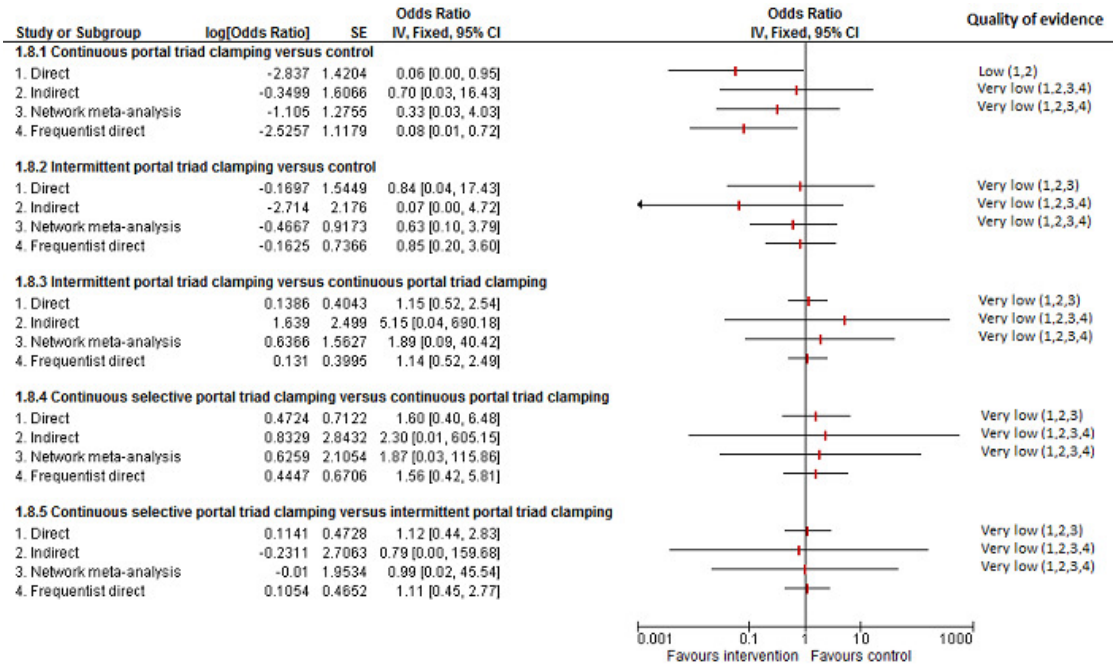
Figure 24. Probability of best treatment: probability of being best, second best, third best, etc. for each treatment for blood transfusion (proportion) (vascular occlusion methods). A probability of more than 90% is a reliable indicator that a treatment is best with regards to the specific outcome. A probability of less than 90% is less reliable. None of the treatments have a 90% probability of being best treatment.Con: continuous; Int: intermittent; HVE: hepatic vascular exclusion; PTC: portal triad clamping.



Direct evidence compared to network meta-analysis

Figure 25 shows the information on direct evidence compared to network meta-analysis. Although the credible intervals overlap, there appears to be some discrepancies between direct and indirect estimates for continuous portal triad clamping versus control, intermittent portal triad clamping versus control, and intermittent portal triad clamping versus continuous portal triad clamping. Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.

Figure 25. Methods of vascular occlusion: blood transfusion (proportion) Forest plot of the comparisons in which direct and indirect estimates were available. Although the confidence intervals overlap, there appear to be some discrepancies between direct and indirect estimates for continuous portal triad clamping versus control, intermittent portal triad clamping versus control, and intermittent portal triad clamping versus continuous portal triad clamping. Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.1Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).2Sample size was low (downgraded by 1 point).3Confidence intervals spanned no effect and clinically significant effect (downgraded by 1 point).4There was substantial or considerable heterogeneity (downgraded by 2 points).



Blood transfusion (red blood cells)

Ten trials reported blood transfusion quantity (red blood cells) (Belghiti 1996; Clavien 1996; Man 1997; Belghiti 1999; Wu 2002; Capussotti 2003; Figueras 2005; Liang 2009; Ni 2013; Si-Yuan 2014). They usedseven treatments in 786 participants. The median and range of the mean blood transfusion quantity (red blood cells) reported for each treatment are as follows.

- Control: 1.50 units and 1.90 units (two trials only).
- Continuous hepatic vascular exclusion: 2.50 units (one trial only).
- Continuous portal triad clamping: 1.80 units (range 0.50 to 30).
- Continuous selective hepatic vascular exclusion: 1.00 unit (one trial only).
- Continuous selective portal triad clamping: 1.20 units and 1.37 units (two trials only).
- Intermittent portal triad clamping: 0.99125 units (range 0.00 to 2.54).
- Intermittent selective portal triad clamping: 0.34 units, 2.24 units (two trials only).

Direct comparison

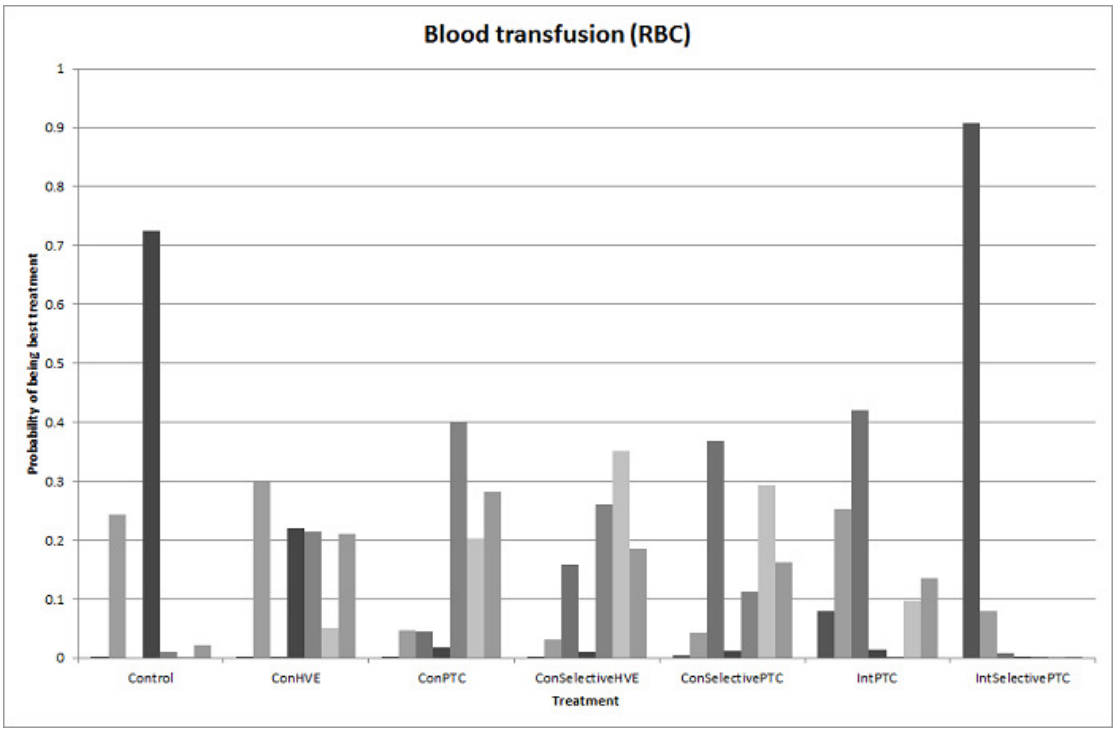
Based on the DIC, we chose the fixed-effect model for comparisons with two or more studies. The blood transfusion quantity (red blood cells) was lower in the group receiving intermittent portal triad clamping than in the control (−1.50, 95% CrI −2.75 to −0.26; 100 participants; 1 study). The blood transfusion quantity (red blood cells) was lower in the group receiving continuous selective hepatic vascular exclusion than in the continuous portal triad clamping group (MD −1.20 units, 95% CrI −2.37 to −0.04; 160 participants; 1 study). The blood transfusion quantity (red blood cells) was lower in the continuous selective portal triad clamping group than in the continuous portal triad clamp-

ing group (MD −0.20 units, 95% CrI −0.31 to −0.09; 120 participants; 1 study). There was no evidence of differences in other comparisons. Exclusion of four trials in which we calculated the mean, standard deviation, or both did not change the conclusions (Man 1997; Belghiti 1999; Wu 2002; Si-Yuan 2014).

Network meta-analysis

Figure 18 shows the network plots. Based on the DIC, we chose the fixed-effect model. Compared with the control group, there was evidence for a lower blood transfusion quantity (red blood cells) with continuous portal triad clamping (MD −1.25 units, 95% CrI −2.39 to −0.10), continuous selective hepatic vascular exclusion (MD −2.45 units, 95% CrI −4.08 to −0.82), continuous selective portal triad clamping (MD −1.45 units, 95% CrI −2.59 to −0.31), intermittent portal triad clamping (MD −1.36 units, 95% CrI −2.48 to −0.23), and intermittent selective portal triad clamping (MD −1.43 units, 95% CrI −2.61 to −0.24). There was no evidence of differences in other comparisons. On excluding the trials in which either mean or standard deviation was not available, there was no evidence of differences in any of the comparisons. Figure 26 shows the probability of each treatment being best, second best, third best, and so on. Figure 20 shows the cumulative probability of a treatment being best.

Figure 26. Probability of best treatment: probability of being best, second best, third best, etc. for each treatment for blood transfusion (red blood cells) (vascular occlusion methods). A probability of more than 90% is a reliable indicator that a treatment is best with regards to the specific outcome. A probability of less than 90% is less reliable. Intermittent selective portal triad clamping has about 90% probability of being best treatment. However, other random and systematic errors make this finding unreliable.Con: continuous; Int: intermittent; HVE: hepatic vascular exclusion; PTC: portal triad clamping.

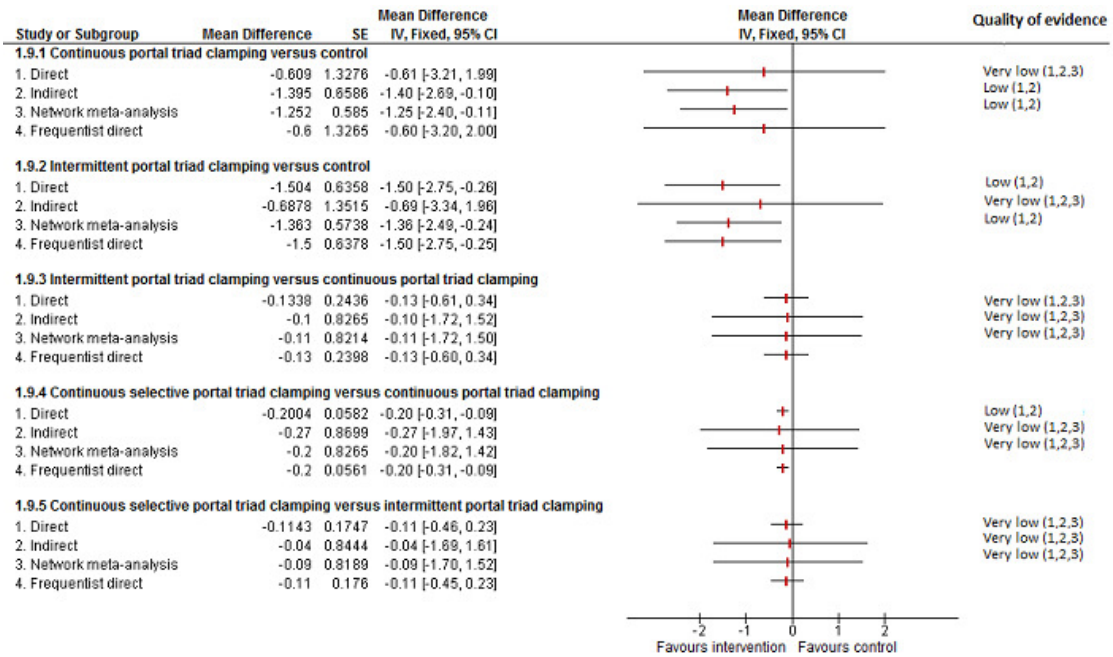


Direct evidence compared to network meta-analysis

Figure 27 shows the information on direct evidence compared to network meta-analysis. There do not appear to be any discrepancies between direct and indirect estimates, although the credible intervals are different (the direct evidence had narrower credible

intervals in four of the five comparisons above) resulting in the differences in the comparisons in which there was evidence for difference. Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence for the comparison 'continuous selective portal triad clamping versus continuous portal triad clamping'. Indirect evidence and network meta-analysis appear to be preferable over direct evidence for the comparison 'continuous portal triad clamping versus control'. Direct evidence and network meta-analysis appear to be preferable over indirect evidence for the comparison 'intermittent portal triad clamping versus control'. There was little apparent difference in the quality of evidence between direct, indirect estimates, and network meta-analysis; so, we could not choose one estimate over the others based on the quality of evidence.

Figure 27. Methods of vascular occlusion:blood transfusion (red blood cells) Forest plot of the comparisons in which direct and indirect estimates were available. There do not appear to be any discrepancies between direct and indirect estimates, although the credible intervals are different (the direct evidence had narrower credible intervals in four of the five comparisons above) resulting in the differences in the comparisons in which there was evidence for difference. Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence for the comparison 'continuous selective portal triad clamping versus continuous portal triad clamping'. Indirect evidence and network meta-analysis appear to be preferable over direct evidence for the comparison 'continuous portal triad clamping versus control'. Direct evidence and network meta-analysis appear to be preferable over indirect evidence for the comparison 'intermittent portal triad clamping versus control'. There was little apparent difference in the quality of evidence between direct, indirect estimates, and network meta-analysis; so, we could not choose one estimate over the others based on the quality of evidence.1Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).2Sample size was low (downgraded by 1 point).3Confidence intervals spanned no effect and clinically significant effect (downgraded by 1 point).



Blood transfusion (platelets)

None of the trials reported this outcome.

Blood transfusion (fresh frozen plasma)

None of the trials reported this outcome.

Blood transfusion (cryoprecipitate)

None of the trials reported this outcome.

Blood loss

Sixteen trials reported blood loss (Belghiti 1996; Man 1997; Belghiti 1999; Wu 2002; Capussotti 2003; Chouker 2004; Figueras 2005; Capussotti 2006; Chen 2006; Liang 2009; Dayangac 2010; Pietsch 2010; Lee 2012; Park 2012; Ni 2013; Si-Yuan 2014). They used seven interventions in 1322 participants. The median and range of the mean blood loss reported for each treatment are as follows.

- Control: 0.489 L (range 0.204 to 2.17).
- Continuous hepatic vascular exclusion: 0.42 L and 1.195 L (two trials only).
- Continuous portal triad clamping: 0.77 L (range 0.2 to 1.38).
- Continuous selective hepatic vascular exclusion: 0.529 L (one trial only).
- Continuous selective portal triad clamping: 0.3 L and 0.649 L (two trials only).
- Intermittent portal triad clamping: 0.671 L (range 0.184 to 1.685).
- Intermittent selective portal triad clamping: 0.735 L and 1.159 L (two trials only)..

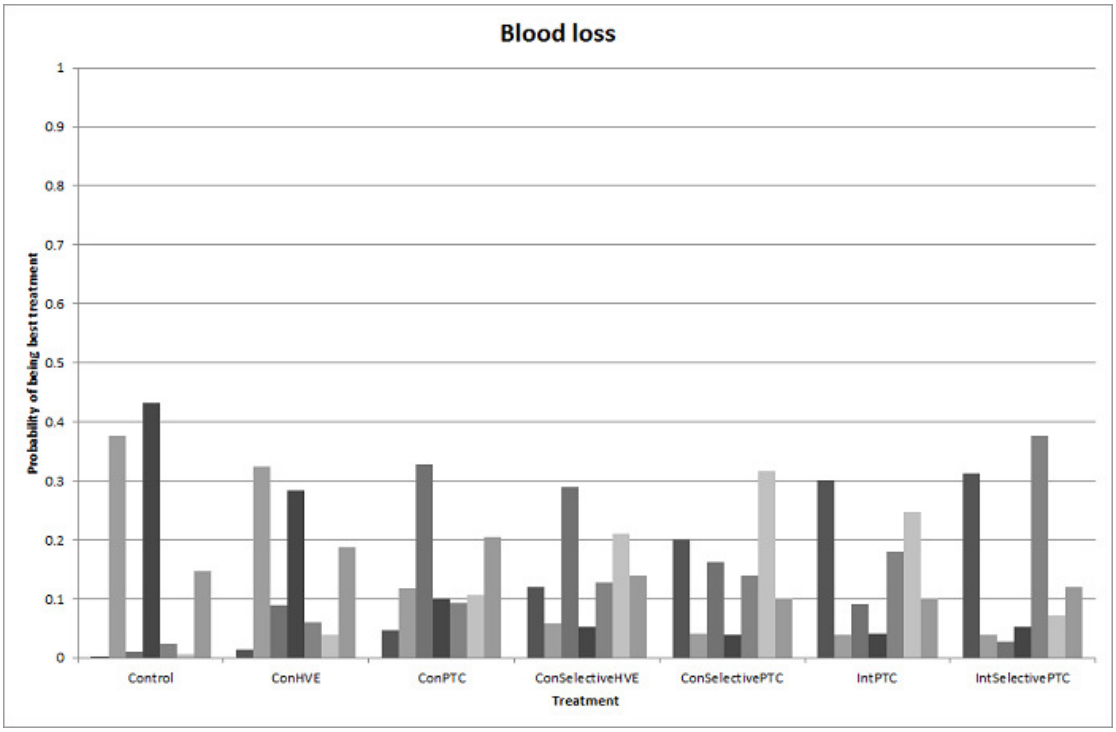
Direct comparison

Based on the DIC, we chose the fixed-effect model for intermittent portal triad clamping versus continuous portal triad clamping and the random-effects model for the remaining comparisons with two or more studies. There was no evidence of differences in blood loss for any of the comparisons. Either the mean, the standard deviation, or both were not available in six trials (Man 1997; Wu 2002; Capussotti 2006; Pietsch 2010; Ni 2013; Si-Yuan 2014). Excluding these trials did not alter the conclusions.

Network meta-analysis

Figure 18 shows the network plots. Based on the DIC, we chose the random-effects model. There was no evidence of differences in blood loss for any of the comparisons. Excluding the six trials in which either the mean, the standard deviation, or both were not available did not alter the results (Man 1997; Wu 2002; Capussotti 2006; Pietsch 2010; Ni 2013; Si-Yuan 2014). Figure 28 shows the probability of each treatment being best, second best, third best, and so on. Figure 20 shows the cumulative probability of a treatment being best.

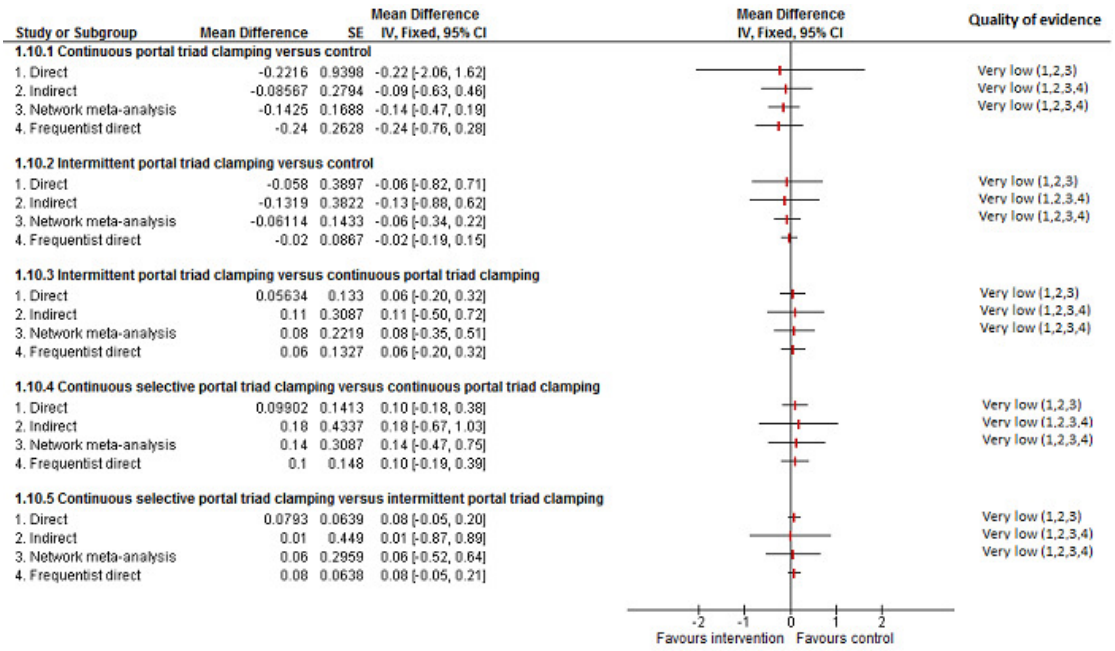
Figure 28. Probability of best treatment: probability of being best, second best, third best, etc. for each treatment for blood loss (vascular occlusion methods). A probability of more than 90% is a reliable indicator that a treatment is best with regards to the specific outcome. A probability of less than 90% is less reliable. None of the treatments have a 90% probability of being best treatment.Con: continuous; Int: intermittent; HVE: hepatic vascular exclusion; PTC: portal triad clamping.



Direct evidence compared to network meta-analysis

Figure 29 shows the information on direct evidence compared to network meta-analysis. There do not appear to be any discrepancies between direct and indirect estimates, although the credible intervals are different (the direct evidence had narrower credible intervals in three of the five comparisons above). Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.

Figure 29. Methods of vascular occlusion:blood loss Forest plot of the comparisons in which direct and indirect estimates were available. There does not appear to be any discrepancies between direct and indirect estimates, although the credible intervals are different (the direct evidence had narrower credible intervals in three of the five comparisons above). Direct evidence appears to be preferable over indirect evidence and network meta-analysis based on the quality of evidence.1Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).2 Sample size was low (downgraded by 1 point).3Confidence intervals spanned no effect and clinically significant effect (downgraded by 1 point).Ç4There was substantial or considerable heterogeneity (downgraded by 2 points).



Major blood loss (proportion)

Three trials reported the proportion of participants experiencing major blood loss (Lee 2012; Ni 2013; Si-Yuan 2014), defined as more than one litre in Lee 2012 and Ni 2013 and as more than two litres in Si-Yuan 2014. The trials used five interventions in 406 participants. The unadjusted proportions of participants experiencing major blood loss are as follows.

- Control: 4/63 (6.3%).
- Continuous portal triad clamping: 8/140 (5.7%).
- Continuous selective hepatic vascular exclusion: 2/80 (2.5%).
- Continuous selective portal triad clamping: 0/60 (0.0%).
- Intermittent portal triad clamping: 5/63 (7.9%).

There was only one trial for each comparison. There was no evidence of differences in major blood loss (proportion) for any of the comparisons.

Hospital stay

Total hospital stay

Ten trials reported total hospital stay (Belghiti 1996; Man 1997; Belghiti 1999; Wu 2002; Figueras 2005; Capussotti 2006; Liang 2009; Lee 2012; Park 2012; Si-Yuan 2014). They used seven treatments in 918 participants. The medians and ranges of the mean hospital stay reported for each treatment are as follows.

- Control: 9 d (range 7 to 19).
- Continuous hepatic vascular exclusion: 22 d (one trial only).
- Continuous portal triad clamping: 14 d (range 13 to 14).
- Continuous selective hepatic vascular exclusion: 10 d (one trial only).
- Continuous selective portal triad clamping: 10 d (one trial only).
- Intermittent portal triad clamping: 10 d (range 8 to 16).
- Intermittent selective portal triad clamping: 8 d and 16 d (two trials only)..

Based on the DIC, we chose the fixed-effect model for compar-

isons with two or more studies. The total hospital stay was lower in the continuous portal triad clamping group than in the continuous hepatic vascular exclusion group (MD −8.00 d, 95% CrI −13.03 to −2.95; 52 participants; 1 study; low-quality evidence: downgraded one point for unclear or high risk of bias in trial and one more point for small sample size). The total hospital stay was lower in the continuous selective hepatic vascular exclusion group than in the continuous portal triad clamping group (MD −2.80 d, 95% CrI −4.13 to −1.47; 160 participants; 1 study; low-quality evidence: downgraded 1 point for unclear or high risk of bias in trial and one more point for small sample size). There was no evidence of differences in other comparisons. Either the mean, the standard deviation, or both were not available in four trials (Man 1997; Wu 2002; Capussotti 2006; Lee 2012). Excluding these trials did not alter the conclusions except for intermittent portal triad clamping versus control. We excluded three of the four trials under this comparison because of the lack of availability of either the mean, the standard deviation, or both (Man 1997; Capussotti 2006; Lee 2012). Excluding these trials, the hospital stay was shorter in the intermittent portal triad clamping group than in the control (MD −3.51 d, 95% CrI −6.85 to −0.16; 50 participants; 1 study).

ITU stay

One trial reported ITU stay (Si-Yuan 2014); the mean ITU stays reported for each treatment are as follows.

- Continuous portal triad clamping: 1.5 d.
- Continuous selective hepatic vascular exclusion: 1.2 d.

The ITU stay was lower in the continuous selective hepatic vascular exclusion group than in the continuous portal triad clamping group (MD −0.30 d, 95% CrI −0.55 to −0.06; 160 participants; 1 study).

Operating time

Twelve trials reported operating time (Belghiti 1996; Clavien 1996; Wu 2002; Capussotti 2003; Figueras 2005; Chen 2006; Liang 2009; Pietsch 2010; Lee 2012; Park 2012; Ni 2013; Si-Yuan 2014). They used seven treatments in 919 participants. The medians and ranges of the mean operating times reported for each treatment are as follows.

- Control: 292 min (range 239 to 339).
- Continuous hepatic vascular exclusion: 133 min and 366 min (two trials only).
- Continuous portal triad clamping: 200 min (range 116 to 301).
- Continuous selective hepatic vascular exclusion: 131 min (one trial only).
- Continuous selective portal triad clamping: 136 min and 236 min (two trials only).
- Intermittent portal triad clamping: 241 min (range 204 to 409).
- Intermittent selective portal triad clamping: 219 min and 399 min (two trials only).

Based on the DIC, we chose the fixed-effect model for continuous portal triad clamping versus control and intermittent selective portal triad clamping versus intermittent portal triad clamping, and we used the random-effects model for the remaining comparisons with two or more studies. The operating time was lower in the intermittent portal triad clamping group than in the continuous selective portal triad clamping group (MD −30.53 min, 95% CrI −49.68 to −11.29; 80 participants; 1 study). There was no evidence of differences in other comparisons. Either the mean, the standard deviation, or both were not available in four trials (Wu 2002; Pietsch 2010; Lee 2012; Si-Yuan 2014). Excluding these trials did not alter the conclusions except for intermittent portal triad clamping versus control. We excluded Lee 2012 from this two-trial comparison because no mean or standard deviation were available (Lee 2012; Park 2012). Excluding this trial, the operating time was longer in the intermittent portal triad clamping group than in the control (MD 49.63 min, 95% CrI 26.72 to 72.55; 50 participants; 1 study; low-quality evidence: downgraded one point for unclear or high risk of bias in trial and one more point for small sample size).

Time needed to return to work

None of the trials reported this outcome.

Difference between Bayesian and frequentist meta-analysis

The interpretation of information and conclusions did not alter by using the frequentist meta-analysis.

Overall summary

There was no evidence of differences between the tested methods of vascular occlusion in any of the reported outcomes of interest for this review other than the following — and they all ought to be considered of low or very low quality .

- The proportion of participants experiencing serious adverse events was lower in the continuous selective portal triad clamping group than in the continuous portal triad clamping group (OR 0.42, 95% CrI 0.18 to 0.96; 120 participants; 1 study).
- The number of serious adverse events was lower in the intermittent portal triad clamping group than in the continuous portal triad clamping group (rate ratio 0.09, 95% CrI 0.00 to 0.56; 86 participants; 1 study).
- The proportion of participants experiencing adverse events was lower in the continuous selective portal triad clamping group than in the continuous portal triad clamping group (OR 0.41, 95% CrI 0.18 to 0.90; 120 participants; 1 study).

- The proportion of participants requiring a blood transfusion was lower in the continuous portal triad clamping group than in the control (OR 0.06, 95% CrI 0.00 to 0.49; 34 participants; 1 study). The proportion of participants requiring a blood transfusion was higher in the continuous portal triad clamping group than in the continuous hepatic vascular exclusion group (OR 5.90, 95% CrI 2.45 to 15.58; 118 participants; 1 study).
- The blood transfusion quantity (red blood cells) was lower with continuous portal triad clamping than in the control (MD −1.25 units, 95% CrI −2.39 to −0.10; network meta-analysis: 786 participants; 10 studies). The blood transfusion quantity (red blood cells) was lower in the intermittent portal triad clamping group than in the control (−1.50, 95% CrI −2.75 to −0.26; 100 participants; 1 study). The blood transfusion quantity (red blood cells) was lower in the continuous selective hepatic vascular exclusion group than in the continuous portal triad clamping group(MD −1.20 units, 95% CrI −2.37 to −0.04; 160 participants; 1 study). The blood transfusion quantity (red blood cells) was lower in the continuous selective portal triad clamping group than in the continuous portal triad clamping group (MD −0.20, 95% CrI −0.31 to −0.09; 120 participants; 1 study).
- The hospital stay was lower in the continuous portal triad clamping group than in the continuous hepatic vascular exclusion group (MD −8.00 d, 95% CrI −13.03 to −2.95; 52 participants; 1 study). The hospital stay was lower in the continuous selective hepatic vascular exclusion group than in the continuous portal triad clamping group (MD −2.80 d, 95% CrI −4.13 to −1.47; 160 participants; 1 study).
- The ITU stay was lower in the continuous selective hepatic vascular exclusion group than in the continuous portal triad clamping group (MD −0.30 d, 95% CrI −0.55 to −0.06; 160 participants; 1 study).
- The operating time was lower in the intermittent portal triad clamping group than in the continuous selective portal triad clamping group (MD −30.53 min, 95% CrI −49.68 to −11.29; 80 participants; 1 study).

Pharmacological interventions

Six trials compared different pharmacological interventions (Shimada 1994; Lentschener 1997; Wong 2003; Lodge 2005; Shao 2006; Wu 2006). We did not perform network meta-analysis since direct comparison and indirect comparison effect estimates (which would enable assessment of inconsistency) were not available for any of the outcomes.

Quality of evidence

The quality of evidence was very low for all the outcomes and comparisons unless specifically indicated within the results. This was because of unclear or high risk of bias in the trials (downgraded by one point), imprecision due to small sample size (downgraded by one point), and wide credible intervals (downgraded by one point) for all outcomes with very low quality of evidence. In addition, we downgraded the quality for blood transfusion (as a proportion of participants requiring one) by two points because of the presence of substantial or considerable heterogeneity in the pair-wise comparison or in the network.

Mortality

Mortality (perioperative)

Two trials reported perioperative mortality (Lodge 2005; Wu 2006). They used three treatments in 399 participants. The unadjusted proportions of perioperative mortality are as follows.

- Control: 3/165 (1.8%).
- Recombinant factor VIIa: 4/126 (3.2%).
- Tranexamic acid: 0/108 (0.0%).

There was no evidence of differences in perioperative mortality for any of the comparisons.

Mortality (longest follow-up)

None of the trials reported this outcome.

Adverse events

Serious adverse events (proportion)

Three trials reported the proportion of participants experiencing serious adverse events (Shimada 1994; Lodge 2005; Shao 2006). They used three treatments in 456 participants. The unadjusted proportions of participants experiencing serious adverse events are as follows.

- Control: 59/160 (36.9%).
- Anti-thrombin III: 4/13 (30.8%).
- Recombinant factor VIIa: 111/283 (39.2%).

There was no evidence of differences in the proportion of participants experiencing serious adverse events for any of the comparisons.

Serious adverse events (number)

Three trials reported the number of serious adverse events (Lodge 2005; Shao 2006; Wu 2006). They used three treatments in 646 participants. The unadjusted rates of serious adverse events (number) are as follows.

- Control: 20/255 (7.8 per 100 participants).

- Recombinant factor VIIa: 35/283 (12.4 per 100 participants).
- Tranexamic acid: 7/108 (6.5 per 100 participants).

There was no evidence of differences in the number of serious adverse events for any of the comparisons.

Adverse events (proportion)

Three trials reported the proportion of participants experiencing adverse events (Shimada 1994; Shao 2006; Wu 2006). A total of four treatments were used in a total of 470 participants in these studies. The unadjusted proportions of adverse events (proportion) are as follows.

- Control: 98/198 (49.5%)
- Anti-thrombin III: 4/13 (30.8%)
- Recombinant factor VIIa: 142/151 (94.0%)
- Tranexamic acid: 14/108 (13.0%).

There was no evidence of differences in the proportion of participants experiencing adverse events for any of the comparisons.

Adverse events (number)

Three trials reported the number of adverse events (number) (Lodge 2005; Shao 2006; Wu 2006). They used three treatments in 646 participants. The unadjusted rates of adverse events (number) are as follows.

- Control: 467/255 (183.1 per 100 participants).
- Recombinant factor VIIa: 824/283 (291.2 per 100 participants).
- Tranexamic acid: 19/108 (17.6 per 100 participants).

There was no evidence of differences in the number of adverse events reported for any of the comparisons.

Health-related quality of life

None of the trials reported this outcome at any time point.

Blood transfusion requirements

Blood transfusion (proportion)

Five trials reported the proportion of participants requiring a blood transfusion (Lentschener 1997; Wong 2003; Lodge 2005; Shao 2006; Wu 2006). They used five treatments in 787 participants. The unadjusted proportions of participants requiring a blood transfusion (proportion) are as follows.

- Control: 93/320 (29.1%).
- Aprotinin: 8/48 (16.7%).
- Desmopressin: 3/30 (10.0%).
- Recombinant factor VIIa: 104/281 (37.0%).
- Tranexamic acid: 0/108 (0.0%).

The the proportion of participants requiring a blood transfusion was lower in the aprotinin group (OR 0.31, 95% CrI 0.11 to 0.78; 97 participants; 1 study; low-quality evidence: downgraded one point for unclear or high risk of bias in trial and one more point for small sample size) and in the tranexamic acid group than in the control (OR 0.01, 95% CrI 0.00 to 0.13; 214 participants; 1 study; low-quality evidence: downgraded one point for unclear or high risk of bias in trial and one more point for small sample size). There was no evidence of differences in other comparisons.

Blood transfusion (red blood cells)

Four trials reported blood transfusion quantity (red blood cells) (Shimada 1994; Lentschener 1997; Lodge 2005; Shao 2006). They used four interventions in 537 participants. The median and range of the mean blood transfusion quantity (red blood cells) reported for each treatment are as follows.

- Control: 2.07 units (range 0.00 to 4.40).
- Anti-thrombin III: 4.80 units (one trial only).
- Aprotinin: 0.63 units (one trial only).
- Recombinant factor VIIa: 0.40 and 3.00 units (two trials only).

We did not perform meta-analysis since none of the studies provided both the mean and the standard deviation. The blood transfusion quantity (red blood cells) was lower in the aprotinin group than in the control (MD −0.94 units; P = 0.015; 97 participants; 1 study). There was no evidence of differences in other comparisons.

Blood transfusion (platelets)

Two trials reported blood transfusion quantity (platelets) (Lentschener 1997; Shao 2006). They used three treatments in 328 participants. No participants received a platelets transfusion in Lentschener 1997 (aprotinin versus control). The median platelets transfused was 0 in both groups in the other trial (Shao 2006; recombinant factor VIIa versus control).

Blood transfusion (fresh frozen plasma)

Three trials reported blood transfusion quantity (fresh frozen plasma) (Lentschener 1997; Wong 2003; Shao 2006). They used four treatments in 388 participants. The median and range of the mean or median blood transfusion quantity (fresh frozen plasma) reported for each treatment are as follows.

- Control: 0.45 units (range 0.00 to 0.80).
- Aprotinin: 0.04 units (one trial only).
- Desmopressin: 0.20 units (one trial only).
- Recombinant factor VIIa: 0.00 units (one trial only).

We did not perform meta-analysis since either mean or standard deviation was not available in two trials (Lentschener 1997; Shao

2006). There was no evidence of differences in blood transfusion quantity (fresh frozen plasma) for any of the comparisons.

Blood transfusion (cryoprecipitate)

None of the trials reported this outcome.

Blood loss

Six trials reported blood loss (Shimada 1994; Lentschener 1997; Wong 2003; Lodge 2005; Shao 2006; Wu 2006). They used six treatments in 810 participants. The median and range of the mean blood loss reported for each treatment are as follows.

- Control: 1.10 L (range 0.50 to 1.65).
- Anti-thrombin III: 1.86 L (one trial only).
- Aprotinin: 1.22 L (one trial only).
- Desmopressin: 0.83 L (one trial only).
- Recombinant factor VIIa: 0.65 L and 1.23 L (two trials only).
- Tranexamic acid: 0.30 L (one trial only).

We did not perform meta-analysis since we imputed the mean, standard deviation, or both in five trials (Shimada 1994; Wong 2003; Lodge 2005; Shao 2006; Wu 2006). The blood loss was lower in the tranexamic acid group than in the control (difference in median: −0.30 L, P < 0.001; 214 participants; 1 study). There was no evidence of any difference in other comparisons.

Major blood loss (proportion)

None of the trials reported this outcome.

Total hospital stay

Hospital stay

One trial (214 participants) reported hospital stay (Wu 2006). The median hospital stays reported for each treatment are as follows.

- Control: 9 d (one trial only).
- Tranexamic acid: 8 d (one trial only).

There was no evidence of difference in median hospital stay between the groups.

ITU stay

None of the trials reported this outcome.

Operating time

Five trials reported operating time (Shimada 1994; Lentschener 1997; Wong 2003; Lodge 2005; Wu 2006). They used six treatments in 580 participants. The medians and ranges of the mean operating times reported for each treatment are as follows.

- Control: 261 min (range 233 to 435).
- Anti-thrombin III: 233 min (one trial only).
- Aprotinin: 232 min (one trial only).
- Desmopressin: 405 min (one trial only).
- Recombinant factor VIIa: 230 min (one trial only).
- Tranexamic acid: 254min (one trial only).

The mean, standard deviation or both were not available from four studies (Shimada 1994; Wong 2003; Lodge 2005; Wu 2006). The operating time was lower in the tranexamic acid group than in the control group (difference in medians −52.20 min; P = 0.003; 214 participants; 1 study; low-quality evidence: downgraded one point for unclear or high risk of bias in trial and one more point for small sample size). There was no evidence of differences in other comparisons.

Time needed to return to work

None of the trials reported this outcome.

Difference between Bayesian and frequentist meta-analysis

The interpretation of information and conclusions did not alter by using the frequentist meta-analysis.

Overall summary

There was no evidence of differences between different pharmacological interventions in any of the reported outcomes of interest for this review other than the following.

- The proportion of participants requiring a blood transfusion was lower in the aprotinin group (OR 0.31, 95% CrI 0.11 to 0.78; 97 participants; 1 study) and in the tranexamic acid group (OR 0.01, 95% CrI 0.00 to 0.13; 214 participants; 1 study) than in the control.
- The blood transfusion quantity (red blood cells) was lower in the aprotinin group than in the control (MD −0.94 units; P = 0.015; 97 participants; 1 study).
- The blood loss was lower in the tranexamic acid group than in the control (difference in median: −0.3 L, P < 0.001; 214 participants; 1 study).
- The operating time was lower in the tranexamic acid group than in the control (difference in medians −52.20 min; P = 0.003; 214 participants; 1 study).

Overall summary across all interventions

Mortality (perioperative)

There was no evidence of differences in perioperative mortality for any of the comparisons for which this information was available.

Mortality at longest follow-up

There was no evidence of differences in mortality at longest follow-up for any of the comparisons for which this information was available.

Serious adverse events (proportion)

- The proportion of participants experiencing serious adverse events was lower in the continuous selective portal triad clamping group than in the continuous portal triad clamping group (OR 0.42, 95% CrI 0.18 to 0.96; 120 participants; 1 study).
- There was no evidence of differences in other comparisons for which this information was available.

Serious adverse events (number)

- The number of serious adverse events was higher in the fibrin sealant group than in the argon beam group (rate ratio 4.81, 95% CrI 1.73 to 17.5; 121 participants; 1 study).
- The number of serious adverse events was lower in the intermittent portal triad clamping group than in the continuous portal triad clamping group (rate ratio 0.09, 95% CrI 0.00 to 0.56; 86 participants; 1 study).
- There was no evidence of differences in other comparisons for which this information was available.

Adverse events (proportion)

- The proportion of participants experiencing adverse events was lower in the continuous selective portal triad clamping group than in the continuous portal triad clamping group (OR 0.41, 95% CrI 0.18 to 0.90; 120 participants; 1 study).
- There was no evidence of differences in other comparisons for which this information was available.

Adverse events (number)

- The number of adverse events was higher with radiofrequency dissecting sealer than with the clamp-crush method (rate ratio 1.85, 95% CrI 1.07 to 3.26; 250 participants; 3 studies) (Bayesian analysis only: both direct and network meta-analysis).
- There was no evidence of differences in other comparisons for which this information was available.

Health-related quality of life

None of the trials reported this outcome.

Blood transfusion (proportion)

- The proportion of participants requiring a blood transfusion was lower in the group receiving an autologous blood donation than in the control (OR 0.18, 95% CrI 0.04 to 0.66; 42 participants; 1 study).
- The proportion of participants requiring a blood transfusion was higher in the low central venous pressure group than in the acute normovolemic haemodilution plus low central venous pressure group (OR 3.19, 95% CrI 1.56 to 6.95; 208 participants; 2 studies).
- The proportion of participants requiring a blood transfusion was lower in the continuous portal triad clamping group than in the control (OR 0.06, 95% CrI 0.00 to 0.49; 34 participants; 1 study). The proportion of participants requiring a blood transfusion was higher in the continuous portal triad clamping group than in the continuous hepatic vascular exclusion group (OR 5.90, 95% CrI 2.45 to 15.58; 118 participants; 1 study).
- The proportion of participants requiring a blood transfusion was lower in the aprotinin group (OR 0.31, 95% CrI 0.11 to 0.78; 97 participants; 1 study) and in the tranexamic acid group than in the control (OR 0.01, 95% CrI 0.00 to 0.13; 214 participants; 1 study).
- There was no evidence of differences in other comparisons for which this information was available.

Blood transfusion (red blood cells)

- Compared to control, the blood transfusion quantity (red blood cells) was lower in the acute normovolemic haemodilution group (MD −1.25 units, 95% CrI −1.75 to −0.74; 20 participants; 1 study) and in the acute normovolemic haemodilution plus hypotension group (MD −1.67 units, 95% CrI −2.06 to −1.32; 20 participants; 1 study). The blood transfusion quantity (red blood cells) was higher in the acute normovolemic haemodilution plus low central venous pressure group than in the control (MD 0.27 units, 95% CrI 0.01 to 0.52; 30 participants; 1 study).
- The blood transfusion quantity (red blood cells) was lower in the hydrojet group than in the cavitron ultrasonic surgical aspirator group (MD −0.98 units, 95% CrI −1.90 to −0.06; 61 participants; 1 study).
- The blood transfusion quantity (red blood cells) was lower in the fibrin sealant group than in the control (MD −0.53 units, 95% CrI −1.00 to −0.07; 122 participants; 2 studies). The blood transfusion quantity (red blood cells) was higher in the fibrin sealant group than in the cyanoacrylate group (MD 2.20 units; 95% CrI 1.59 to 2.81; 30 participants; 1 study).

- The blood transfusion quantity (red blood cells) was lower with continuous portal triad clamping than control (MD −1.25 units, 95% CrI −2.39 to −0.10; network meta-analysis: 786 participants; 10 studies). The blood transfusion quantity (red blood cells) was lower in the intermittent portal triad clamping group than in the control (−1.50, 95% CrI −2.75 to −0.26; 100 participants; 1 study). The blood transfusion quantity (red blood cells) was lower in the continuous selective hepatic vascular exclusion group than in the continuous portal triad clamping group (MD −1.20 units, 95% CrI −2.37 to −0.04; 160 participants; 1 study). The blood transfusion quantity (red blood cells) was lower in the continuous selective portal triad clamping group than in the continuous portal triad clamping group (MD −0.20, 95% CrI −0.31 to −0.09; 120 participants; 1 study).
- The blood transfusion quantity (red blood cells) was lower in the aprotinin group than in the control (MD −0.94; P = 0.015; 97 participants; 1 study).
- There was no evidence of differences in other comparisons for which this information was available.

Blood transfusion (platelets)

There was no evidence of differences in blood transfusion quantity (platelets) in any of the comparisons for which this information was available.

Blood transfusion (fresh frozen plasma)

- The blood transfusion quantity (fresh frozen plasma) was lower in the low central venous pressure group than in the control (MD −2.48 units, 95% CrI −3.58 to −1.37; 50 participants; 1 study).
- The blood transfusion quantity (fresh frozen plasma) was lower in the fibrin sealant group than in the cyanoacrylate group (MD −0.81 units, 95% CrI −1.04 to −0.62; 30 participants; 1 study). The blood transfusion quantity (fresh frozen plasma) was higher in the oxidised cellulose group than in the fibrin sealant group (MD 0.53 units, 95% CrI 0.36 to 0.71; 80 participants; 2 studies).
- There was no evidence of differences in other comparisons for which this information was available.

Blood transfusion (cryoprecipitate)

There was no evidence of differences in blood transfusion quantity (cryoprecipitate) in any of the comparisons for which this information was available.

Blood loss

- The blood loss was lower in the acute normovolemic haemodilution plus hypotension group (MD −0.25 L; 95% CrI −0.37 to −0.13; 20 participants; 1 study) and in the low central venous pressure group than in the control (MD −0.34 L, 95% CrI −0.46 to −0.22; 237 participants; 4 studies). The blood loss was lower in the acute normovolemic haemodilution plus hypotension group than in the acute normovolemic haemodilution group (MD −0.25; 95% CrI −0.40 to −0.10; 20 participants; 1 study).
- The blood loss was lower in the tranexamic acid group than in the control (difference in median: −0.3 L, P < 0.001; 214 participants; 1 study).
- There was no evidence of differences in other comparisons for which this information was available.

Major blood loss (proportion)

There was no evidence of differences in the proportion of participants experiencing major blood loss in any of the comparisons for which this information was available.

Hospital stay

- The total hospital stay was lower in the low central venous pressure group than in the control (MD −2.42 d, 95% CrI −3.91 to −0.94; 197 participants; 3 studies).
- The total hospital stay was lower in the continuous portal triad clamping group than in the continuous hepatic vascular exclusion group (MD −8.00 d, 95% CrI −13.03 to −2.95; 52 participants; 1 study). The total hospital stay was lower in the continuous selective hepatic vascular exclusion group than in the continuous portal triad clamping group (MD −2.80 d, 95% CrI −4.13 to −1.47; 160 participants; 1 study).
- There was no evidence of differences in other comparisons for which this information was available.

ITU stay

- The ITU stay was lower in the continuous selective hepatic vascular exclusion group than in the continuous portal triad clamping group (MD −0.30 d, 95% CrI −0.55 to −0.06; 160 participants; 1 study).
- There was no evidence of differences in other comparisons for which this information was available.

Operating time

- The operating time was lower in the low central venous pressure group than in the control (MD −15.32 min, 95% CrI −29.03 to −1.69; 192 participants; 4 studies).
- The operating time was lower in the stapler resection group than in the clamp-crush method group with frequentist meta-analysis (MD −31.00 min, 95% CI −60.40 to −1.60; 130 participants; 1 study) (frequentist analysis only).

- The operating time was higher in the fibrin sealant and collagen group than in the control (MD 19.72 min, 95% CrI 2.93 to 36.57; 300 participants; 1 study).
- The operating time was lower in the intermittent portal triad clamping group than in the continuous selective portal triad clamping group (MD −30.53 min, 95% CrI −49.68 to −11.29; 80 participants; 1 study).
- The operating time was lower in the tranexamic acid group than in the control (difference in medians −52.20 min; P = 0.003; 214 participants; 1 study).
- There was no evidence of differences in other comparisons for which this information was available.

Time needed to return to work

None of the trials reported this outcome.

Subgroup analysis

We did not perform subgroup analyses because of the paucity of data.

Reporting bias

For outcomes with 10 or more trials, we explored reporting bias using funnel plots. There were nine comparisons with at least 10 trials. Of these, there was no evidence of funnel plot asymmetry on visualisation for perioperative mortality for methods of parenchymal transection, methods of dealing with cut surface, or methods of vascular occlusion. There was funnel plot asymmetry in the remaining six comparisons, all of which fall under the comparison of different methods of vascular occlusion: adverse events (proportion), blood transfusion (proportion), blood transfusion (red blood cells), blood loss, hospital stay, and operating time. The funnels plots of blood transfusion (proportion), blood transfusion (red blood cells), and blood loss are shown in Figure 30, Figure 31, and Figure 32.

Figure 30. Funnel plot of blood transfusion (proportion): The funnel plot shows funnel plot asymmetry (i.e. some trials with large variance with large effects favouring one treatment were not matched by other trials with similarly large variance with large effects favouring the other treatment). This may be evidence of reporting bias or could be because of heterogeneity between the studies.

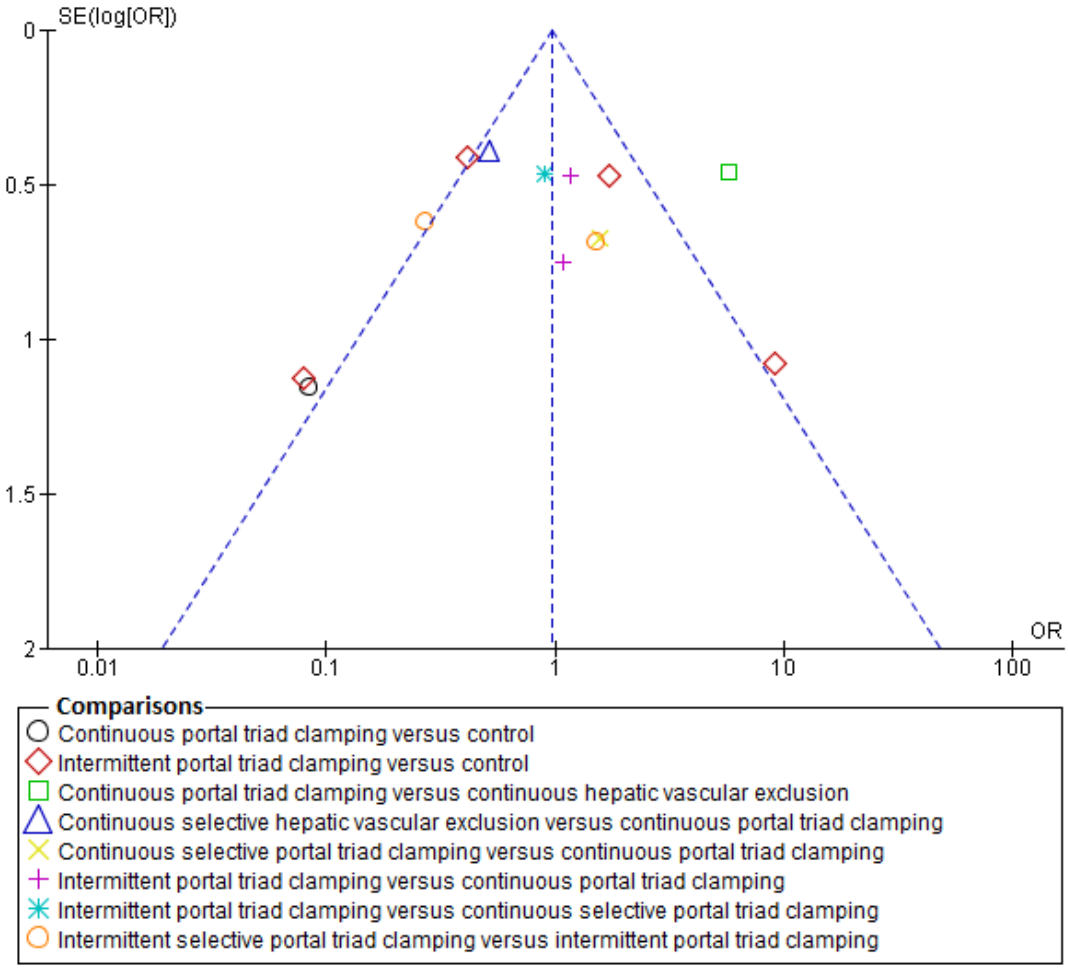


Figure 31. Funnel plot of blood transfusion (red blood cells): The funnel plot shows funnel plot asymmetry (i.e. some trials with large variance with large effects favouring one treatment were not matched by other trials with similarly large variance with large effects favouring the other treatment). This may be evidence of reporting bias or could be because of heterogeneity between the studies.

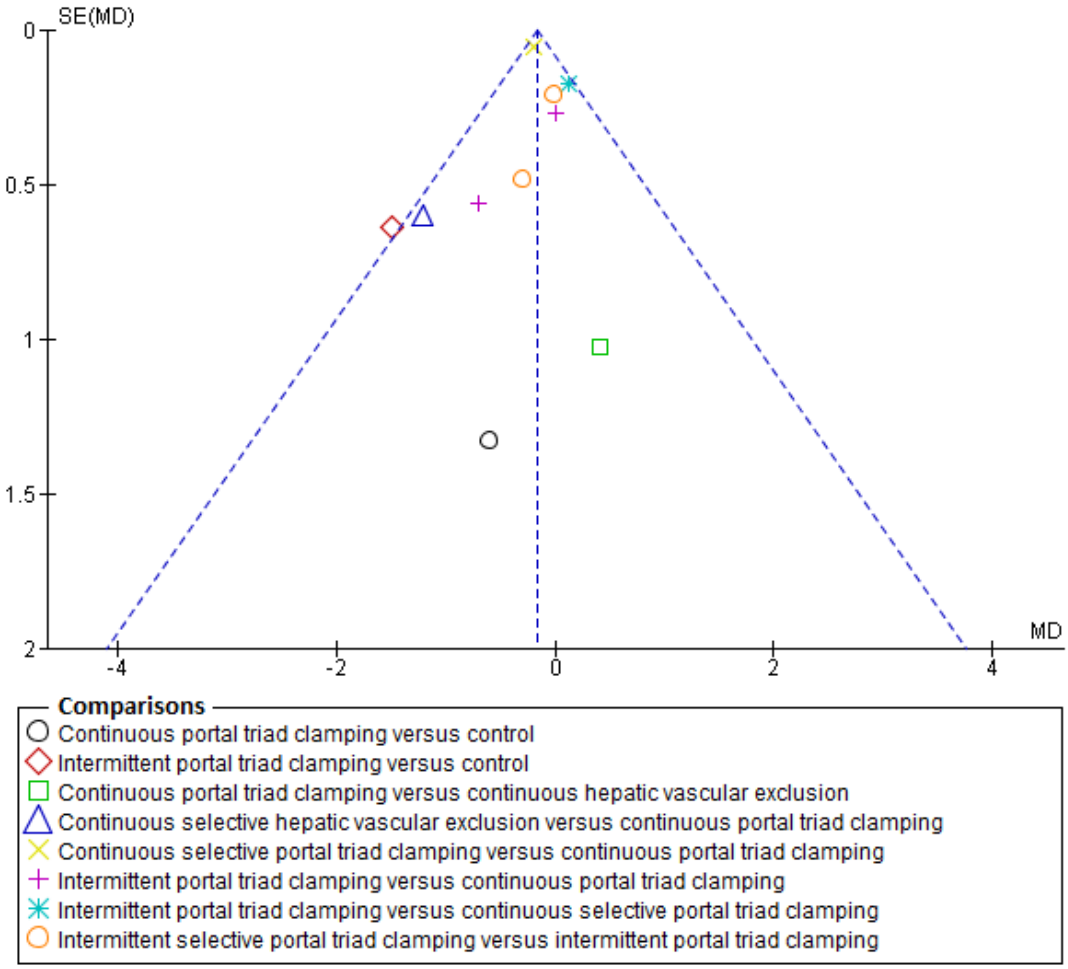
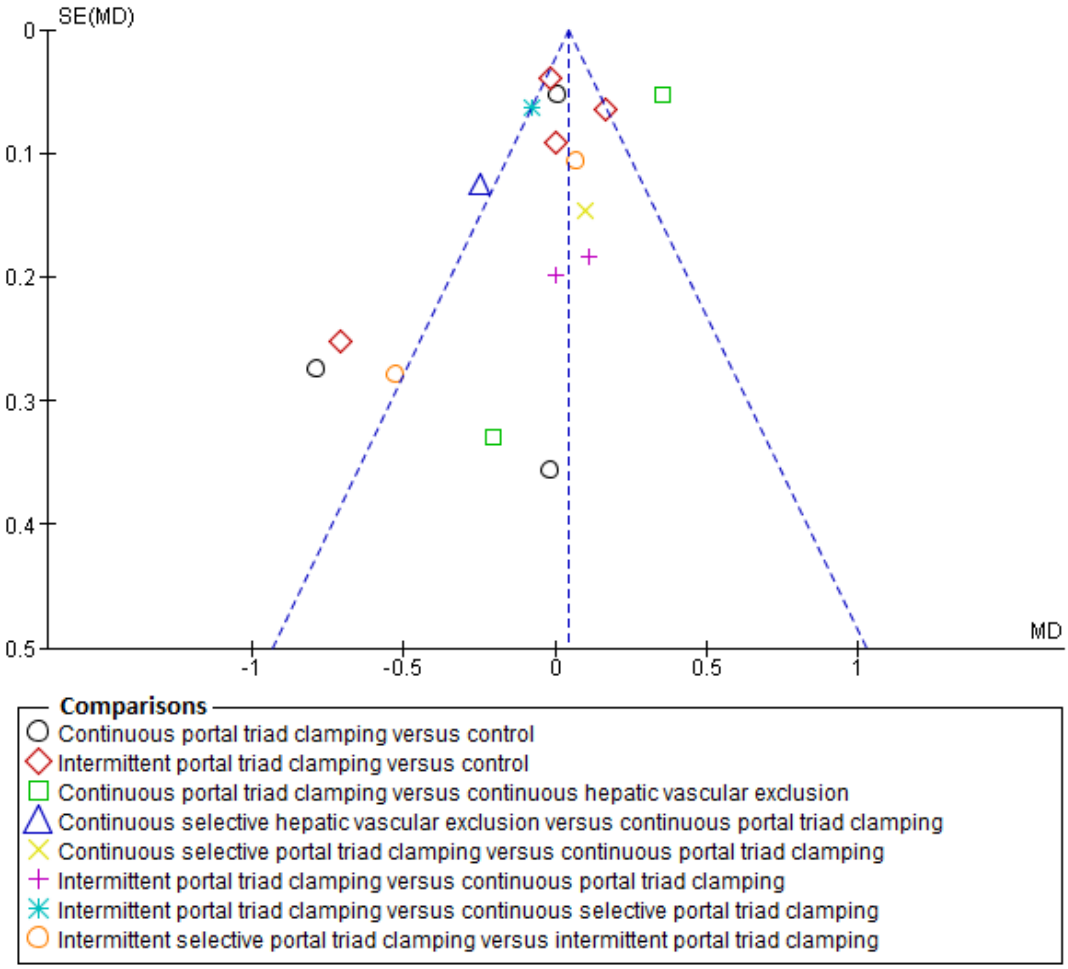


Figure 32. Funnel plot of blood loss: The funnel plot shows funnel plot asymmetry (i.e. some trials with large variance with large effects favouring one treatment were not matched by other trials with similarly large variance with large effects favouring the other treatment). This may be evidence of reporting bias or could be because of heterogeneity between the studies.



Since none of the comparisons had 10 or more trials, we did not perform Egger's test to assess the funnel plot asymmetry.

DISCUSSION

Summary of main results

In this updated network meta-analysis, we compared all the interventions aimed at decreasing blood loss and blood transfusion requirements in people undergoing liver resection. We included 67 randomised clinical trials involving 6197 participants in this review. A total of 5771 participants from 64 trials provided data for one or more outcomes assessed.

In order to perform a network meta-analysis, it is necessary to satisfy the transitivity assumption, that is, the participants had to be sufficiently similar across the pair-wise comparisons. While some trials restricted their participant recruitment to those with cirrhotic livers or those who were undergoing major liver resections, others did not. Although there is no clear evidence for an interaction between the presence of cirrhosis or extent of liver resection and the treatment effect, lack of evidence supporting an interaction does not mean that one does not exist. For example, experimen-

tal research has shown that cirrhotic livers are more susceptible to ischaemia than normal livers (Figueras 1997; Jang 2008). So vascular occlusion may be beneficial in limiting blood loss in people without cirrhosis while the same treatment may be harmful in people with cirrhotic liver. When different trials use different types of participants (with regards to the presence of cirrhosis), this may lead to problems with clinical heterogeneity in pair-wise comparisons and undermine the transivitiy assumption in network meta-analysis. Similarly, a method of treating the cut surface may be more beneficial in people undergoing major liver resections with larger cut surfaces than in those undergoing minor liver resections with smaller cut surfaces that bleed. In the presence of sufficient data, we could have assessed the interaction between the treatment effects and the presence of cirrhosis and the extent of liver resection; however, this was not possible because of paucity of data. So we are unable to comment on the transitivity assumption. We performed network meta-analyses only when direct and indirect effect estimates for one of more comparisons in a network. This allowed us to evaluate inconsistency in the network. Although we did not find any inconsistency in the networks, lack of evidence of inconsistency did not indicate that the results were consistent. With the paucity of data due to few trials and few participants under each comparison, we were unable to make any firm conclusions about inconsistency. Likewise, the paucity of data decreases the confidence in the results of the network meta-analysis. As a result of these limitations, readers should interpret our network meta-analysis with caution. Nevertheless, these results provide relative estimates between treatments that have not been compared in head-to-head comparisons.

We present the summary of findings in the Summary of findings for the main comparison, Appendix 9, and Appendix 10, as well as in the Results section. There was no evidence of differences in most of the comparisons, and where such differences existed, they were in single trials, mostly of small sample size. Without confirmation of the findings in additional trials, combined with lack of reporting in some (possibly because of selective outcome reporting), the evidence from these single trials is not reliable. So we discuss only the evidence that was available in more than one trial below. Of the primary outcomes, the only comparison showing evidence of a difference was in the number of adverse events, which was higher with radiofrequency dissecting sealer than with the clamp-crush method (rate ratio 1.85, 95% CrI 1.07 to 3.26; 250 participants; 3 studies). However, even for this comparison, the credible intervals overlap a clinically non-significant difference (i.e. < 20% difference). So, there is significant uncertainty in the difference in the number of adverse events between those operated on with the radiofrequency dissecting sealer compared to the clamp-crush method due to imprecision in addition to the uncertainty caused by the risk of bias in the trials.

There was no evidence of a reduction in mortality for any of the interventions. Major blood loss may cause multiorgan failure leading to sepsis and death. Mortality was generally low in all the groups compared to that reported in previous studies (Finch 2007). This may be because of the careful selection of participants included in randomised clinical trials compared to a consecutive patient series, which report the results of all liver resections. We have provided the sample size calculations based on the mortality observed in the control groups of 1.8%. To demonstrate a significant 20% relative reduction in mortality (20% relative risk reduction) from 1.8% to 1.4%, approximately 38,000 participants are required for a single direct comparison with one intervention. As shown in the Appendix 7, the effective sample size in an indirect comparison involving just three treatments is only a fraction of the number of participants included in the trials. For example, 10,000 participants included in the indirect comparisons is equivalent to fewer than 2000 'direct' participants in the absence of heterogeneity and fewer than 1000 'direct' participants in the presence of moderate heterogeneity. Even without these complicated calculations, one can easily observe that the credible intervals were very wide, meaning that we cannot rule out a significant benefit or harm for different treatments in terms of mortality. Approximately 16.7% of people in the control group (as defined above) developed serious adverse events. To demonstrate a significant 20% relative reduction in serious adverse events (20% relative risk reduction) from 16.7% to 13.4%, approximately 3592 participants are required for a single direct comparison with a specific intervention. This critical mass of information has not been reached, and there is a significant risk of both type I (alpha) and type II (beta) random errors, that is, there is a significant risk of making false positive and false negative conclusions. Given the number of participants required to show a significant benefit of treatment with relation to mortality and serious adverse events, it is unlikely that trials of the adequate magnitude will be funded.

Of the secondary outcomes, the main outcome measure of the included trials was blood loss and transfusion requirement. The only comparisons with more than one trial where there was evidence of difference were the following: the proportion of participants requiring a blood transfusion was higher in the low central venous pressure group than in the acute normovolemic haemodilution plus low central venous pressure group; blood transfusion (red blood cells) was lower in the fibrin sealant group than in the control; blood transfusion (fresh frozen plasma) was higher in the oxidised cellulose group than in the fibrin sealant group; and blood loss, total hospital stay, and operating time were lower with low central venous pressure than in the control. Trials measured blood loss in different ways. Most reports did not specify whether they measured the amount of blood obtained in the suction, weighed the swabs, or measured the decrease in haemoglobin. In any case, this is only important if the intervention decreases the blood transfusion requirements, operating time, or serious adverse events. Except for low central venous pressure, which decreases blood loss, operating time, and hospital stay, none of the interventions consistently lowered the blood transfusion requirements or improved other clinical outcomes.

Approximately 21.8% of people in the control group required a blood transfusion. Decreasing this need can reduce transfusion-related anaphylactic reactions and transmission of transfusion-related diseases. In addition, there are significant costs associated with blood transfusion, so this is an important outcome. To demonstrate a (significant) 20% relative reduction in serious adverse events (20% relative risk reduction) from 21.8% to 17.4%, approximately 2600 participants are required for a single direct comparisonwith a specific intervention. This critical mass of information has not been reached, and there is significant risk of both alpha and beta random errors in secondary outcomes also.

None of the trials reported quality of life, which is an important outcome used to assess the cost-effectiveness of a treatment in a state-funded healthcare system. Given that the quality of life would depend upon various factors including perioperative complications, length of hospital stay, and time to return to work, it is likely to be easier to demonstrate a significant difference in quality of life if the treatment is effective than to demonstrate a difference in mortality or serious adverse events. Future randomised clinical trials should use a validated quality of life measure as one of the outcomes. Serious adverse events are likely to result in decreased quality of life for patients and increased costs to the healthcare provider and are, therefore, more important endpoints than a modest decrease in blood transfusion. Length of total hospital stay and intensive therapy unit stay are important to the patients, their carers, and the healthcare funders. These should be reported in future trials assessing interventions to decrease blood loss or blood transfusion requirements. None of the trials reported time taken to return to work, which is an important outcome for the patient and their carers in the absence of significant sickness benefit and is an important outcome for the healthcare provider in a state-funded healthcare system with significant sickness benefits.

The major purpose of using different methods of liver resection is to limit blood loss and blood transfusion requirements. Some methods do not require any additional equipment (e.g. vascular occlusion), while other methods do (e.g. cavitron ultrasonic surgical aspirator or radiofrequency dissecting sealer). None of the interventions that require special equipment were better than the clamp-crush method in terms of blood transfusion requirements or other important patient-oriented outcomes and hence cannot be recommended over the standard. However, as mentioned previously, there is a significant risk of random errors because of the small sample sizes and possibly important benefits or harms.

Overall completeness and applicability of evidence

The participants included in this trial underwent elective open liver resection and were generally anaesthetically fit. The findings of this review are applicable only to such patients.

Quality of the evidence

The overall quality of evidence was low or very low as shown in Summary of findings for the main comparison, Appendix 9, and Appendix 10. The risk of bias was high in many of the domains in the trials. Using appropriate methods of randomisation and reporting the method of randomisation adequately will decrease selection bias. While surgeons who perform the surgery cannot be blinded to the treatments, it is possible to blind the surgeons who are involved in the day-to-day postoperative management of the patient. While it may be difficult to blind the anaesthetist to the treatment groups, using objective criteria for transfusion may overcome the problem of bias due to lack of blinding with regards to intraoperative blood transfusion (NHS Blood and Transplant 2007). The intensivist involved in the postoperative care of the patient can be easily blinded. Objective criteria for detection of complications along with the postoperative management of the patient by a healthcare team not involved in the operation can decrease detection and performance bias. Even if blinding of participants and healthcare providers was excluded as a criterion to classify a trial as being at low risk of bias (i.e. even if we considered that trials were at low risk of bias if they were classified as low risk of bias in all domains other than blinding of participants and healthcare providers), we would not have classified any of the trials as being at low risk of bias. With regards to dropouts, randomising the participants after confirming that the tumour can be removed can avoid postrandomisation dropouts due to metastatic spread identified at the time of laparotomy. This can decrease attrition bias. Reporting all the important clinical outcomes can decrease selective reporting bias.

There was heterogeneity in some of the comparisons, which resulted in downgrading the level of evidence, but we did not observe heterogeneity in most of the comparisons in which there were two or more trials. However, it was not possible to assess the consistency of evidence in many comparisons because of the presence of single trials.

The effect estimates were wide with the credible intervals spanning either 0.80 (a 20% reduction) or 1.20 (a 20% increase), which both can be considered clinically significant effects. The total number of participants included in the analysis was only a small fraction of the required sample size even without adjustment for heterogeneity. These findings indicate that there is significant risk of imprecision in all the comparisons. Future trials should be adequately powered to decrease the risk of random errors. There was no indirectness of evidence for any of the outcomes. Although we did not find any reporting bias since the paucity of trials precluded the creation of funnel plots, many of the trials did not adequately report a number of important outcomes. Only 25 trials (37.3%) reported mortality and serious adverse events, although these outcomes ought to be routinely measured in trials comparing interventions aimed at limiting blood loss. This suggests indirect evidence of reporting bias.

Potential biases in the review process

We selected a range of databases without any language restrictions and conducted the meta-analysis according to the NICE TSU (Dias 2012a; Dias 2012b; Dias 2012c; Dias 2013a; Dias 2013b; Dias 2013c; Dias 2013d; Dias 2013e). We performed network meta-analysis only when the treatments were connected to each other and only when it was possible to obtain the direct and indirect estimates for a comparison. This allowed us to evaluate the quality of evidence of direct estimates, indirect estimates, and network meta-analysis estimates, choosing the estimates with the best quality of evidence. These are the strengths of the review process.
The major potential source of bias was that we considered each of these interventions (different methods of cardiopulmonary interventions, parenchymal transection methods, methods of dealing with raw surface, vascular occlusion methods, and pharmacological interventions) as separate networks. This was due to the lack of sufficient information in the trials (which resulted in very few trials in the previous version) and the design of the trials. In many of the trials, the surgeons involved in the trial were allowed to choose their method of liver resection apart from the factor being randomised. This design is based on the assumption that the other factors are independent of each other, that is, there is no interaction between the factors, or the choice of one factor is not dependent upon the choice of another factor. There is no evidence to support or refute this assumption. However, if we planned to include only trials in which all the factors were included, we would not even have been able to include as many trials as we did in the previous version, as we have now included all the interventions aimed at limiting blood loss and blood transfusion requirements during liver resection. Each of the factors are independent of other, i.e. the method of parenchymal transection does not affect the method of vascular occlusion that the surgeons use. However, it is quite possible that there were interactions between the different methods. For example, when a parenchymal transection method with high blood loss was chosen, additional interventions such as fibrin glue may have been used to deal with the cut surface (although there is currently no evidence that fibrin glue is effective). Such use may not necessarily mean that there was an interaction unless there was a systematic difference in the use of the other methods for limiting blood loss between the intervention and control. However, it is only possible to assess this if there are details about all the methods to decrease blood loss from the trial report. Future trials should describe the methods used for reducing blood loss even if it was not the factor being randomised. It is only possible to assess the presence of interaction (i.e. the intervention is more effective or less effective depending upon the presence or absence of a second factor) in well-designed factorial trials. However, the sample size required to detect interaction is much higher than the usual primary analysis of the 'margins'. It is highly unlikely that trials powered to measure interactions can be conducted because of this very large sample size.
We excluded studies that compared variations in the methods listed in Table 1, Table 2, Table 3, and Table 4 and treated variations in the method as single treatment. For example, we included intermittent portal triad clamping of differing durations as a single treatment and did not include comparisons of different methods of intermittent portal triad clamping, unless trials compared them with a different method of vascular occlusion. Hence, this review does not provide information on whether one variation is better than another. We imputed the standard deviations when they were not available from the trials. We performed a sensitivity analysis in all these situations, and there were no changes in results.
Another major limitation of the review was the paucity of data. Many of the networks had few closed loops (i.e. where direct and indirect evidence was available for a particular comparison). Along with this, there were few trials included under each comparison. This also makes the assessment of inconsistency underpowered. Lack of evidence of inconsistency should not be considered the same as lack of inconsistency. This paucity of data decreases the confidence in the results of the network meta-analysis.
Different interventions may have different effects based on on the extent of liver resection and whether the underlying liver was diseased. However, we were unable to assess this because of paucity of data.
We included only randomised clinical trials in this review. While this is the best way to prevent arriving at biased false conclusions on the benefits of a treatment, the harms of treatment may not be fully captured. This is because of the highly selected group of people who enter into randomised clinical trials compared to clinical practice. In addition, randomised clinical trials may not report rare or late serious adverse events, simply due to their generally small sample size and short duration of follow-up.

Agreements and disagreements with other studies or reviews

This is an update of ourfirst network meta-analysis on methods to reduce blood loss during liver resection from 2014 (Simillis 2014). In that review, we concluded that liver resection using a radiofrequency dissecting sealer without vascular occlusion or fibrin sealant may increase serious adverse events. In that review as well, we highlighted the paucity of data. Previously, we also compared individual components included in this review and concluded that intermittent vascular occlusion and the clamp-crush method may decrease blood loss (Gurusamy 2009a; Gurusamy 2009b). In this review, we concluded that there is no evidence for any significant advantage of different methods of liver resection with regards to blood loss. The differences in conclusion may be because of the decreased importance that we have given to single trials of small sample size and inclusion of trials in which the methods were not reported or when the other aspects of liver resection other than the component being compared were chosen in a non-random manner.

AUTHORS' CONCLUSIONS

Implications for practice

Paucity of data meant that we could not assess the transitivity assumption or inconsistency for most analyses. When direct and indirect comparisons were available, network meta-analysis provided additional effect estimates for comparisons where there were no direct comparisons. However, the paucity of data decreases the confidence in the results of the network meta-analysis. Low-quality evidence suggests that liver resection using a radiofrequency dissecting sealer may be associated with more adverse events than with the clamp-crush method. Low-quality evidence also suggests that the proportion of participants requiring a blood transfusion was higher in the groups receiving low central venous pressure than in those receiving acute normovolemic haemodilution plus low central venous pressure; very low-quality evidence suggests that blood transfusion quantity (red blood cells) was lower in the fibrin sealant group than in the control; blood transfusion quantity (fresh frozen plasma) was higher in the oxidised cellulose group than in the fibrin sealant group; and blood loss, total hospital stay, and operating time were lower with low central venous pressure than control. There is no evidence to suggest that using special equipment for liver resection is of any benefit in decreasing the mortality, morbidity, or blood transfusion requirements (very low-quality evidence). Radiofrequency dissecting sealer should not be used outside the clinical trial setting since there is low-quality evidence for increased harm without any evidence of benefits. In addition, it should be noted that the sample size was small and the credible intervals were wide, and considerable benefit or harm with a specific method of liver resection cannot be ruled out.

Implications for research

Trials need to be conducted and reported according to the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) statement (www.spirit-statement.org/) and the CONSORT (Consolidated Standards for Reporting of Trials) statement (www.consort-statement.org). Future randomised clinical trials ought to include people at higher anaesthetic risk eligible for liver resection and to blind outcome assessors.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Arita 2005

Methods	Randomised clinical trial
Participants	Country: Japan Number randomised: 80 Postrandomisation dropouts: 0 (0%) Revised sample size: 80 Average age: 67 years Women: 20 (25%) Number of cirrhotics: 21 (26.3%) Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): not stated Further details of methods of liver resection 1. Vascular occlusion: variable 2. Parenchymal transection: factor being randomised 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Patients undergoing liver resection 2. Age 20-79 years 3. An acceptable clotting profile Exclusion criteria: inflow occlusion at the hepatic hilum proved impossible at laparotomy
Interventions	Participants were randomly assigned to 2 groups. Group 1: radiofrequency dissecting sealer (n = 40) Group 2: clamp-crush method (n = 40) Radiofrequency dissecting sealer: Tissue Link (Valley Lab)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, number of serious adverse events, proportion of people with any adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, and length of hospital stay
Notes	Authors provided replies in March 2016.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomization was done by the minimization procedure with stratification by age (less than 65 versus 65 years or more), indocyanine green retention rate at 15 min (ICG-R15) (less than 20 versus 20 per cent or more) and

Arita 2005 (*Continued*)

		type of resection (minor or major). Resection of two or more Couinaud segments was defined as 'major"'
Allocation concealment (selection bias)	Low risk	Quote: "The assignments were done by an internet-accessed registration system administered by the independent randomization service University Hospital Medical Information Network in Japan"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (author replies): "Patients were informed just of a study plan, but did not know which cohort they belonged to. However, surgeons, of course, could not be blinded because of the nature of study"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The outcome assessors were not blinded".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Low risk	Quote: "This work was supported by a grant from the Kanae Foundation for Life-Socio-medical service"
Other bias	Low risk	Comment: no other bias

Bektas 2014

Methods	Randomised clinical trial
Participants	Country: Germany Number randomised: 70 Postrandomisation dropouts: not stated Revised sample size: 70 Average age: 57 years Women: 31 (44.3%) Number of cirrhotics: 2 (2.9%) Number of major liver resections: 33 (47.1%) Number of right hepatectomies: not stated Follow-up (months): 1 Further details of methods of liver resection 1. Vascular occlusion: intermittent portal triad clamping 2. Parenchymal transection: different types of liver resection 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria

Bektas 2014 (*Continued*)

	1. Adult patients undergoing elective liver resection 2. Requirement for additional haemostatic measures because of persistent oozing from cut surface Exclusion criteria: arterial or venous bleeding
Interventions	Participants were randomly assigned to 2 groups. Group 1: fibrin sealant (n = 35) Group 2: control (n = 35) Fibrin sealant: TISSEEL (Baxter Health Corporation) Spray; 5 mL of fibrinogen with synthetic aprotinin and 5 mL of thrombin (500 IU/mL)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, number of serious adverse events, proportion of people with any adverse events, and number of adverse events
Notes	Authors provided replies in March 2016.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: " Subjects were randomized at a ratio of 1:1 to receive either FS or MC according to a predetermined randomization scheme stratified by study center using the random number generator algorithm of Wichmann and Hill as modified by McLeod" Comment: FS: fibrin sealant; MC: manual compression.
Allocation concealment (selection bias)	Low risk	Quote: "On the day of surgery, the randomization envelope number was obtained from an electronic data capture system. The randomization envelope assigned was opened in the operating room after confirmation of the intraoperative eligibility criteria and clamping of the hilar vessels in the hepatoduodenal ligament (i.e., Pringle maneuver)"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (author reply): "the patient was blinded to the treatment administered. Blinding of the investigator (surgeon) was not possible due to the difference in procedures (spray administration of fibrin sealant vs. manual compression with a surgical gauze swab"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (author reply): "The investigator assessed intra-operative time to hemostasis and other outcome measures, i.e., outcome was assessed unblinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all patients were included for the clinical outcomes
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.

Bektas 2014 (*Continued*)

Vested interest bias	High risk	Quote: "This clinical research was sponsored by Baxter Innovations GmbH, Vienna, Austria"
Other bias	Low risk	Comment: no other bias

Belghiti 1996

Methods	Randomised clinical trial
Participants	Country: France Number randomised: 52 Postrandomisation dropouts: 8 (15.4%) Revised sample size: 44 Average age: 46 years Women: 31 (70.5%) Number of cirrhotics: 0 (0%) Number of major liver resections: 44 (100%) Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: clamp-crush or cavitron ultrasonic surgical aspirator 3. Fibrin glue: yes 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Patients undergoing elective major liver resections 2. Non-cirrhotic livers Exclusion criteria: encasement of blood vessels .
Interventions	Participants were randomly assigned to 2 groups. Group 1: continuous portal triad clamping (n = 24) Group 2: continuous hepatic vascular exclusion (n = 28) Hepatic vascular exclusion by encircling the entire retrohepatic inferior vena cava
Outcomes	The outcomes reported were: short-term mortality, number of serious adverse events, number of adverse events, operative blood loss, quantity of blood transfused (red cell transfusion or whole blood), length of hospital stay, and operating time
Notes	Reasons for postrandomisation dropouts: cross-over to other group (n = 4 in each group)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Belghiti 1996 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Belghiti 1999

Methods	Randomised clinical trial
Participants	Country: France Number randomised: 86 Postrandomisation dropouts: 0 (0%) Revised sample size: 86 Average age: 51 years Women: 39 (45.3%) Number of cirrhotics: not stated Number of major liver resections: 39 (45.3%) Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: cavitron ultrasonic surgical aspirator 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: low central venous pressure 6. Autologous transfusion: not stated Inclusion criteria 1. Elective resections 2. Total vascular exclusion not required because of involvement of the cavosuprahepatic junction or the inferior vena cava 3. No simultaneous bilioenteric anastomosis or associated gastro- intestinal

Belghiti 1999 (*Continued*)

	procedures
Interventions	Participants were randomly assigned to 2 groups. Group 1: continuous portal triad clamping (n = 42) Group 2: intermittent portal triad clamping (n = 44) Continuous portal triad clamping: until end of transection Intermittent portal triad clamping: 15 min on and 5 min off until hepatectomy
Outcomes	The outcomes reported were: short-term mortality, number of serious adverse events, proportion of people with any adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), and length of hospital stay
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Capussotti 2003

Methods	Randomised clinical trial
Participants	Country: Italy Number randomised: 35 Postrandomisation dropouts: not stated Revised sample size: 35

	Average age: 63 years Women: 8 (22.9%) Number of cirrhotics: 35 (100%) Number of major liver resections: 8 (22.9%) Number of right hepatectomies: 2 (5.7%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: clamp-crush 3. Fibrin glue: fibrin glue used 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Patients with hepatocellular carcinoma and liver cirrhosis who underwent liver resection 2. Age < 75 years 3. Child-Pugh class A
Interventions	Participants were randomly assigned to 2 groups Group 1: continuous portal triad clamping (n = 18) Group 2: intermittent portal triad clamping (n = 17) Intermittent portal triad clamping: 15 min on and 5 min off
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Randomization to the type of clamping was assigned by computer generated random numbers"
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.

Capussotti 2003 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Capussotti 2006

Methods	Randomised clinical trial
Participants	Country: Italy Number randomised: 126 Postrandomisation dropouts: 0 (0%) Revised sample size: 126 Average age: 64 years Women: 51 (40.5%) Number of cirrhotics: 19 (15.1%) Number of major liver resections: 56 (44.4%) Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: clamp-crush or bipolar dissecting sealer 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: low central venous pressure 6. Autologous transfusion: not stated Inclusion criteria: patients with resectable liver tumours Exclusion criteria: patients requiring concomitant bowel or bile duct resection or total vascular exclusion
Interventions	Participants were randomly assigned to 2 groups. Group 1: intermittent portal triad clamping (n = 63) Group 2: control (n = 63) Intermittent portal triad clamping: 15 min on and 5 min off
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, operative blood loss, proportion of people requiring blood transfusion, and length of hospital stay
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Capussotti 2006 (*Continued*)

Random sequence generation (selection bias)	Low risk	Quote: "Randomization took place intraoperatively and was performed with a computerized random-number generator"
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Capussotti 2012

Methods	Randomised clinical trial
Participants	Country: Italy Number randomised: 66 Postrandomisation dropouts: 1 (1.5%) Revised sample size: 65 Average age: 62 years Women: 39 (60%) Number of cirrhotics: 5 (7.7%) Number of major liver resections: 65 (100%) Number of right hepatectomies: 65 (100%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: clamp-crush, bipolar dissecting sealer 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Patients aged 18-80 years old scheduled for right hepatectomy 2. Estimated future remnant liver (FRL) before or after portal vein embolisation ≥ 25 % in patients with a normal liver or ≥ 30 % in those with intense preoperative chemotherapy or ≥ 40 % in cirrhotic patients

	3. Indocyanine green (ICG) retention rate at 15 min ≤ 10 % in cirrhotic patients Exclusion criteria 1. Concomitant resection of segment 1 or the bile duct 2. Suspected infiltration of IVC based on preoperative imaging studies 3. Very high-risk patient according to the American Society of Anesthesiologists (ASA) physical score (ASA score IV) and emergency surgery
Interventions	Participants were randomly assigned to 2 groups. Group 1: anterior approach (n = 33) Group 2: control (n = 32)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, number of adverse events, operative blood loss, proportion of people with major blood loss, proportion of people requiring blood transfusion, length of hospital stay, and operating time
Notes	Reasons for postrandomisation dropouts: not stated

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Random sequence was performed using a computerised random number generator"
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Low risk	Quote: "there has been no significant financial support for this work that could have influenced its outcome"
Other bias	Low risk	Comment: no other bias

Chapman 2000

Methods	Randomised clinical trial
Participants	Country: USA Number randomised: 80 Postrandomisation dropouts: 13 (16.3%) Revised sample size: 67 Average age: 58 years Women: 38 (56.7%) Number of cirrhotics: not stated Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing elective liver resection .
Interventions	Participants were randomly assigned to 2 groups. Group 1: fibrin sealant (n = 38) Group 2: collagen (n = 29) Fibrin sealant: Costasis (Cohesion Technologies) - bovine thrombin and collagen combined with patient's own plasma Collagen: Instat (Johnson & Johnson)
Outcomes	The outcomes reported were: short-term mortality, quantity of blood transfused (red cell transfusion or whole blood), and operating time
Notes	Reasons for postrandomisation dropouts: surgery cancelled (n = 8), study co-ordinator not available (n = 1), other reasons (n = 4); 7 in intervention and 6 in control

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Thus, separate computer generated randomization schedules of treatment group assignment placed in sealed envelopes were used for each clinical site and for each type of surgery"
Allocation concealment (selection bias)	Unclear risk	Quote: "Thus, separate computer generated randomization schedules of treatment group assignment placed in sealed envelopes were used for each clinical site and for each type of surgery". Comment: further details of sealed envelope were not avail-

Chapman 2000 (*Continued*)

		able
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: morbidity was not reported.
Vested interest bias	High risk	Quote: "This work was supported in part by Cohesion Technologies Inc, Palo Alto, Calif"
Other bias	Low risk	Comment: no other bias

Chen 2006

Methods	Randomised clinical trial
Participants	Country: China Number randomised: 118 Postrandomisation dropouts: not stated Revised sample size: 118 Average age: 41 years Women: 14 (11.9%) Number of cirrhotics: 118 (100%) Number of major liver resections: 102 (86.4%) Number of right hepatectomies: 0 (0%) Follow-up (months): 1 Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: clamp-crush method 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients with cirrhosis and hepatocellular carcinoma undergoing minor or major right sided liver resections Exclusion criteria 1. Patients with extrahepatic spread or who required concomitant non-shunt operation 2. Splenectomy 3. Multiple liver resection

Chen 2006 (*Continued*)

	4. Extended right or left hepatectomy
Interventions	Participants were randomly assigned to 2 groups. Group 1: continuous portal triad clamping (n = 58) Group 2: continuous hepatic vascular exclusion (n = 60) Hepatic vascular exclusion by encircling the entire infrahepatic inferior vena cava
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, operative blood loss, proportion of people requiring blood transfusion, and operating time
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Low risk	Quote: "This work was supported by the key clinical project fund [No. 321 (2001)] from the Chinese Ministry of Public Health"
Other bias	Low risk	Comment: no other bias

Choi 2007

Methods	Randomised clinical trial
Participants	Country: South Korea Number randomised: 62 Postrandomisation dropouts: not stated Revised sample size: 62

	Average age: 55 years Women: 18 (29%) Number of cirrhotics: not stated Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: factor being randomised 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing liver resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: low central venous pressure (n = 30) Group 2: control (n = 32) Low central venous pressure: by restricting flow from legs
Outcomes	The outcomes reported were: operative blood loss, length of hospital stay, and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.

Choi 2007 (*Continued*)

Other bias	Low risk	Comment: no other bias

Chouker 2004

Methods	Randomised clinical trial
Participants	Country: Germany Number randomised: 46 Postrandomisation dropouts: 12 (26.1%) Revised sample size: 34 Average age: 61 years Women: 11 (32.4%) Number of cirrhotics: 0 (0%) Number of major liver resections: 8 (23.5%) Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Non-cirrhotic adult patients (> 18 years) undergoing elective liver resection 2. ASA status I to III Exclusion criteria 1. History of myocardial infarction in the last 6 months 2. Haemotological disorder 3. Additional planned gastrointestinal surgery
Interventions	Participants were randomly assigned to 2 groups. Group 1: continuous portal triad clamping (n = 19) Group 2: control (n = 15)
Outcomes	The outcomes reported were: operative blood loss and proportion of people requiring blood transfusion
Notes	Reasons for postrandomisation dropouts: patients in this trial were randomised to 3 groups out of which 2 are eligible for this review. The reason for dropout in the included groups was not available. There were 4 dropouts in intervention group and 8 dropouts in control group

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Chouker 2004 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "A blinded allocation of surgeons/anaesthesists was not feasible"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Clavien 1996

Methods	Randomised clinical trial
Participants	Country: International multicentric trial Number randomised: 17 Postrandomisation dropouts: 2 (11.8%) Revised sample size: 15 Average age: 63 years Women: 4 (26.7%) Number of cirrhotics: 6 (40%) Number of major liver resections: 15 (100%) Number of right hepatectomies: 15 (100%) Follow-up (months): 3 months Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing right hepatectomy
Interventions	Participants were randomly assigned to 2 groups. Group 1: continuous portal triad clamping (n = 8) Group 2: control (n = 7) Note: after every 1 h of continuous portal triad clamping (or 30 min for cirrhotic patients)

Clavien 1996 (*Continued*)

	, the clamp was released for 10 min before reclamping
Outcomes	The outcomes reported were: short-term mortality, quantity of blood transfused (red cell transfusion or whole blood), and operating time
Notes	Reasons for postrandomisation dropouts: cardiac transplant patient (n = 1), haemodynamic instability during surgery (n = 1)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: morbidity was not reported.
Vested interest bias	Low risk	Quote: "Supported by a grant from the Medical Research Council of Canada and by a special grant from the Toronto Hospital, University of Toronto, Toronto"
Other bias	Low risk	Comment: no other bias

Dayangac 2010

Methods	Randomised clinical trial
Participants	Country: Turkey Number randomised: 72 Postrandomisation dropouts: 0 (0%) Revised sample size: 72 Average age: 39 years. Women: not stated Number of cirrhotics: not stated Number of major liver resections: 72 (100%)

Dayangac 2010 (*Continued*)

	Number of right hepatectomies: 72 (100%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing right donor hepatectomy
Interventions	Participants were randomly assigned to 2 groups. Group 1: continuous portal triad clamping (n = 36) Group 2: control (n = 36)
Outcomes	The outcome reported was: operative blood loss.
Notes	Authors provided replies in March 2016.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote (author reply): "The patients were randomly assigned by coin tossing"
Allocation concealment (selection bias)	Low risk	Quote: "Neither participants, nor investigators could foresee the assignment, because the coin tossing was performed by the chief operating room nurse at the time of incision"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (author reply): "Yes, all the patients and all of the transplant nurses, coordinators, and physicians (except the senior donor surgeon, who performed all hepatectomies) were blinded"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote (author reply): "Yes, at the end of the study, I performed all the analyses on the prospectively collected data. As the outcome assessor, I was blinded until the end of the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Low risk	Quote (author reply): "There was no direct or indirect financial support"

Dayangac 2010 (*Continued*)

Other bias	Low risk	Comment: no other bias

De Boer 2012

Methods	Randomised clinical trial
Participants	Country: Netherlands Number randomised: 310 Postrandomisation dropouts: 0 (0%) Revised sample size: 310 Average age: 62 years Women: 151 (48.7%) Number of cirrhotics: 0 (0%) Number of major liver resections: 160 (51.6%) Number of right hepatectomies: not stated Follow-up (months): 1 Further details of methods of liver resection 1. Vascular occlusion: with and without inflow occlusion 2. Parenchymal transection: clamp-crush, cavitron ultrasonic surgical aspirator, electric coagulation based, combined 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: at least 1 liver segment or a nonanatomical resection Exclusion criteria 1. Wedge resections 2. Concomitant extrahepatic bile duct resection or bowel resection 3. Cirrhosis 4. Haemostatic disorders 5. Polycystic liver disease 6. Pregnancy 7. History of hypersensitivity or allergic reaction to any plasma derived product
Interventions	Participants were randomly assigned to 2 groups. Group 1: fibrin sealant (n = 156) Group 2: control (n = 154) Fibrin sealant: Quixil (Johnson & Johnson Medical) spray; 5 mL of fibrinogen and tranexamic acid and 5 mL of thrombin
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, operative blood loss, and proportion of people requiring blood transfusion
Notes	Authors provided replies in March 2016.

Risk of bias

De Boer 2012 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (author reply): "A statistician, who was not otherwise involved in the conduct of the study prepared the randomization list, using a computer random number generator"
Allocation concealment (selection bias)	Low risk	Quote: "Treatment allocation employed a sequentially numbered opaque and sealed envelope system"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Surgeons could not be kept unaware of treatment allocation, but patients, local investigators responsible for data gathering, data analysts, and radiologists did remain unaware of the study group assignment"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Surgeons could not be kept unaware of treatment allocation, but patients, local investigators responsible for data gathering, data analysts, and radiologists did remain unaware of the study group assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all patients were included for the clinical outcomes
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	High risk	Quote: "This study was supported by the Fund for Medical Technology Assessment of the University Medical Center Groningen and by Johnson & Johnson Medical"
Other bias	Low risk	Comment: no other bias

Doklestic 2012

Methods	Randomised clinical trial
Participants	Country: Serbia Number randomised: 60 Postrandomisation dropouts: not stated Revised sample size: 60 Average age: 58 years Women: 40 (66.7%) Number of cirrhotics: 0 (0%) Number of major liver resections: 20 (51.6%) Number of right hepatectomies: not stated Follow-up (months): 1 Further details of methods of liver resection 1. Vascular occlusion: intermittent portal triad clamping 2. Parenchymal transection: factor being randomised 3. Fibrin glue: not stated

	4. Pharmacological methods: not stated 5. Cardiopulmonary methods: low central venous pressure 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing hepatectomy for benign or malignant tumours in patients with adequate functional reserve of the heart, lungs, and kidneys Exclusion criteria: cirrhosis
Interventions	Participants were randomly assigned to 3 groups. Group 1: clamp-crush method (n = 20) Group 2: cavitron ultrasonic surgical aspirator (n = 20) Group 3: radiofrequency dissecting sealer (LIGASURE) (n = 20)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, operative blood loss, proportion of people requiring blood transfusion, length of hospital stay, length of intensive therapy unit stay, and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Quote: "The randomization was performed on the day prior to surgery using the sealed envelopes; each group consisted of 20 subjects". Comment: further details of sealed envelope method were not available
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Low risk	Quote: "This study was supported by funding by funding from the Ministry of Education and Science of the Republic

Doklestic 2012 (*Continued*)

		of Serbia"
Other bias	Low risk	Comment: no other bias

El-Kharboutly 2004

Methods	Randomised clinical trial
Participants	Country: Egypt Number randomised: 40 Postrandomisation dropouts: not stated Revised sample size: 40 Average age: 51 years Women: 17 (42.5%) Number of cirrhotics: 40 (100%) Number of major liver resections: 25 (62.5%) Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: intermittent portal triad clamping 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: factor being randomised 6. Autologous transfusion: not stated Inclusion criteria: cirrhotic patients undergoing liver resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: control (n = 20) Group 2: low central venous pressure (n = 20) Low central venous pressure: nitroglycerine
Outcomes	The outcomes reported were: number of serious adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Quote: "Patients were randomly (closed envelope method) ". Comment: further details of sealed envelope method were not available

El-Kharboutly 2004 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Figueras 2005

Methods	Randomised clinical trial
Participants	Country: Spain Number randomised: 80 Postrandomisation dropouts: 0 (0%) Revised sample size: 80 Average age: 62 years Women: 21 (26.3%) Number of cirrhotics: 39 (48.8%) Number of major liver resections: 0 (0%) Number of right hepatectomies: 0 (0%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing minor liver resection Exclusion criteria: patients requiring concomitant bowel resection or contralateral hepatic resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: intermittent portal triad clamping (n = 39) Group 2: intermittent selective portal triad clamping (n = 41) Intermittent clamping: 15 min on and 5 min off

Figueras 2005 (*Continued*)

Outcomes	The outcomes reported were: short-term mortality, number of serious adverse events, proportion of people with any adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), length of hospital stay, and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Quote: "Randomization was performed using sealed envelopes". Comment: further details of sealed envelope method were not available
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.
Vested interest bias	Low risk	Quote: "This is study was partially supported by a grant from 'August Pi i Sunyer Foundation', Ciutat Sanitaria i Universitaria de Bellvitge, Barcelona, Spain; and by a grant from 'Fundacio August Pi i Sunyer', Hospital Universitario de Bellvitge, Barcelona, Spain"
Other bias	Low risk	Comment: no other bias

Figueras 2007

Methods	Randomised clinical trial
Participants	Country: Spain Number randomised: 300 Postrandomisation dropouts: 0 (0%) Revised sample size: 300

Figueras 2007 (*Continued*)

	Average age: 61 years Women: 195 (65%) Number of cirrhotics: 21 (7%) Number of major liver resections: 181 (60.3%) Number of right hepatectomies: 112 (37.3%) Follow-up (months): 6 Further details of methods of liver resection 1. Vascular occlusion: intermittent portal triad or selective clamping 2. Parenchymal transection: cavitron ultrasonic surgical aspirator 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria:patients undergoing liver resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: fibrin sealant plus collagen (n = 150) Group 2: control (n = 150) Fibrin sealant spray: Tissucol Collagen: collagen sponge (Johnson & Johnson) Note: in both groups, bleeding from raw surface was controlled using argon beam coagulator or Tissuelink
Outcomes	The outcomes reported were: short-term mortality, number of serious adverse events, proportion of people with any adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), length of hospital stay, and operating time
Notes	Authors provided replies in March 2016.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote (author reply): "Random list was generated by a computer"
Allocation concealment (selection bias)	Low risk	Quote (author reply): "For patient allocation among groups we used consecutive sealed opaque envelopes"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "The patients were blinded as well as the healthcare providers. After finishing the liver resection the envelope was opened and the surgeon applied the technique of the allocated group". Comment: further details of blinding were not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "The data manager and assessors were also blinded". Comment: further details of blinding were not available.

Figueras 2007 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Low risk	Quote (author reply): "Supported in part by a grant from Fundacio Bellvitge, Barcelona, Spain. The study was not funded because the hemostatic product was approved by the agencia española del medicamento"
Other bias	Low risk	Comment: no other bias

Fischer 2011

Methods	Randomised clinical trial
Participants	Country: European multicentre trial Number randomised: 119 Postrandomisation dropouts: 13 (10.9%) Revised sample size: 106 Average age: 61 years Women: 49 (46.2%) Number of cirrhotics: 0 (0%) Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: a mixture of approaches 2. Parenchymal transection: a mixture of approaches 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Patients > 18 years of age 2. Elective liver resection 3. Women of child-bearing potential use adequate contraception (contraceptive pill or intrauterine device) 4. At least segmental resection (anatomic/nonanatomic) of the liver Exclusion criteria 1. Only minor (i.e. oozing) or moderate haemorrhage persisting after primary operative haemostatic procedures 2. Evidence of coagulation disorders including haemophilia A or B and von Willebrand disease 3. History of allergic reactions after application of human fibrinogen, human thrombin, and/or collagen of any origin 4. Evidence of cirrhosis 5. Emergency operation

Fischer 2011 (*Continued*)

	6. Present drug or alcohol abuse 7. Pregnant or breastfeeding woman 8. Participation in a clinical trial < 30 d before inclusion in present trial 9. Participation in a clinical trial concomitantly with present trial 10. Serious operative complications 11. Prior portal vein embolisation 12. Any fibrin glue haemostatic (including tachocombs) or coagulation method having been used before randomisation
Interventions	Participants were randomly assigned to 2 groups. Group 1: fibrin sealant (n = 54) Group 2: argon beam coagulator (n = 52) Fibrin sealant: Tachosil (Nycomed)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events and proportion of people with any adverse events
Notes	Reasons for postrandomisation dropouts: lost to follow-up or discontinued (6 in TachoSil group and 7 in control group)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Low risk	Quote: "Clinical monitoring, centralized telephone randomization, data management, and statistics were done by Quintiles Ltd"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "This trial was open, because blinding for surgeons and outcome assessors was not possible owing to the nature of the interventions and the primary end point"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "This trial was open, because blinding for surgeons and outcome assessors was not possible owing to the nature of the interventions and the primary end point"
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	High risk	Quote: "This study was fully sponsored by Nycomed".
Other bias	Low risk	Comment: no other bias

Franceschi 2006

Methods	Randomised clinical trial
Participants	Country: USA Number randomised: 153 Postrandomisation dropouts: not stated Revised sample size: 153 Average age: not stated Women: not stated Number of cirrhotics: not stated Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): 1 Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing liver resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: fibrin sealant (n = not stated) Group 2: collagen (n = not stated) Fibrin sealant: CryoSeal FS Collagen: Instat (Ethicon)
Outcomes	None of the outcomes of interest were reported
Notes	Number of participants in each group was not stated. There were no significant difference in blood loss, operating time, hospital stay, or complications

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.

Franceschi 2006 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Frilling 2005

Methods	Randomised clinical trial
Participants	Country: European multicentre trial Number randomised: 121 Postrandomisation dropouts: 0 (0%) Revised sample size: 121 Average age: not stated Women: not stated Number of cirrhotics: not stated Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: a mixture of approaches 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing elective liver resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: fibrin sealant (n = 59) Group 2: argon beam coagulator (n = 62) Fibrin sealant: Tachosil
Outcomes	The outcomes reported were: short-term mortality, number of serious adverse events, proportion of people with any adverse events, and number of adverse events
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.

Frilling 2005 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Quote: "Allocation was concealed by the use of sealed treatment code envelopes, which were opened when the patients had fulfilled the eligibility criteria". Comment: further details of sealed envelope method were not available
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The trial was open, since the appearance of TachoSil precluded blinding"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The trial was open, since the appearance of TachoSil precluded blinding"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Genyk 2014

Methods	Randomised clinical trial
Participants	Country: USA Number randomised: 224 Postrandomisation dropouts: not stated Revised sample size: 224 Average age: not stated Women: not stated Number of cirrhotics: not stated Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing liver resection with minor to moderate bleeding from the resection area after primary control of arterial bleeding or major venous haemorrhage

Genyk 2014 (*Continued*)

Interventions	Participants were randomly assigned to 2 groups. Group 1: fibrin sealant (n = 114) Group 2: oxidised cellulose (n = 110) Fibrin sealant: Tachosil Oxidised cellulose: Surgicel
Outcomes	The outcomes reported were: proportion of people with any adverse events
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Gugenheim 2011

Methods	Randomised clinical trial
Participants	Country: France Number randomised: 58 Postrandomisation dropouts: not stated Revised sample size: 58 Average age: 62 years Women: 31 (53.4%) Number of cirrhotics: 9 (15.5%) Number of major liver resections: 31 (53.4%)

	Number of right hepatectomies: 20 (34.5%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: cavitron ultrasonic surgical aspirator 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Patients undergoing elective open liver resection 2. Raw liver surface > 16 square cm
Interventions	Participants were randomly assigned to 2 groups. Group 1: fibrin sealant (n = 29) Group 2: plasmajet coagulator (n = 29) Fibrin sealant: fibrin glue (no further details)
Outcomes	The outcomes reported were: short-term mortality and proportion of people with serious adverse events
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Quote: "Random assignment was done by opening an envelope in which allotted treatment was hidden". Comment: further details of sealed envelope method were not available
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: morbidity was not reported adequately.
Vested interest bias	Unclear risk	Comment: this information was not available.

Gugenheim 2011 (*Continued*)

Other bias	Low risk	Comment: no other bias

Guo 2013

Methods	Randomised clinical trial
Participants	Country: China Number randomised: 30 Postrandomisation dropouts: not stated Revised sample size: 30 Average age: 65 years Women: 8 (26.7%) Number of cirrhotics: not stated Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: factor being randomised 6. Autologous transfusion: not stated Inclusion criteria 1. Patients under liver resection for cancer 2. ASA I - II 3. Aged 60-70 years with body weight of 45-74 kg 4. No severe dysfunction of liver, kidney, or coagulation system 5. No severe pulmonary or cardiovascular diseases 6. No anticoagulation medication in the previous 2 weeks 7. Preoperative haematocrit (HCT) > 35% 8. Haemoglobin (HB) > 120 g/L
Interventions	Participants were randomly assigned to 2 groups. Group 1: acute normovolemic haemodilution plus low central venous pressure (n = 15) Group 2: control (n = 15) Acute normovolemic dilution plus low central venous pressure: blood withdrawn to a target of 28% haemocrit and replaced with fluid; target for central venous pressure was not reported
Outcomes	The outcomes reported were: operative blood loss and quantity of blood transfused (red cell transfusion or whole blood)
Notes	-
Risk of bias	

Guo 2013 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Low risk	Quote: "The study is supported by Ningbo Medical Technology Foundation 200612"
Other bias	Low risk	Comment: no other bias

Guo 2014

Methods	Randomised clinical trial
Participants	Country: China Number randomised: 60 Postrandomisation dropouts: not stated Revised sample size: 60 Average age: 50 years Women: 22 (36.7%) Number of cirrhotics: not stated Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: factor being randomised 6. Autologous transfusion: not stated Inclusion criteria 1. Patients undergoing liver resection

Guo 2014 (*Continued*)

	2. Age 35-71 3. BMI 18-28 kg/m^2 4. Haematocrit ≥ 35% 5. Haemoglobin ≥ 110 g/L 6. Normal endocrine and coagulation function before operation 7. No portal hypertension 8. No disease of the brain, heart, lung, or kidney
Interventions	Participants were randomly assigned to 3 groups. Group 1: control (n = 20) Group 2: low central venous pressure (n = 20) Group 3: low central venous pressure + acute normovolemic haemodilution (n = 20) Low central venous pressure: fluid restriction and nitroglycerine Acute normovolemic haemodilution plus low central venous pressure: withdrawal of blood to a target haematocrit of 30% and replacement with colloids
Outcomes	The outcomes reported were: operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Low risk	Quote: "The study is supported by Outstanding Leaders Training Program of Pudong Health Bureau of Shanghai Grant no:PWR12013-03 and funded by Disciplines Group Construction Project of Pudong Health Bureau of Shanghai Grant no:PWZxq2014-06"
Other bias	Low risk	Comment: no other bias.

Hasegawa 2002

Methods	Randomised clinical trial
Participants	Country: Japan Number randomised: 80 Postrandomisation dropouts: 1 (1.3%) Revised sample size: 79 Average age: 65 years Women: not stated Number of cirrhotics: 35 (44.3%) Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: intermittent portal triad clamping or selective occlusion 2. Parenchymal transection: clamp-crush or cavitron ultrasonic surgical aspirator 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: factor being randomised 6. Autologous transfusion: none Inclusion criteria: patients scheduled to undergo hepatic resection for the removal of tumours were entered into this trial Exclusion criteria: patients with severe pulmonary dysfunction (< 70% vital capacity, or 1 second forced expiratory volume divided by forced vital capacity < 60%)
Interventions	Participants were randomly assigned to 2 groups. Group 1: control (n = 39) Group 2: hypoventilation (n = 40)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (cryoprecipitate), length of hospital stay, and operating time
Notes	Authors provided replies in March 2016. Reasons for postrandomisation dropouts: did not undergo liver resection

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "In the operating room, eligible patients were randomly assigned to the normoventilation or hypoventilation groups by the minimization method."
Allocation concealment (selection bias)	Low risk	Quote: "In the operating room, eligible patients were randomly assigned to the normoventilation or hypoventilation groups by the minimization method "

Hasegawa 2002 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote (author reply): "Only 2 investigators (K.H. and R. O.), who were not involved in the hepatic resections, had seen the results of the randomization procedure, and they were able to decide to alter the respiratory conditions without consulting with the surgeon. The intervention of this study was hypoventilation during liver parenchyma division, while the control was normoventilation. Both are done by anesthesiologists, which could be blinded to the surgeons and the enrolled patients"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (author reply): "Outcome assessors were not blinded. The outcome measures including blood loss and central venous pressure were evaluated by nurses and anesthesiologists as the outcome assessors"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there was 1 postrandomisation dropout. This was because the patient did not undergo liver resection. This postrandomisation dropout is unlikely to affect the effect estimates for people undergoing liver resection
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.
Vested interest bias	Low risk	Quote: "This work was supported by a grant-in-aid for scientific research from the Ministry of Education, Science, and Culture of Japan (grant 12470252) (Drs Kubota and Makuuchi)"
Other bias	Low risk	Comment: no other bias

Ikeda 2009

Methods	Randomised clinical trial
Participants	Country: Japan Number randomised: 120 Postrandomisation dropouts: 0 (0%) Revised sample size: 120 Average age: 66 years Women: 39 (32.5%) Number of cirrhotics: 27 (22.5%) Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: intermittent portal triad clamping or hemihepatic occlusion 2. Parenchymal transection: factor being randomised 3. Fibrin glue: not stated 4. Pharmacological methods: not stated

	5. Cardiopulmonary methods: not stated 6. Autologous transfusion: no Inclusion criteria 1. Patients undergoing liver resection 2. Age 20-85 years 3. An acceptable clotting profile Exclusion criteria 1. Requirement for bilioenteric anastomoses 2. Cases where inflow occlusion is not possible
Interventions	Participants were randomly assigned to 2 groups. Group 1: radiofrequency dissecting sealer (n = 60) Group 2: clamp-crush method (n = 60) Radiofrequency dissecting sealer: ligasure
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, and length of hospital stay
Notes	Authors provided replies in March 2016.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "the assignments were generated by an internet-accessed randomization system supported by Mebix Inc."
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "In this study, results of assignment were not blinded"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "In this study, results of assignment were not blinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Low risk	Quote: "Supported by grants from the Public Trust Surgery Research Fund, the Japanese Clinical Oncology Fund, the Public Trust Haraguchi Memorial Cancer Research Fund, the JSPS Fujita Memorial Fund for Medical Research; and a grant-in-aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan

Ikeda 2009 (*Continued*)

		(grant 18790955)"
Other bias	Low risk	Comment: no other bias

Jarnagin 2008

Methods	Randomised clinical trial
Participants	Country: USA Number randomised: 135 Postrandomisation dropouts: 5 (3.7%) Revised sample size: 130 Average age: 53 years Women: 61 (46.9%) Number of cirrhotics: not stated Number of major liver resections: 130 (100%) Number of right hepatectomies: 53 (40.8%) Follow-up (months): 3 Further details of methods of liver resection 1. Vascular occlusion: intermittent portal triad clamping 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: factor being randomised 6. Autologous transfusion: not stated Inclusion criteria 1. Adult patients (> 18 years) undergoing elective major liver resection 2. Preoperative Hb ≥ 11 g/dL for men and ≥ 10 g/dL for women Exclusion criteria 1. Active coronary artery disease (exceptions for cardiac stress study showing no reversible ischaemia within 30 d) 2. History of cerebrovascular disease 3. History of congestive heart failure 4. Uncontrolled hypertension 5. Restrictive or obstructive pulmonary disease (COPD) 6. Renal dysfunction 7. Abnormal coagulation parameters 8. Presence of active infection 9. Evidence of hepatic metabolic disorder 10. Preoperative autologous blood donation
Interventions	Participants were randomly assigned to 2 groups. Group 1: acute normovolemic haemodilution plus low central venous pressure (n = 63) Group 2: low central venous pressure (n = 67) Acute normovolemic haemodilution: blood was withdrawn and replaced by colloids and crystalloids to reach a haemocrit target of 8 gm/dL Low central venous pressure was maintained < 5 H_20 using fluid restriction and pharmacologic manipulation

Jarnagin 2008 (*Continued*)

Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, operative blood loss, proportion of people with major blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), quantity of blood transfused (fresh frozen plasma), length of hospital stay, and operating time
Notes	Reasons for postrandomisation dropouts: not clearly stated

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "The generation of the randomization sequences was performed in the Office of Clinical Research at Memorial Sloan-Kettering Cancer Center (MSKCC) by a statistician completely blinded to patient clinical data ". Comment: the method of random sequence generation was not reported
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Kajikawa 1994

Methods	Randomised clinical trial
Participants	Country: Japan Number randomised: 42 Postrandomisation dropouts: not stated Revised sample size: 42 Average age: not stated Women: not stated

	Number of cirrhotics: 42 (100%) Number of major liver resections: 12 (28.6%) Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: factor being randomised Inclusion criteria: cirrhotic patients undergoing liver resection for HCC
Interventions	Participants were randomly assigned to 2 groups. Group 1: autologous blood donation (n = 21) Group 2: control (n = 21) Note: autologous blood donation group was further randomised to recombinant erythropoietin and no erythropoietin
Outcomes	The outcomes reported were: operative blood loss, proportion of people with major blood loss, proportion of people requiring blood transfusion, and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Kakaei 2013

Methods	Randomised clinical trial
Participants	Country: Iran Number randomised: 45 Postrandomisation dropouts: not stated Revised sample size: 45 Average age: 48 years Women: 27 (60%) Number of cirrhotics: 0 (0%) Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge. Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: clamp-crush method 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients aged 18-75 years old undergoing liver resection for resectable mass Exclusion criteria 1. Patients with chronic liver disease 2. Coagulopathy not corrected with treatment before the surgery 3. Death during surgery 4. Operation discontinuation due to severe acidosis or coagulopathy 5. Acute liver failure diagnosed with severe acidosis and severe uncontrolled INR Patients in need of resurgery due to bleeding or bile leak from liver other than resection site
Interventions	Participants were randomly assigned to 3 groups. Group 1: fibrin sealant (n = 15) Group 2: oxidised cellulose (n = 15) Group 3: cyanoacrylate (n = 15) Oxidised cellulose: Surgicel (Ethicon Inc) Fibrin sealant: Tachosil (Takeda Pharmaceuticals) Cyanoacrylate: Glubran 2 (GEM S.R.L.)
Outcomes	The outcomes reported were: number of serious adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), quantity of blood transfused (fresh frozen plasma), and length of hospital stay
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement

Kakaei 2013 (*Continued*)

Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly assigned to these 3 groups by a web-based calculator available in this web address: http://www.randomizer.org"
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Blinding for surgeons was not possible owing to the nature of the used materials' consistency (spongy TachoSil knitted fabric Surgicel and liquid Glubran 2) and their packages"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "The postoperative assessors were completely blinded to which agents were used for each patient". Comment: it is not clear how the assessment was done if the surgeons were not blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	High risk	Comment: mortality was not reported.
Vested interest bias	Low risk	Quote: "This research was financially supported by the Vice Chancellor for Research, Tabriz University of Medical Sciences, Iran"
Other bias	Low risk	Comment: no other bias

Kato 2008

Methods	Randomised clinical trial
Participants	Country: Japan Number randomised: 85 Postrandomisation dropouts: 0 (0%) Revised sample size: 85 Average age: 66 years Women: not stated Number of cirrhotics: not stated Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): not stated Further details of methods of liver resection 1. Vascular occlusion: intermittent portal triad clamping 2. Parenchymal transection: cavitron ultrasonic surgical aspirator 3. Fibrin glue: fibrin glue used 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: factor being randomised 6. Autologous transfusion: not stated

Kato 2008 (*Continued*)

	Inclusion criteria: patients undergoing liver resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: low central venous pressure (n = 43) Group 2: control (n = 42) Low central venous pressure: by inferior IVC clamping
Outcomes	The outcomes reported were: short-term mortality, operative blood loss, proportion of people requiring blood transfusion, length of hospital stay
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Eighty-five patients who underwent hepatic resection between June 2002 and May 2006 were randomly assigned to an IVC clamping or an IVC nonclamping group by the minimization method "
Allocation concealment (selection bias)	Low risk	Quote: "Eighty-five patients who underwent hepatic resection between June 2002 and May 2006 were randomly assigned to an IVC clamping or an IVC nonclamping group by the minimization method "
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: morbidity was not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Koea 2013

Methods	Randomised clinical trial
Participants	Country: European and Australian multicentre trial Number randomised: 84 Postrandomisation dropouts: 0 (0%) Revised sample size: 84 Average age: 65 years Women: 36 (42.9%) Number of cirrhotics: not stated Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: older than 18 years of age and required urgent or elective hepatic resection and were able to provide written, informed consent Exclusion criteria 1. Admitted for trauma surgery 2. Undergoing a liver transplant for fulminant hepatic failure 3. Active sepsis around the liver 4. Known tolerance to blood products or one of the components of the fibrin pad 5. Unwilling to receive blood products 6. Known and current alcohol or drug abuser 7. Pregnant or breastfeeding 8. Participated in another investigational drug or device research study within the previous 30 d
Interventions	Participants were randomly assigned to 2 groups. Group 1: fibrin sealant (n = 45) Group 2: oxidised cellulose (n = 39) Fibrin sealant: Fibrin Pad Oxidised cellulose: no further details
Outcomes	None of the outcomes of interest were reported.
Notes	Authors provided replies in March 2016.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Random allocation of patients to the FP or SoC groups was generated by a computer program and validated by a secondary statistician".

Koea 2013 (*Continued*)

		Comment: FP: Fibrin Pad; SoC: standard of care.
Allocation concealment (selection bias)	Low risk	Quote: "The allocation was on sequentially numbered concealed envelopes"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote (author reply): "The patients were blinded regarding the treatment, but health care providers can't be blinded given the obvious difference in the nature of the test products"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (author reply): "Outcomes assessor for outcomes not specific for research may include hospital staff which may not be aware of the research nor the treatment assignment. The collection of the outcomes information for analysis was done by research staff that is aware of the treatment assignment. However, the information collected is verified with the hospital source documents"
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: although the authors call this intention-to-treat analysis, only an 'as-treated' analysis is presented
Selective reporting (reporting bias)	High risk	Comment: none of the outcomes of interest were presented for the randomised patients
Vested interest bias	High risk	Quote: "Financial and product support was provided by Ethicon Inc, Sommervile, New Jersey, USA"
Other bias	Low risk	Comment: no other bias

Kohno 1992

Methods	Randomised clinical trial
Participants	Country: Japan Number randomised: 62 Postrandomisation dropouts: 0 (0%) Revised sample size: 62 Average age: 62 years Women: 14 (22.6%) Number of cirrhotics: 46 (74.2%) Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): not stated Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated

Kohno 1992 (*Continued*)

	5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing liver resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: collagen (n = 31) Group 2: fibrin sealant (n = 31) Collagen: Avitene (Alcon Inc) Fibrin sealant: Beriplast P (Beringwerke AB)
Outcomes	The outcomes reported were: short-term mortality, number of serious adverse events, number of adverse events, operative blood loss, and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Koo 2005

Methods	Randomised clinical trial
Participants	Country: South Korea Number randomised: 50 Postrandomisation dropouts: not stated Revised sample size: 50

Koo 2005 (*Continued*)

	Average age: 53 years Women: 14 (28%) Number of cirrhotics: not stated Number of major liver resections: 38 (76%) Number of right hepatectomies: 27 (54%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: No vascular occlusion. 2. Parenchymal transection: factor being randomised 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: adults scheduled for elective hepatectomy Exclusion criteria 1. Known cardiopulmonary diseases 2. Patients with dysphagia 3. Hiatal hernia 4. Oesophageal disease
Interventions	Participants were randomly assigned to 2 groups. Group 1: clamp-crush method (n = 25) Group 2: cavitron ultrasonic surgical aspirator (n = 25)
Outcomes	The outcomes reported were: proportion of people with any adverse events, operative blood loss, and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Quote: "Randomization was performed by opening a sealed envelope before induction of anaesthesia". Comment: further information on sealed envelope system were not available
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.

Koo 2005 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Kostopanagiotou 2007

Methods	Randomised clinical trial
Participants	Country: Greece Number randomised: 35 Postrandomisation dropouts: 7 (20%) Revised sample size: 28 Average age: 52 years Women: 11 (39.3%) Number of cirrhotics: 0 (0%) Number of major liver resections: 16 (57.1%) Number of right hepatectomies: 11 (39.3%) Follow-up (months): 12 Further details of methods of liver resection 1. Vascular occlusion: hepatic vascular exclusion 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: factor being randomised Inclusion criteria 1. Non-cirrhotic patients undergoing elective liver resections 2. ASA II or III Exclusion criteria: receiving immunosuppressive drugs
Interventions	Participants were randomly assigned to 2 groups. Group 1: autologous blood donation (n = 15) Group 2: control (n = 13) Autologous blood donation: 2 units of blood were withdrawn before surgery
Outcomes	The outcomes reported were: short-term mortality, long-term mortality, proportion of people with any adverse events, operative blood loss, quantity of blood transfused (red cell transfusion or whole blood), length of hospital stay, and operating time
Notes	Reasons for postrandomisation dropouts: requirement of allogenic transfusion in autologous group or did not require any transfusion (4 in intervention group and 3 in control group)

Kostopanagiotou 2007 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Lee 2012

Methods	Randomised clinical trial
Participants	Country: Hong Kong, China Number randomised: 126 Postrandomisation dropouts: 0 (0%) Revised sample size: 126 Average age: 59 years Women: 32 (25.4%) Number of cirrhotics: 54 (42.9%) Number of major liver resections: 62 (49.2%) Number of right hepatectomies: 39 (31%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: cavitron ultrasonic surgical aspirator 3. Fibrin glue: yes 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: low central venous pressure 6. Autologous transfusion: not stated Inclusion criteria:

Lee 2012 (*Continued*)

	adult patients (> 18 years) undergoing elective open liver resection Exclusion criteria 1. Portal vein thrombosis, portal vein embolisation, or requiring portal vein resection 2. Hepatic artery thrombosis 3. Previous transarterial chemoembolization (TACE) or chemoirradiation 4. Ruptured hepatocellular carcinoma (HCC) 5. Repeat hepatectomy 6. Patients in whom concomitant bowel or bile duct resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: intermittent portal triad clamping (n = 63) Group 2: control (n = 63) Intermittent portal triad clamping: 15 min on and 5 min off
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, number of adverse events, operative blood loss, proportion of people with major blood loss, proportion of people requiring blood transfusion, length of hospital stay, operating time
Notes	Authors provided replies in March 2016.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "The computer-generated numbers were kept in sealed envelopes."
Allocation concealment (selection bias)	Low risk	Quote (author reply): "The randomisation code was put in the sealed opaque envelops with consecutive number before the start of the study by a clerical staff not related to the study. An envelop was provided by research assistant consecutively and was brought to the theatre on day of surgery. The envelop was opened by the operation nurse or anesthetist independent to the study when and only if the surgical team confirm feasibility of proceeding to liver resection according to the study protocol intra-operatively"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Patients and surgeons were not blinded to the randomization result"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (author reply): "The outcome assessors for blood loss were not blinded to the surgeons (because we felt operating surgeons should know about the degree of intra-operative blood loss). But the actual recording procedure were performed by independent OT nurses and anaesthetists in the particular operation. The blood loss was measure by measuring all the blood collected in the suction bottle and weighing

Lee 2012 (*Continued*)

		the gauzes in different phases of the operation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Low risk	Quote (author reply): "The study received no external funding. It was supported by the team's own private funding"
Other bias	Low risk	Comment: no other bias

Lentschener 1997

Methods	Randomised clinical trial
Participants	Country: France Number randomised: 109 Postrandomisation dropouts: 12 (11%) Revised sample size: 97 Average age: 54 years Women: 45 (46.4%) Number of cirrhotics: not stated Number of major liver resections: 63 (64.9%) Number of right hepatectomies: 34 (35.1%) Follow-up (months): not stated Further details of methods of liver resection 1. Vascular occlusion: intermittent portal triad clamping 2. Parenchymal transection: Kelly clamp 3. Fibrin glue: fibrin glue used 4. Pharmacological methods: factor being randomised 5. Cardiopulmonary methods: none 6. Autologous transfusion: not stated Inclusion criteria: adult patients undergoing elective liver resection Exclusion criteria 1. Known allergy to aprotinin or possible previous exposure to the drug 2. Pregnancy 3. Any possible bleeding disorder or inherited bleeding disorder 4. Previous venous or arterial thrombosis or any biological abnormality likely to induce thrombosis 5. Impaired renal function 6. Age < 18 years
Interventions	Participants were randomly assigned to 2 groups. Group 1: aprotinin (n = 48) Group 2: control (n = 49) Aprotinin: loading dose: 2 X 10^6 kIU of aprotinin over a 20 min period after induction of anaesthesia

Lentschener 1997 (*Continued*)

	Continuous infusion: 5 x 10^5 kIU per h administered by an infusion pump until skin closure Additional bolus: 5 X 10^5 kIU of aprotinin was infused every 3 transfused red blood cell packs Control: placebo
Outcomes	The outcomes reported were: long-term mortality, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), quantity of blood transfused (platelets), quantity of blood transfused (fresh frozen plasma), and operating time
Notes	Reasons for postrandomisation dropouts: tumour could not be removed (n = 6), wrong pre-operative histological assessment (n = 5), and extension of incision to a thoracotomy (n = 1)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: " Patients were assigned in a double blind fashion by means of a computer-generated code to receive either aprotinin or the equivalent volume of placebo"
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: a placebo was used. It was not clear whether the anaesthetists and surgeons performing the surgery and the patients were aware of the groups
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "An identical-appearing placebo was prepared by a nurse not involved in latter assessment. Each patient in the control group received equivalent volumes of the placebo (0. 9% saline solution) at the respective times"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	Unclear risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Unclear risk	Quote: "This study was conducted independently of, but partially supported by, Assistance Publique-Hopitaux de Paris, Bayer Pharma France and the Associations Claude Bernard and Mises au Point en Anesthesie-Reanimation"
Other bias	Unclear risk	Comment: no other bias

Lesurtel 2005

Methods	Randomised clinical trial
Participants	Country: Switzerland Number randomised: 75 Postrandomisation dropouts: not stated Revised sample size: 75 Average age: 57 years Women: 34 (45.3%) Number of cirrhotics: 0 (0%) Number of major liver resections: 45 (60%) Number of right hepatectomies: 23 (30.6%) Follow-up (months): 3 Further details of methods of liver resection 1. Vascular occlusion: no vascular occlusion 2. Parenchymal transection: factor being randomised 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Patients undergoing partial liver resection for tumours 2. Acceptable coagulation profile Exclusion criteria 1. Living liver donors 2. Cirrhotic patients 3. Cholestatic patients
Interventions	Participants were randomly assigned to 3 groups. Group 1: radiofrequency dissecting sealer (n = 25) Group 2: cavitron ultrasonic surgical aspirator (n = 25) Group 3: hydrojet (n = 25) Radiofrequency dissecting sealer: Tissue Link Hydrojet: Helix Hydro-Jet A fourth group with clamp-crush and vascular occlusion was excluded since there was difference in the co-intervention between the groups
Outcomes	The outcomes reported were: short-term mortality, number of serious adverse events, number of adverse events, proportion of people requiring blood transfusion, length of hospital stay, and length of intensive therapy unit stay
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.

Lesurtel 2005 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	High risk	Quote: "Supported in an equivalent amount by Erbe (Tubingen, Germany), Tissuelink (Dover, NH), and Tyco Healthcare (Mansfield, MA). Dr. Selzner and Dr. Petrowsky are the recipients of the Novartis fellowship in HPB surgery and liver transplantation"
Other bias	Low risk	Comment: no other bias

Liang 2009

Methods	Randomised clinical trial
Participants	Country: China Number randomised: 80 Postrandomisation dropouts: 0 (0%) Revised sample size: 80 Average age: 49 years Women: 22 (27.5%) Number of cirrhotics: 36 (45%) Number of major liver resections: 23 (28.8%) Number of right hepatectomies: 6 (7.5%) Follow-up (months): 1 Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: clamp-crush 3. Fibrin glue: not stated 4. Pharmacological methods: None 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Patients undergoing liver resection 2. Tumours confined to one half of the liver 3. Hilar dissection was feasible

Liang 2009 (*Continued*)

	Exclusion criteria: patients requiring concomitant gastrointestinal procedures or bilioenteric anastomosis
Interventions	Participants were randomly assigned to 2 groups. Group 1: continuous selective portal triad clamping (n = 40) Group 2: intermittent portal triad clamping (n = 40) Intermittent portal triad clamping: 20 min on and 5 min off
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), length of hospital stay, and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Low risk	Quote: "The study was supported by the Basic Research Foundation of Sichuan Province of China (05JY29-005-3) "
Other bias	Low risk	Comment: no other bias

Liu 1993

Methods	Randomised clinical trial
Participants	Country: Taiwan Number randomised: 40 Postrandomisation dropouts: 0 (0%) Revised sample size: 40 Average age: 60 years Women: 3 (7.5%) Number of cirrhotics: 22 (55%) Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing liver resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: fibrin sealant (n = 20) Group 2: control (n = 20) Fibrin sealant: name not available
Outcomes	The outcomes reported were: operative blood loss, quantity of blood transfused (red cell transfusion or whole blood), and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.

Liu 1993 (*Continued*)

Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Liu 2006

Methods	Randomised clinical trial
Participants	Country: Hong Kong, China Number randomised: 136 Postrandomisation dropouts: 16 (11.8%) Revised sample size: 120 Average age: 52 years Women: 17 (14.2%) Number of cirrhotics: 38 (31.7%) Number of major liver resections: 120 (100%) Number of right hepatectomies: 120 (100%) Follow-up (months): 20 Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: cavitron ultrasonic surgical aspirator 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Patients undergoing right hepatectomy 2. HCC
Interventions	Participants were randomly assigned to 2 groups. Group 1: anterior approach (n = 60) Group 2: control (n = 60)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with any adverse events, operative blood loss, proportion of people with major blood loss, proportion of people requiring blood transfusion, length of hospital stay, length of intensive therapy unit stay, and operating time
Notes	Reasons for postrandomisation dropouts: 7 and 9 in intervention and control groups; Non-HCC on histology (n = 8); segmentectomy (n = 1); palliative resection (n = 7)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Liu 2006 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Quote: "A total of 136 patients were randomized initially to have either anterior approach hepatectomy (AA group) or conventional approach resection (CA group) by drawing consecutive sealed envelopes". Comment: further information on sealed envelope system were not available
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The randomization was made known to the operating surgeon only when the disease was deemed suitable for curative resection"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "All patients received the same postoperative care by the same team of surgeons in the intensive care unit during the early postoperative course"
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.
Vested interest bias	Low risk	Quote: "Supported by the Earmarked Research Grant of the Research Grants Council of Hong Kong"
Other bias	Low risk	Comment: no other bias

Lodge 2005

Methods	Randomised clinical trial
Participants	Country: European multicentre trial Number randomised: 204 Postrandomisation dropouts: 19 (9.3%) Revised sample size: 185 Average age: 57 years Women: 92 (49.7%) Number of cirrhotics: 0 (0%) Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: mixture of methods 2. Parenchymal transection: not stated 3. Fibrin glue: no 4. Pharmacological methods: factor being randomised 5. Cardiopulmonary methods: not stated

	6. Autologous transfusion: no Inclusion criteria 1. Non-cirrhotic adults (≥ 18 years of age) scheduled to undergo partial hepatectomy for liver cancer/metastasis, benign tumors, or both 2. Planned anatomical resection of 3 or more segments of the liver or planned nonanatomical resection of a volume equivalent to 2 or more segments of the liver parenchyma Exclusion criteria 1. Known hereditary bleeding disorders 2. The planned use of autologous blood transfusion 3. Low molecular weight heparin before hepatectomy 4. Tissue glue or haemodilution therapy during surgery or haemostatic drugs for prophylactic purposes 5. Renal insufficiency requiring dialysis 6. Clinically documented portal vein or deep vein thrombosis or a history of the latter within the preceding 6 months 7. Severe cardiovascular disease or previous myocardial/pulmonary infarction or stroke within the preceding 6 months 8. Anticoagulation therapy not discontinued within 48 h before surgery 9. Active bleeding 10. Use of nonsteroidal antiinflammatory drugs within 7 d before surgery
Interventions	Participants were randomly assigned to 2 groups. Group 1: recombinant factor viia (n = 126) Group 2: control (n = 59) Recombinant factor VIIa: first dose: slow intravenous injection (20 mcg/kg or 80 mcg/kg) within 5 min before incision. Second dose: identical dose was given 5 h after incision if the surgery time was anticipated to exceed 6 h Control: placebo
Outcomes	The outcomes reported were: short-term mortality, long-term mortality, proportion of people with serious adverse events, number of serious adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), and operating time
Notes	Reasons for postrandomisation dropouts: did not receive drug (n = 4); did not undergo hepatectomy (n = 15)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was computer-generated and was performed after patient eligibility assessments on the day of surgery by means of a central interactive voice response system set up by Novo Nordisk A/S"

Lodge 2005 (*Continued*)

Allocation concealment (selection bias)	Low risk	Quote: "Randomization was computer-generated and was performed after patient eligibility assessments on the day of surgery by means of a central interactive voice response system set up by Novo Nordisk A/S"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The current randomized, controlled, double-blind, multi-national trial was designed to evaluate the efficacy and safety of rFVIIa in noncirrhotic patients undergoing major liver resection. To maintain blinding, an equal volume of trial drug per body weight was administered to all patients, irrespective of treatment group allocation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The current randomized, controlled, double-blind, multi-national trial was designed to evaluate the efficacy and safety of rFVIIa in noncirrhotic patients undergoing major liver resection. To maintain blinding, an equal volume of trial drug per body weight was administered to all patients, irrespective of treatment group allocation"
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	High risk	Quote: "The authors thank the patients and the hospital staff participating in the trial, as well as Allan Blemings, M. Sc. (Statistician), and Karsten Soendergaard, M.Sc. (Clinical Researcher), both at Novo Nordisk A/S, Copenhagen, Denmark"
Other bias	Low risk	Comment: no other bias

Lupo 2007

Methods	Randomised clinical trial
Participants	Country: Italy Number randomised: 51 Postrandomisation dropouts: 1 (2%) Revised sample size: 50 Average age: 62 years Women: 14 (28%) Number of cirrhotics: 7 (14%) Number of major liver resections: 21 (42%) Number of right hepatectomies: 9 (18%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: no vascular occlusion

Lupo 2007 (*Continued*)

	2. Parenchymal transection: factor being randomised 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing potentially curative liver resection for primary or secondary liver cancers
Interventions	Participants were randomly assigned to 2 groups. Group 1: radiofrequency dissecting sealer (n = 24) Group 2: clamp-crush method (n = 26) Radiofrequency dissecting sealer: radionics needles
Outcomes	The outcomes reported were: short-term mortality, number of serious adverse events, number of adverse events, proportion of people requiring blood transfusion, length of hospital stay, and operating time
Notes	Authors provided replies in March 2016. Reasons for postrandomisation dropouts: did not undergo liver resection

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "The patients were assigned, in the operating room, by random-number tables to undergo RF-R (even numbers) or resection by the clamp-crushing method (odd numbers) " Comment: RF-R: radiofrequency radiation
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Authors replied that patients and healthcare providers were blinded". Comment: further information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Authors replied that outcome assessors were blinded". Comment: further information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there was 1 postrandomisation dropout. This was because the patient did not undergo liver resection. This postrandomisation dropout is unlikely to affect the effect estimates for people undergoing liver resection
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.

Lupo 2007 (*Continued*)

Vested interest bias	Low risk	Quote: "The authors replied that there was no external funding"
Other bias	Low risk	Comment: no other bias

Man 1997

Methods	Randomised clinical trial
Participants	Country: Hong Kong, China Number randomised: 100 Postrandomisation dropouts: not stated Revised sample size: 100 Average age: 56 years Women: 19 (19%) Number of cirrhotics: 29 (29%) Number of major liver resections: 69 (69%) Number of right hepatectomies: 14 (14%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: cavitron ultrasonic surgical aspirator 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria Adult patients undergoing liver resection Exclusion criteria Requiring concomitant bowel resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: intermittent portal triad clamping (n = 50) Group 2: control (n = 50) Intermittent portal triad clamping: 20 min on and 5 min off
Outcomes	The outcomes reported were: short-term mortality, number of serious adverse events, proportion of people with any adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), and length of hospital stay
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Man 1997 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.
Vested interest bias	Low risk	Quote: "Research Grant Council of Hong Kong in funding the study"
Other bias	Low risk	Comment: no other bias

Man 2003

Methods	Randomised clinical trial
Participants	Country: Hong Kong, China Number randomised: 40 Postrandomisation dropouts: 0 (0%) Revised sample size: 40 Average age: 50 years Women: 11 (27.5%) Number of cirrhotics: not stated Number of major liver resections: 26 (65%) Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients with resectable tumours.
Interventions	Participants were randomly assigned to 2 groups. Group 1: intermittent portal triad clamping (n = 20)

Man 2003 (*Continued*)

	Group 2: control (n = 20) Intermittent portal triad clamping: 20 min on and 5 min off (until resection is completed or a maximum of 6 cycles)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with any adverse events, and proportion of people requiring blood transfusion
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Matot 2002

Methods	Randomised clinical trial
Participants	Country: Israel Number randomised: 78 Postrandomisation dropouts: not stated Revised sample size: 78 Average age: 57 years Women: 47 (60.3%) Number of cirrhotics: 0 (0%) Number of major liver resections: 78 (100%) Number of right hepatectomies: not stated Follow-up (months): until discharge

Matot 2002 (*Continued*)

	Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: factor being randomised 6. Autologous transfusion: not stated Inclusion criteria 1. Adults (> 18 years) undergoing major elective resection 2. Haematocrit > 36% 3. ASA I or II 4. No cardiovascular or pulmonary disease, or severe hepatic metabolic disorder
Interventions	Participants were randomly assigned to 2 groups. Group 1: acute normovolemic haemodilution + low central venous pressure (n = 39) Group 2: low central venous pressure (n = 39) Acute normovolemic haemodilution: blood was withdrawn and replaced by colloids to reach a haemocrit target of 24% Low central venous pressure was achieved by fluid restriction
Outcomes	The outcomes reported were: short-term mortality, number of serious adverse events, proportion of people with any adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "On admission to the operating room, patients who met inclusion criteria were randomly assigned (random numbers) to one of two groups"
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The anesthesiologist making decisions regarding transfusion was not blinded to patient group assignment"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Subsequent blood loss was estimated by assessment of the suction bottles, sponges, and the surgical drapes and gowns by an anesthesiologist who was not aware of the patient's group assignment". Comment: Not clear whether other outcomes were assessed by a blinded observer

Matot 2002 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.
Vested interest bias	Low risk	Quote: "Supported by a grant from the Joint Research Fund of the Hebrew University and Hadassah, Jerusalem, Israel"
Other bias	Low risk	Comment: no other bias

Moench 2014

Methods	Randomised clinical trial
Participants	Country: Germany Number randomised: 128 Postrandomisation dropouts: 1 (0.8%) Revised sample size: 127 Average age: 61 years Women: 53 (41.7%) Number of cirrhotics: 0 (0%) Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): 3 Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: a number of parenchymal transection techniques 3. Fibrin glue: factor being randomised 4. Pharmacological methods: none 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: non-cirrhotic adult patients undergoing elective open liver resection Exclusion criteria 1. Coagulation disorders 2. Klatskin tumour 3. Participation in another clinical study within 30 d 4. Pregnancy or breastfeeding 5. Concurrent or previous therapy with systemic pharmacologic agents promoting blood clotting (including but not limited to tranexamic acid, activated factor VIII, and aprotinin) 6. Known allergy or hypersensitivity to human thrombin or to human fibrinogen or to riboflavin or to proteins of bovine origin. 7. Resection area estimated by operating surgeon to be less than 16 cm^2 8. An infected wound area 9. Persistent major bleeding or no bleeding after primary operative haemostatic procedures

Interventions	Participants were randomly assigned to 2 groups. Group 1: collagen (n = 62) Group 2: fibrin sealant (n = 65) Collagen: sangustop fleece (Aesculap AG) Fibrin sealant: Tachosil (Nycomed)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, number of serious adverse events, proportion of people with any adverse events, and number of adverse events
Notes	Authors provided replies in March 2016. Reasons for postrandomisation dropouts: the resection area was dry

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Lists with a block size of 4 were generated for each participating center prior to the initiation of the study using the Software RandList of the DatInf GmbH (Tübingen, Germany)"
Allocation concealment (selection bias)	Low risk	Quote: "A1:1 intraoperative randomization was performed using identical looking, sealed, and numbered opaque envelopes"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "ESSCALIVER is a single-blinded trial, i.e., patients were not informed about their assignment in order to increase reliability of secondary outcomes, assessed during the follow-up visits". Comment: healthcare providers were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Due to the appearance of the products used and the differences in their application, blinding of the primary outcome assessor was not possible"
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: the outcomes stated in the protocol wer reported.
Vested interest bias	High risk	Quote (author reply): "The study was sponsored by Aesculap AG (Tuttlingen , Germany). Clinical Monitoring and data management were contracted to Centrial GmbH (Tübingen, Germany). Statistical planning and analysis was performed by Dr.M.Koehler GmbH (Freiburg, Germany)"
Other bias	Low risk	Comment: no other bias

Muratore 2014

Methods	Randomised clinical trial
Participants	Country: Italy Number randomised: 100 Postrandomisation dropouts: 0 (0%) Revised sample size: 100 Average age: 65 years Women: 38 (38%) Number of cirrhotics: not stated Number of major liver resections: 10 (10%) Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: factor being randomised 3. Fibrin glue: none. 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: low central venous pressure 6. Autologous transfusion: not stated Inclusion criteria 1. Patients undergoing elective liver resection 2. Good hepatic function (Child Pugh - A or indocyanine green (ICG) clearance ≤ 15%) 3. Good cardiac and renal function Exclusion criteria 1. Clotting disorders 2. Requiring bile duct resection or vascular resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: clamp-crush method (n = 50) Group 2: radiofrequency dissecting sealer (n = 50) Radiofrequency dissecting sealer: ligasure (Covidien)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with any adverse events, operative blood loss, proportion of people requiring blood transfusion, and length of hospital stay
Notes	Authors provided replies in March 2016.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Patients were assigned to treatment at the ratio of 1:1 according to a computer-generated randomization list by means of STATA software (version 10©; StataCorp LP, College Station, TX, USA)".

Muratore 2014 (*Continued*)

Allocation concealment (selection bias)	Low risk	Quote (author reply): "The details of the randomization series were unknown to any of the invesigators and were contained in sealed envelopes, each bearing outside the name of the hospital and a number. After the patient was deemed resectable in the operating room, the numbered envelope was opened at the central office and the card inside told if the patient was kellyclasia or ligasure group. This information was given to the surgeon performing the operation"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote (author reply): "Patients and healthcare providers were blinded". Comment: further details were not available.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote (author reply): "Outcome assessors were not blinded".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "There were no postrandomisation dropouts".
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Low risk	Quote (author reply): "The study was funded by the participating hospitals"
Other bias	Low risk	Comment: no other bias

Ni 2013

Methods	Randomised clinical trial
Participants	Country: China Number randomised: 120 Postrandomisation dropouts: 0 (0%) Revised sample size: 120 Average age: 56 years Women: 28 (23.3%) Number of cirrhotics: 120 (100%) Number of major liver resections: 15 (12.5%) Number of right hepatectomies: 3 (2.5%) Follow-up (months): until discharge Further details of methods of liver resection: 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: clamp-crush method 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: low central venous pressure 6. Autologous transfusion: not stated

	Inclusion criteria 1. Elective liver resection 2. No major concomitant surgical procedures such as bowel or bile duct resection 3. Total or selective vascular inflow/outflow occlusion was not required because of the site or extent of tumour 4. Tumours which were located either in the right or left hemiliver 5. Extent of partial hepatectomy was a hemihepatectomy or less 6. Compensated cirrhosis with Child-Pugh class A or B 7. Eastern cooperative oncology group performance status 0-1
Interventions	Participants were randomly assigned to 2 groups. Group 1: continuous portal triad clamping (n = 60) Group 2: continuous selective portal triad clamping (n = 60)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, operative blood loss, proportion of people with major blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Low risk	Quote: "The patients were randomly assigned to the Pringle manoeuvre group or to the hemi-hepatic vascular inflow occlusion group by drawing sealed and opaque envelops from a box containing 120 prearranged envelopes"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Low risk	Quote: "This study was supported by the State Key Project on Infectious Diseases of China (2012ZX10002010,

Ni 2013 (*Continued*)

		2012ZX10002016), Nature Science Fund for Creative Research Groups, China (30921006,81221061,81201940) and Innovation Program of Shanghai Municipal Education Commission (09ZZ82)"
Other bias	Low risk	Comment: no other bias

Noun 1996

Methods	Randomised clinical trial
Participants	Country: France Number randomised: 82 Postrandomisation dropouts: not stated Revised sample size: 82 Average age: 51 years Women: 39 (47.6%) Number of cirrhotics: 7 (8.5%) Number of major liver resections: 34 (41.5%) Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: varied 2. Parenchymal transection: clamp-crush method or cavitron ultrasonic surgical aspirator 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing elective liver resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: fibrin sealant (n = 38) Group 2: control (n = 44) Fibrin sealant: Biocol
Outcomes	The outcomes reported were: proportion of people with serious adverse events, proportion of people with any adverse events, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), length of hospital stay, and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.

Noun 1996 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: participants were excluded from complications because drains were not inserted or drainage data was not available
Selective reporting (reporting bias)	High risk	Comment: mortality and severity of morbidity were not reported
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Ollinger 2013

Methods	Randomised clinical trial
Participants	Country: European multicentre trial Number randomised: 50 Postrandomisation dropouts: not stated Revised sample size: 50 Average age: 62 years Women: 20 (40%) Number of cirrhotics: 0 (0%) Number of major liver resections: 21 (42%) Number of right hepatectomies: 15 (30%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: varied 2. Parenchymal transection: not stated 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Non-urgent, open hepatic surgery 2. Age ≥ 18 years and had a target bleeding site of generalised minor or moderate bleeding that persisted on the cut surface of the liver in which haemostasis was not achieved utilising conventional methods and which necessitated the use of a topical haemostatic

Ollinger 2013 (*Continued*)

	Exclusion criteria 1. Laparoscopic procedure that would require the study treatment to be applied through a trocar 2. Were scheduled for a subsequent surgical procedure at the target bleeding site 3. Documented history of cirrhosis 4. Had severe coagulopathy 5. Had a total bilirubin level of ≥ 2.5 mg/dL 6. Had an active local infection at the target bleeding site 7. Were pregnant 8. Had a life expectancy of < 3 months 9. Had received a liver transplant 10. Had been treated with an investigational drug or device within 30 d of enrolment 11. Any incidental preoperative finding was deemed by the investigator to have potentially jeopardised the safety or welfare of the patient
Interventions	Participants were randomly assigned to 2 groups. Group 1: oxidised cellulose (n = 32) Group 2: fibrin sealant (n = 18) Oxidised cellulose: Veriset (Covidien) Fibrin sealant: Tachosil (Nycomed)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, quantity of blood transfused (red cell transfusion or whole blood), quantity of blood transfused (fresh frozen plasma) , length of hospital stay, length of intensive therapy unit stay, and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "This study was a prospective, non-inferiority, multicentre, twoarm, randomized, patient-blinded study to compare a haemostatic patch (Veriset™) with a fibrinogenand thrombin-coated collagen patch (TachoSil®; control) in the management of bleeding during hepatic surgery"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "This study was a prospective, non-inferiority, multicentre, twoarm, randomized, patient-blinded study to compare a haemostatic patch (Veriset™) with a fibrinogenand thrombin-coated collagen patch (TachoSil®; control) in the management of bleeding during hepatic surgery"

Ollinger 2013 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	High risk	Quote: "This study was sponsored by Covidien, Inc. ".
Other bias	Low risk	Comment: no other bias

Park 2012

Methods	Randomised clinical trial
Participants	Country: South Korea Number randomised: 53 Postrandomisation dropouts: 3 (5.7%) Revised sample size: 50 Average age: 31 years Women: 11 (22%) Number of cirrhotics: 0 (0%) Number of major liver resections: 50 (100%) Number of right hepatectomies: 50 (100%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: donors underwent right hemihepatectomy and recipients received right hemiliver grafts Exclusion criteria 1. Recipient had experienced fulminant hepatic failure 2. The graft-to-recipient body weight ratio (GRWR) was < 0.9% 3. A frozen biopsy sample from the donor liver showed > 30% macrovesicular steatosis before donor hemihepatectomy 4. The transplant was ABO-incompatible 5. The recipient had previously undergone organ transplantation 6. The recipient had undergone or was scheduled to undergo multiorgan transplantation
Interventions	Participants were randomly assigned to 2 groups. Group 1: intermittent portal triad clamping (n = 25) Group 2: control (n = 25) Intermittent portal triad clamping: 15 min on and 5 min off

Park 2012 (*Continued*)

Outcomes	The outcomes reported were: proportion of people with serious adverse events, operative blood loss, length of hospital stay, and operating time
Notes	Reasons for postrandomisation dropouts: graft-to-recipent body weight ratio < 0.9%

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The donor-recipient pairs were randomized (1:1) into 2 groups (IHIO and control groups) at the time of anesthesia induction for donors via the extraction of a black or white (but otherwise identical) stone from an unseen box" Comment: IHIO: intermittent hepatic inflow occlusion
Allocation concealment (selection bias)	Low risk	Quote: "The donor-recipient pairs were randomized (1:1) into 2 groups (IHIO and control groups) at the time of anesthesia induction for donors via the extraction of a black or white (but otherwise identical) stone from an unseen box"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported adequately
Vested interest bias	Low risk	Quote: "This study was funded by the Clinical Research Development Program (CRS1091811)"
Other bias	Low risk	Comment: no other bias

Pietsch 2010

Methods	Randomised clinical trial
Participants	Country: Germany Number randomised: 25 Postrandomisation dropouts: not stated Revised sample size: 25 Average age: 56 years

Pietsch 2010 (*Continued*)

	Women: 11 (44%) Number of cirrhotics: not stated Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing elective liver resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: continuous portal triad clamping (n = 14) Group 2: control (n = 11)
Outcomes	The outcomes reported were: operative blood loss and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Porte 2012

Methods	Randomised clinical trial
Participants	Country: Netherlands Number randomised: 56 Postrandomisation dropouts: not stated Revised sample size: 56 Average age: 61 years Women: 20 (35.7%) Number of cirrhotics: not stated Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: factor being randomised 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing liver resection and having diffuse bleeding
Interventions	Participants were randomly assigned to 2 groups. Group 1: fibrin sealant (n = 39) Group 2: gelatin (n = 17) Fibrin sealant: Fibrocaps (ProFibrix)
Outcomes	None of the outcomes of interest were reported.
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.

Porte 2012 (*Continued*)

Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Rahbari 2014

Methods	Randomised clinical trial
Participants	Country: Germany Number randomised: 130 Postrandomisation dropouts: 0 (0%) Revised sample size: 130 Average age: 61 years Women: 60 (46.2%) Number of cirrhotics: 2 (1.5%) Number of major liver resections: 73 (56.2%) Number of right hepatectomies: 43 (33.1%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: variable 3. Fibrin glue: variable 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: low central venous pressure 6. Autologous transfusion: not stated Inclusion criteria 1. Patients undergoing liver resection 2. A minimum age of 18 years 3. Feasibility of stapler and clamp-crushing transection techniques based on preoperative imaging (absence of a fairly curved or angled resection line) Exclusion criteria 1. Concomitant extrahepatic resection was planned 2. Already participating in concurrent intervention trials 3. Expected lack of compliance were also excluded 4. Impaired mental state or language difficulties
Interventions	Participants were randomly assigned to 2 groups. Group 1: clamp-crush method (n = 65) Group 2: stapler resection (n = 65) Stapler: Autosuture EndoGIA stapler (Covidien)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, operative blood loss, quantity of blood transfused (red cell transfusion or whole blood), quantity of blood transfused (fresh frozen plasma), length of hospital stay, length of intensive therapy unit stay, and operating time

Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A block randomisation list is generated by the Institute for Medical Biometrics and Informatics (IMBI) applying SAS (SAS™ Version 9.1., SAS Institute Inc., Cary, USA) "
Allocation concealment (selection bias)	Low risk	Quote: "Randomization was carried out during surgery using consecutively numbered opaque and sealed envelopes, once the operating surgeon had confirmed resectability"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Patients were blinded to the study intervention. Blinding of the staff in the operating room was not feasible"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Therefore, a third party blinded to the allocated treatment group assessed postoperative outcomes"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	High risk	Quote: "The trial was funded by the Department of General, Visceral and Transplant Surgery, University of Heidelberg, Germany. M.K., P.S., M.W.B and J.W. received speaker's honoraria from Covidien"
Other bias	Low risk	Comment: no other bias

Rau 2001

Methods	Randomised clinical trial
Participants	Country: Germany Number randomised: 61 Postrandomisation dropouts: not stated Revised sample size: 61 Average age: 62 years Women: 25 (41%) Number of cirrhotics: not stated Number of major liver resections: 24 (39.3%) Number of right hepatectomies: not stated

	Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: portal triad clamping 2. Parenchymal transection: factor being randomised 3. Fibrin glue: variable 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Liver resection for liver metastases 2. Parenchymal hepatic resection rate < 50% 3. Child-Pugh class A
Interventions	Participants were randomly assigned to 2 groups. Group 1: cavitron ultrasonic surgical aspirator (n = 30) Group 2: hydrojet (n = 31) Hydrojet: jet cutter
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, operative blood loss, quantity of blood transfused (red cell transfusion or whole blood)
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	High risk	Comment: severity of postoperative morbidity was not reported
Vested interest bias	Unclear risk	Comment: this information was not available.

Rau 2001 (*Continued*)

Other bias	Low risk	Comment: no other bias

Savlid 2013

Methods	Randomised clinical trial
Participants	Country: Sweden Number randomised: 100 Postrandomisation dropouts: 0 (0%) Revised sample size: 100 Average age: 65 years Women: 41 (41%) Number of cirrhotics: 2 (2%) Number of major liver resections: 71 (71%) Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: variable 2. Parenchymal transection: factor being randomised 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Patients undergoing elective liver resection (removal of 2 or more segments) 2. Feasible to use cavitron ultrasonic surgical aspirator or stapler
Interventions	Participants were randomly assigned to 2 groups. Group 1: cavitron ultrasonic surgical aspirator (n = 50) Group 2: stapler resection (n = 50) Stapler: Endostapler (Covidien)
Outcomes	The outcomes reported were: short-term mortality, number of serious adverse events, number of adverse events, operative blood loss, quantity of blood transfused (red cell transfusion or whole blood), length of hospital stay, and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "The randomization was completed by the use of opaque, sealed envelopes with computer-generated random numbers in blocks of 10 (5:5)"

Savlid 2013 (*Continued*)

Allocation concealment (selection bias)	Low risk	Quote: "The randomization was completed by the use of opaque, sealed envelopes with computer-generated random numbers in blocks of 10 (5:5)"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	High risk	Quote: "This study was supported by an unconditional research grant by Covidien Sweden AB "
Other bias	Low risk	Comment: no other bias

Shao 2006

Methods	Randomised clinical trial
Participants	Country: Asian multicentre trial Number randomised: 235 Postrandomisation dropouts: 14 (6%) Revised sample size: 221 Average age: 52 years Women: 38 (17.2%) Number of cirrhotics: 231 (104.5%) Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: factor being randomised 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: cirrhotic patients (> 21 years of age) scheduled for partial hepatectomy as a result of liver cancer or benign tumors (> 5 cm, involving ≥ 2 segments or located centrally) Exclusion criteria 1. History of portal vein thrombosis

	2. Documented deep vein thrombosis 3. Symptoms of severe cardiovascular disease 4. Previous myocardial/pulmonary infarction or stroke 5. Renal insufficiency requiring dialysis 6. Use of anticoagulation therapy within 48 h of surgery 7. Life expectancy of less than 1 month owing to known metastasis 8. Other major abdominal surgery planned during the partial hepatectomy 9. Synchronous liver and intestinal resections 10. Previous partial hepatectomy
Interventions	Participants were randomly assigned to 2 groups. Group 1: control (n = 76) Group 2: recombinant factor via (n = 155) Recombinant factor VIIa: brand not stated Dose: 50 or 100 mcg/kg before skin incision over 2 min and repeated every 2 h until a maximum of 4 doses Control: placebo
Outcomes	The outcomes reported were: proportion of people with serious adverse events, number of serious adverse events, proportion of people with any adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), quantity of blood transfused (platelets), and quantity of blood transfused (fresh frozen plasma)
Notes	Reasons for postrandomisation dropouts: did not receive intervention (n = 11); lost-to follow-up (n = 2); withdrew consent (n = 1)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "A multicenter, randomized, double-blind, placebo-controlled trial". Comment: further information on blinding was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "a multicenter, randomized, double-blind, placebo-controlled trial". Comment: further information on blinding was not available.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.

Shao 2006 (*Continued*)

Selective reporting (reporting bias)	High risk	Comment: mortality was not reported.
Vested interest bias	High risk	Comment: one of the co-authors belonged to a pharmaceutical industry
Other bias	Low risk	Comment: no other bias

Shimada 1994

Methods	Randomised clinical trial
Participants	Country: Japan Number randomised: 24 Postrandomisation dropouts: not stated Revised sample size: 24 Average age: 63 years Women: 4 (16.7%) Number of cirrhotics: 13 (54.2%) Number of major liver resections: 10 (41.7%) Number of right hepatectomies: 9 (37.5%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: factor being randomised 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients with hepatocellular carcinoma undergoing liver resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: antithrombin iii (n = 13) Group 2: control (n = 11) Antithrombin concentrate: 1500 IU IV over 30 min: immediately before the operation, just before hepatic division, and immediately after operation
Outcomes	The outcomes reported were: proportion of people with serious adverse events, proportion of people with any adverse events, operative blood loss, quantity of blood transfused (red cell transfusion or whole blood), and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.

Shimada 1994 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	High risk	Comment: mortality and severity of morbidity were nor reported
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Si-Yuan 2014

Methods	Randomised clinical trial
Participants	Country: China Number randomised: 160 Postrandomisation dropouts: 0 (0%) Revised sample size: 160 Average age: 49 years Women: 36 (22.5%) Number of cirrhotics: 98 (61.3%) Number of major liver resections: 112 (70%) Number of right hepatectomies: 53 (33.1%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: factor being randomised 2. Parenchymal transection: not stated 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: low central venous pressure 6. Autologous transfusion: not stated Inclusion criteria 1. Patients who were surgically fit to receive partial hepatectomy 2. Resectable tumour which had invaded one or more major hepatic vein or was adjacent to the hepatocaval junction 3. No other concomitant major surgical procedures such as bowel or bile duct resection 4. No tumour invasion of IVC

	5. Child-Pugh class A or B 6. Patient aged between 16 and 65 years
Interventions	Participants were randomly assigned to 2 groups. Group 1: continuous portal triad clamping (n = 80) Group 2: continuous selective hepatic vascular exclusion (n = 80)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, operative blood loss, proportion of people with major blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), length of hospital stay, length of intensive therapy unit stay, operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Low risk	Quote: "All eligible patients were randomly assigned to the Pringle manoeuvre and selective hepatic vascular occlusion group by drawing sealed, consecutively numbered, and opaque envelopes after abdominal exploration had confirmed resectability"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Smyrniotis 2005

Methods	Randomised clinical trial
Participants	Country: Greece Number randomised: 82 Postrandomisation dropouts: 0 (0%) Revised sample size: 82 Average age: 64 years Women: 17 (20.7%) Number of cirrhotics: 12 (14.6%) Number of major liver resections: 60 (73.2%) Number of right hepatectomies: 31 (37.8%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: selective hepatic vascular exclusion 2. Parenchymal transection: factor being randomised 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: low central venous pressure 6. Autologous transfusion: not stated Inclusion criteria: patients who underwent liver resection for benign or malignant tumours
Interventions	Participants were randomly assigned to 2 groups. Group 1: sharp transection (n = 41) Group 2: clamp-crush method (n = 41) Sharp transection: using scalpel
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, proportion of people with any adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), length of hospital stay, length of intensive therapy unit stay, and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.

Smyrniotis 2005 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

Takayama 2001

Methods	Randomised clinical trial
Participants	Country: Japan Number randomised: 132 Postrandomisation dropouts: 0 (0%) Revised sample size: 132 Average age: 62 years Women: not stated Number of cirrhotics: 45 (34.1%) Number of major liver resections: 43 (32.6%) Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: intermittent total or selective portal triad clamping 2. Parenchymal transection: factor being randomised 3. Fibrin glue: used 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria 1. Partial hepatectomy for tumor resection or graft harvest 2. Hepatic function of Child-Pugh class A or B 3. Acceptable clotting profile 4. Adequate functional reserve of the heart, lungs, and kidneys
Interventions	Participants were randomly assigned to 2 groups. Group 1: cavitron ultrasonic surgical aspirator (n = 66) Group 2: clamp-crush method (n = 66)
Outcomes	The outcomes reported were: short-term mortality, proportion of people with serious adverse events, number of serious adverse events, proportion of people with any adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, length of hospital stay

Takayama 2001 (*Continued*)

Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Unclear risk	Comment: mortality and morbidity were reported.
Vested interest bias	Unclear risk	Quote: "This work was supported in part by a grant-in-aid for cancer research from the Ministry of Health and Welfare, Tokyo, Japan". Comment: only part of the funding information was available.
Other bias	Low risk	Comment: no other bias

Wang 2006

Methods	Randomised clinical trial
Participants	Country: China Number randomised: 52 Postrandomisation dropouts: 2 (3.8%) Revised sample size: 50 Average age: 46 years Women: 10 (20%) Number of cirrhotics: 29 (58%) Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: varied

Wang 2006 (*Continued*)

	2. Parenchymal transection: clamp-crush 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: factor being randomised 6. Autologous transfusion: not stated Inclusion criteria: patients with hepatocellular carcinoma undergoing liver resection
Interventions	Participants were randomly assigned to 2 groups. Group 1: low central venous pressure (n = 25) Group 2: control (n = 25) Low central venous pressure: by limiting fluid, nitroglycerine, and furosemide
Outcomes	The outcomes reported were: proportion of people with any adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), quantity of blood transfused (fresh frozen plasma) , length of hospital stay, and operating time
Notes	Reasons for postrandomisation dropouts: hepatectomy was not performed because of cardiac arrest or because it was not possible to demarcate the tumour

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Quote: "By the sealed envelope method, the patients were blindly randomized into Lcentral venous pressure group (n = 25) and control group (n = 27) at the beginning of the operation". Comment: further details of sealed envelope method were not available
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were postrandomisation dropouts.
Selective reporting (reporting bias)	High risk	Comment: mortality and severity of morbidity were not reported
Vested interest bias	Unclear risk	Comment: this information was not available.

Wang 2006 (*Continued*)

Other bias	Low risk	Comment: no other bias

Wong 2003

Methods	Randomised clinical trial
Participants	Country: Hong Kong, China Number randomised: 60 Postrandomisation dropouts: 0 (0%) Revised sample size: 60 Average age: 51 years Women: 23 (38.3%) Number of cirrhotics: 23 (38.3%) Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: varied 2. Parenchymal transection: cavitron ultrasonic surgical aspirator 3. Fibrin glue: not stated 4. Pharmacological methods: factor being randomised 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: adult patients scheduled for hepatectomy Exclusion criteria 1. Patients with coronary artery disease 2. Congenital or acquired coagulation disorders other than liver cirrhosis 3. Blood sodium level < 130 mmol/L 4. Non-steroidal anti-inflammatory drug or aspirin ingestion within seven d of scheduled surgery 5. History of thrombovascular disorders or pulmonary thromboembolism
Interventions	Participants were randomly assigned to 2 groups. Group 1: desmopressin (n = 30) Group 2: control (n = 30) Desmopressin: 30 mcg/kg shortly after induction Control: placebo
Outcomes	The outcomes reported were: operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (fresh frozen plasma), and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Wong 2003 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Quote: "Patient randomization was by drawing a sealed envelope specifying a prescription for either desmopressin or placebo, which was then prepared by an independent investigator and blinded to the patient, attending anesthesiologist and surgeon". Comment: further details of sealed envelope method were not available
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Patient randomization was by drawing a sealed envelope specifying a prescription for either desmopressin or placebo, which was then prepared by an independent investigator and blinded to the patient, attending anesthesiologist and surgeon"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Patient randomization was by drawing a sealed envelope specifying a prescription for either desmopressin or placebo, which was then prepared by an independent investigator and blinded to the patient, attending anesthesiologist and surgeon"
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: 1 patient who had heavy bleeding in control group was excluded for blood loss
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Low risk	Quote: "This study was supported by a Hong Kong University CRCG grant (10202115/20013/20100/323/01)"
Other bias	Low risk	Comment: no other bias

Wu 2002

Methods	Randomised clinical trial
Participants	Country: Taiwan Number randomised: 58 Postrandomisation dropouts: 0 (0%) Revised sample size: 58 Average age: 55 years Women: 10 (17.2%) Number of cirrhotics: 58 (100%) Number of major liver resections: 20 (34.5%) Number of right hepatectomies: 0 (0%) Follow-up (months): until discharge Further details of methods of liver resection

	1. Vascular occlusion: factor being randomised 2. Parenchymal transection: clamp-crush method 3. Fibrin glue: not stated 4. Pharmacological methods: not stated 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: cirrhotic patients who had no previous biliary operations and no preoperative therapies and whose main tumour was located at the central portion of the liver (defined as Couinaud segments 4, 5, and 8) without having directly invaded the hepatic hilar plate Exclusion criteria 1. Patients requiring extended right or left hepatectomy 2. Patients requiring hepatic vascular exclusion
Interventions	Participants were randomly assigned to 2 groups. Group 1: intermittent portal triad clamping (n = 28) Group 2: intermittent selective portal triad clamping (n = 30) Intermittent portal triad clamping: 15 min on and 5 min off Intermittent selective portal triad clamping: 30 min on and 5 min off
Outcomes	The outcomes reported were: short-term mortality, number of serious adverse events, proportion of people with any adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, quantity of blood transfused (red cell transfusion or whole blood), length of hospital stay, and operating time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Quote: "If the tumour condition and procedures fulfilled the aforementioned criteria, randomization was performed by opening a sealed envelope after the abdomen was explored". Comment: further details of sealed envelope method were not available
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.

Wu 2002 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts.
Selective reporting (reporting bias)	Low risk	Comment: mortality and morbidity were reported.
Vested interest bias	Low risk	Quote: "This study was supported in part by grant NSC 902314-075A-018 from the National Science Council, Taipei, Taiwan"
Other bias	Low risk	Comment: no other bias

Wu 2006

Methods	Randomised clinical trial
Participants	Country: Taiwan Number randomised: 217 Postrandomisation dropouts: 3 (1.4%) Revised sample size: 214 Average age: 60 years Women: 57 (26.6%) Number of cirrhotics: 110 (51.4%) Number of major liver resections: 38 (17.8%) Number of right hepatectomies: 18 (8.4%) Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: varied 2. Parenchymal transection: clamp-crush method 3. Fibrin glue: not stated 4. Pharmacological methods: factor being randomised 5. Cardiopulmonary methods: not stated 6. Autologous transfusion: not stated Inclusion criteria: patients undergoing liver resections
Interventions	Participants were randomly assigned to 2 groups. Group 1: tranexamic acid (n = 108) Group 2: control (n = 106) Tranexamic acid: 500 mg just before the surgery followed by 250 4 times a day for 3 d
Outcomes	The outcomes reported were: short-term mortality, number of serious adverse events, proportion of people with any adverse events, number of adverse events, operative blood loss, proportion of people requiring blood transfusion, length of hospital stay, and operating time
Notes	Reasons for postrandomisation dropouts: liver resection not completed because of presence of more extensive disease

Risk of bias

Wu 2006 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Quote: "The randomization was double-blinded in a sealed envelope". Comment: further details of sealed envelope method were not available
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Neither surgeons nor medical staffs knew whether patients were enrolled in group A or group B "
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Neither surgeons nor medical staffs knew whether patients were enrolled in group A or group B "
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: although there were 3 postrandomisation drop-outs, this was because liver resection could not be carried out
Selective reporting (reporting bias)	High risk	Comment: severity of morbidity was not reported.
Vested interest bias	Unclear risk	Quote: "Supported in part by a grant from National Science Council, Taiwan (No. 92-2314-B-075A-006) ". Comment: only part of the funding information was available.
Other bias	Low risk	Comment: no other bias

Yao 2006

Methods	Randomised clinical trial
Participants	Country: China Number randomised: 30 Postrandomisation dropouts: not stated Revised sample size: 30 Average age: not stated Women: 14 (46.7%) Number of cirrhotics: not stated Number of major liver resections: not stated Number of right hepatectomies: not stated Follow-up (months): until discharge Further details of methods of liver resection 1. Vascular occlusion: not stated 2. Parenchymal transection: not stated 3. Fibrin glue: not stated

	4. Pharmacological methods: not stated 5. Cardiopulmonary methods: factor being randomised 6. Autologous transfusion: not stated Inclusion criteria 1. Patients undergoing liver resection for tumours 2. Good heart, liver, kidney, and coagulation function
Interventions	Participants were randomly assigned to 3 groups. Group 1: acute normovolemic haemodilution (n = 10) Group 2: acute normovolemic haemodilution with hypotension (n = 10) Group 3: control (n = 10) Acute normovolemic haemodilution: withdrawal of blood and replacement with fluids to maintain a target haematocrit of 30% Acute normovolemic haemodilution With controlled hypotension: in addition to acute normovolemic haemodilution, sodium nitroprusside was used; target blood pressure not known
Outcomes	The outcomes reported were: operative blood lossand quantity of blood transfused (red cell transfusion or whole blood)
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: this information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: this information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: this information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: this information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: this information was not available.
Selective reporting (reporting bias)	High risk	Comment: mortality and morbidity were not reported.
Vested interest bias	Unclear risk	Comment: this information was not available.
Other bias	Low risk	Comment: no other bias

ABO: blood group incompatible; **ASA**: American Society of Anesthesiologists; **HCC**: hepatocellular carcinoma; **INR**: international normalised ratio; **IU**: international unit; **IVC**: infrahepatic inferior vena cava; **kIU**: kilo international units.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Arru 2007	Not a randomised clinical trial
Azoulay 2005	Not a randomised clinical trial
Bellolio 2012	Not a randomised clinical trial
Beppu 2012	Not a randomised clinical trial
Broek 2011	Comparison of 2 methods of intermittent Pringle manoeuvre of different duration
Chapman 2007	Variations of thrombin
Correa-Gallego 2015	Not an intervention targeted at decreasing blood loss
Dello 2012	Comparison of 2 different methods of intermittent portal triad clamping
Dominioni 2014	Not a randomised clinical trial
El-Moghazy 2009	Comparison of minor variations of same transection method
Esaki 2006	Comparison of 2 different methods of intermittent portal triad clamping
Feldheiser 2015	Not an intervention targeted at decreasing blood loss
Figueras 2003	Not a comparison with main focus on blood loss
Frankel 2013	Different methods of selection for acute normovolemic haemodilution
Gonzalez 2009	Comment on Figueras 2007
Gotohda 2015	Different methods of treatment of raw surface were allowed in control group
Grobmyer 2009	The intervention was started 1 day after operation and used only in selected patients undergoing surgery
Hamady 2015	Comment on an excluded trial (Rahbari 2011)
Hanyong 2015	Vascular occlusion was used in only method of parenchymal transection
Harimoto 2011	Different methods of suturing on the raw surface of the liver

(*Continued*)

Hashimoto 2007	Different methods of autologous blood donation (pre-operative or pre-operative + intra-operative)
Kaibori 2013	Variations in cavitron ultrasonic surgical aspirator technique
Kim 2007	Comparison of 2 different methods of intermittent portal triad clamping
Kim 2008	Not a randomised clinical trial
Le Treut 1995	Not a randomised clinical trial
Levit 2012	Comparison of interventions that were not of interest for this review
Li 2013	In the control group, 2 different forms of vascular occlusion were used
Li 2015	Not a randomised clinical trial
Lu 2014	Low central venous pressure was used in fast-track group, but this was combined with a number of other measures in the intervention group only
Man 2002	Not a randomised clinical trial
Nagano 2009	Not a randomised clinical trial
Narita 2012	Not a randomised clinical trial
NCT01651182	Not a randomised clinical trial
Obiekwe 2014	Quasi-randomised study (alternate assignment)
Palibrk 2012	Not a randomised clinical trial
Petras 2009	Comment on Richter 2009
Petrowsky 2006	Ischaemic preconditioning was applied only in 1 group
Rahbari 2011	Different methods of achieving low central venous pressure
Rau 1995	Started as a randomised clinical trial but did not continue because of problems with nozzles of jet cutter. So, the report consisted of non-randomised patients
Richter 2009	In this randomised clinical trial, if the patients did not undergo liver resection, the envelopes were resealed and returned to the pool of sealed envelopes. The allocation concealment is not adequate in this trial
Ryu 2010	Comparison of different methods of low central venous pressure
Saiura 2006	Comparison of variations in clamp-crush method
Saiura 2014	Comparison of variations in clamp-crush method

(*Continued*)

Schilling 2009	Comment on Richter 2009
Schwartz 2004	In the control group a number of topical haemostatic agents were used
Shu 2014	In this study, patients were divided into 4 groups - people who received blood transfusion and ulinastatin, people who received blood transfusion but not ulinastatin, people who received ulinastatin but not blood transfusion, and people who did not receive blood transfusion or ulinastatin. Although the authors randomised patients to ulinastatin or control, they ensured that the number of patients in each group was the same, i. e. the number of people in ulinastatin group who received blood transfusion was 50% and the number of people in control group who received blood transfusion was 50%. This would have seriously impaired the randomisation to the extent that we feel that this is not a randomised clinical at all
Si-Yuan 2011	Used continuous and intermittent portal triad clamping depending upon transection time with vascular occlusion being the factor randomised
Smyrniotis 2002	Quasi-randomised (random sequence generated by hospital number)
Smyrniotis 2003a	Quasi-randomised (random sequence generated by hospital number)
Smyrniotis 2003b	Quasi-randomised (random sequence generated by hospital number)
Smyrniotis 2006	Ischaemic preconditioning was applied to only one of the groups
Standl 1998	Variations in autologous blood donation
Strobel 2012	Commentary on Lee 2012
Strobel 2014	Commentary on Rahbari 2014
Takatsuki 2015	Not a randomised clinical trial
Torzilli 2008	Variations in clamp-crush method
Vlad 2014	Not a randomised clinical trial
Wang 2010	Not a randomised clinical trial
Wang 2011	Not a randomised clinical trial
Yang 2012	Not a randomised clinical trial
Yang 2013	Variations in selective hepatic vascular exclusion
Yin 2003	Not a randomised clinical trial
Zhang 2014	Variations in portal triad clamping

(*Continued*)

Zhu 2012	Different methods of low central venous pressure

Characteristics of studies awaiting assessment *[ordered by study ID]*

Bochicchio 2015

Methods	Randomised clinical trial
Participants	Patients undergoing different types of surgical procedures
Interventions	Fibrin sealant versus gelatin
Outcomes	Adverse events
Notes	Attempts were made to contact the authors in September 2016.

Chapman 2006

Methods	Randomised clinical trial
Participants	Patients undergoing different types of surgical procedures
Interventions	Recombinant thrombin versus placebo
Outcomes	Adverse events
Notes	Attempts were made to contact the authors in September 2016.

Wright 2015

Methods	Randomised clinical trial
Participants	Adult patients undergoing major oncologic surgery
Interventions	Pre-operative tranexamic acid
Outcomes	Proportion requiring transfusion
Notes	We were unable to obtain further contact details of the author from the institution

Characteristics of ongoing studies *[ordered by study ID]*

Chen 2015

Trial name or title	Usefulness of BiClamp forceps for liver resection: a randomized clinical trial
Methods	Randomised clinical trial
Participants	Inclusion criteria 1. Above 18 years of age 2. Elective hepatic resection due to benign or malignant hepatobiliary disease 3. Child-Pugh class A or B liver function 4. Informed consent Exclusion criteria 1. Participation in concurrent intervention trials with interference in the outcome of this study. Laparoscopic hepatectomy. 2. Preoperative liver function evaluation: Child-Pugh class C 3. Lack of compliance 4. Pregnancy or lactation
Interventions	BiClamp forceps versus clamp-crush methods for liver parenchymal transection
Outcomes	Primary outcome: total intraoperative blood loss Secondary outcomes • Operation time • Duration of postoperative hospital stay • Mortality • Postoperative morbidity
Starting date	1 October 2014
Contact information	Jiang-ming Chen (email: chenjm10@126.com)
Notes	NCT02197481

Schmidt 2008

Trial name or title	Influence of two different resection techniques (conventional liver resection versus anterior approach) of liver metastases from colorectal cancer on hematogenous tumor cell dissemination - prospective randomized multicenter trial
Methods	Randomised clinical trial
Participants	Inclusion criteria • Patients being considered for a potentially curative (R0) right hepatectomy, extended right hepatectomy, or right trisegmentectomy for colorectal liver metastases • Age ≥ 18 years • Absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol, follow-up schedules or from signing informed consent • No evidence of active or former concurrent malignant diseases (except non-melanous skin cancer) Exclusion criteria

Schmidt 2008 (*Continued*)

	• Any extrahepatic disease, even if this will be resected concomitantly • Liver cirrhosis • Grossly positive lymph nodes in the hepatoduodenal ligament • Positive margins after liver resection (R1) • Patients with an intraoperative blood loss of ≥ 2000 cc will be excluded from the analysis of tumour cell detection in blood samples but will be included in the rest of the analyses
Interventions	Anterior approach versus conventional approach
Outcomes	• Overall survival • Blood loss • Duration time of resection • Number of blood products transfused • Postoperative complications
Starting date	Not stated
Contact information	J Weitz (email: jeurgen.weitz@med.uni-heidelberg.ed
Notes	ISN45066244

DATA AND ANALYSES

Comparison 1. Anterior approach vs conventional approach

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality (perioperative)	2		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Anterior approach vs conventional approach	2	185	Odds Ratio (M-H, Fixed, 95% CI)	0.27 [0.05, 1.32]
2 Serious adverse events (proportion)	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 Anterior approach vs conventional approach	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Adverse events (proportion)	2		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Anterior approach vs conventional approach	2	185	Odds Ratio (M-H, Fixed, 95% CI)	0.89 [0.48, 1.64]
4 Adverse events (number)	1		Rate Ratio (Fixed, 95% CI)	Totals not selected
4.1 Anterior approach vs conventional approach	1		Rate Ratio (Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Blood transfusion (proportion)	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 Anterior approach vs conventional approach	2	185	Odds Ratio (M-H, Random, 95% CI)	0.60 [0.05, 6.74]
6 Major blood loss (proportion)	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 Anterior approach vs conventional approach	2	185	Odds Ratio (M-H, Random, 95% CI)	0.56 [0.09, 3.41]

Comparison 2. Autologous blood donation vs control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Adverse events (proportion)	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Autologous blood donation vs control	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Blood transfusion (proportion)	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 Autologous blood donation vs control	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Blood transfusion (red blood cell)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Autologous blood donation vs control	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Blood loss	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.1 Autologous blood donation vs control	2	70	Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.37, 0.34]
5 Major blood loss (proportion)	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

5.1 Autologous blood donation vs control	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Total hospital stay	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1 Autologous blood donation vs control	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Operating time	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 Autologous blood donation vs control	2	70	Mean Difference (IV, Fixed, 95% CI)	-3.79 [-34.28, 26.70]

Comparison 3. Cardiopulmonary interventions

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality (perioperative)	4		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Hypoventilation vs control	1	79	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Low central venous pressure vs control	1	85	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure	2	208	Odds Ratio (M-H, Fixed, 95% CI)	2.91 [0.29, 28.70]
2 Serious adverse events (proportion)	2		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 Hypoventilation vs control	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Serious adverse events (number)	2		Rate Ratio (Fixed, 95% CI)	Totals not selected
3.1 Low central venous pressure vs control	1		Rate Ratio (Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure	1		Rate Ratio (Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Adverse events (proportion)	4		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Hypoventilation vs control	1	79	Odds Ratio (M-H, Fixed, 95% CI)	1.33 [0.53, 3.34]
4.2 Low central venous pressure vs control	1	50	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.21, 3.03]
4.3 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure	2	208	Odds Ratio (M-H, Fixed, 95% CI)	0.68 [0.37, 1.23]
5 Adverse events (number)	2		Rate Ratio (Fixed, 95% CI)	Totals not selected
5.1 Low central venous pressure vs control	1		Rate Ratio (Fixed, 95% CI)	0.0 [0.0, 0.0]

5.2 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure	1		Rate Ratio (Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Blood transfusion (proportion)	6		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Hypoventilation vs control	1	79	Odds Ratio (M-H, Fixed, 95% CI)	0.71 [0.15, 3.40]
6.2 Low central venous pressure vs control	3	175	Odds Ratio (M-H, Fixed, 95% CI)	0.49 [0.21, 1.13]
6.3 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure	2	208	Odds Ratio (M-H, Fixed, 95% CI)	3.09 [1.49, 6.42]
7 Blood transfusion (red blood cell)	6		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 Acute normovolemic haemodilution vs control	1	20	Mean Difference (IV, Fixed, 95% CI)	-1.25 [-1.74, -0.75]
7.2 Acute normovolemic haemodilution plus hypotension vs control	1	20	Mean Difference (IV, Fixed, 95% CI)	-1.66 [-2.05, -1.28]
7.3 Acute normovolemic haemodilution plus low central venous pressure vs control	1	30	Mean Difference (IV, Fixed, 95% CI)	0.27 [0.02, 0.51]
7.4 Low central venous pressure vs control	2	90	Mean Difference (IV, Fixed, 95% CI)	-1.60 [-2.26, -0.93]
7.5 Acute normovolemic haemodilution plus hypotension vs acute normovolemic haemodilution	1	20	Mean Difference (IV, Fixed, 95% CI)	-0.42 [-0.74, -0.10]
7.6 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure	2	208	Mean Difference (IV, Fixed, 95% CI)	0.16 [-0.63, 0.95]
8 Blood transfusion (fresh frozen plasma)	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.1 Low central venous pressure vs control	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Blood transfusion (cryoprecipitate)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
9.1 Hypoventilation vs control	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Blood loss	9		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.1 Acute normovolemic haemodilution vs control	1	20	Mean Difference (IV, Fixed, 95% CI)	0.00 [-0.10, 0.11]
10.2 Acute normovolemic haemodilution plus hypotension vs control	1	20	Mean Difference (IV, Fixed, 95% CI)	-0.25 [-0.36, -0.14]

10.3 Acute normovolemic haemodilution plus low central venous pressure vs control	1	30	Mean Difference (IV, Fixed, 95% CI)	0.02 [-0.03, 0.08]
10.4 Hypoventilation vs control	1	79	Mean Difference (IV, Fixed, 95% CI)	0.0 [-1.12, 1.12]
10.5 Low central venous pressure vs control	4	237	Mean Difference (IV, Fixed, 95% CI)	-0.34 [-0.47, -0.22]
10.6 Acute normovolemic haemodilution plus hypotension vs acute normovolemic haemodilution	1	20	Mean Difference (IV, Fixed, 95% CI)	-0.25 [-0.39, -0.11]
10.7 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure	2	208	Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.32, 0.15]
11 Major blood loss (proportion)	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
11.1 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Hospital stay	5		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
12.1 Hypoventilation vs control	1	79	Mean Difference (IV, Fixed, 95% CI)	0.0 [-3.79, 3.79]
12.2 Low central venous pressure vs control	3	197	Mean Difference (IV, Fixed, 95% CI)	-2.43 [-3.93, -0.94]
12.3 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure	1	130	Mean Difference (IV, Fixed, 95% CI)	0.0 [-2.96, 2.96]
13 Operating time	7		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.1 Acute normovolemic haemodilution plus low central venous pressure vs control	1	40	Mean Difference (IV, Fixed, 95% CI)	-17.0 [-42.78, 8.78]
13.2 Hypoventilation vs control	1	79	Mean Difference (IV, Fixed, 95% CI)	0.0 [-88.21, 88.21]
13.3 Low central venous pressure vs control	4	192	Mean Difference (IV, Fixed, 95% CI)	-17.41 [-31.14, -3.67]
13.4 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure	3	248	Mean Difference (IV, Fixed, 95% CI)	13.63 [-4.11, 31.38]

Comparison 4. Methods of parenchymal transection

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality (perioperative)	11		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Cavitron ultrasonic surgical aspirator vs clamp-crush method	2	172	Odds Ratio (M-H, Fixed, 95% CI)	0.18 [0.01, 4.01]
1.2 Radiofrequency dissecting sealer vs clamp-crush method	5	390	Odds Ratio (M-H, Fixed, 95% CI)	1.85 [0.38, 8.97]
1.3 Sharp transection method vs clamp-crush method	1	82	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.4 Stapler vs clamp-crush method	1	130	Odds Ratio (M-H, Fixed, 95% CI)	2.07 [0.36, 11.69]
1.5 Hydrojet vs cavitron ultrasonic surgical aspirator	2	111	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.19, 5.17]
1.6 Radiofrequency dissecting sealer vs cavitron ultrasonic surgical aspirator	2	90	Odds Ratio (M-H, Fixed, 95% CI)	0.66 [0.11, 4.05]
1.7 Stapler vs cavitron ultrasonic surgical aspirator	1	100	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.8 Radiofrequency dissecting sealer vs hydrojet	1	50	Odds Ratio (M-H, Fixed, 95% CI)	0.18 [0.01, 4.04]
2 Serious adverse events (proportion)	7		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Cavitron ultrasonic surgical aspirator vs clamp-crush method	2	172	Odds Ratio (M-H, Fixed, 95% CI)	0.35 [0.09, 1.35]
2.2 Radiofrequency dissecting sealer vs clamp-crush method	3	240	Odds Ratio (M-H, Fixed, 95% CI)	0.85 [0.27, 2.63]
2.3 Sharp transection method vs clamp-crush method	1	82	Odds Ratio (M-H, Fixed, 95% CI)	2.11 [0.36, 12.20]
2.4 Stapler vs clamp-crush method	1	130	Odds Ratio (M-H, Fixed, 95% CI)	1.26 [0.58, 2.75]
2.5 Hydrojet vs cavitron ultrasonic surgical aspirator	1	61	Odds Ratio (M-H, Fixed, 95% CI)	0.62 [0.10, 4.00]
2.6 Radiofrequency dissecting sealer vs cavitron ultrasonic surgical aspirator	1	40	Odds Ratio (M-H, Fixed, 95% CI)	1.0 [0.06, 17.18]
3 Serious adverse events (number)	5		Rate Ratio (Fixed, 95% CI)	Subtotals only
3.1 Cavitron ultrasonic surgical aspirator vs clamp-crush method	1	132	Rate Ratio (Fixed, 95% CI)	0.67 [0.11, 3.99]
3.2 Radiofrequency dissecting sealer vs clamp-crush method	2	130	Rate Ratio (Fixed, 95% CI)	3.34 [1.08, 10.31]
3.3 Hydrojet vs cavitron ultrasonic surgical aspirator	1	50	Rate Ratio (Fixed, 95% CI)	1.50 [0.25, 8.98]

3.4 Radiofrequency dissecting sealer vs cavitron ultrasonic surgical aspirator	1	50	Rate Ratio (Fixed, 95% CI)	1.50 [0.25, 8.98]
3.5 Stapler vs cavitron ultrasonic surgical aspirator	1	100	Rate Ratio (Fixed, 95% CI)	1.33 [0.56, 3.16]
3.6 Radiofrequency dissecting sealer vs hydrojet	1	50	Rate Ratio (Fixed, 95% CI)	1.0 [0.20, 4.95]
4 Adverse events (proportion)	8		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Cavitron ultrasonic surgical aspirator vs clamp-crush method	3	222	Odds Ratio (M-H, Fixed, 95% CI)	1.30 [0.73, 2.34]
4.2 Radiofrequency dissecting sealer vs clamp-crush method	3	220	Odds Ratio (M-H, Fixed, 95% CI)	0.92 [0.51, 1.64]
4.3 Sharp transection method vs clamp-crush method	1	82	Odds Ratio (M-H, Fixed, 95% CI)	1.11 [0.46, 2.68]
4.4 Stapler vs clamp-crush method	1	130	Odds Ratio (M-H, Fixed, 95% CI)	1.06 [0.53, 2.12]
4.5 Hydrojet vs cavitron ultrasonic surgical aspirator	1	61	Odds Ratio (M-H, Fixed, 95% CI)	0.29 [0.07, 1.24]
4.6 Radiofrequency dissecting sealer vs cavitron ultrasonic surgical aspirator	1	40	Odds Ratio (M-H, Fixed, 95% CI)	1.86 [0.52, 6.61]
5 Adverse events (number)	7		Rate Ratio (Fixed, 95% CI)	Subtotals only
5.1 Cavitron ultrasonic surgical aspirator vs clamp-crush method	1	132	Rate Ratio (Fixed, 95% CI)	1.56 [0.83, 2.93]
5.2 Radiofrequency dissecting sealer vs clamp-crush method	3	250	Rate Ratio (Fixed, 95% CI)	1.67 [0.95, 2.94]
5.3 Sharp transection method vs clamp-crush method	1	82	Rate Ratio (Fixed, 95% CI)	1.12 [0.57, 2.21]
5.4 Hydrojet vs cavitron ultrasonic surgical aspirator	1	50	Rate Ratio (Fixed, 95% CI)	0.88 [0.32, 2.41]
5.5 Radiofrequency dissecting sealer vs cavitron ultrasonic surgical aspirator	1	50	Rate Ratio (Fixed, 95% CI)	1.12 [0.43, 2.92]
5.6 Stapler vs cavitron ultrasonic surgical aspirator	1	100	Rate Ratio (Fixed, 95% CI)	1.16 [0.63, 2.14]
5.7 Radiofrequency dissecting sealer vs hydrojet	1	50	Rate Ratio (Fixed, 95% CI)	1.29 [0.48, 3.45]
6 Blood transfusion (proportion)	8		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Cavitron ultrasonic surgical aspirator vs clamp-crush method	2	172	Odds Ratio (M-H, Fixed, 95% CI)	1.37 [0.29, 6.59]
6.2 Radiofrequency dissecting sealer vs clamp-crush method	5	390	Odds Ratio (M-H, Fixed, 95% CI)	1.13 [0.63, 2.03]
6.3 Sharp transection method vs clamp-crush method	1	82	Odds Ratio (M-H, Fixed, 95% CI)	0.80 [0.32, 2.01]
6.4 Hydrojet vs cavitron ultrasonic surgical aspirator	1	50	Odds Ratio (M-H, Fixed, 95% CI)	1.0 [0.30, 3.28]

6.5 Radiofrequency dissecting sealer vs cavitron ultrasonic surgical aspirator	2	90	Odds Ratio (M-H, Fixed, 95% CI)	0.77 [0.29, 2.09]
6.6 Radiofrequency dissecting sealer vs hydrojet	1	50	Odds Ratio (M-H, Fixed, 95% CI)	0.53 [0.15, 1.93]
7 Blood transfusion (red blood cell)	4		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7.1 Sharp transection method vs clamp-crush method	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 Stapler vs clamp-crush method	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 Hydrojet vs cavitron ultrasonic surgical aspirator	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.4 Stapler vs cavitron ultrasonic surgical aspirator	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Blood transfusion (fresh frozen plasma)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.1 Stapler vs clamp-crush method	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Blood loss	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
9.1 Cavitron ultrasonic surgical aspirator vs clamp-crush method	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Hydrojet vs cavitron ultrasonic surgical aspirator	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Operating time	6		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.1 Cavitron ultrasonic surgical aspirator vs clamp-crush method	2	90	Mean Difference (IV, Fixed, 95% CI)	27.47 [-2.87, 57.81]
10.2 Radiofrequency dissecting sealer vs clamp-crush method	2	90	Mean Difference (IV, Fixed, 95% CI)	16.11 [-11.45, 43.67]
10.3 Sharp transection method vs clamp-crush method	1	82	Mean Difference (IV, Fixed, 95% CI)	-6.0 [-90.85, 78.85]
10.4 Stapler vs clamp-crush method	1	130	Mean Difference (IV, Fixed, 95% CI)	-31.0 [-60.40, -1.60]
10.5 Radiofrequency dissecting sealer vs cavitron ultrasonic surgical aspirator	1	40	Mean Difference (IV, Fixed, 95% CI)	25.0 [-96.48, 146.48]
10.6 Stapler vs cavitron ultrasonic surgical aspirator	1	100	Mean Difference (IV, Fixed, 95% CI)	-26.0 [-87.12, 35.12]

Comparison 5. Methods of dealing with cut surface

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality (perioperative)	10		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Fibrin sealant vs control	2	380	Odds Ratio (M-H, Fixed, 95% CI)	3.56 [0.73, 17.35]
1.2 Fibrin sealant and collagen vs control	1	300	Odds Ratio (M-H, Fixed, 95% CI)	3.08 [0.61, 15.53]
1.3 Fibrin sealant vs argon beam	2	227	Odds Ratio (M-H, Fixed, 95% CI)	1.37 [0.46, 4.03]
1.4 Fibrin sealant vs collagen	3	256	Odds Ratio (M-H, Fixed, 95% CI)	0.90 [0.24, 3.32]
1.5 Oxidised cellulose vs fibrin sealant	1	50	Odds Ratio (M-H, Fixed, 95% CI)	0.55 [0.03, 9.33]
1.6 Plasmajet vs fibrin sealant	1	58	Odds Ratio (M-H, Fixed, 95% CI)	0.64 [0.10, 4.16]
2 Serious adverse events (proportion)	7		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Fibrin sealant vs control	3	457	Odds Ratio (M-H, Fixed, 95% CI)	1.03 [0.64, 1.65]
2.2 Fibrin sealant vs argon beam	1	106	Odds Ratio (M-H, Fixed, 95% CI)	0.62 [0.25, 1.55]
2.3 Fibrin sealant vs collagen	1	127	Odds Ratio (M-H, Fixed, 95% CI)	1.57 [0.73, 3.38]
2.4 Oxidised cellulose vs fibrin sealant	1	50	Odds Ratio (M-H, Fixed, 95% CI)	0.57 [0.17, 1.87]
2.5 Plasmajet vs fibrin sealant	1	58	Odds Ratio (M-H, Fixed, 95% CI)	0.14 [0.02, 1.22]
3 Serious adverse events (number)	6		Rate Ratio (Fixed, 95% CI)	Subtotals only
3.1 Fibrin sealant vs control	1	70	Rate Ratio (Fixed, 95% CI)	0.94 [0.48, 1.86]
3.2 Fibrin sealant and collagen vs control	1	300	Rate Ratio (Fixed, 95% CI)	1.32 [0.76, 2.29]
3.3 Fibrin sealant vs argon beam	1	121	Rate Ratio (Fixed, 95% CI)	4.47 [1.50, 13.27]
3.4 Fibrin sealant vs collagen	2	189	Rate Ratio (Fixed, 95% CI)	1.22 [0.76, 1.98]
3.5 Fibrin sealant vs cyanoacrylate	1	30	Rate Ratio (Fixed, 95% CI)	1.0 [0.06, 15.99]
3.6 Oxidised cellulose vs cyanoacrylate	1	30	Rate Ratio (Fixed, 95% CI)	4.00 [0.45, 35.79]
3.7 Oxidised cellulose vs fibrin sealant	1	30	Rate Ratio (Fixed, 95% CI)	4.00 [0.45, 35.79]
4 Adverse events (proportion)	9		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Fibrin sealant versus control	3	457	Odds Ratio (M-H, Fixed, 95% CI)	0.80 [0.55, 1.17]
4.2 Fibrin sealant and collagen vs control	1	300	Odds Ratio (M-H, Fixed, 95% CI)	1.0 [0.59, 1.71]
4.3 Fibrin sealant vs argon beam	2	227	Odds Ratio (M-H, Fixed, 95% CI)	0.97 [0.58, 1.64]
4.4 Fibrin sealant vs collagen	1	127	Odds Ratio (M-H, Fixed, 95% CI)	0.95 [0.46, 1.93]
4.5 Oxidised cellulose vs fibrin sealant	2	274	Odds Ratio (M-H, Fixed, 95% CI)	0.77 [0.30, 2.01]
5 Adverse events (number)	5		Rate Ratio (Fixed, 95% CI)	Subtotals only
5.1 Fibrin sealant vs control	1	70	Rate Ratio (Fixed, 95% CI)	1.01 [0.75, 1.36]
5.2 Fibrin sealant vs argon beam	1	121	Rate Ratio (Fixed, 95% CI)	1.12 [0.75, 1.66]

5.3 Fibrin sealant vs collagen	2	189	Rate Ratio (Fixed, 95% CI)	1.13 [0.90, 1.42]
5.4 Fibrin sealant vs cyanoacrylate	1	30	Rate Ratio (Fixed, 95% CI)	1.50 [0.25, 8.98]
5.5 Oxidised cellulose vs cyanoacrylate	1	30	Rate Ratio (Fixed, 95% CI)	3.50 [0.73, 16.85]
5.6 Oxidised cellulose vs fibrin sealant	1	30	Rate Ratio (Fixed, 95% CI)	2.33 [0.60, 9.02]
6 Blood transfusion (proportion)	4		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Fibrin sealant vs control	2	392	Odds Ratio (M-H, Fixed, 95% CI)	1.04 [0.61, 1.76]
6.2 Fibrin sealant and collagen vs control	1	300	Odds Ratio (M-H, Fixed, 95% CI)	1.52 [0.88, 2.61]
6.3 Fibrin sealant vs cyanoacrylate	1	30	Odds Ratio (M-H, Fixed, 95% CI)	3.25 [0.52, 20.37]
6.4 Oxidised cellulose vs cyanoacrylate	1	30	Odds Ratio (M-H, Fixed, 95% CI)	2.36 [0.36, 15.45]
6.5 Oxidised cellulose vs fibrin sealant	1	30	Odds Ratio (M-H, Fixed, 95% CI)	0.73 [0.15, 3.49]
7 Blood transfusion (red blood cell)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
7.1 Fibrin sealant vs control	2	122	Mean Difference (IV, Random, 95% CI)	-0.53 [-1.00, -0.06]
7.2 Fibrin sealant and collagen vs control	1	300	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.16, 0.14]
7.3 Fibrin sealant vs collagen	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7.4 Fibrin sealant vs cyanoacrylate	1	30	Mean Difference (IV, Random, 95% CI)	2.2 [1.59, 2.81]
7.5 Oxidised cellulose vs cyanoacrylate	1	30	Mean Difference (IV, Random, 95% CI)	-0.27 [-0.81, 0.27]
7.6 Oxidised cellulose vs fibrin sealant	2	80	Mean Difference (IV, Random, 95% CI)	-1.76 [-2.00, 0.47]
8 Blood transfusion (fresh frozen plasma)	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
8.1 Fibrin sealant vs cyanoacrylate	1	30	Mean Difference (IV, Fixed, 95% CI)	-0.8 [-1.01, -0.59]
8.2 Oxidised cellulose vs cyanoacrylate	1	30	Mean Difference (IV, Fixed, 95% CI)	-0.27 [-0.55, 0.01]
8.3 Oxidised cellulose vs fibrin sealant	2	80	Mean Difference (IV, Fixed, 95% CI)	0.53 [0.35, 0.71]
9 Blood loss	5		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
9.1 Fibrin sealant vs control	2	350	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.13, 0.33]
9.2 Fibrin sealant and collagen vs control	1	300	Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.06, 0.19]
9.3 Fibrin sealant vs collagen	1	62	Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.54, 0.68]
9.4 Fibrin sealant vs cyanoacrylate	1	30	Mean Difference (IV, Fixed, 95% CI)	0.11 [-0.20, 0.43]
9.5 Oxidised cellulose vs cyanoacrylate	1	30	Mean Difference (IV, Fixed, 95% CI)	-0.08 [-0.35, 0.19]
9.6 Oxidised cellulose vs fibrin sealant	1	30	Mean Difference (IV, Fixed, 95% CI)	-0.19 [-0.45, 0.06]
10 Total hospital stay	4		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.1 Fibrin sealant vs control	1	82	Mean Difference (IV, Fixed, 95% CI)	-0.5 [-2.45, 1.45]

10.2 Fibrin sealant and collagen vs control	1	300	Mean Difference (IV, Fixed, 95% CI)	0.70 [-1.83, 3.23]
10.3 Fibrin sealant vs cyanoacrylate	1	30	Mean Difference (IV, Fixed, 95% CI)	-1.34 [-3.61, 0.93]
10.4 Oxidised cellulose vs cyanoacrylate	1	30	Mean Difference (IV, Fixed, 95% CI)	-0.67 [-3.12, 1.78]
10.5 Oxidised cellulose vs fibrin sealant	2	80	Mean Difference (IV, Fixed, 95% CI)	0.25 [-1.84, 2.33]
11 ITU stay	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
11.1 Oxidised cellulose vs fibrin sealant	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Operating time	5		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
12.1 Fibrin sealant vs control	2	122	Mean Difference (IV, Fixed, 95% CI)	-14.55 [-52.86, 23.76]
12.2 Fibrin sealant and collagen vs control	1	300	Mean Difference (IV, Fixed, 95% CI)	19.0 [2.09, 35.91]
12.3 Fibrin sealant vs collagen	1	62	Mean Difference (IV, Fixed, 95% CI)	-4.0 [-44.33, 36.33]
12.4 Oxidised cellulose vs fibrin sealant	1	50	Mean Difference (IV, Fixed, 95% CI)	5.40 [-70.13, 80.93]

Comparison 6. Methods of vascular occlusion

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality (perioperative)	14		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Continuous portal triad clamping vs control	1	15	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Intermittent portal triad clamping vs control	4	392	Odds Ratio (M-H, Fixed, 95% CI)	0.63 [0.16, 2.44]
1.3 Continuous portal triad clamping vs continuous hepatic vascular exclusion	2	170	Odds Ratio (M-H, Fixed, 95% CI)	3.39 [0.34, 33.33]
1.4 Continuous selective hepatic vascular exclusion vs continuous portal triad clamping	1	160	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.5 Continuous selective portal triad clamping vs continuous portal triad clamping	1	120	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.6 Intermittent portal triad clamping vs continuous portal triad clamping	2	121	Odds Ratio (M-H, Fixed, 95% CI)	0.19 [0.02, 1.64]
1.7 Intermittent portal triad clamping vs continuous selective portal triad clamping	1	80	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

1.8 Intermittent selective portal triad clamping vs intermittent portal triad clamping	2	138	Odds Ratio (M-H, Fixed, 95% CI)	2.93 [0.12, 74.00]
2 Serious adverse events (proportion)	8		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Intermittent portal triad clamping vs control	3	302	Odds Ratio (M-H, Fixed, 95% CI)	1.16 [0.55, 2.44]
2.2 Continuous portal triad clamping vs continuous hepatic vascular exclusion	1	118	Odds Ratio (M-H, Fixed, 95% CI)	0.68 [0.11, 4.22]
2.3 Continuous selective hepatic vascular exclusion vs continuous portal triad clamping	1	160	Odds Ratio (M-H, Fixed, 95% CI)	0.20 [0.01, 4.13]
2.4 Continuous selective portal triad clamping vs continuous portal triad clamping	1	120	Odds Ratio (M-H, Fixed, 95% CI)	0.43 [0.19, 0.98]
2.5 Intermittent portal triad clamping vs continuous portal triad clamping	1	35	Odds Ratio (M-H, Fixed, 95% CI)	0.47 [0.07, 2.96]
2.6 Intermittent portal triad clamping vs continuous selective portal triad clamping	1	80	Odds Ratio (M-H, Fixed, 95% CI)	4.33 [0.46, 40.61]
3 Serious adverse events (number)	5		Rate Ratio (Fixed, 95% CI)	Subtotals only
3.1 Intermittent portal triad clamping vs control	1	100	Rate Ratio (Fixed, 95% CI)	1.50 [0.42, 5.32]
3.2 Continuous portal triad clamping vs continuous hepatic vascular exclusion	1	52	Rate Ratio (Fixed, 95% CI)	0.23 [0.03, 2.00]
3.3 Intermittent portal triad clamping vs continuous portal triad clamping	1	86	Rate Ratio (Fixed, 95% CI)	0.12 [0.01, 0.95]
3.4 Intermittent selective portal triad clamping vs intermittent portal triad clamping	2	138	Rate Ratio (Fixed, 95% CI)	1.26 [0.53, 2.99]
4 Adverse events (proportion)	12		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Intermittent portal triad clamping vs control	4	392	Odds Ratio (M-H, Fixed, 95% CI)	1.27 [0.83, 1.94]
4.2 Continuous portal triad clamping vs continuous hepatic vascular exclusion	1	118	Odds Ratio (M-H, Fixed, 95% CI)	0.89 [0.41, 1.96]
4.3 Continuous selective hepatic vascular exclusion vs continuous portal triad clamping	1	160	Odds Ratio (M-H, Fixed, 95% CI)	0.47 [0.20, 1.13]

4.4 Continuous selective portal triad clamping vs continuous portal triad clamping	1	120	Odds Ratio (M-H, Fixed, 95% CI)	0.41 [0.19, 0.93]
4.5 Intermittent portal triad clamping vs continuous portal triad clamping	2	121	Odds Ratio (M-H, Fixed, 95% CI)	0.67 [0.29, 1.56]
4.6 Intermittent portal triad clamping vs continuous selective portal triad clamping	1	80	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.29, 2.52]
4.7 Intermittent selective portal triad clamping vs intermittent portal triad clamping	2	138	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.42, 1.75]
5 Adverse events (number)	6		Rate Ratio (Fixed, 95% CI)	Subtotals only
5.1 Intermittent portal triad clamping vs control	2	226	Rate Ratio (Fixed, 95% CI)	1.19 [0.80, 1.76]
5.2 Continuous portal triad clamping vs continuous hepatic vascular exclusion	1	52	Rate Ratio (Fixed, 95% CI)	0.61 [0.29, 1.32]
5.3 Intermittent portal triad clamping vs continuous portal triad clamping	1	86	Rate Ratio (Fixed, 95% CI)	0.64 [0.31, 1.32]
5.4 Intermittent selective portal triad clamping vs intermittent portal triad clamping	2	138	Rate Ratio (Fixed, 95% CI)	1.17 [0.72, 1.91]
6 Blood transfusion (proportion)	13		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Continuous portal triad clamping vs control	1	34	Odds Ratio (M-H, Fixed, 95% CI)	0.08 [0.01, 0.80]
6.2 Intermittent portal triad clamping vs control	4	392	Odds Ratio (M-H, Fixed, 95% CI)	0.82 [0.50, 1.35]
6.3 Continuous portal triad clamping vs continuous hepatic vascular exclusion	1	118	Odds Ratio (M-H, Fixed, 95% CI)	5.66 [2.29, 14.00]
6.4 Continuous selective hepatic vascular exclusion vs continuous portal triad clamping	1	160	Odds Ratio (M-H, Fixed, 95% CI)	0.51 [0.24, 1.11]
6.5 Continuous selective portal triad clamping vs continuous portal triad clamping	1	120	Odds Ratio (M-H, Fixed, 95% CI)	1.56 [0.42, 5.82]
6.6 Intermittent portal triad clamping vs continuous portal triad clamping	2	121	Odds Ratio (M-H, Fixed, 95% CI)	1.14 [0.52, 2.49]
6.7 Intermittent portal triad clamping vs continuous selective portal triad clamping	1	80	Odds Ratio (M-H, Fixed, 95% CI)	0.90 [0.36, 2.23]

6.8 Intermittent selective portal triad clamping vs intermittent portal triad clamping	2	138	Odds Ratio (M-H, Fixed, 95% CI)	0.58 [0.25, 1.36]
7 Blood transfusion (red blood cell)	10		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 Continuous portal triad clamping vs control	1	15	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-3.20, 2.00]
7.2 Intermittent portal triad clamping vs control	1	100	Mean Difference (IV, Fixed, 95% CI)	-1.5 [-2.75, -0.25]
7.3 Continuous portal triad clamping vs continuous hepatic vascular exclusion	1	52	Mean Difference (IV, Fixed, 95% CI)	0.40 [-1.61, 2.41]
7.4 Continuous selective hepatic vascular exclusion vs continuous portal triad clamping	1	160	Mean Difference (IV, Fixed, 95% CI)	-1.20 [-2.38, -0.02]
7.5 Continuous selective portal triad clamping vs continuous portal triad clamping	1	120	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-0.31, -0.09]
7.6 Intermittent portal triad clamping vs continuous portal triad clamping	2	121	Mean Difference (IV, Fixed, 95% CI)	-0.13 [-0.60, 0.34]
7.7 Intermittent portal triad clamping vs continuous selective portal triad clamping	1	80	Mean Difference (IV, Fixed, 95% CI)	0.11 [-0.23, 0.46]
7.8 Intermittent selective portal triad clamping vs intermittent portal triad clamping	2	138	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.45, 0.32]
8 Blood loss	16		Mean Difference (IV, Random, 95% CI)	Subtotals only
8.1 Continuous portal triad clamping vs control	3	131	Mean Difference (IV, Random, 95% CI)	-0.24 [-0.76, 0.27]
8.2 Intermittent portal triad clamping vs control	4	402	Mean Difference (IV, Random, 95% CI)	-0.02 [-0.19, 0.15]
8.3 Continuous portal triad clamping vs continuous hepatic vascular exclusion	2	170	Mean Difference (IV, Random, 95% CI)	0.17 [-0.35, 0.68]
8.4 Continuous selective hepatic vascular exclusion vs continuous portal triad clamping	1	160	Mean Difference (IV, Random, 95% CI)	-0.25 [-0.49, -0.00]
8.5 Continuous selective portal triad clamping vs continuous portal triad clamping	1	120	Mean Difference (IV, Random, 95% CI)	0.10 [-0.19, 0.39]
8.6 Intermittent portal triad clamping vs continuous portal triad clamping	2	121	Mean Difference (IV, Random, 95% CI)	0.06 [-0.20, 0.32]

8.7 Intermittent portal triad clamping vs continuous selective portal triad clamping	1	80	Mean Difference (IV, Random, 95% CI)	-0.08 [-0.20, 0.05]
8.8 Intermittent selective portal triad clamping vs intermittent portal triad clamping	2	138	Mean Difference (IV, Random, 95% CI)	-0.17 [-0.74, 0.39]
9 Major blood loss (proportion)	3		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
9.1 Intermittent portal triad clamping vs control	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Continuous selective hepatic vascular exclusion vs continuous portal triad clamping	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Continuous selective portal triad clamping vs continuous portal triad clamping	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Total hospital stay	10		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.1 Intermittent portal triad clamping vs control	4	402	Mean Difference (IV, Fixed, 95% CI)	0.32 [-0.64, 1.28]
10.2 Continuous portal triad clamping vs continuous hepatic vascular exclusion	1	52	Mean Difference (IV, Fixed, 95% CI)	-8.0 [-13.05, -2.95]
10.3 Continuous selective hepatic vascular exclusion vs continuous portal triad clamping	1	160	Mean Difference (IV, Fixed, 95% CI)	-2.80 [-4.13, -1.47]
10.4 Intermittent portal triad clamping vs continuous portal triad clamping	1	86	Mean Difference (IV, Fixed, 95% CI)	1.0 [-2.82, 4.82]
10.5 Intermittent portal triad clamping vs continuous selective portal triad clamping	1	80	Mean Difference (IV, Fixed, 95% CI)	-0.27 [-1.60, 1.06]
10.6 Intermittent selective portal triad clamping vs intermittent portal triad clamping	2	138	Mean Difference (IV, Fixed, 95% CI)	-0.67 [-2.40, 1.06]
11 ITU stay	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
11.1 Continuous selective hepatic vascular exclusion vs continuous portal triad clamping	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Operating time	12		Mean Difference (IV, Random, 95% CI)	Subtotals only
12.1 Continuous portal triad clamping vs control	2	40	Mean Difference (IV, Random, 95% CI)	-45.87 [-95.61, 3.87]
12.2 Intermittent portal triad clamping vs control	2	176	Mean Difference (IV, Random, 95% CI)	25.66 [-31.57, 82.89]
12.3 Continuous portal triad clamping vs continuous hepatic vascular exclusion	2	170	Mean Difference (IV, Random, 95% CI)	-29.32 [-82.75, 24.10]

12.4 Continuous selective hepatic vascular exclusion vs continuous portal triad clamping	1	160	Mean Difference (IV, Random, 95% CI)	-7.20 [-63.42, 49.02]
12.5 Continuous selective portal triad clamping vs continuous portal triad clamping	1	120	Mean Difference (IV, Random, 95% CI)	20.0 [-0.00, 40.00]
12.6 Intermittent portal triad clamping vs continuous portal triad clamping	1	35	Mean Difference (IV, Random, 95% CI)	13.40 [-41.28, 68.08]
12.7 Intermittent portal triad clamping vs continuous selective portal triad clamping	1	80	Mean Difference (IV, Random, 95% CI)	-32.17 [-51.50, -12.84]
12.8 Intermittent selective portal triad clamping vs intermittent portal triad clamping	2	138	Mean Difference (IV, Random, 95% CI)	8.64 [-10.16, 27.45]

Comparison 7. Pharmacological interventions

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality (perioperative)	2		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Recombinant factor VIIa vs control	1	185	Odds Ratio (M-H, Fixed, 95% CI)	0.61 [0.13, 2.83]
1.2 Tranexamic acid vs control	1	214	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Serious adverse events (proportion)	3		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Anti-thrombin III vs control	1	24	Odds Ratio (M-H, Fixed, 95% CI)	1.19 [0.20, 6.99]
2.2 Recombinant factor VIIa vs control	2	432	Odds Ratio (M-H, Fixed, 95% CI)	1.10 [0.58, 2.09]
3 Serious adverse events (number)	3		Rate Ratio (Fixed, 95% CI)	Subtotals only
3.1 Recombinant factor VIIa vs control	2	432	Rate Ratio (Fixed, 95% CI)	1.46 [0.75, 2.84]
3.2 Tranexamic acid vs control	1	214	Rate Ratio (Fixed, 95% CI)	0.86 [0.31, 2.37]
4 Adverse events (proportion)	3		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Anti-thrombin III vs control	1	24	Odds Ratio (M-H, Fixed, 95% CI)	0.53 [0.10, 2.84]
4.2 Recombinant factor VIIa vs control	1	232	Odds Ratio (M-H, Fixed, 95% CI)	1.04 [0.34, 3.21]
4.3 Tranexamic acid vs control	1	214	Odds Ratio (M-H, Fixed, 95% CI)	0.78 [0.36, 1.67]
5 Adverse events (number)	3		Rate Ratio (Fixed, 95% CI)	Subtotals only
5.1 Recombinant factor VIIa vs control	2	432	Rate Ratio (Fixed, 95% CI)	0.98 [0.87, 1.10]
5.2 Tranexamic acid vs control	1	214	Rate Ratio (Fixed, 95% CI)	0.78 [0.43, 1.42]
6 Blood transfusion (proportion)	5		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only

6.1 Aprotinin vs control	1	97	Odds Ratio (M-H, Fixed, 95% CI)	0.32 [0.12, 0.82]
6.2 Desmopressin vs control	1	60	Odds Ratio (M-H, Fixed, 95% CI)	0.56 [0.12, 2.57]
6.3 Recombinant factor VIIa vs control	2	416	Odds Ratio (M-H, Fixed, 95% CI)	0.94 [0.62, 1.43]
6.4 Tranexamic acid vs control	1	214	Odds Ratio (M-H, Fixed, 95% CI)	0.02 [0.00, 0.40]
7 Blood transfusion (fresh frozen plasma)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 Desmopressin vs control	1	60	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-1.39, 0.19]
8 Blood loss	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
8.1 Aprotinin vs control	1	97	Mean Difference (IV, Fixed, 95% CI)	-0.44 [-0.87, 0.00]
9 Hospital stay	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
9.1 Tranexamic acid vs control	1	214	Mean Difference (IV, Fixed, 95% CI)	-1.0 [-3.06, 1.06]
10 Operating time	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.1 Aprotinin vs control	1	97	Mean Difference (IV, Fixed, 95% CI)	-1.0 [-30.08, 28.08]

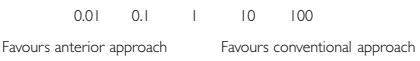
Analysis 1.1. Comparison 1 Anterior approach vs conventional approach, Outcome 1 Mortality (perioperative).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 1 Anterior approach vs conventional approach

Outcome: 1 Mortality (perioperative)

Study or subgroup	Anterior approach n/N	Conventional approach n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Anterior approach vs conventional approach					
Capussotti 2012	1/33	1/32		14.3 %	0.97 [0.06, 16.18]
Liu 2006	1/60	6/60		85.7 %	0.15 [0.02, 1.31]
Subtotal (95% CI)	**93**	**92**		**100.0 %**	**0.27 [0.05, 1.32]**
Total events: 2 (Anterior approach), 7 (Conventional approach)					
Heterogeneity: Chi^2 = 1.06, df = 1 (P = 0.30); I^2 =6%					
Test for overall effect: Z = 1.61 (P = 0.11)					

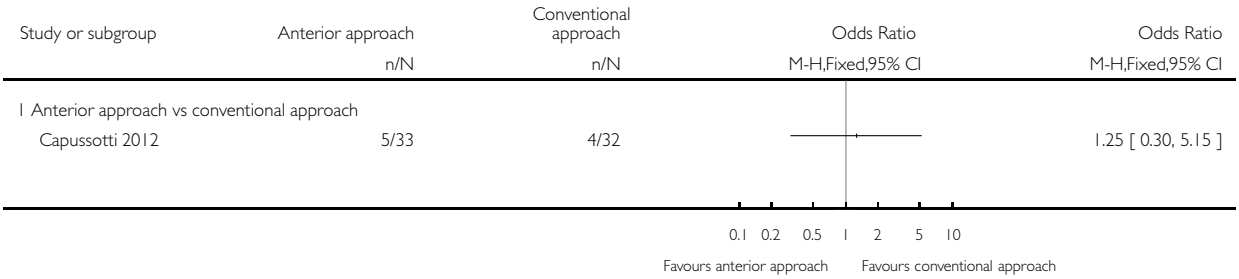


Analysis 1.2. Comparison 1 Anterior approach vs conventional approach, Outcome 2 Serious adverse events (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 1 Anterior approach vs conventional approach

Outcome: 2 Serious adverse events (proportion)

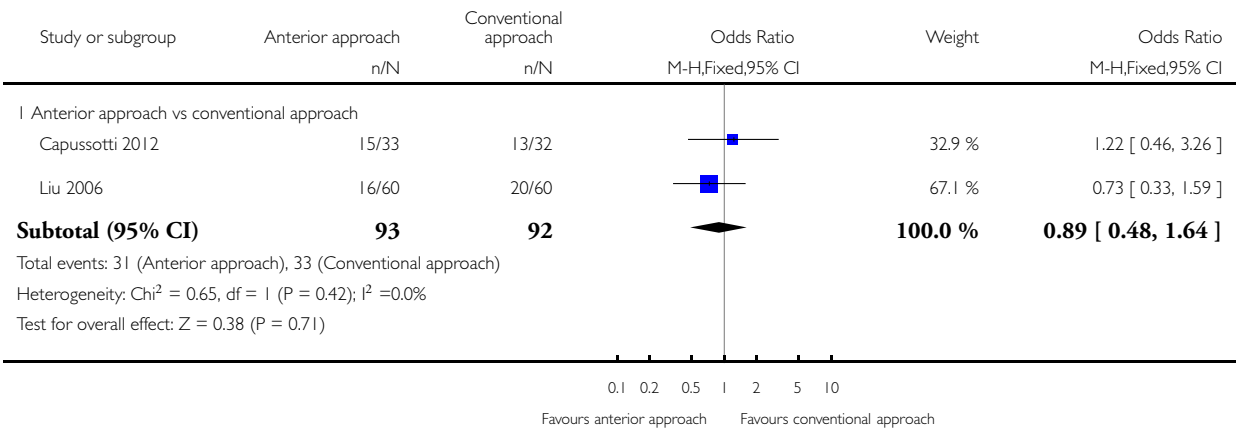


Analysis 1.3. Comparison 1 Anterior approach vs conventional approach, Outcome 3 Adverse events (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 1 Anterior approach vs conventional approach

Outcome: 3 Adverse events (proportion)

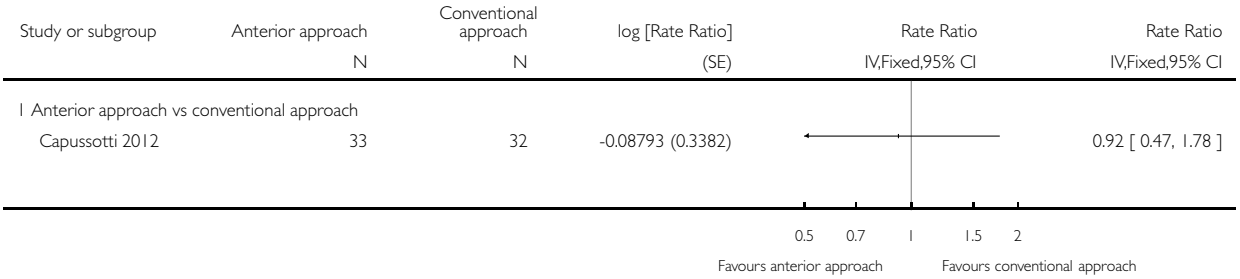


Analysis 1.4. Comparison 1 Anterior approach vs conventional approach, Outcome 4 Adverse events (number).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 1 Anterior approach vs conventional approach

Outcome: 4 Adverse events (number)

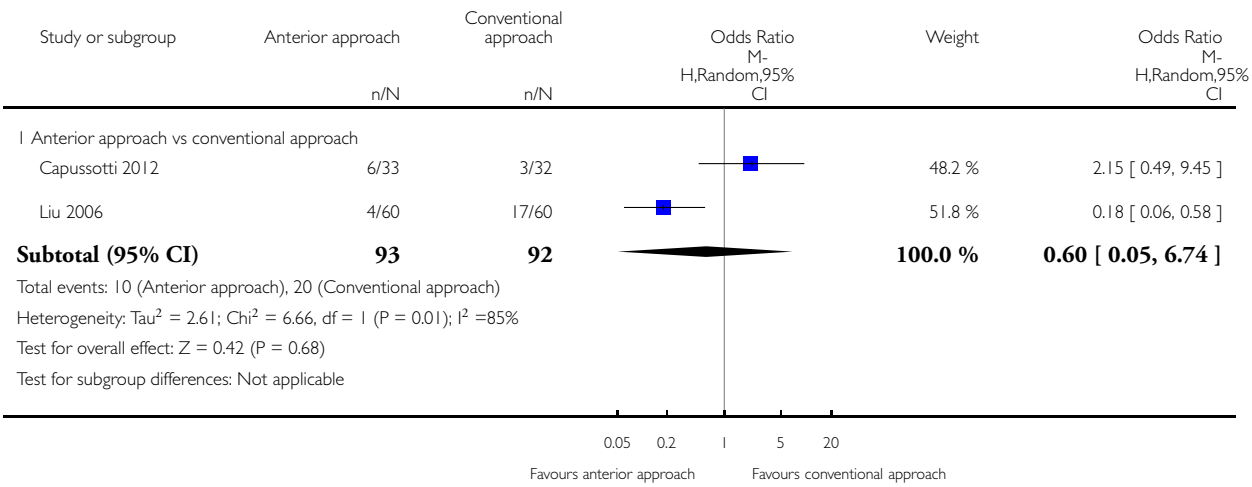


Analysis 1.5. Comparison 1 Anterior approach vs conventional approach, Outcome 5 Blood transfusion (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 1 Anterior approach vs conventional approach

Outcome: 5 Blood transfusion (proportion)

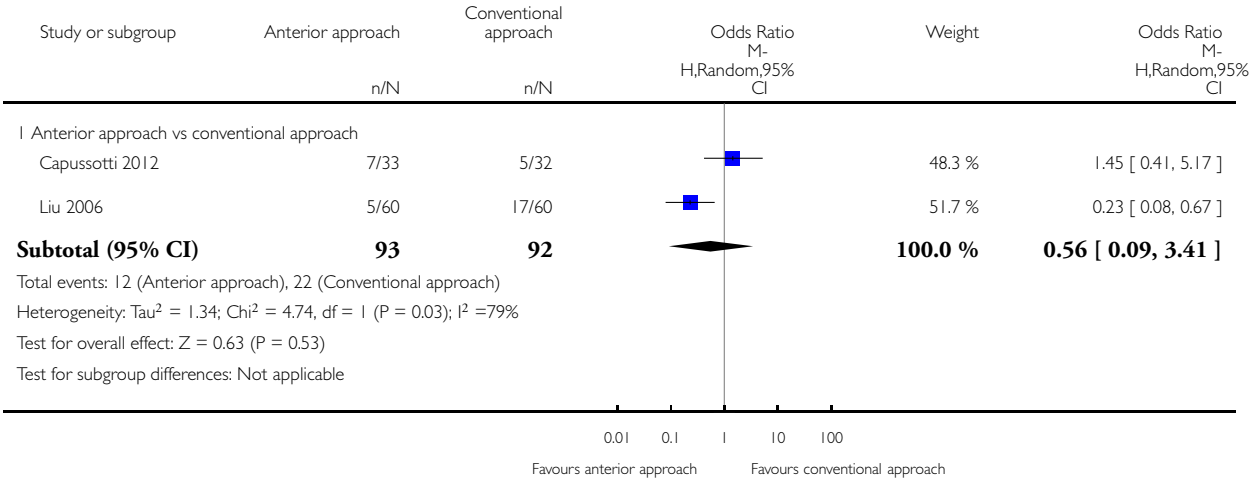


Analysis 1.6. Comparison 1 Anterior approach vs conventional approach, Outcome 6 Major blood loss (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 1 Anterior approach vs conventional approach

Outcome: 6 Major blood loss (proportion)



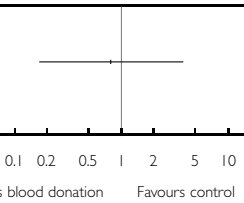
Analysis 2.1. Comparison 2 Autologous blood donation vs control, Outcome 1 Adverse events (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 2 Autologous blood donation vs control

Outcome: 1 Adverse events (proportion)

Study or subgroup	Autologous blood donation n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
1 Autologous blood donation vs control				
Kostopanagiotou 2007	5/15	5/13		0.80 [0.17, 3.77]



Analysis 2.2. Comparison 2 Autologous blood donation vs control, Outcome 2 Blood transfusion (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 2 Autologous blood donation vs control

Outcome: 2 Blood transfusion (proportion)

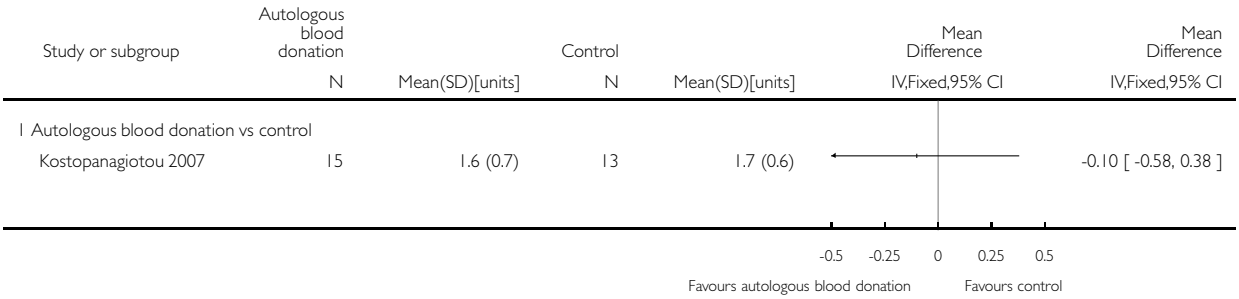
Study or subgroup	Autologous blood donation n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
1 Autologous blood donation vs control				
Kajikawa 1994	5/21	13/21		0.19 [0.05, 0.73]

Analysis 2.3. Comparison 2 Autologous blood donation vs control, Outcome 3 Blood transfusion (red blood cell).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 2 Autologous blood donation vs control

Outcome: 3 Blood transfusion (red blood cell)

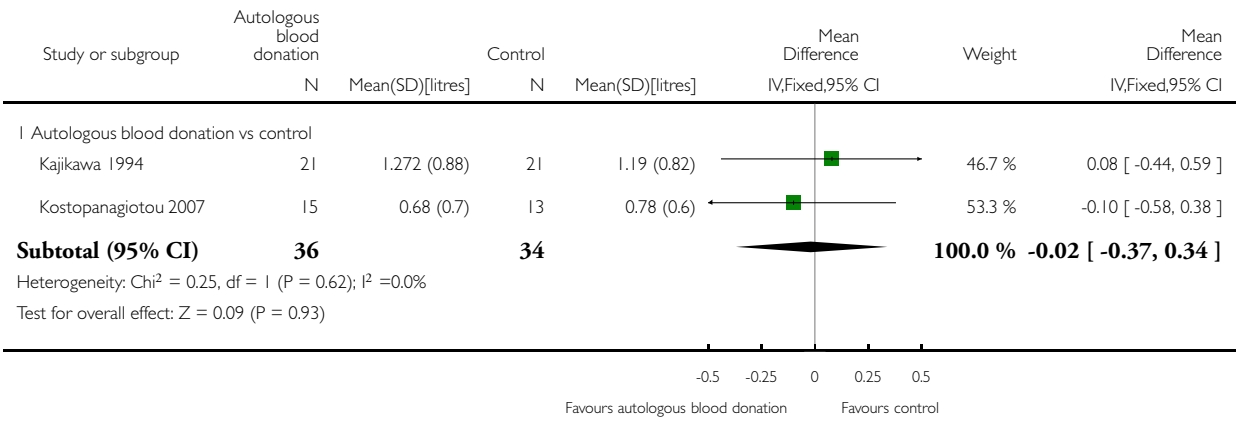


Analysis 2.4. Comparison 2 Autologous blood donation vs control, Outcome 4 Blood loss.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 2 Autologous blood donation vs control

Outcome: 4 Blood loss

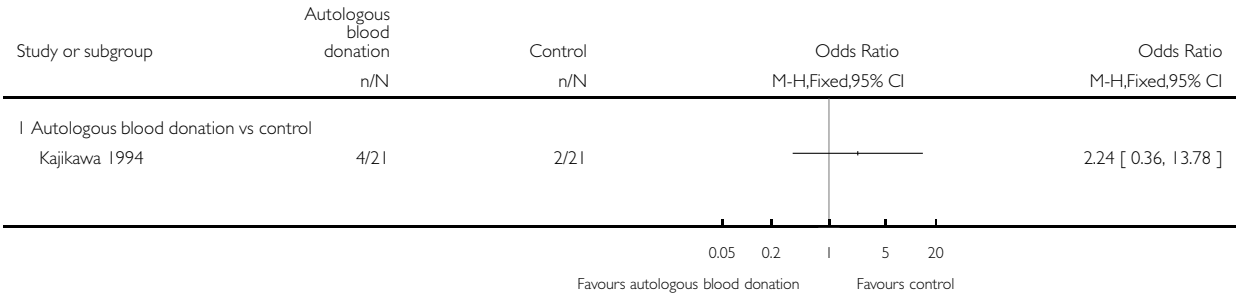


Analysis 2.5. Comparison 2 Autologous blood donation vs control, Outcome 5 Major blood loss (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 2 Autologous blood donation vs control

Outcome: 5 Major blood loss (proportion)

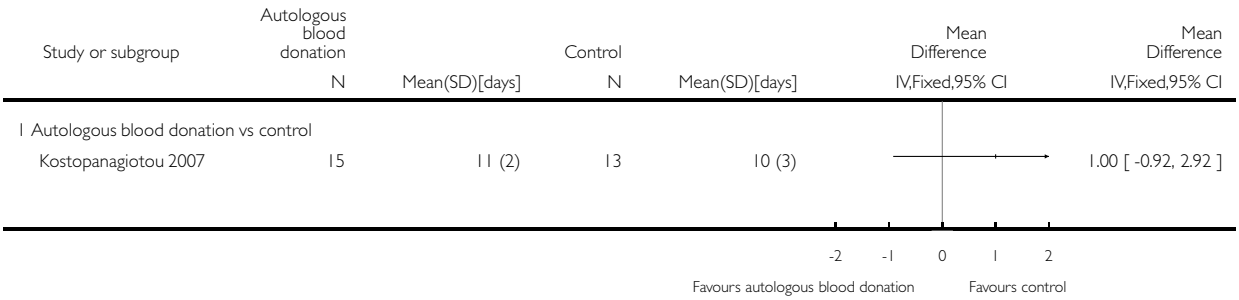


Analysis 2.6. Comparison 2 Autologous blood donation vs control, Outcome 6 Total hospital stay.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 2 Autologous blood donation vs control

Outcome: 6 Total hospital stay

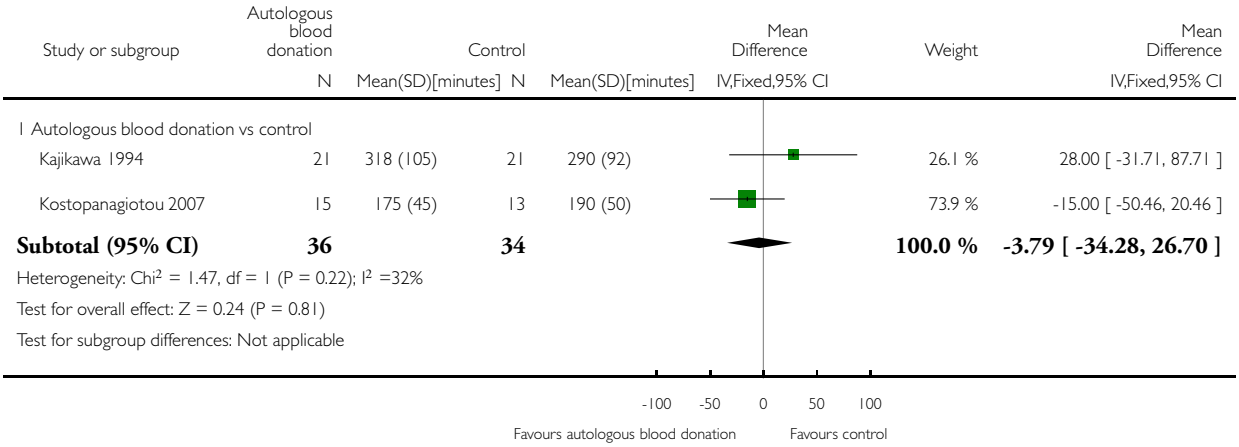


Analysis 2.7. Comparison 2 Autologous blood donation vs control, Outcome 7 Operating time.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 2 Autologous blood donation vs control

Outcome: 7 Operating time



Analysis 3.1. Comparison 3 Cardiopulmonary interventions, Outcome 1 Mortality (perioperative).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 3 Cardiopulmonary interventions

Outcome: 1 Mortality (perioperative)

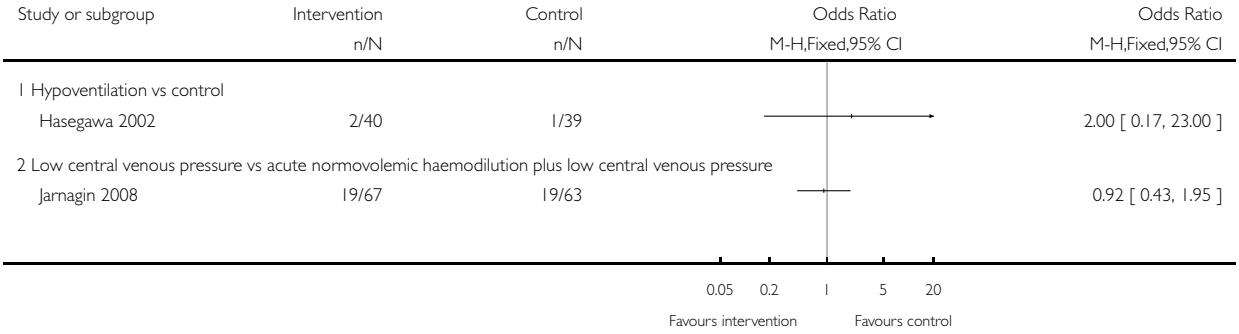
Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Hypoventilation vs control					
Hasegawa 2002	0/40	0/39			Not estimable
Subtotal (95% CI)	**40**	**39**			**Not estimable**
Total events: 0 (Intervention), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
2 Low central venous pressure vs control					
Kato 2008	0/43	0/42			Not estimable
Subtotal (95% CI)	**43**	**42**			**Not estimable**
Total events: 0 (Intervention), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
3 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure					
Jarnagin 2008	3/67	1/63		100.0 %	2.91 [0.29, 28.70]
Matot 2002	0/39	0/39			Not estimable
Subtotal (95% CI)	**106**	**102**		**100.0 %**	**2.91 [0.29, 28.70]**
Total events: 3 (Intervention), 1 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.91 (P = 0.36)					

Analysis 3.2. Comparison 3 Cardiopulmonary interventions, Outcome 2 Serious adverse events (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 3 Cardiopulmonary interventions

Outcome: 2 Serious adverse events (proportion)

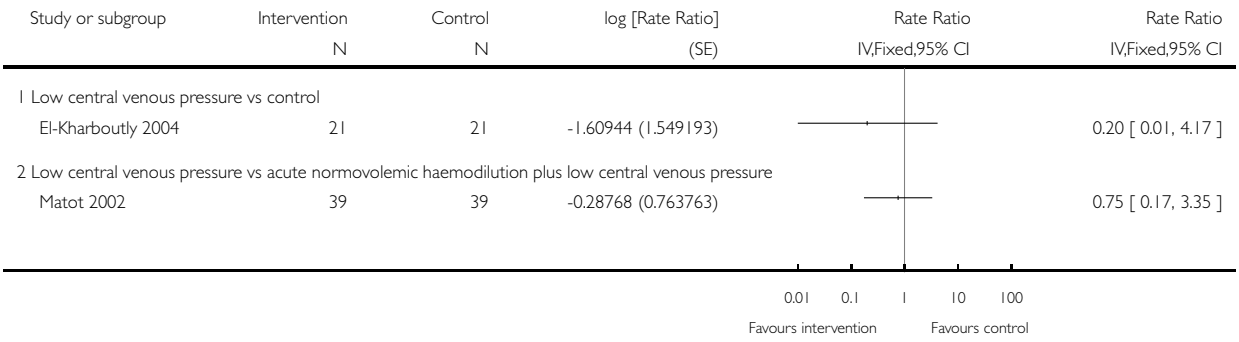


Analysis 3.3. Comparison 3 Cardiopulmonary interventions, Outcome 3 Serious adverse events (number).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 3 Cardiopulmonary interventions

Outcome: 3 Serious adverse events (number)

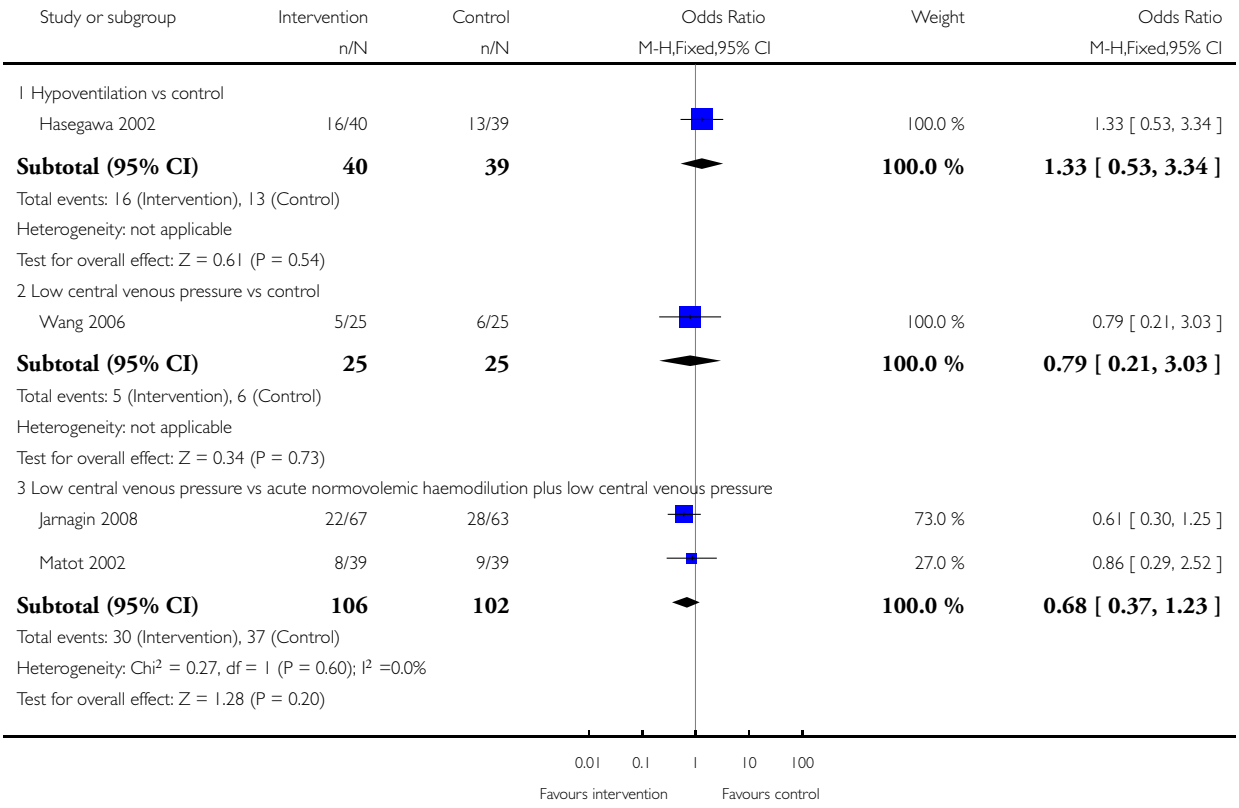


Analysis 3.4. Comparison 3 Cardiopulmonary interventions, Outcome 4 Adverse events (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 3 Cardiopulmonary interventions

Outcome: 4 Adverse events (proportion)



Analysis 3.5. Comparison 3 Cardiopulmonary interventions, Outcome 5 Adverse events (number).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 3 Cardiopulmonary interventions

Outcome: 5 Adverse events (number)

Study or subgroup	Intervention N	Control N	log [Rate Ratio] (SE)	Rate Ratio IV,Fixed,95% CI	Rate Ratio IV,Fixed,95% CI
1 Low central venous pressure vs control					
El-Kharboutly 2004	20	20	-0.69315 (0.707107)		0.50 [0.13, 2.00]
2 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure					
Matot 2002	39	39	0 (0.408248)		1.00 [0.45, 2.23]

Analysis 3.6. Comparison 3 Cardiopulmonary interventions, Outcome 6 Blood transfusion (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 3 Cardiopulmonary interventions

Outcome: 6 Blood transfusion (proportion)

Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Hypoventilation vs control					
Hasegawa 2002	3/40	4/39		100.0 %	0.71 [0.15, 3.40]
Subtotal (95% CI)	**40**	**39**		**100.0 %**	**0.71 [0.15, 3.40]**
Total events: 3 (Intervention), 4 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.43 (P = 0.67)					
2 Low central venous pressure vs control					
El-Kharboutly 2004	9/20	11/20		38.9 %	0.67 [0.19, 2.33]
Kato 2008	0/43	0/42			Not estimable
Wang 2006	8/25	14/25		61.1 %	0.37 [0.12, 1.17]

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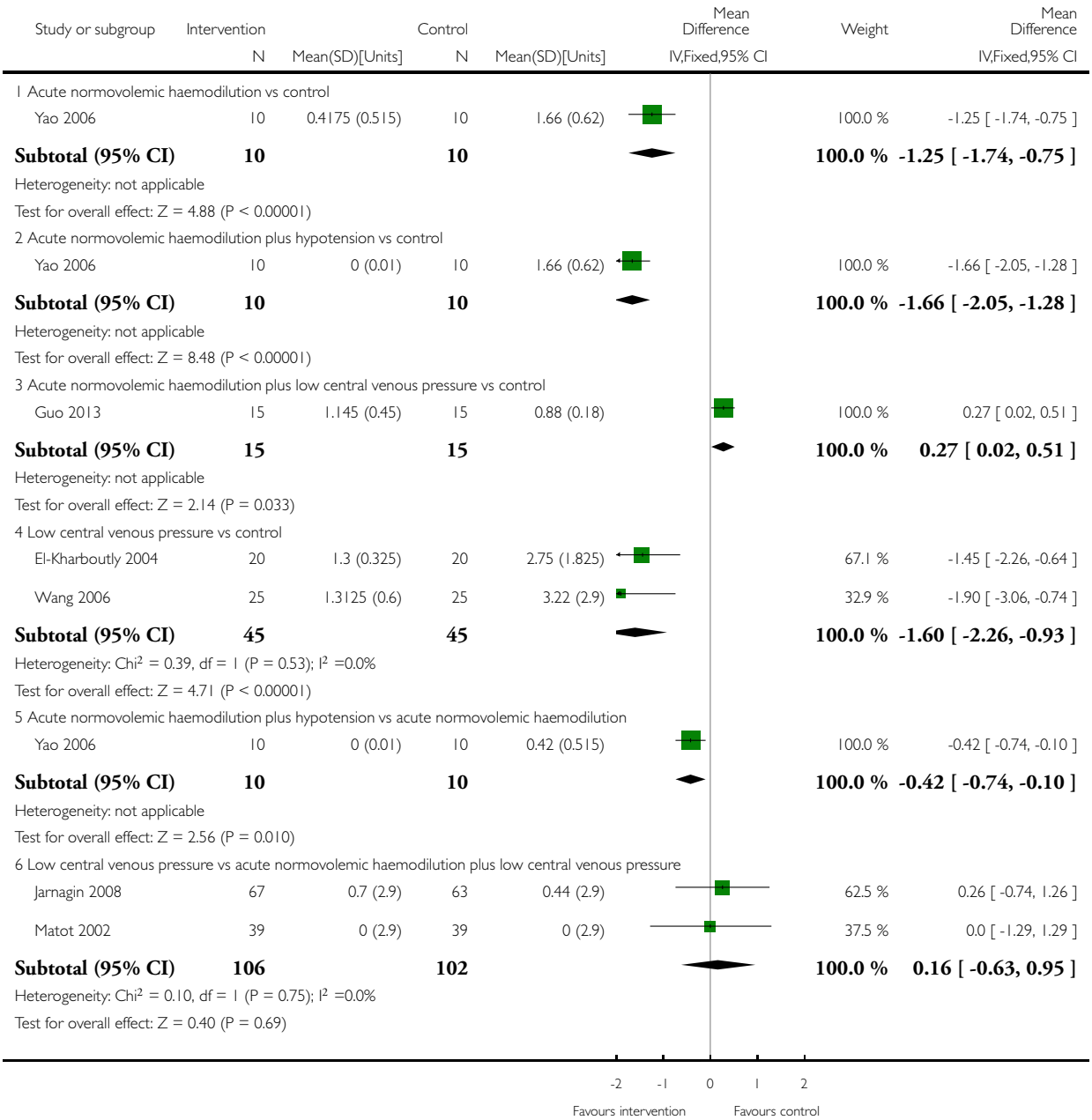
Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Subtotal (95% CI)	**88**	**87**		**100.0 %**	**0.49 [0.21, 1.13]**
Total events: 17 (Intervention), 25 (Control)					
Heterogeneity: Chi^2 = 0.47, df = 1 (P = 0.49); I^2 =0.0%					
Test for overall effect: Z = 1.68 (P = 0.093)					
3 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure					
Jarnagin 2008	17/67	8/63		70.6 %	2.34 [0.93, 5.89]
Matot 2002	14/39	4/39		29.4 %	4.90 [1.44, 16.66]
Subtotal (95% CI)	**106**	**102**		**100.0 %**	**3.09 [1.49, 6.42]**
Total events: 31 (Intervention), 12 (Control)					
Heterogeneity: Chi^2 = 0.90, df = 1 (P = 0.34); I^2 =0.0%					
Test for overall effect: Z = 3.03 (P = 0.0025)					

Analysis 3.7. Comparison 3 Cardiopulmonary interventions, Outcome 7 Blood transfusion (red blood cell).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 3 Cardiopulmonary interventions

Outcome: 7 Blood transfusion (red blood cell)



Analysis 3.8. Comparison 3 Cardiopulmonary interventions, Outcome 8 Blood transfusion (fresh frozen plasma).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 3 Cardiopulmonary interventions

Outcome: 8 Blood transfusion (fresh frozen plasma)

Study or subgroup	Intervention N	Mean(SD)[units]	Control N	Mean(SD)[units]	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Low central venous pressure vs control						
Wang 2006	25	1.752 (1)	25	4.23 (2.63)		-2.48 [-3.58, -1.37]
2 Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure						
Jarnagin 2008	67	0.28 (2.63)	63	0.17 (2.63)		0.11 [-0.79, 1.01]

Analysis 3.9. Comparison 3 Cardiopulmonary interventions, Outcome 9 Blood transfusion (cryoprecipitate).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 3 Cardiopulmonary interventions

Outcome: 9 Blood transfusion (cryoprecipitate)

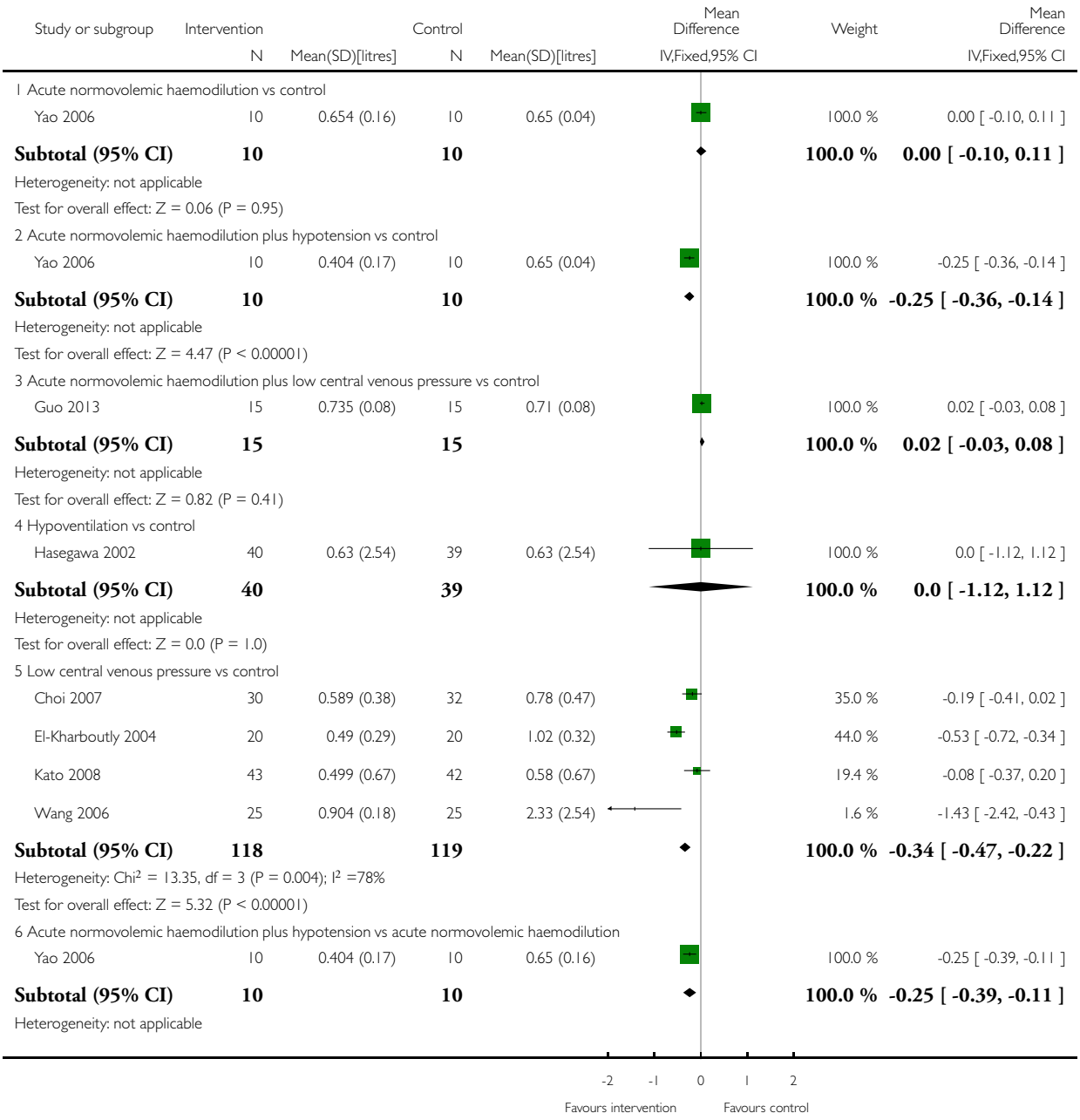
Study or subgroup	Intervention N	Mean(SD)[units]	Control N	Mean(SD)[units]	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Hypoventilation vs control						
Hasegawa 2002	40	0.052 (0.19)	39	0.08 (0.23)		-0.02 [-0.12, 0.07]

Analysis 3.10. Comparison 3 Cardiopulmonary interventions, Outcome 10 Blood loss.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 3 Cardiopulmonary interventions

Outcome: 10 Blood loss



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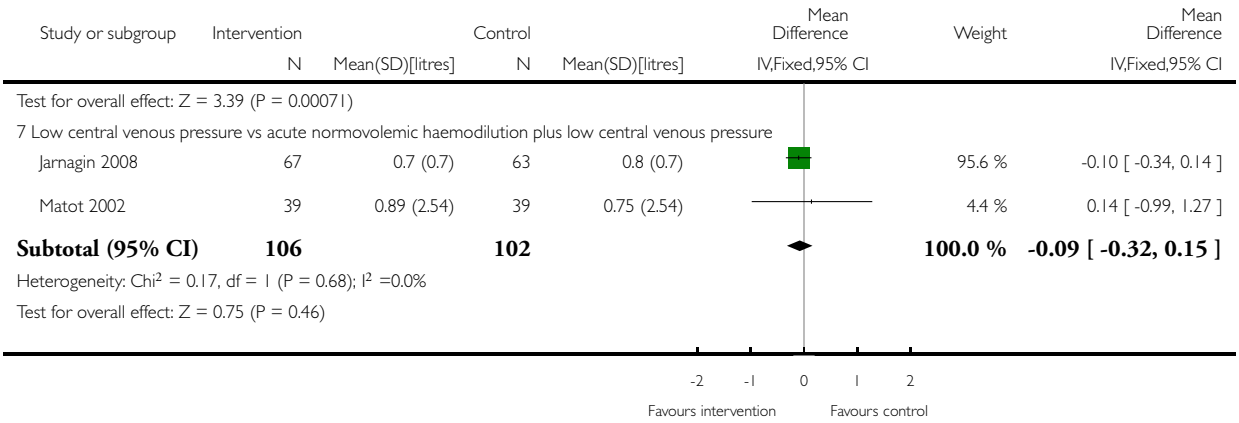
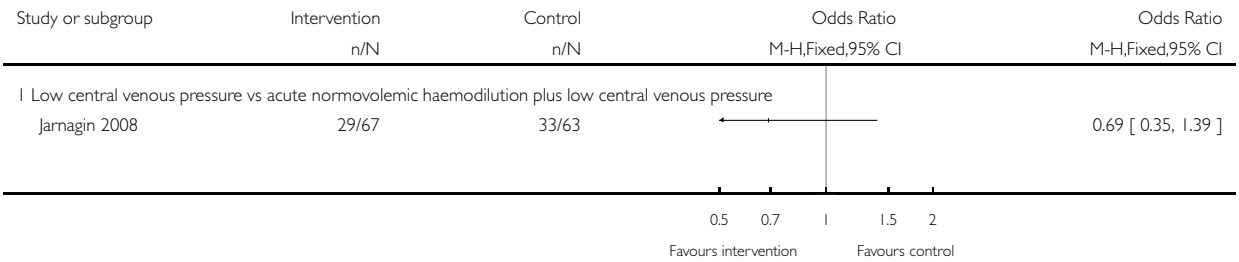


Analysis 3.11. Comparison 3 Cardiopulmonary interventions, Outcome 11 Major blood loss (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 3 Cardiopulmonary interventions

Outcome: 11 Major blood loss (proportion)

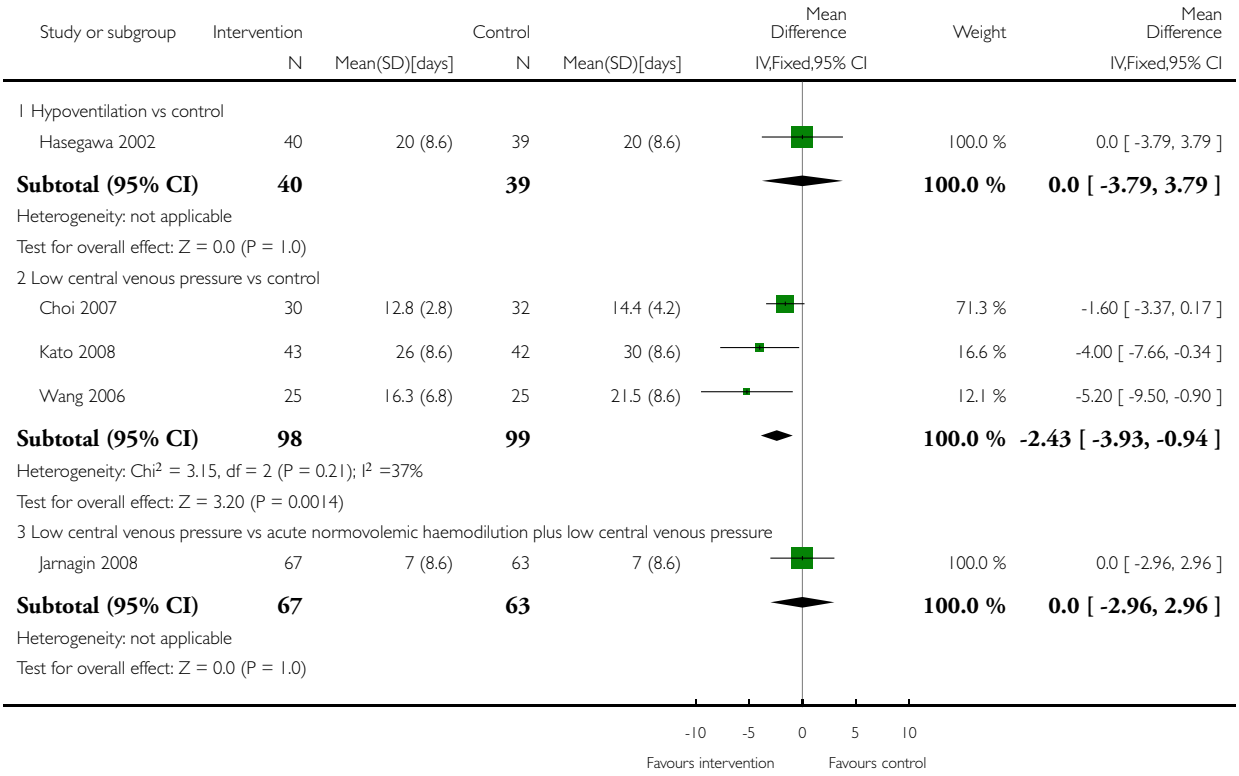


Analysis 3.12. Comparison 3 Cardiopulmonary interventions, Outcome 12 Hospital stay.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 3 Cardiopulmonary interventions

Outcome: 12 Hospital stay

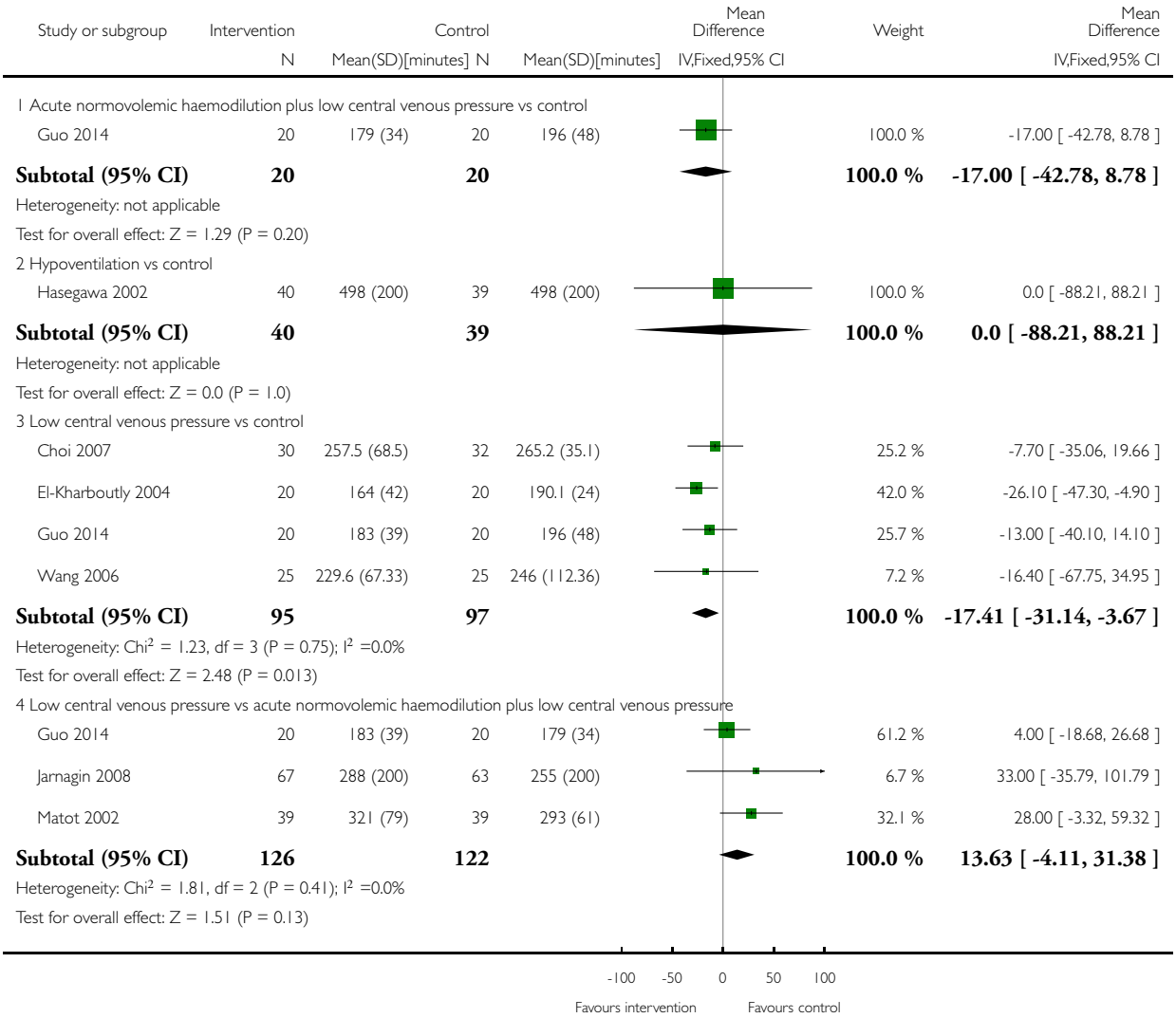


Analysis 3.13. Comparison 3 Cardiopulmonary interventions, Outcome 13 Operating time.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 3 Cardiopulmonary interventions

Outcome: 13 Operating time

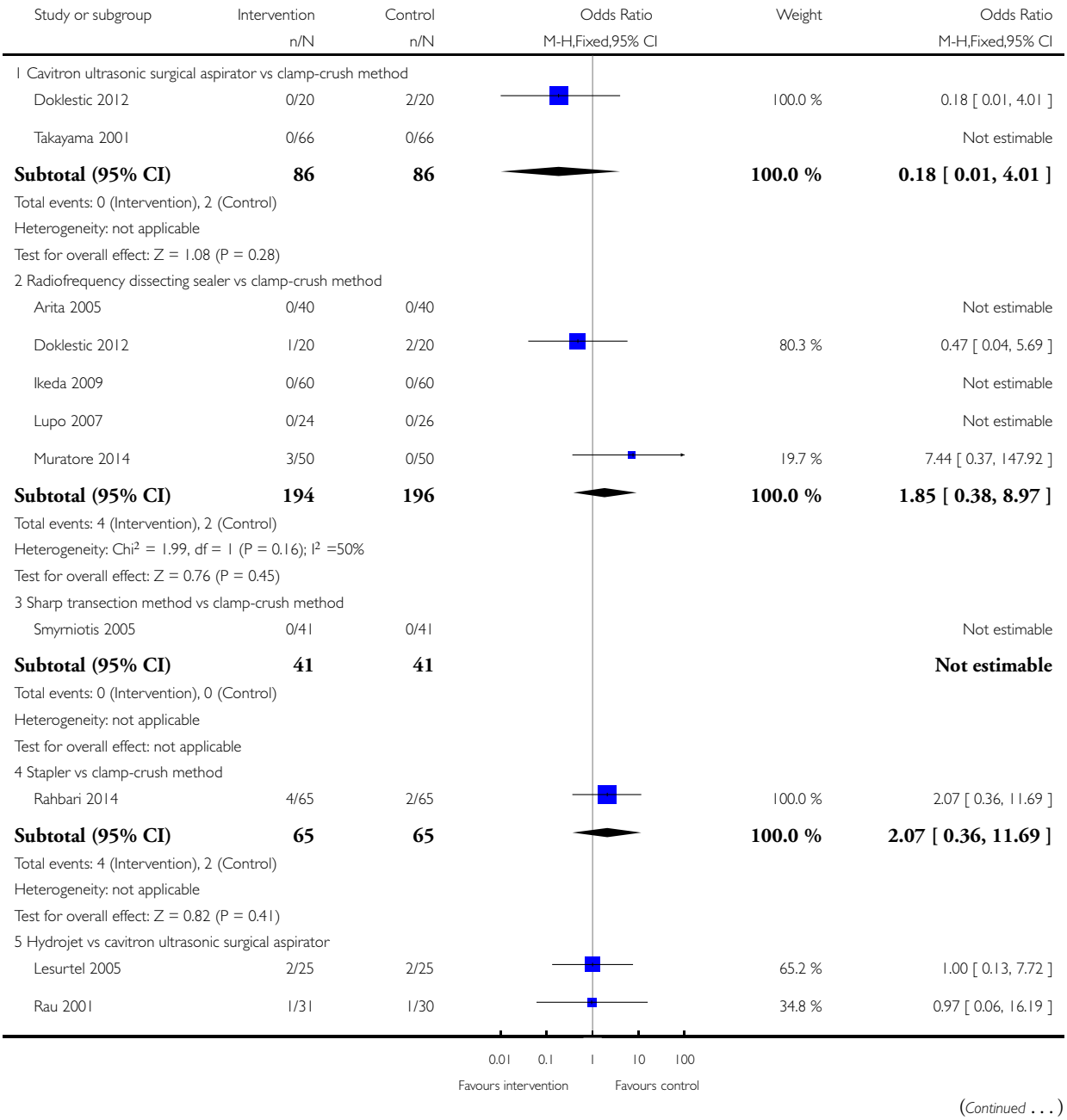


Analysis 4.1. Comparison 4 Methods of parenchymal transection, Outcome 1 Mortality (perioperative).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 4 Methods of parenchymal transection

Outcome: 1 Mortality (perioperative)



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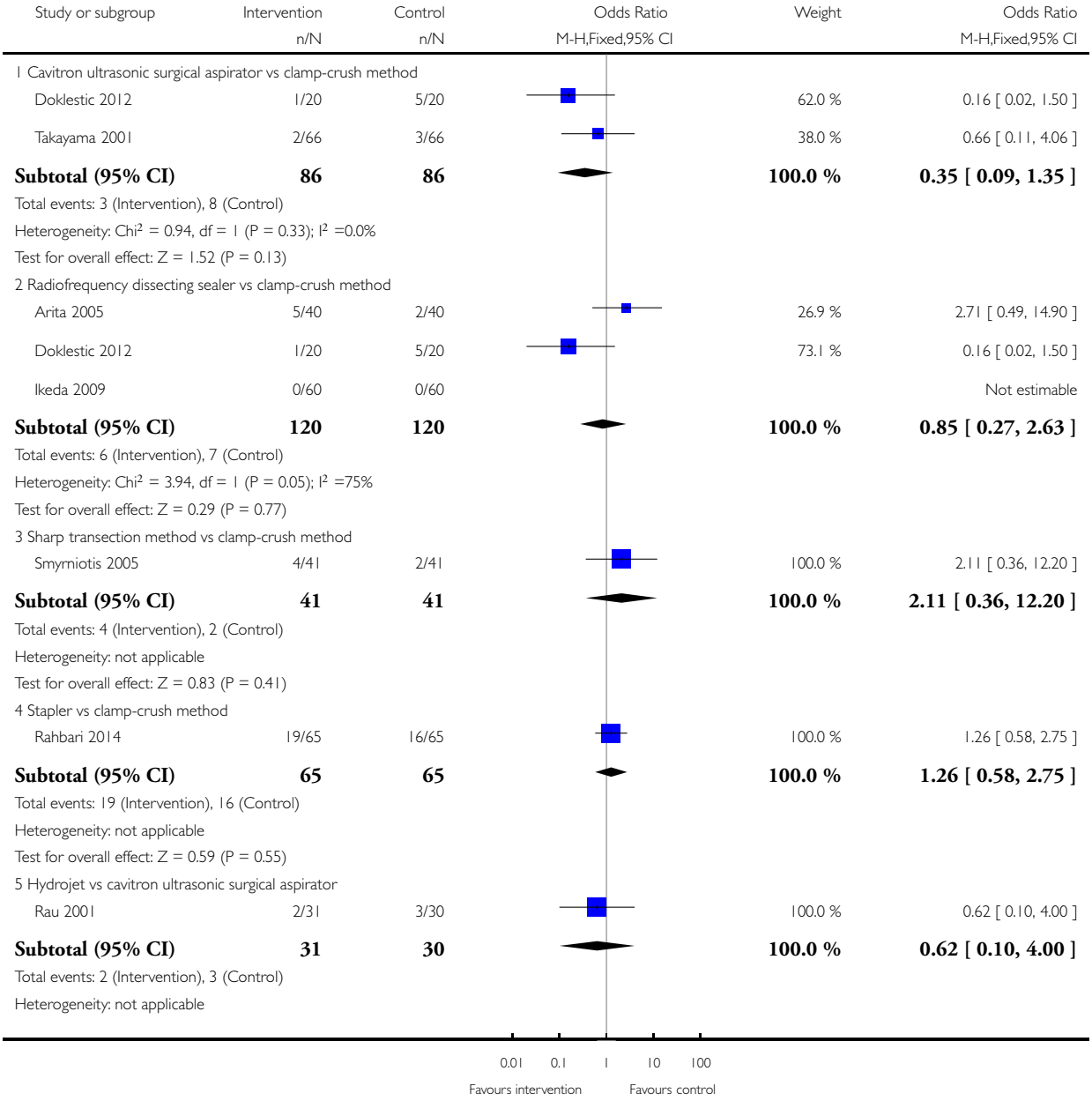
Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Subtotal (95% CI)	**56**	**55**		**100.0 %**	**0.99 [0.19, 5.17]**
Total events: 3 (Intervention), 3 (Control)					
Heterogeneity: Chi^2 = 0.00, df = 1 (P = 0.98); I^2 =0.0%					
Test for overall effect: Z = 0.01 (P = 0.99)					
6 Radiofrequency dissecting sealer vs cavitron ultrasonic surgical aspirator					
Doklestic 2012	1/20	0/20		15.9 %	3.15 [0.12, 82.16]
Lesurtel 2005	0/25	2/25		84.1 %	0.18 [0.01, 4.04]
Subtotal (95% CI)	**45**	**45**		**100.0 %**	**0.66 [0.11, 4.05]**
Total events: 1 (Intervention), 2 (Control)					
Heterogeneity: Chi^2 = 1.54, df = 1 (P = 0.21); I^2 =35%					
Test for overall effect: Z = 0.45 (P = 0.65)					
7 Stapler vs cavitron ultrasonic surgical aspirator					
Savlid 2013	0/50	0/50			Not estimable
Subtotal (95% CI)	**50**	**50**			**Not estimable**
Total events: 0 (Intervention), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
8 Radiofrequency dissecting sealer vs hydrojet					
Lesurtel 2005	0/25	2/25		100.0 %	0.18 [0.01, 4.04]
Subtotal (95% CI)	**25**	**25**		**100.0 %**	**0.18 [0.01, 4.04]**
Total events: 0 (Intervention), 2 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.07 (P = 0.28)					

Analysis 4.2. Comparison 4 Methods of parenchymal transection, Outcome 2 Serious adverse events (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 4 Methods of parenchymal transection

Outcome: 2 Serious adverse events (proportion)



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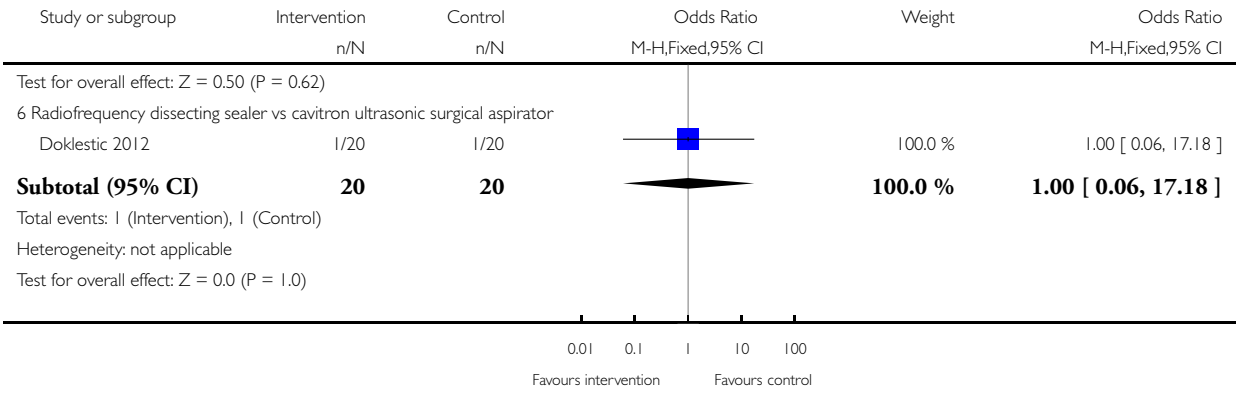
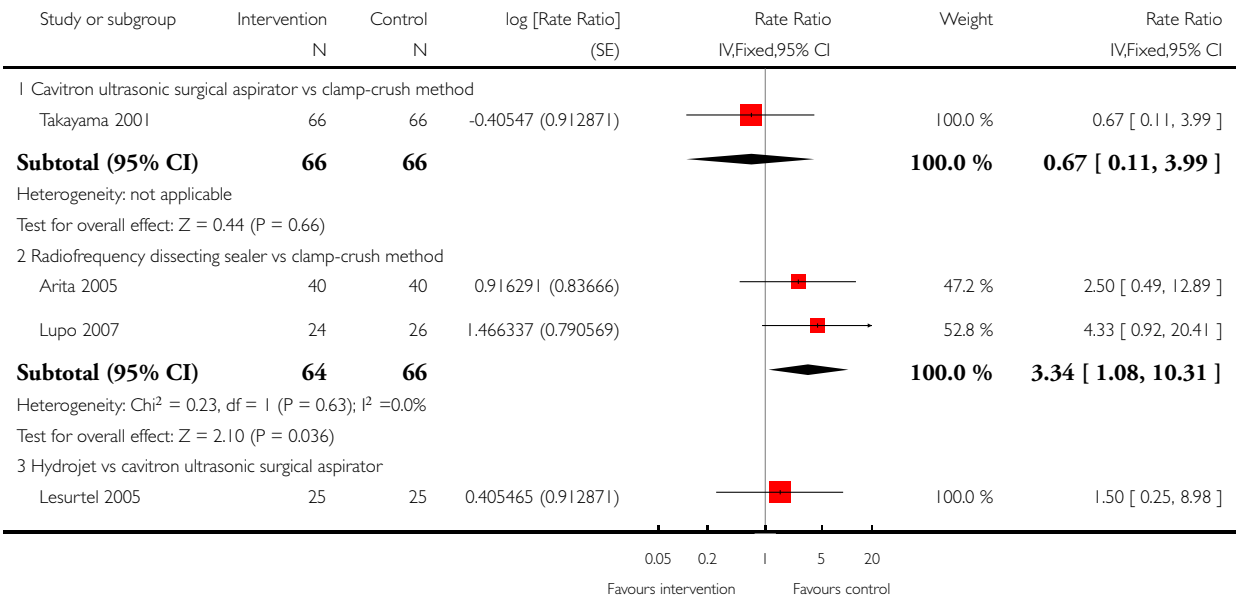


Analysis 4.3. Comparison 4 Methods of parenchymal transection, Outcome 3 Serious adverse events (number).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 4 Methods of parenchymal transection

Outcome: 3 Serious adverse events (number)



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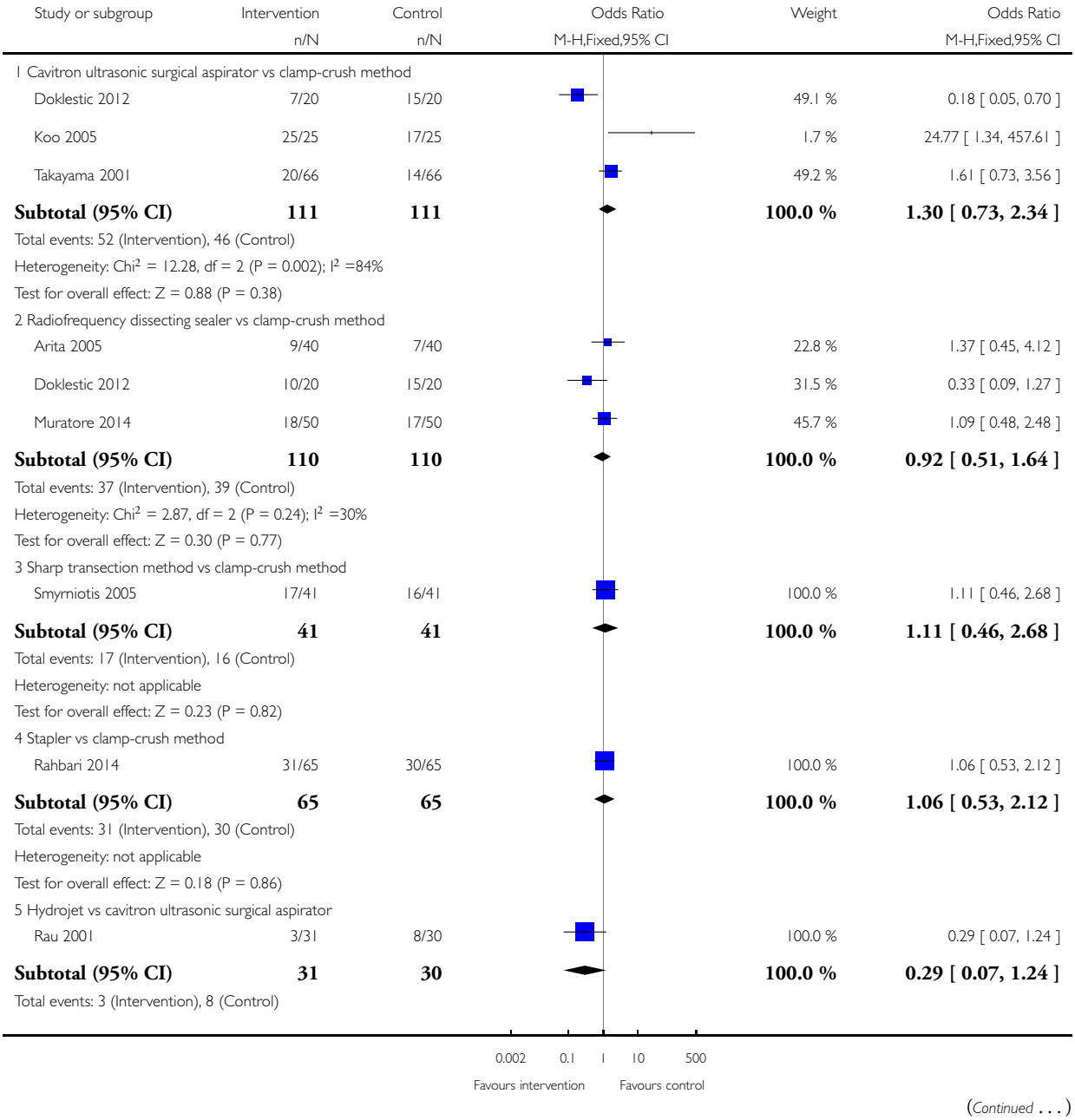
Study or subgroup	Intervention N	Control N	log [Rate Ratio] (SE)	Rate Ratio IV,Fixed,95% CI	Weight	Rate Ratio IV,Fixed,95% CI
Subtotal (95% CI)	**25**	**25**			**100.0 %**	**1.50 [0.25, 8.98]**
Heterogeneity: not applicable						
Test for overall effect: Z = 0.44 (P = 0.66)						
4 Radiofrequency dissecting sealer vs cavitron ultrasonic surgical aspirator						
Lesurtel 2005	25	25	0.405465 (0.912871)		100.0 %	1.50 [0.25, 8.98]
Subtotal (95% CI)	**25**	**25**			**100.0 %**	**1.50 [0.25, 8.98]**
Heterogeneity: not applicable						
Test for overall effect: Z = 0.44 (P = 0.66)						
5 Stapler vs cavitron ultrasonic surgical aspirator						
Savlid 2013	50	50	0.287682 (0.440959)		100.0 %	1.33 [0.56, 3.16]
Subtotal (95% CI)	**50**	**50**			**100.0 %**	**1.33 [0.56, 3.16]**
Heterogeneity: not applicable						
Test for overall effect: Z = 0.65 (P = 0.51)						
6 Radiofrequency dissecting sealer vs hydrojet						
Lesurtel 2005	25	25	0 (0.816497)		100.0 %	1.00 [0.20, 4.95]
Subtotal (95% CI)	**25**	**25**			**100.0 %**	**1.00 [0.20, 4.95]**
Heterogeneity: not applicable						
Test for overall effect: Z = 0.0 (P = 1.0)						

Analysis 4.4. Comparison 4 Methods of parenchymal transection, Outcome 4 Adverse events (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 4 Methods of parenchymal transection

Outcome: 4 Adverse events (proportion)



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Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Heterogeneity: not applicable					
Test for overall effect: Z = 1.66 (P = 0.096)					
6 Radiofrequency dissecting sealer vs cavitron ultrasonic surgical aspirator					
Doklestic 2012	10/20	7/20		100.0 %	1.86 [0.52, 6.61]
Subtotal (95% CI)	**20**	**20**		**100.0 %**	**1.86 [0.52, 6.61]**
Total events: 10 (Intervention), 7 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.96 (P = 0.34)					

Analysis 4.5. Comparison 4 Methods of parenchymal transection, Outcome 5 Adverse events (number).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 4 Methods of parenchymal transection

Outcome: 5 Adverse events (number)

Study or subgroup	Intervention N	Control N	log [Rate Ratio] (SE)	Rate Ratio IV,Fixed,95% CI	Weight	Rate Ratio IV,Fixed,95% CI
1 Cavitron ultrasonic surgical aspirator vs clamp-crush method						
Takayama 2001	66	66	0.446287 (0.320156)		100.0 %	1.56 [0.83, 2.93]
Subtotal (95% CI)	**66**	**66**			**100.0 %**	**1.56 [0.83, 2.93]**
Heterogeneity: not applicable						
Test for overall effect: Z = 1.39 (P = 0.16)						
2 Radiofrequency dissecting sealer vs clamp-crush method						
Arita 2005	40	40	0.251314 (0.503953)		32.8 %	1.29 [0.48, 3.45]
Ikeda 2009	60	60	0.310155 (0.396958)		52.9 %	1.36 [0.63, 2.97]
Lupo 2007	24	26	1.871802 (0.763763)		14.3 %	6.50 [1.45, 29.04]
Subtotal (95% CI)	**124**	**126**			**100.0 %**	**1.67 [0.95, 2.94]**
Heterogeneity: Chi^2 = 3.70, df = 2 (P = 0.16); I^2 =46%						
Test for overall effect: Z = 1.78 (P = 0.075)						
3 Sharp transection method vs clamp-crush method						

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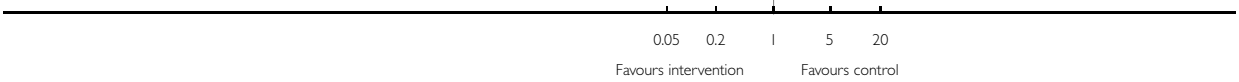
Study or subgroup	Intervention N	Control N	log [Rate Ratio] (SE)	Rate Ratio IV,Fixed,95% CI	Weight	Rate Ratio IV,Fixed,95% CI
Smyrniotis 2005	41	41	0.117783 (0.343592)		100.0 %	1.12 [0.57, 2.21]
Subtotal (95% CI)	**41**	**41**			**100.0 %**	**1.12 [0.57, 2.21]**
Heterogeneity: not applicable						
Test for overall effect: Z = 0.34 (P = 0.73)						
4 Hydrojet vs cavitron ultrasonic surgical aspirator						
Lesurtel 2005	25	25	-0.13353 (0.517549)		100.0 %	0.88 [0.32, 2.41]
Subtotal (95% CI)	**25**	**25**			**100.0 %**	**0.88 [0.32, 2.41]**
Heterogeneity: not applicable						
Test for overall effect: Z = 0.26 (P = 0.80)						
5 Radiofrequency dissecting sealer vs cavitron ultrasonic surgical aspirator						
Lesurtel 2005	25	25	0.117783 (0.485913)		100.0 %	1.12 [0.43, 2.92]
Subtotal (95% CI)	**25**	**25**			**100.0 %**	**1.12 [0.43, 2.92]**
Heterogeneity: not applicable						
Test for overall effect: Z = 0.24 (P = 0.81)						
6 Stapler vs cavitron ultrasonic surgical aspirator						
Savlid 2013	50	50	0.146603 (0.313187)		100.0 %	1.16 [0.63, 2.14]
Subtotal (95% CI)	**50**	**50**			**100.0 %**	**1.16 [0.63, 2.14]**
Heterogeneity: not applicable						
Test for overall effect: Z = 0.47 (P = 0.64)						
7 Radiofrequency dissecting sealer vs hydrojet						
Lesurtel 2005	25	25	0.251314 (0.503953)		100.0 %	1.29 [0.48, 3.45]
Subtotal (95% CI)	**25**	**25**			**100.0 %**	**1.29 [0.48, 3.45]**
Heterogeneity: not applicable						
Test for overall effect: Z = 0.50 (P = 0.62)						

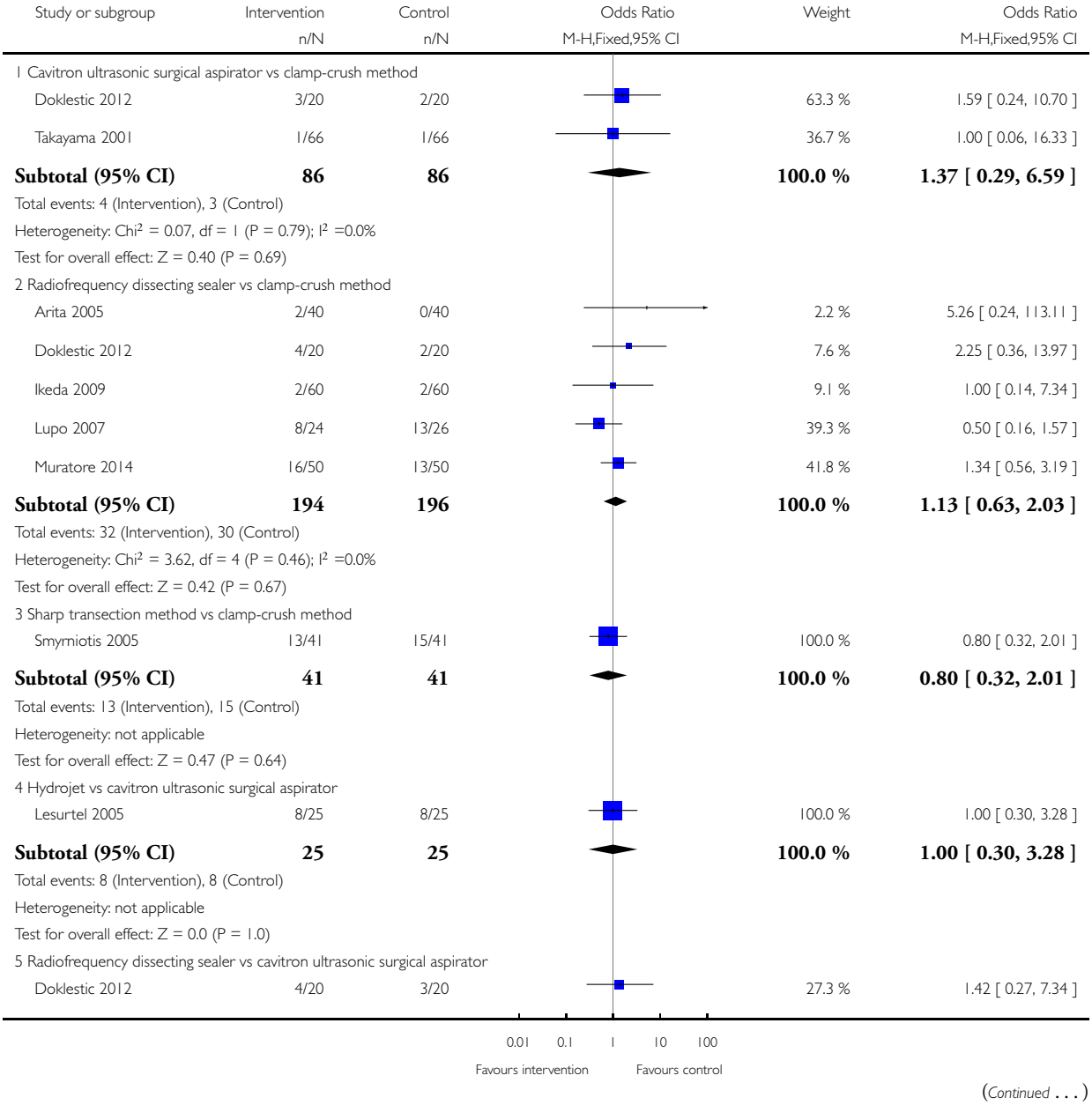


Analysis 4.6. Comparison 4 Methods of parenchymal transection, Outcome 6 Blood transfusion (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 4 Methods of parenchymal transection

Outcome: 6 Blood transfusion (proportion)



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Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Lesurtel 2005	5/25	8/25		72.7 %	0.53 [0.15, 1.93]
Subtotal (95% CI)	**45**	**45**		**100.0 %**	**0.77 [0.29, 2.09]**
Total events: 9 (Intervention), 11 (Control)					
Heterogeneity: Chi^2 = 0.85, df = 1 (P = 0.36); I^2 =0.0%					
Test for overall effect: Z = 0.51 (P = 0.61)					
6 Radiofrequency dissecting sealer vs hydrojet					
Lesurtel 2005	5/25	8/25		100.0 %	0.53 [0.15, 1.93]
Subtotal (95% CI)	**25**	**25**		**100.0 %**	**0.53 [0.15, 1.93]**
Total events: 5 (Intervention), 8 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.96 (P = 0.34)					

Analysis 4.7. Comparison 4 Methods of parenchymal transection, Outcome 7 Blood transfusion (red blood cell).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 4 Methods of parenchymal transection

Outcome: 7 Blood transfusion (red blood cell)

Study or subgroup	Intervention N	Mean(SD)[units]	Control N	Mean(SD)[units]	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Sharp transection method vs clamp-crush method						
Smyrniotis 2005	41	0 (2.3)	41	0 (2.3)		0.0 [-1.00, 1.00]
2 Stapler vs clamp-crush method						
Rahbari 2014	65	1.1 (1.6)	65	1.2 (2.3)		-0.10 [-0.78, 0.58]
3 Hydrojet vs cavitron ultrasonic surgical aspirator						
Rau 2001	31	1.5 (1.69)	30	2.48 (1.99)		-0.98 [-1.91, -0.05]
4 Stapler vs cavitron ultrasonic surgical aspirator						
Savlid 2013	50	4 (2.3)	50	4 (2.3)		0.0 [-0.90, 0.90]

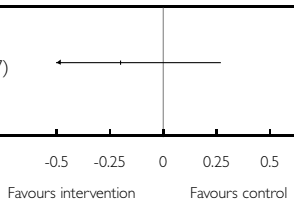
Analysis 4.8. Comparison 4 Methods of parenchymal transection, Outcome 8 Blood transfusion (fresh frozen plasma).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 4 Methods of parenchymal transection

Outcome: 8 Blood transfusion (fresh frozen plasma)

Study or subgroup	Intervention N	Mean(SD)[units]	Control N	Mean(SD)[units]	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Stapler vs clamp-crush method						
Rahbari 2014	65	0.3 (0.9)	65	0.5 (1.7)		-0.20 [-0.67, 0.27]



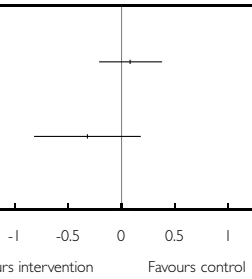
Analysis 4.9. Comparison 4 Methods of parenchymal transection, Outcome 9 Blood loss.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 4 Methods of parenchymal transection

Outcome: 9 Blood loss

Study or subgroup	Intervention N	Mean(SD)[litres]	Control N	Mean(SD)[litres]	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Cavitron ultrasonic surgical aspirator vs clamp-crush method						
Koo 2005	25	0.875 (0.58)	25	0.79 (0.47)		0.08 [-0.21, 0.38]
2 Hydrojet vs cavitron ultrasonic surgical aspirator						
Rau 2001	31	1.479 (1)	30	1.8 (1)		-0.32 [-0.82, 0.18]

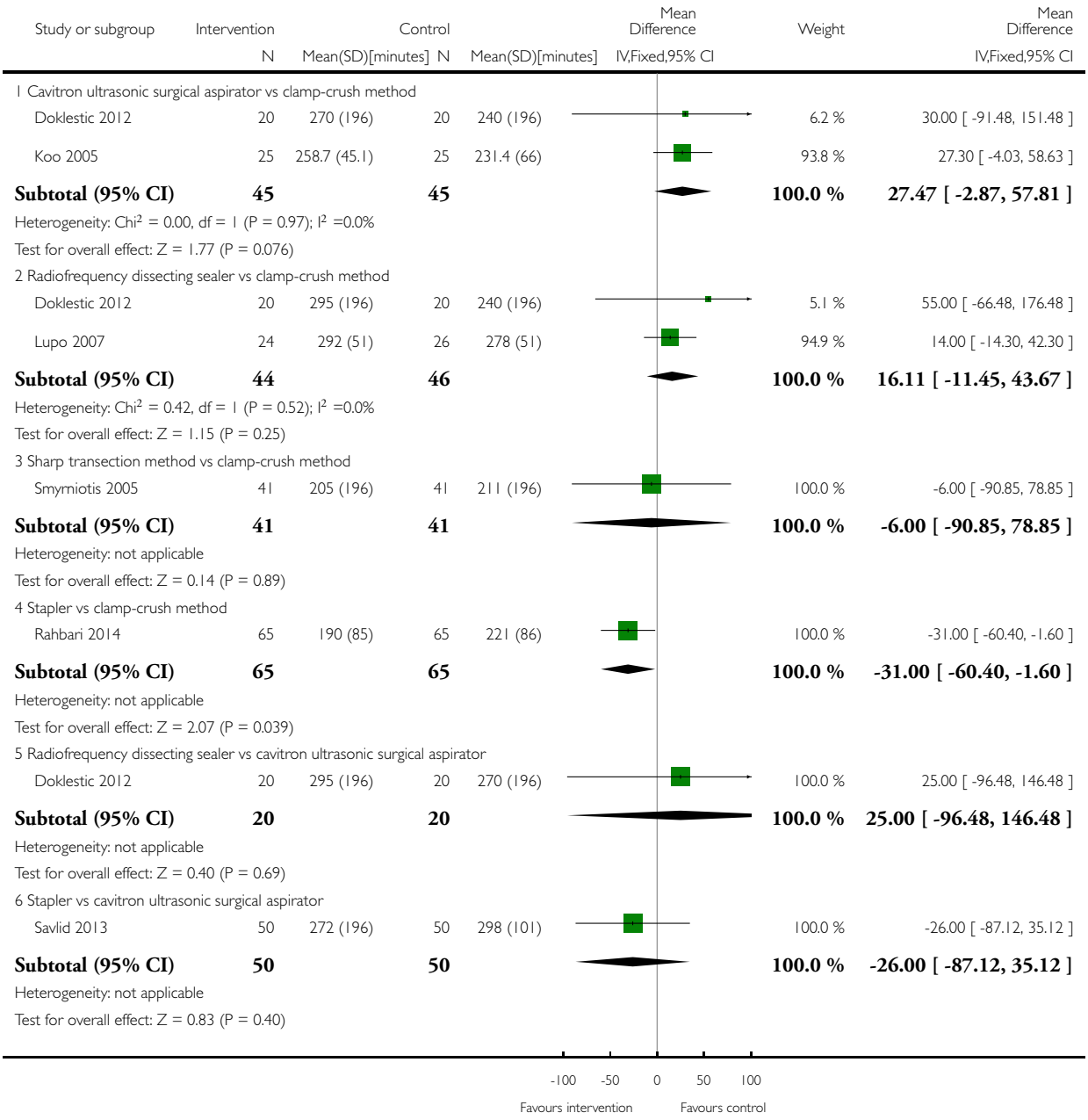


Analysis 4.10. Comparison 4 Methods of parenchymal transection, Outcome 10 Operating time.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 4 Methods of parenchymal transection

Outcome: 10 Operating time

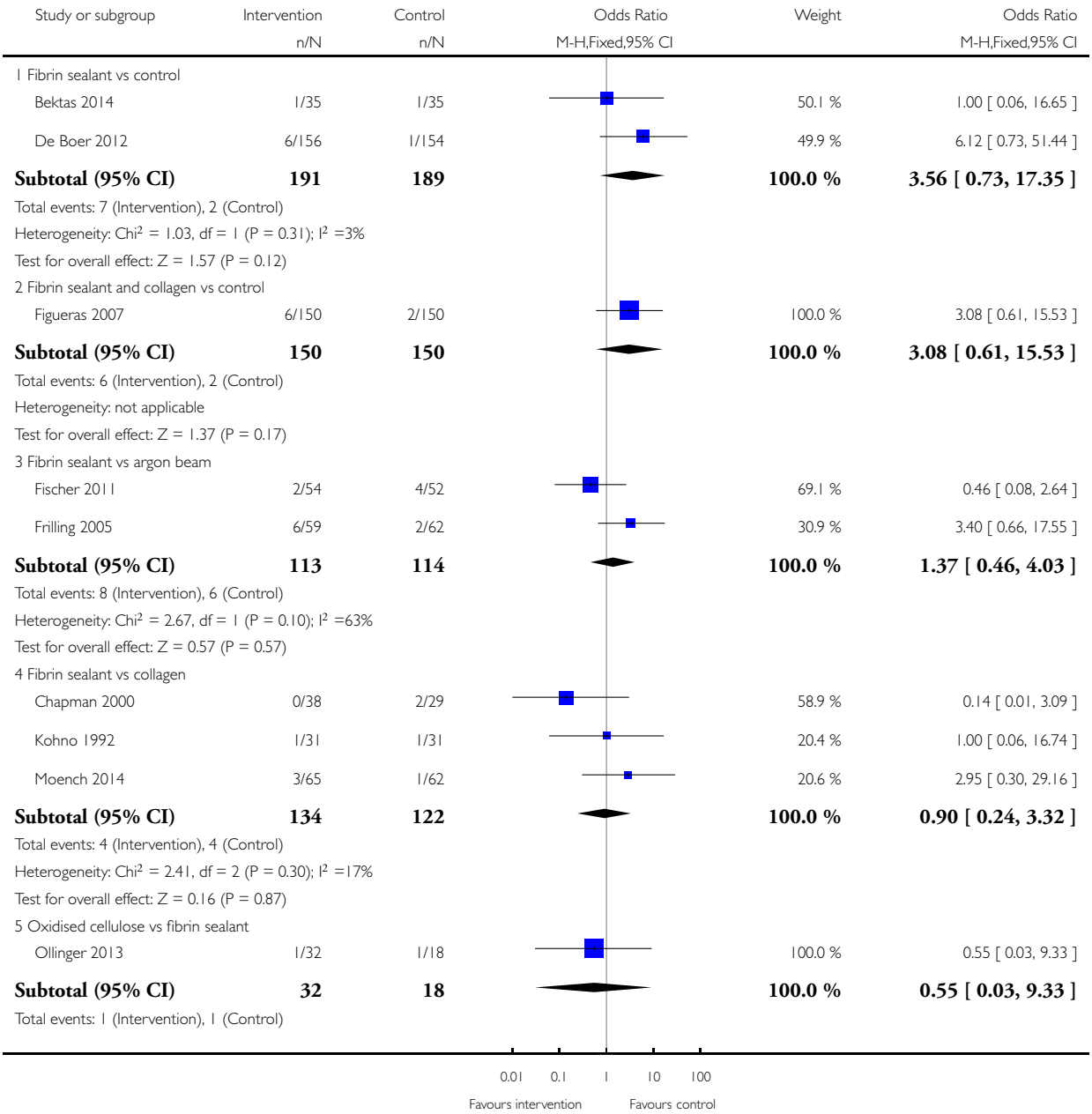


Analysis 5.1. Comparison 5 Methods of dealing with cut surface, Outcome 1 Mortality (perioperative).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 5 Methods of dealing with cut surface

Outcome: 1 Mortality (perioperative)



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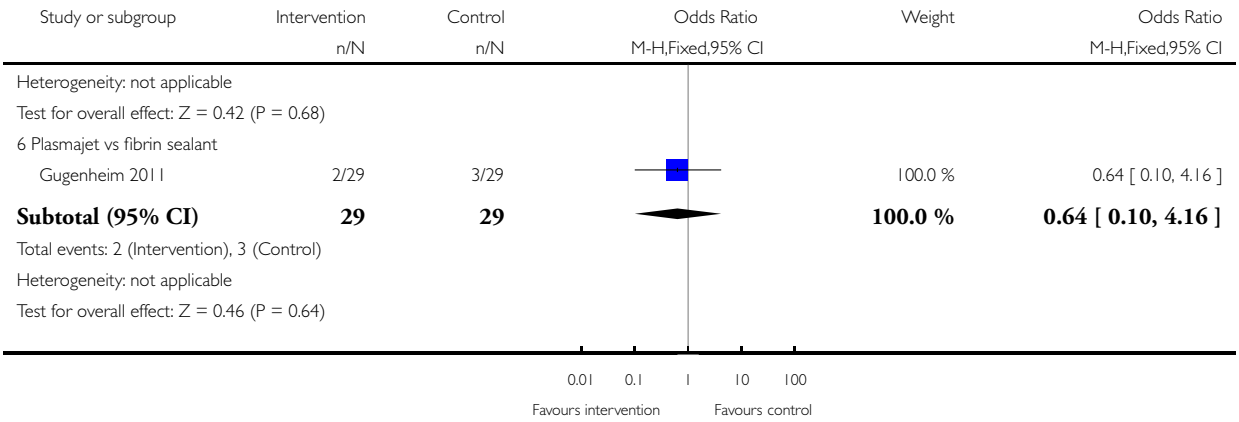
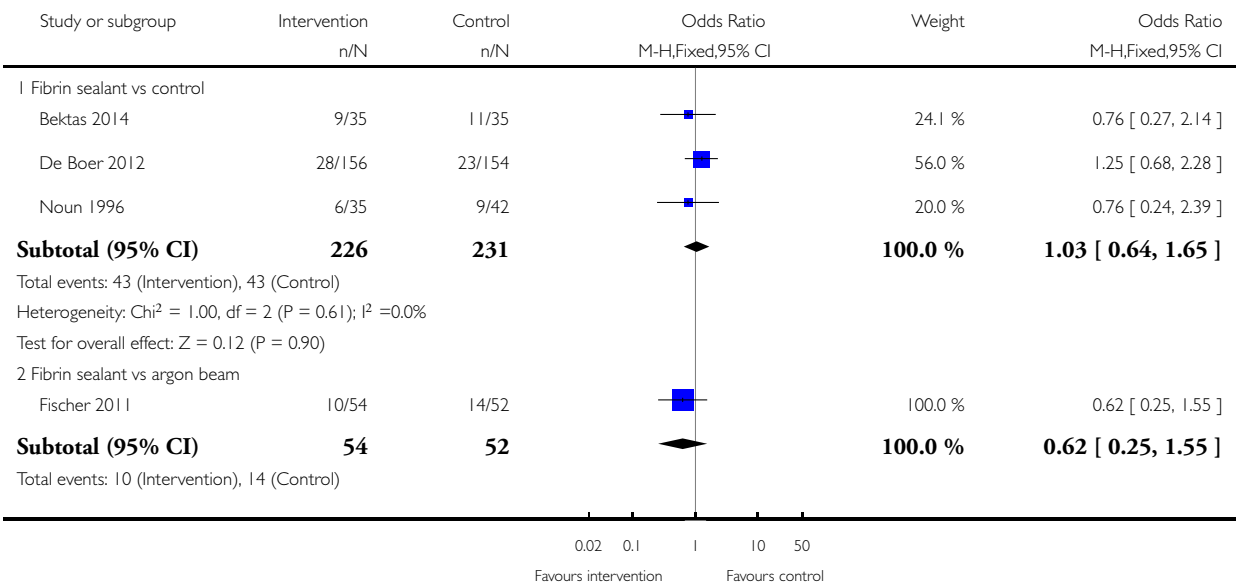


Analysis 5.2. Comparison 5 Methods of dealing with cut surface, Outcome 2 Serious adverse events (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 5 Methods of dealing with cut surface

Outcome: 2 Serious adverse events (proportion)



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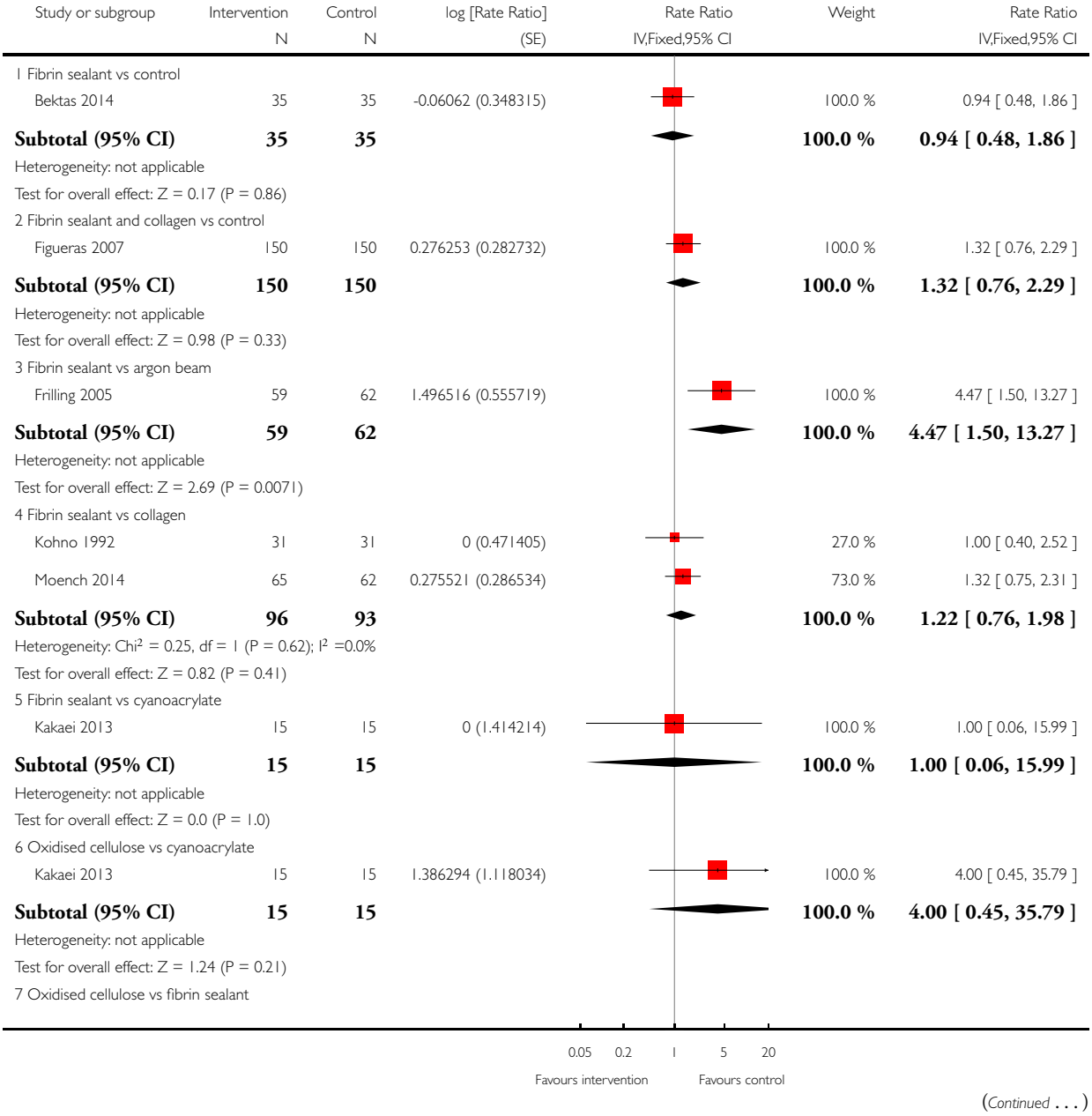
Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Heterogeneity: not applicable					
Test for overall effect: Z = 1.03 (P = 0.30)					
3 Fibrin sealant vs collagen					
Moench 2014	23/65	16/62		100.0 %	1.57 [0.73, 3.38]
Subtotal (95% CI)	**65**	**62**		**100.0 %**	**1.57 [0.73, 3.38]**
Total events: 23 (Intervention), 16 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.17 (P = 0.24)					
4 Oxidised cellulose vs fibrin sealant					
Ollinger 2013	10/32	8/18		100.0 %	0.57 [0.17, 1.87]
Subtotal (95% CI)	**32**	**18**		**100.0 %**	**0.57 [0.17, 1.87]**
Total events: 10 (Intervention), 8 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.93 (P = 0.35)					
5 Plasmajet vs fibrin sealant					
Gugenheim 2011	1/29	6/29		100.0 %	0.14 [0.02, 1.22]
Subtotal (95% CI)	**29**	**29**		**100.0 %**	**0.14 [0.02, 1.22]**
Total events: 1 (Intervention), 6 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.78 (P = 0.075)					

Analysis 5.3. Comparison 5 Methods of dealing with cut surface, Outcome 3 Serious adverse events (number).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 5 Methods of dealing with cut surface

Outcome: 3 Serious adverse events (number)



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Study or subgroup	Intervention N	Control N	log [Rate Ratio] (SE)	Rate Ratio IV,Fixed,95% CI	Weight	Rate Ratio IV,Fixed,95% CI
Kakaei 2013	15	15	1.386294 (1.118034)		100.0 %	4.00 [0.45, 35.79]
Subtotal (95% CI)	**15**	**15**			**100.0 %**	**4.00 [0.45, 35.79]**
Heterogeneity: not applicable						
Test for overall effect: Z = 1.24 (P = 0.21)						

Analysis 5.4. Comparison 5 Methods of dealing with cut surface, Outcome 4 Adverse events (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 5 Methods of dealing with cut surface

Outcome: 4 Adverse events (proportion)

Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Fibrin sealant versus control					
Bektas 2014	26/35	27/35		11.7 %	0.86 [0.29, 2.56]
De Boer 2012	82/156	89/154		71.8 %	0.81 [0.52, 1.27]
Noun 1996	10/35	15/42		16.5 %	0.72 [0.27, 1.89]
Subtotal (95% CI)	**226**	**231**		**100.0 %**	**0.80 [0.55, 1.17]**
Total events: 118 (Intervention), 131 (Control)					
Heterogeneity: Chi^2 = 0.06, df = 2 (P = 0.97); I^2 =0.0%					
Test for overall effect: Z = 1.15 (P = 0.25)					
2 Fibrin sealant and collagen vs control					
Figueras 2007	35/150	35/150		100.0 %	1.00 [0.59, 1.71]
Subtotal (95% CI)	**150**	**150**		**100.0 %**	**1.00 [0.59, 1.71]**
Total events: 35 (Intervention), 35 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					
3 Fibrin sealant vs argon beam					
Fischer 2011	25/54	28/52		53.9 %	0.74 [0.34, 1.59]

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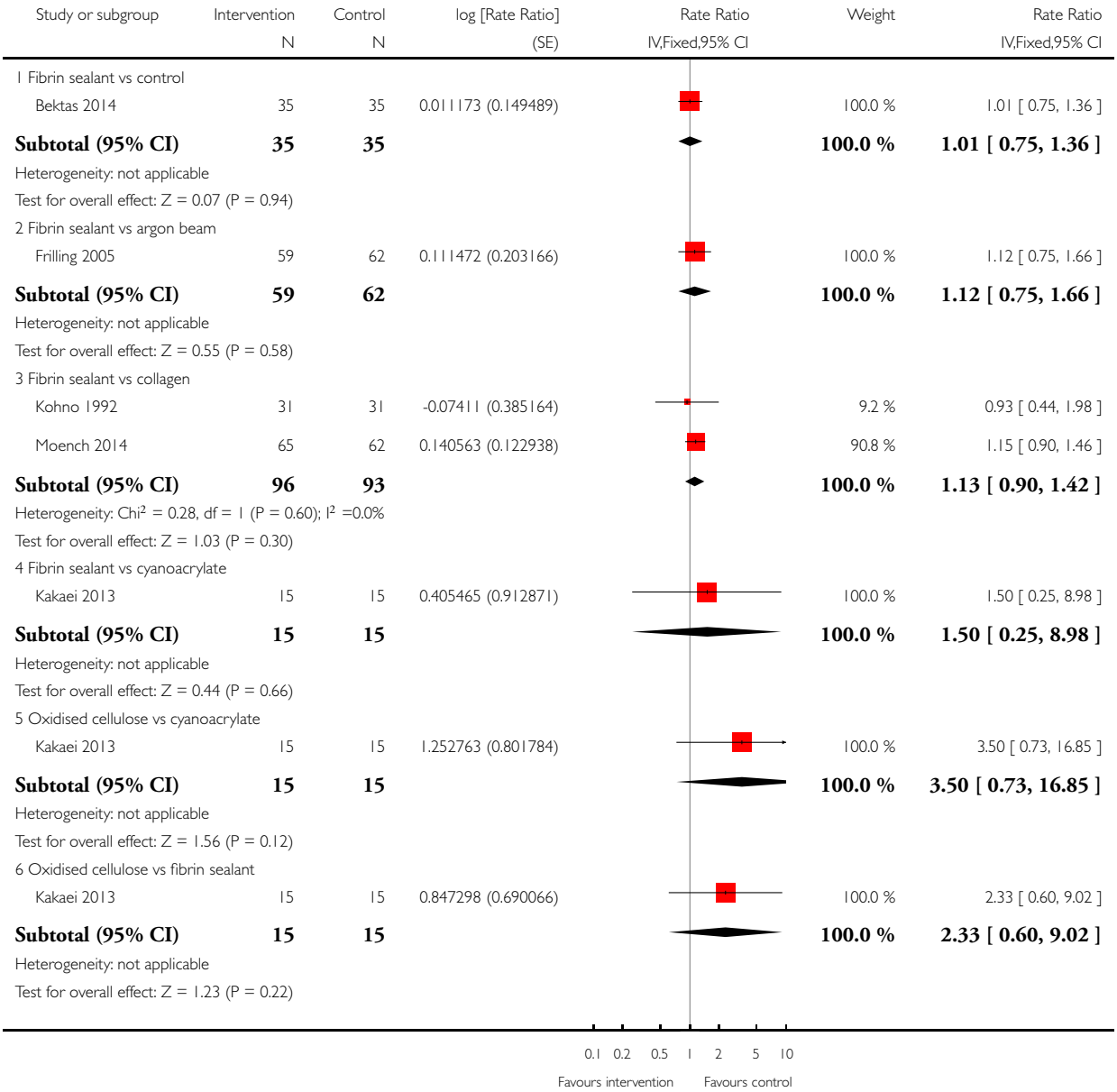
Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Frilling 2005	26/59	24/62		46.1 %	1.25 [0.60, 2.58]
Subtotal (95% CI)	**113**	**114**		**100.0 %**	**0.97 [0.58, 1.64]**
Total events: 51 (Intervention), 52 (Control)					
Heterogeneity: Chi^2 = 0.95, df = 1 (P = 0.33); I^2 =0.0%					
Test for overall effect: Z = 0.10 (P = 0.92)					
4 Fibrin sealant vs collagen					
Moench 2014	39/65	38/62		100.0 %	0.95 [0.46, 1.93]
Subtotal (95% CI)	**65**	**62**		**100.0 %**	**0.95 [0.46, 1.93]**
Total events: 39 (Intervention), 38 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.15 (P = 0.88)					
5 Oxidised cellulose vs fibrin sealant					
Genyk 2014	4/110	5/114		48.4 %	0.82 [0.22, 3.15]
Ollinger 2013	23/32	14/18		51.6 %	0.73 [0.19, 2.82]
Subtotal (95% CI)	**142**	**132**		**100.0 %**	**0.77 [0.30, 2.01]**
Total events: 27 (Intervention), 19 (Control)					
Heterogeneity: Chi^2 = 0.02, df = 1 (P = 0.90); I^2 =0.0%					
Test for overall effect: Z = 0.53 (P = 0.60)					

Analysis 5.5. Comparison 5 Methods of dealing with cut surface, Outcome 5 Adverse events (number).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 5 Methods of dealing with cut surface

Outcome: 5 Adverse events (number)

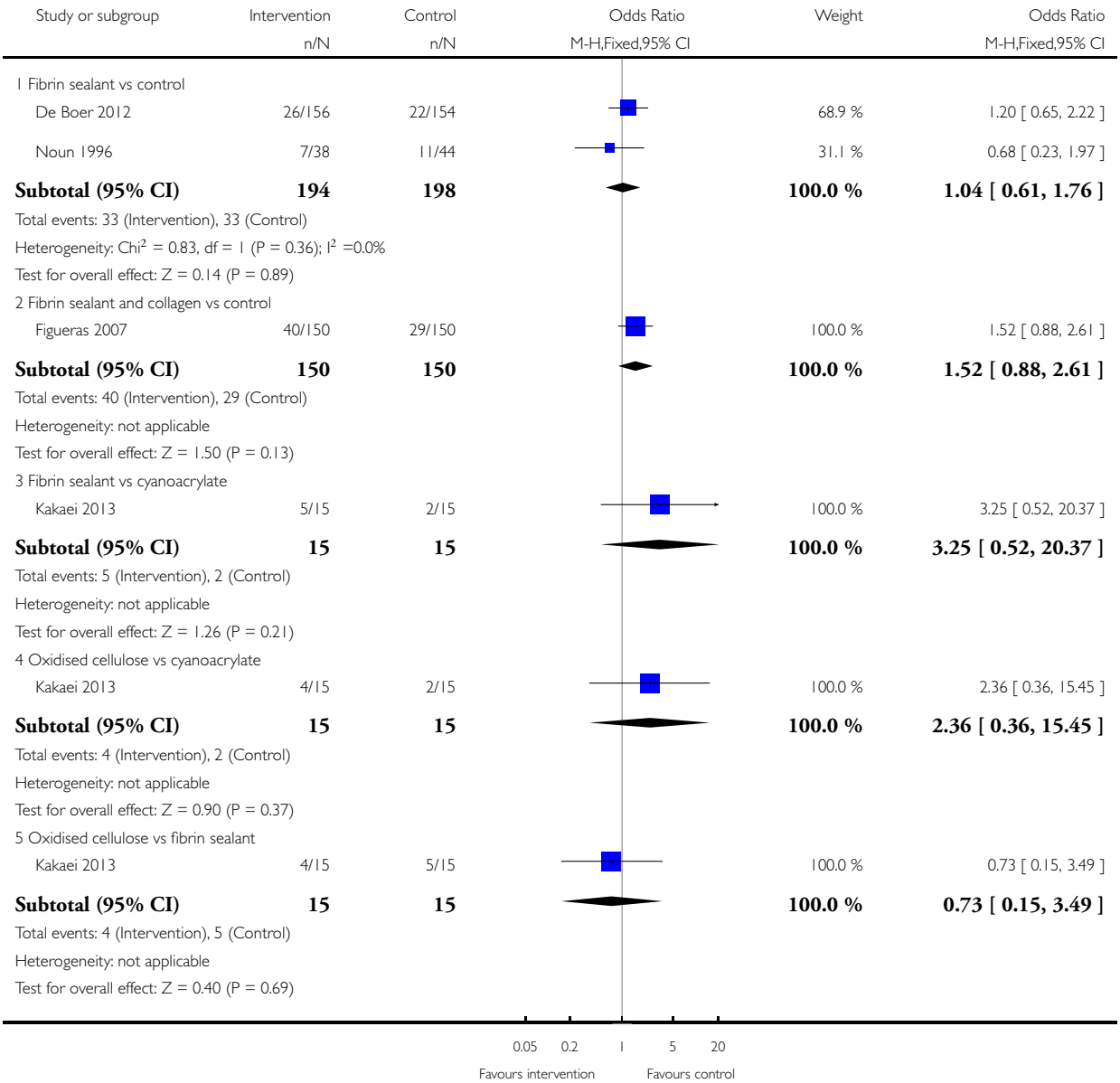


Analysis 5.6. Comparison 5 Methods of dealing with cut surface, Outcome 6 Blood transfusion (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 5 Methods of dealing with cut surface

Outcome: 6 Blood transfusion (proportion)

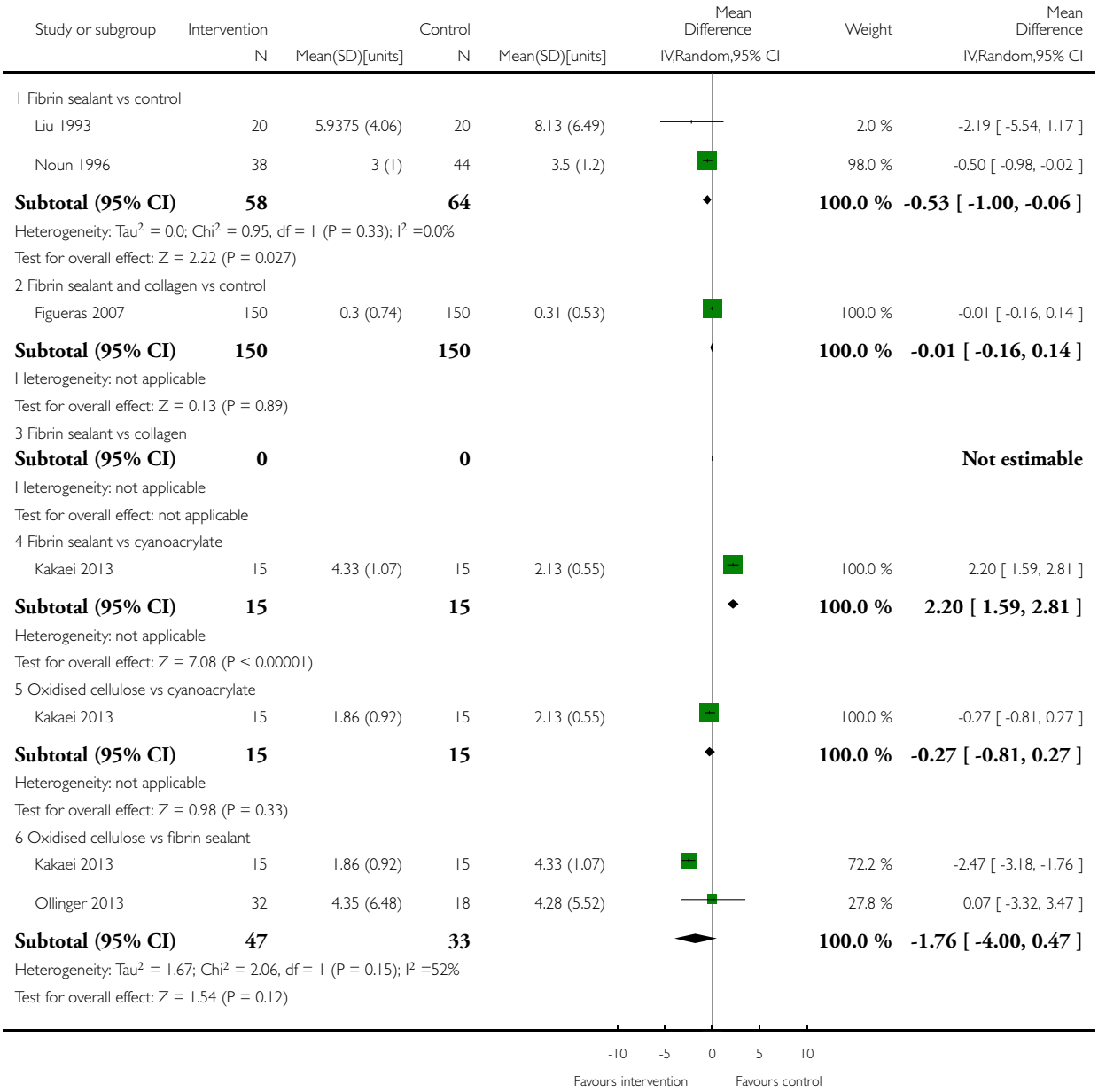


Analysis 5.7. Comparison 5 Methods of dealing with cut surface, Outcome 7 Blood transfusion (red blood cell).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 5 Methods of dealing with cut surface

Outcome: 7 Blood transfusion (red blood cell)



Analysis 5.8. Comparison 5 Methods of dealing with cut surface, Outcome 8 Blood transfusion (fresh frozen plasma).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 5 Methods of dealing with cut surface

Outcome: 8 Blood transfusion (fresh frozen plasma)

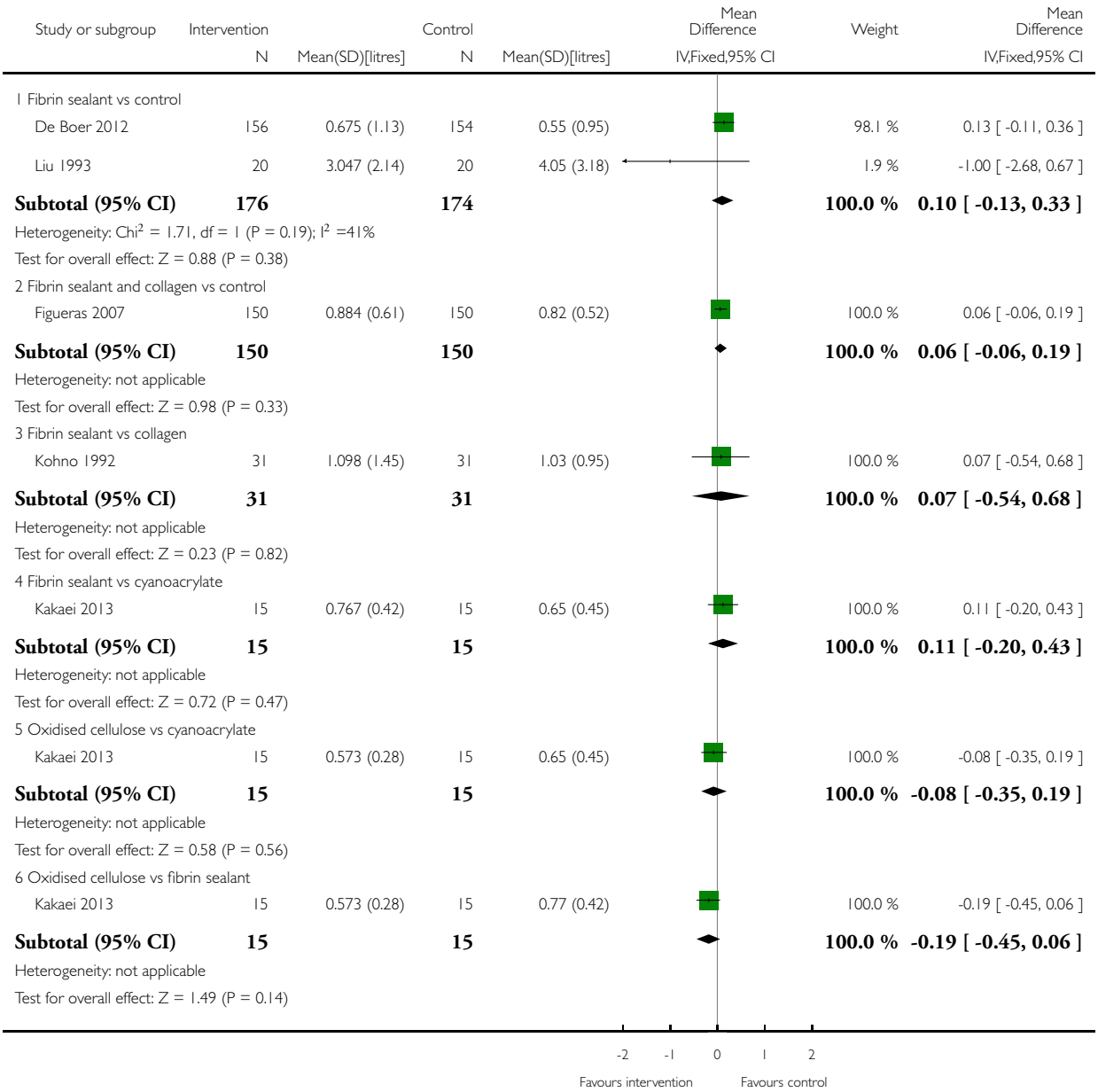
Study or subgroup	Intervention N	Mean(SD)[units]	Control N	Mean(SD)[units]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Fibrin sealant vs cyanoacrylate							
Kakaei 2013	15	0 (0.01)	15	0.8 (0.42)		100.0 %	-0.80 [-1.01, -0.59]
Subtotal (95% CI)	**15**		**15**			**100.0 %**	**-0.80 [-1.01, -0.59]**
Heterogeneity: not applicable							
Test for overall effect: Z = 7.38 (P < 0.00001)							
2 Oxidised cellulose vs cyanoacrylate							
Kakaei 2013	15	0.53 (0.36)	15	0.8 (0.42)		100.0 %	-0.27 [-0.55, 0.01]
Subtotal (95% CI)	**15**		**15**			**100.0 %**	**-0.27 [-0.55, 0.01]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.89 (P = 0.059)							
3 Oxidised cellulose vs fibrin sealant							
Kakaei 2013	15	0.53 (0.36)	15	0 (0.01)		99.9 %	0.53 [0.35, 0.71]
Ollinger 2013	32	20.12 (6.84)	18	17.64 (10.64)		0.1 %	2.48 [-2.98, 7.94]
Subtotal (95% CI)	**47**		**33**			**100.0 %**	**0.53 [0.35, 0.71]**
Heterogeneity: Chi^2 = 0.49, df = 1 (P = 0.48); I^2 =0.0%							
Test for overall effect: Z = 5.73 (P < 0.00001)							

Analysis 5.9. Comparison 5 Methods of dealing with cut surface, Outcome 9 Blood loss.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 5 Methods of dealing with cut surface

Outcome: 9 Blood loss

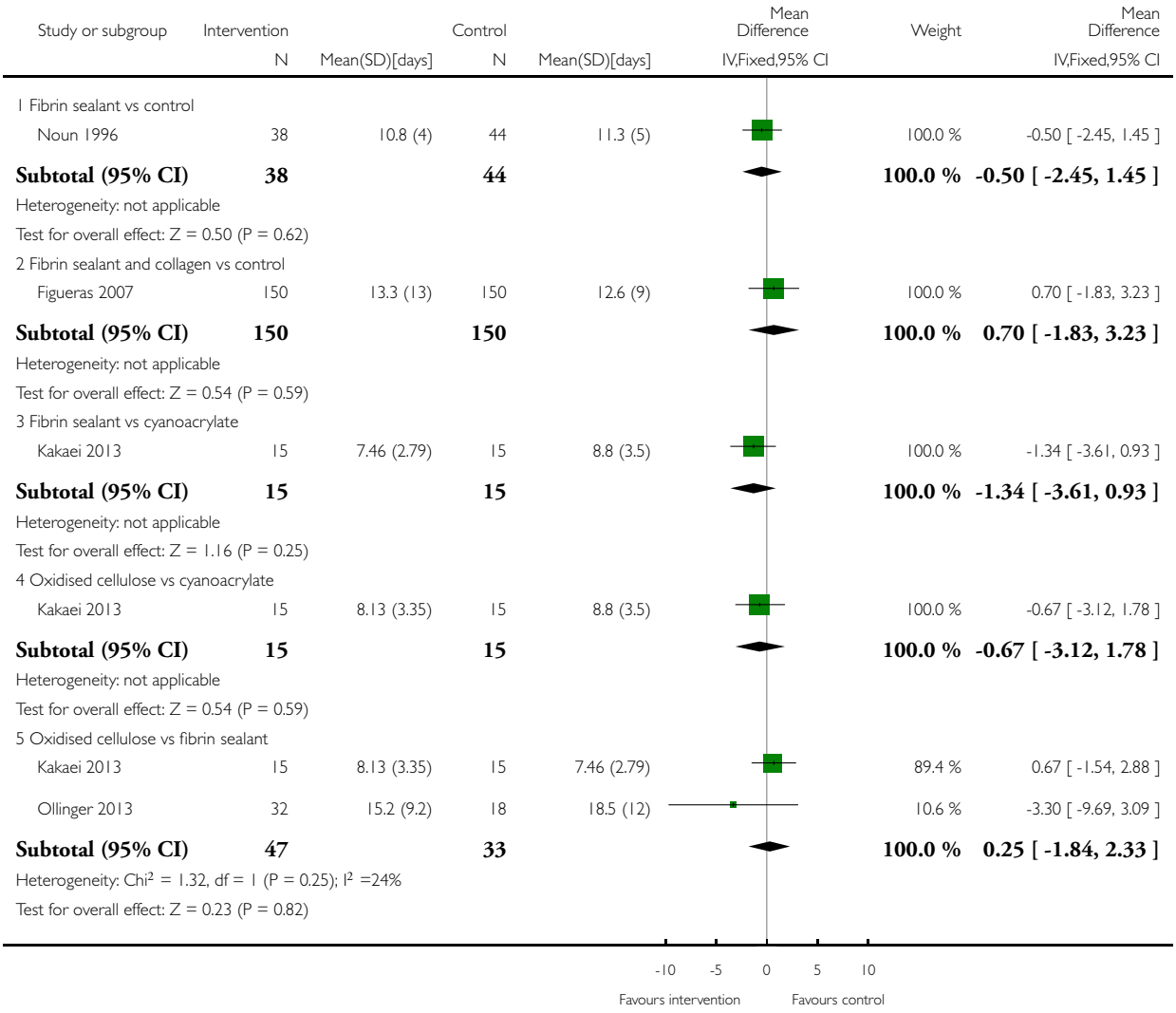


Analysis 5.10. Comparison 5 Methods of dealing with cut surface, Outcome 10 Total hospital stay.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 5 Methods of dealing with cut surface

Outcome: 10 Total hospital stay



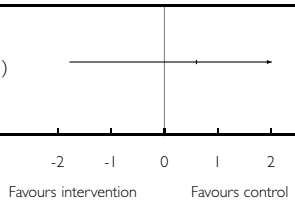
Analysis 5.11. Comparison 5 Methods of dealing with cut surface, Outcome 11 ITU stay.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 5 Methods of dealing with cut surface

Outcome: 11 ITU stay

Study or subgroup	Intervention N	Mean(SD)[days]	Control N	Mean(SD)[days]	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Oxidised cellulose vs fibrin sealant						
Ollinger 2013	32	2.8 (6.3)	18	2.2 (2.1)		0.60 [-1.79, 2.99]



Analysis 5.12. Comparison 5 Methods of dealing with cut surface, Outcome 12 Operating time.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 5 Methods of dealing with cut surface

Outcome: 12 Operating time

Study or subgroup	Intervention N	Mean(SD)[minutes]	Control N	Mean(SD)[minutes]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Fibrin sealant vs control							
Liu 1993	20	294.5 (64.3)	20	343 (184)		20.1 %	-48.50 [-133.92, 36.92]
Noun 1996	38	252 (90)	44	258 (108)		79.9 %	-6.00 [-48.86, 36.86]
Subtotal (95% CI)	**58**		**64**			**100.0 %**	**-14.55 [-52.86, 23.76]**
Heterogeneity: Chi^2 = 0.76, df = 1 (P = 0.38); I^2 =0.0%							
Test for overall effect: Z = 0.74 (P = 0.46)							
2 Fibrin sealant and collagen vs control							
Figueras 2007	150	282 (76.3)	150	263 (73.1)		100.0 %	19.00 [2.09, 35.91]
Subtotal (95% CI)	**150**		**150**			**100.0 %**	**19.00 [2.09, 35.91]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.20 (P = 0.028)							

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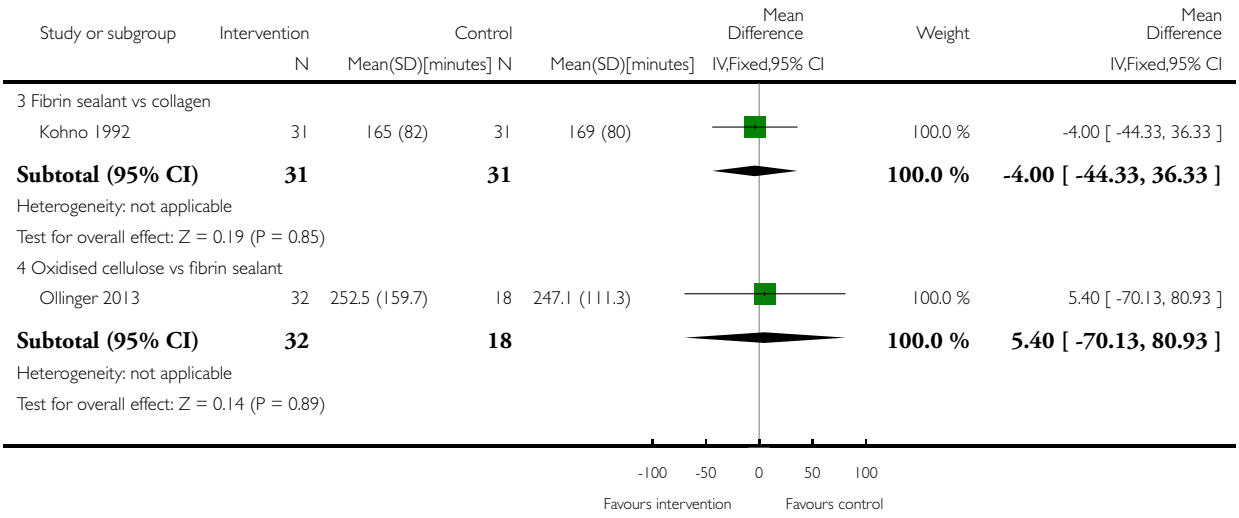
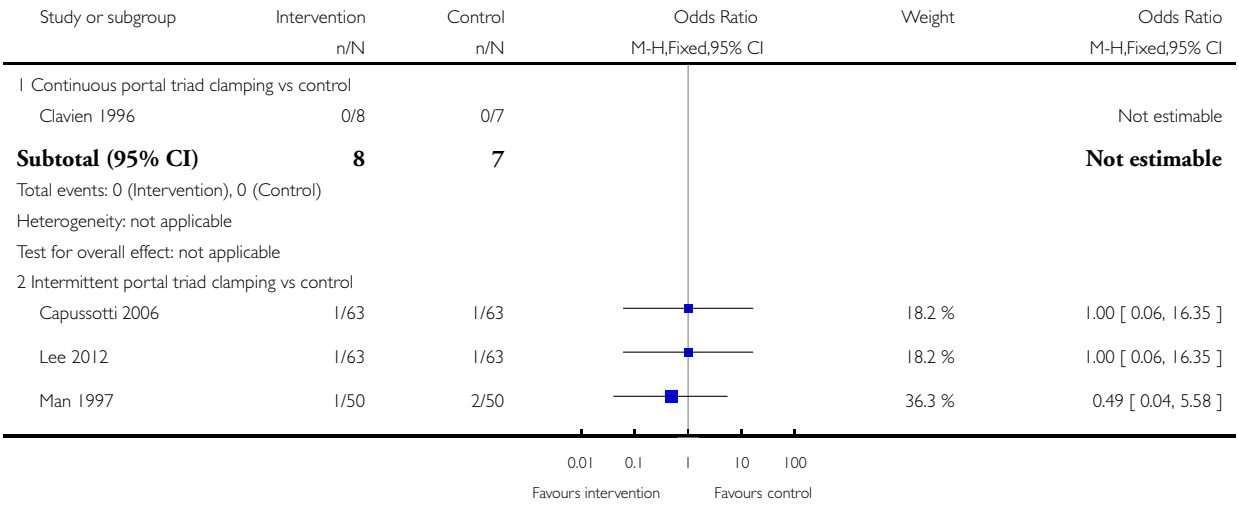


Analysis 6.1. Comparison 6 Methods of vascular occlusion, Outcome 1 Mortality (perioperative).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 6 Methods of vascular occlusion

Outcome: 1 Mortality (perioperative)



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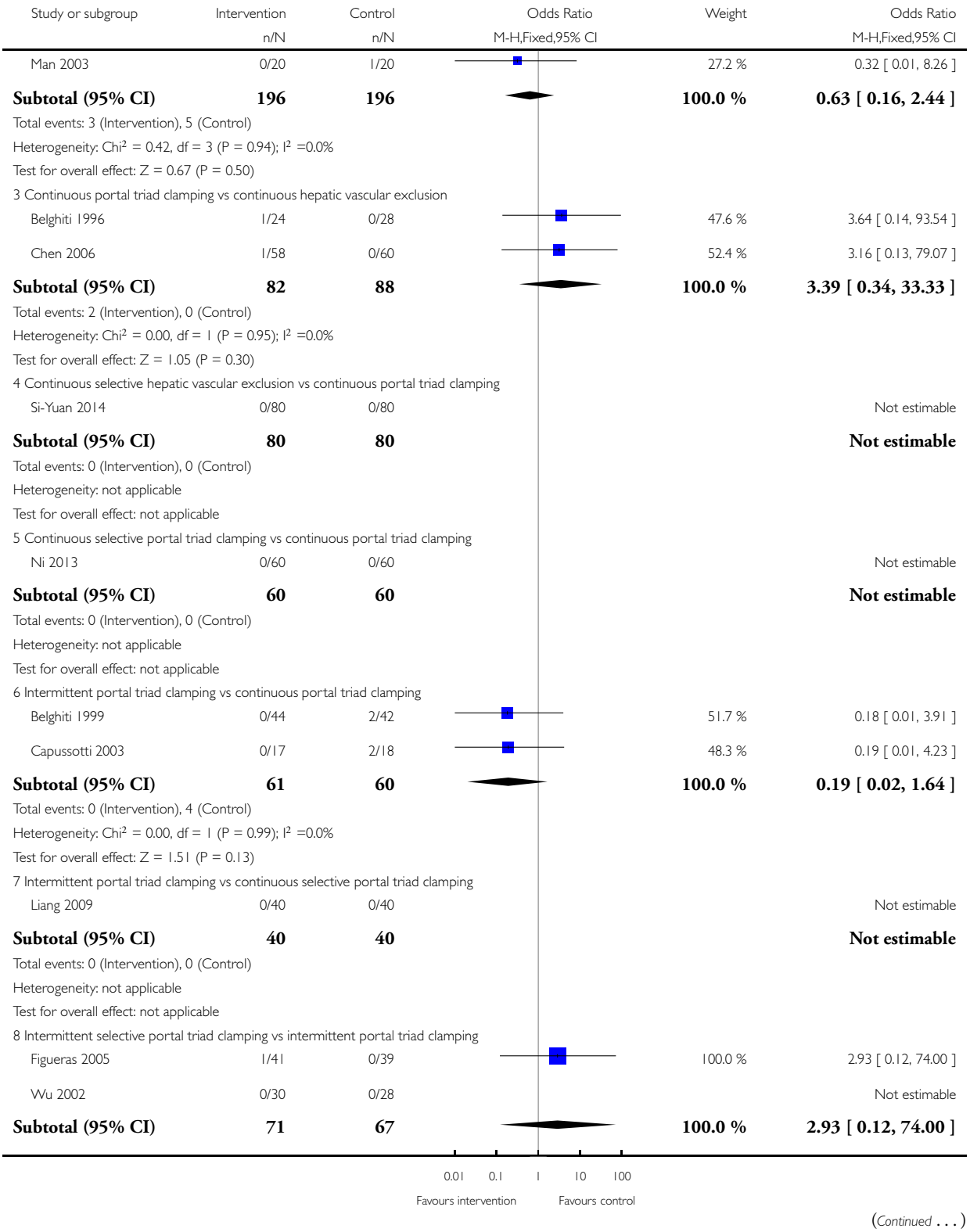

Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Man 2003	0/20	1/20		27.2 %	0.32 [0.01, 8.26]
Subtotal (95% CI)	**196**	**196**		**100.0 %**	**0.63 [0.16, 2.44]**
Total events: 3 (Intervention), 5 (Control)					
Heterogeneity: Chi² = 0.42, df = 3 (P = 0.94); I² =0.0%					
Test for overall effect: Z = 0.67 (P = 0.50)					
3 Continuous portal triad clamping vs continuous hepatic vascular exclusion					
Belghiti 1996	1/24	0/28		47.6 %	3.64 [0.14, 93.54]
Chen 2006	1/58	0/60		52.4 %	3.16 [0.13, 79.07]
Subtotal (95% CI)	**82**	**88**		**100.0 %**	**3.39 [0.34, 33.33]**
Total events: 2 (Intervention), 0 (Control)					
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.95); I² =0.0%					
Test for overall effect: Z = 1.05 (P = 0.30)					
4 Continuous selective hepatic vascular exclusion vs continuous portal triad clamping					
Si-Yuan 2014	0/80	0/80			Not estimable
Subtotal (95% CI)	**80**	**80**			**Not estimable**
Total events: 0 (Intervention), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
5 Continuous selective portal triad clamping vs continuous portal triad clamping					
Ni 2013	0/60	0/60			Not estimable
Subtotal (95% CI)	**60**	**60**			**Not estimable**
Total events: 0 (Intervention), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
6 Intermittent portal triad clamping vs continuous portal triad clamping					
Belghiti 1999	0/44	2/42		51.7 %	0.18 [0.01, 3.91]
Capussotti 2003	0/17	2/18		48.3 %	0.19 [0.01, 4.23]
Subtotal (95% CI)	**61**	**60**		**100.0 %**	**0.19 [0.02, 1.64]**
Total events: 0 (Intervention), 4 (Control)					
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.99); I² =0.0%					
Test for overall effect: Z = 1.51 (P = 0.13)					
7 Intermittent portal triad clamping vs continuous selective portal triad clamping					
Liang 2009	0/40	0/40			Not estimable
Subtotal (95% CI)	**40**	**40**			**Not estimable**
Total events: 0 (Intervention), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
8 Intermittent selective portal triad clamping vs intermittent portal triad clamping					
Figueras 2005	1/41	0/39		100.0 %	2.93 [0.12, 74.00]
Wu 2002	0/30	0/28			Not estimable
Subtotal (95% CI)	**71**	**67**		**100.0 %**	**2.93 [0.12, 74.00]**

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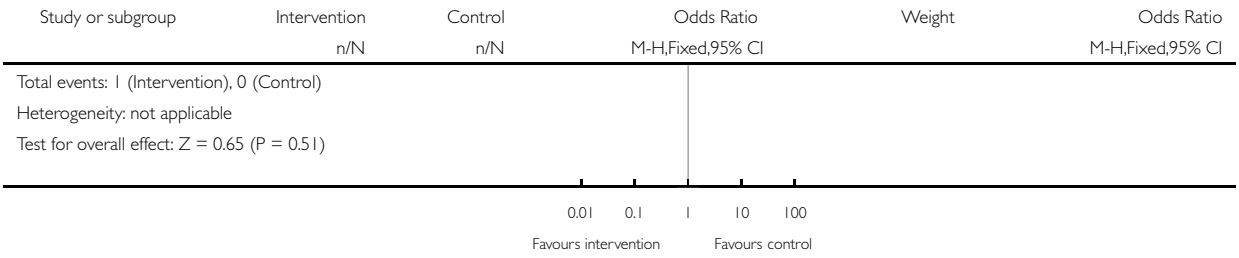
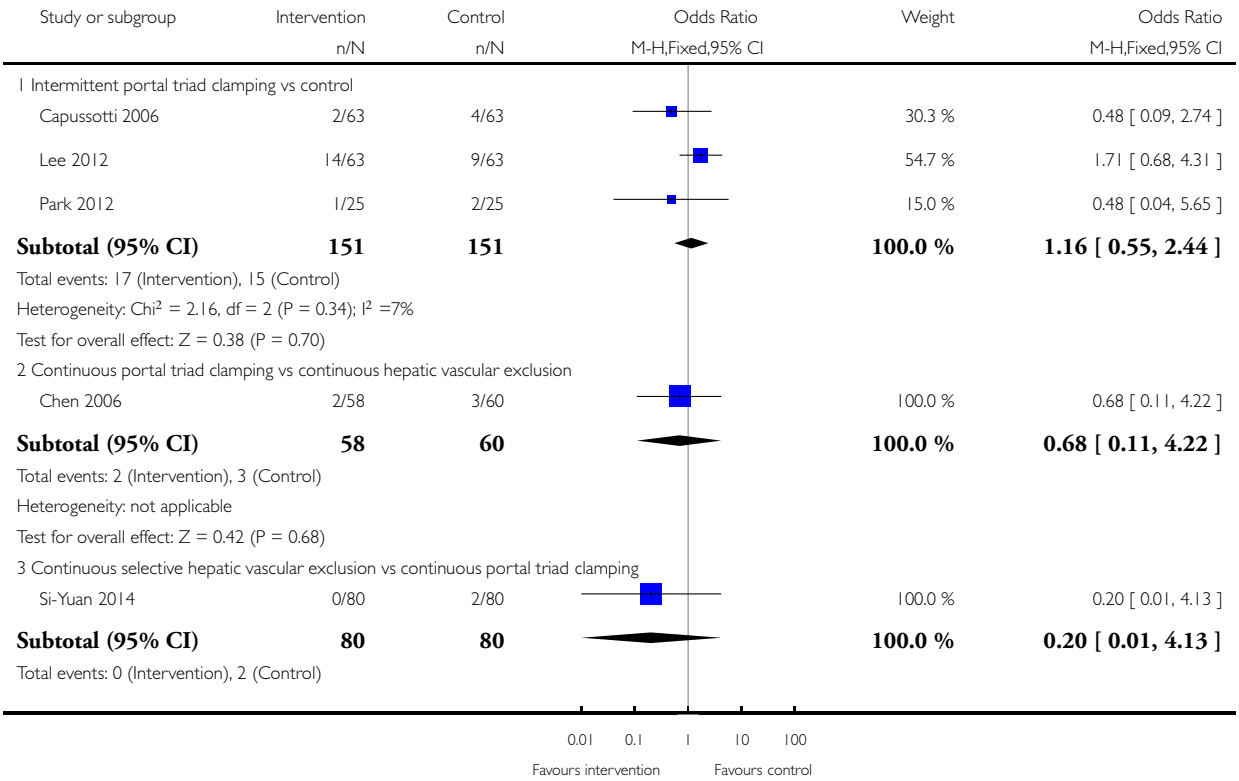


Analysis 6.2. Comparison 6 Methods of vascular occlusion, Outcome 2 Serious adverse events (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 6 Methods of vascular occlusion

Outcome: 2 Serious adverse events (proportion)



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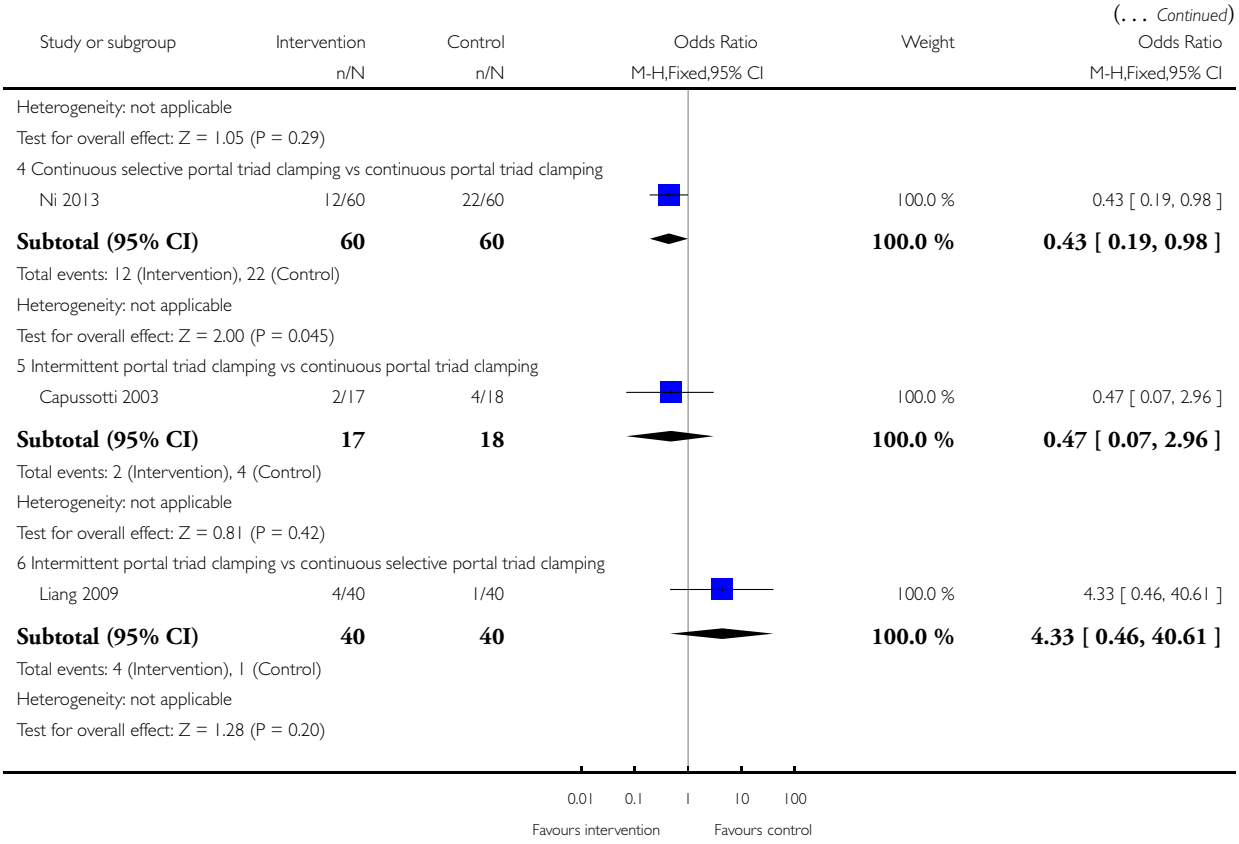
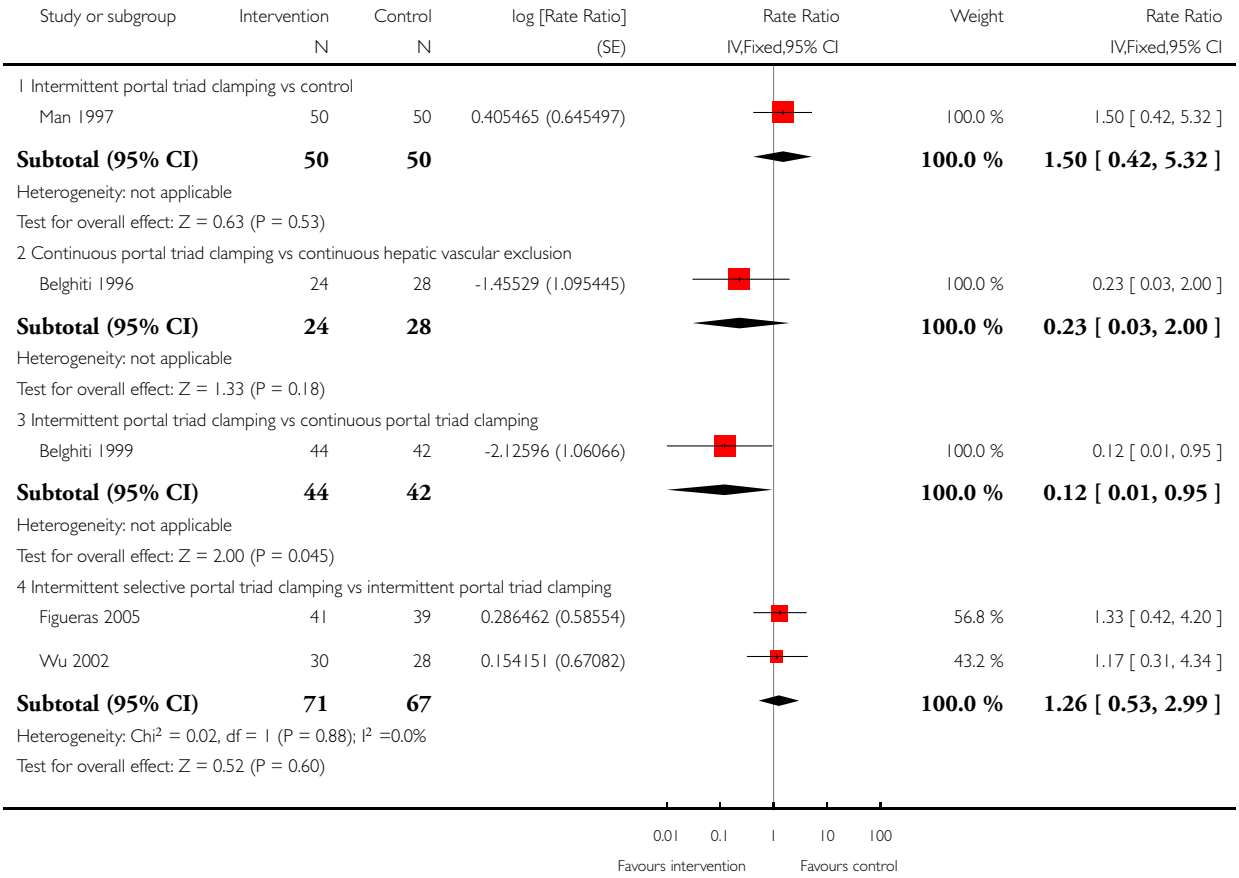


Analysis 6.3. Comparison 6 Methods of vascular occlusion, Outcome 3 Serious adverse events (number).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 6 Methods of vascular occlusion

Outcome: 3 Serious adverse events (number)

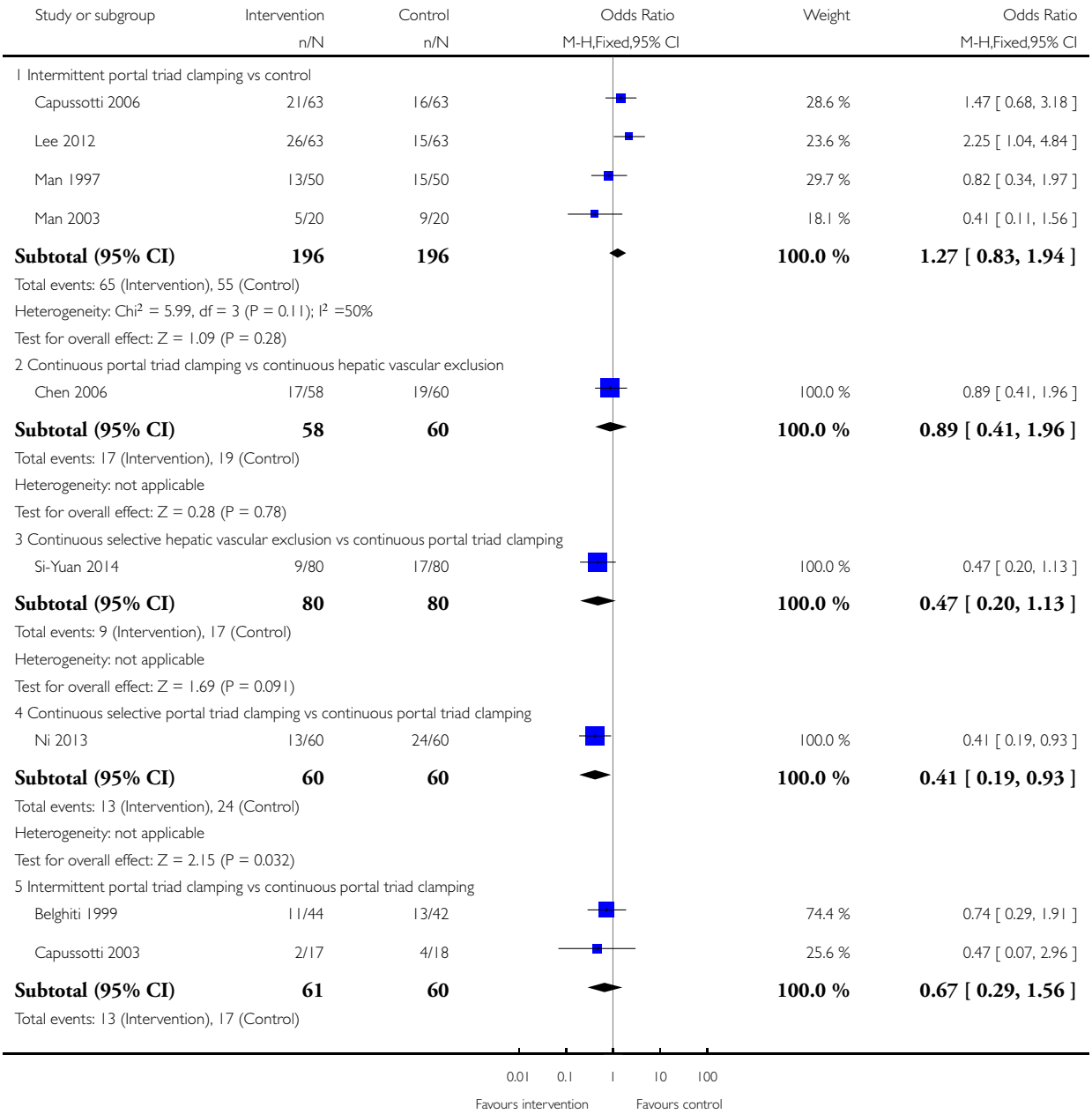


Analysis 6.4. Comparison 6 Methods of vascular occlusion, Outcome 4 Adverse events (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 6 Methods of vascular occlusion

Outcome: 4 Adverse events (proportion)



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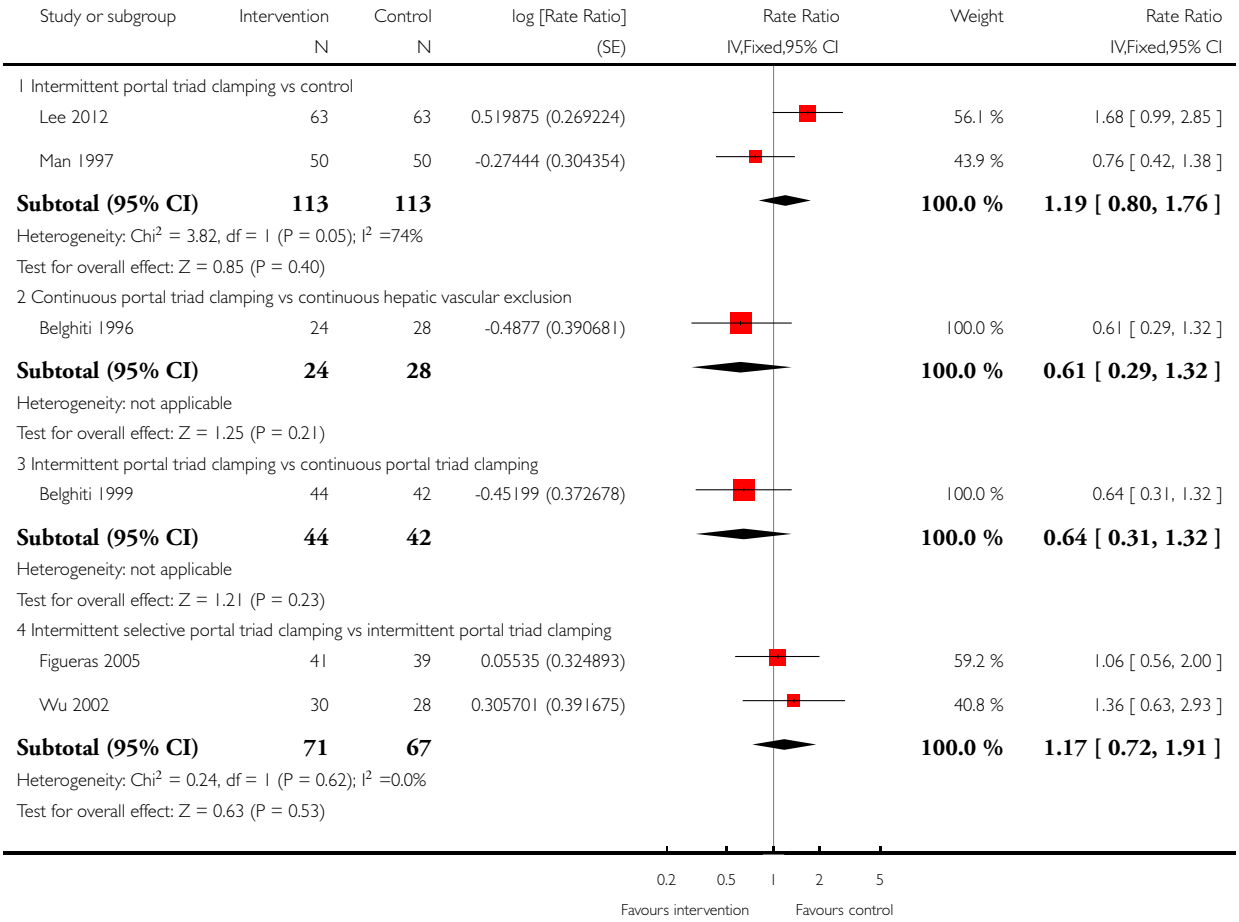
Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Heterogeneity: Chi^2 = 0.19, df = 1 (P = 0.66); I^2 =0.0%					
Test for overall effect: Z = 0.93 (P = 0.35)					
6 Intermittent portal triad clamping vs continuous selective portal triad clamping					
Liang 2009	8/40	9/40		100.0 %	0.86 [0.29, 2.52]
Subtotal (95% CI)	**40**	**40**		**100.0 %**	**0.86 [0.29, 2.52]**
Total events: 8 (Intervention), 9 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.27 (P = 0.78)					
7 Intermittent selective portal triad clamping vs intermittent portal triad clamping					
Figueras 2005	12/41	15/39		66.3 %	0.66 [0.26, 1.68]
Wu 2002	10/30	8/28		33.7 %	1.25 [0.41, 3.82]
Subtotal (95% CI)	**71**	**67**		**100.0 %**	**0.86 [0.42, 1.75]**
Total events: 22 (Intervention), 23 (Control)					
Heterogeneity: Chi^2 = 0.73, df = 1 (P = 0.39); I^2 =0.0%					
Test for overall effect: Z = 0.42 (P = 0.68)					

Analysis 6.5. Comparison 6 Methods of vascular occlusion, Outcome 5 Adverse events (number).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 6 Methods of vascular occlusion

Outcome: 5 Adverse events (number)

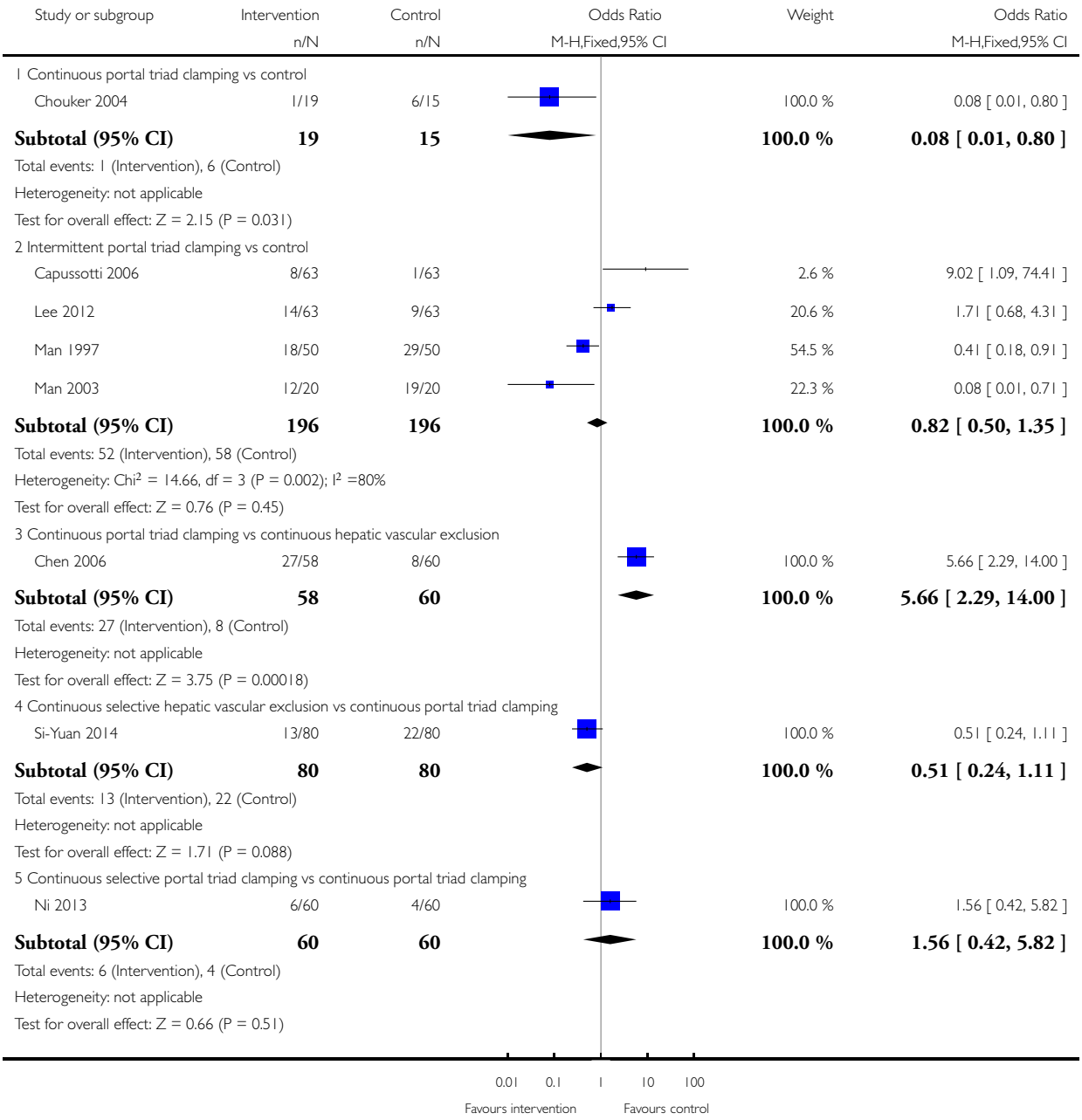


Analysis 6.6. Comparison 6 Methods of vascular occlusion, Outcome 6 Blood transfusion (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 6 Methods of vascular occlusion

Outcome: 6 Blood transfusion (proportion)



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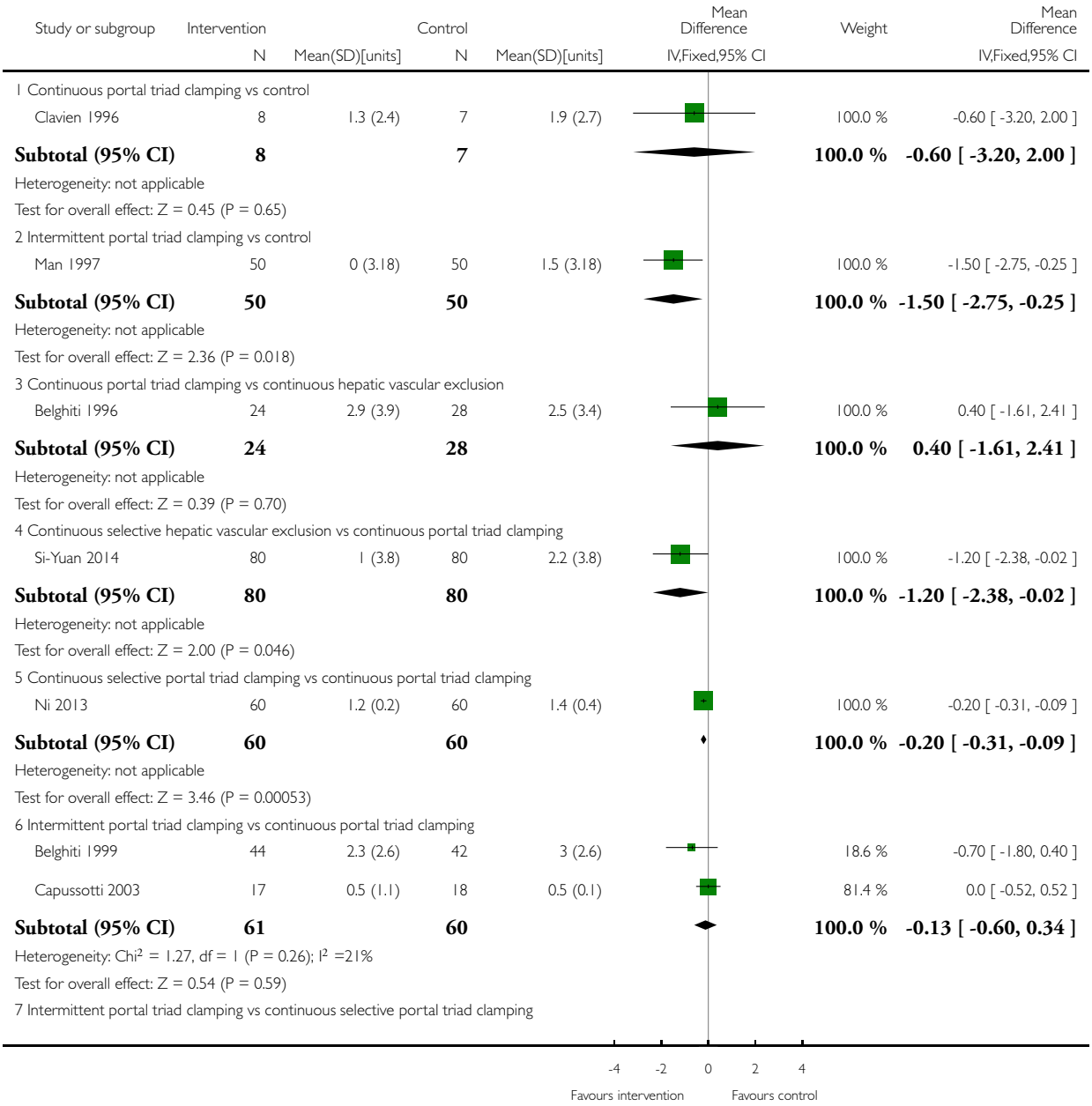
Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
6 Intermittent portal triad clamping vs continuous portal triad clamping					
Belghiti 1999	14/44	12/42		70.9 %	1.17 [0.46, 2.93]
Capussotti 2003	5/17	5/18		29.1 %	1.08 [0.25, 4.70]
Subtotal (95% CI)	**61**	**60**		**100.0 %**	**1.14 [0.52, 2.49]**
Total events: 19 (Intervention), 17 (Control)					
Heterogeneity: Chi^2 = 0.01, df = 1 (P = 0.93); I^2 =0.0%					
Test for overall effect: Z = 0.33 (P = 0.74)					
7 Intermittent portal triad clamping vs continuous selective portal triad clamping					
Liang 2009	14/40	15/40		100.0 %	0.90 [0.36, 2.23]
Subtotal (95% CI)	**40**	**40**		**100.0 %**	**0.90 [0.36, 2.23]**
Total events: 14 (Intervention), 15 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.23 (P = 0.82)					
8 Intermittent selective portal triad clamping vs intermittent portal triad clamping					
Figueras 2005	6/41	4/39		25.3 %	1.50 [0.39, 5.78]
Wu 2002	5/30	12/28		74.7 %	0.27 [0.08, 0.90]
Subtotal (95% CI)	**71**	**67**		**100.0 %**	**0.58 [0.25, 1.36]**
Total events: 11 (Intervention), 16 (Control)					
Heterogeneity: Chi^2 = 3.47, df = 1 (P = 0.06); I^2 =71%					
Test for overall effect: Z = 1.26 (P = 0.21)					

Analysis 6.7. Comparison 6 Methods of vascular occlusion, Outcome 7 Blood transfusion (red blood cell).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 6 Methods of vascular occlusion

Outcome: 7 Blood transfusion (red blood cell)



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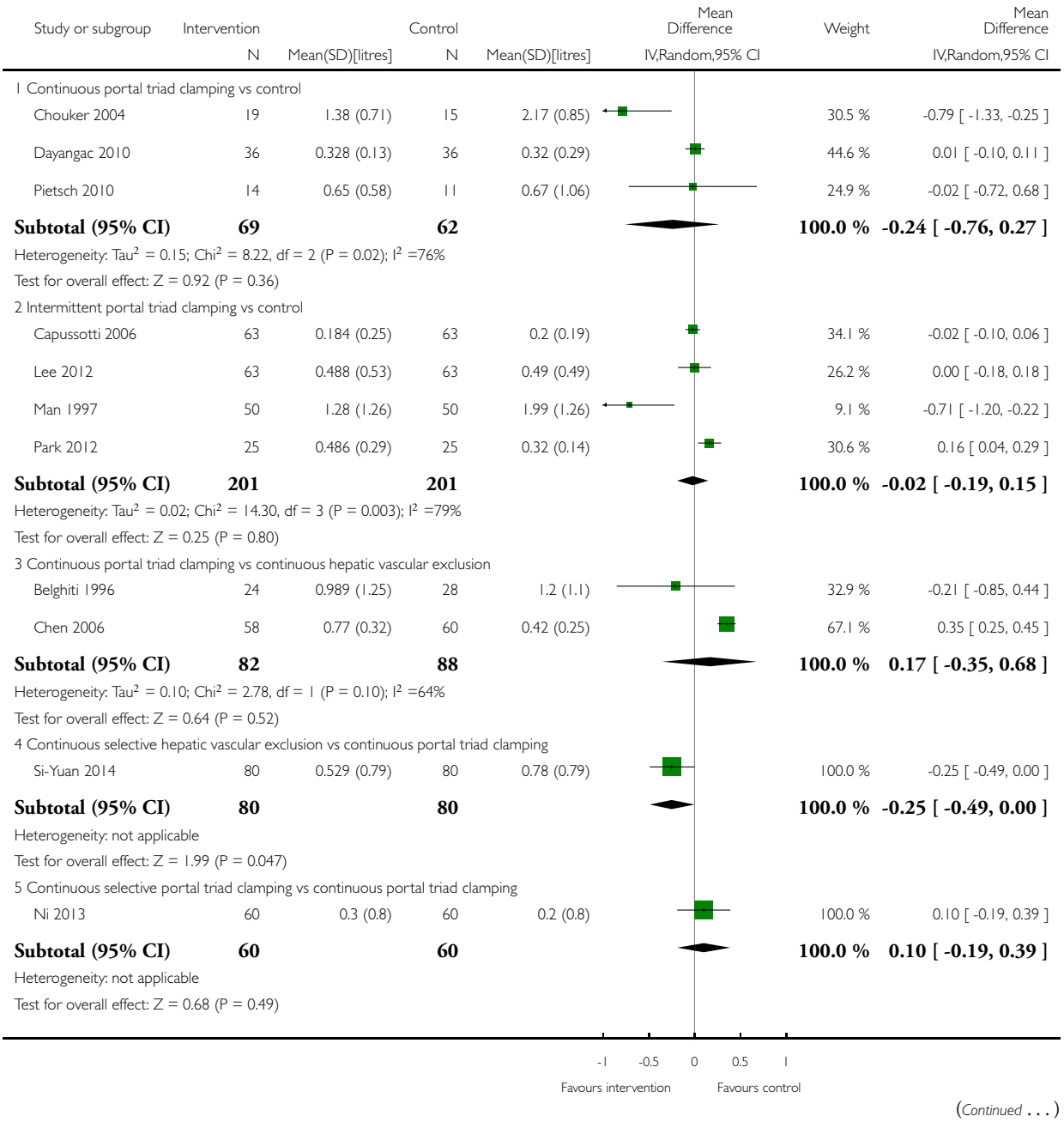
Study or subgroup	Intervention N	Mean(SD)[units]	Control N	Mean(SD)[units]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Liang 2009	40	1.4825 (0.95)	40	1.37 (0.58)		100.0 %	0.11 [-0.23, 0.46]
Subtotal (95% CI)	**40**		**40**			**100.0 %**	**0.11 [-0.23, 0.46]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.65 (P = 0.51)							
8 Intermittent selective portal triad clamping vs intermittent portal triad clamping							
Figueras 2005	41	0.34 (0.9)	39	0.36 (1)		83.6 %	-0.02 [-0.44, 0.40]
Wu 2002	30	2.24 (2.2)	28	2.54 (1.4)		16.4 %	-0.30 [-1.25, 0.64]
Subtotal (95% CI)	**71**		**67**			**100.0 %**	**-0.07 [-0.45, 0.32]**
Heterogeneity: Chi^2 = 0.29, df = 1 (P = 0.59); I^2 =0.0%							
Test for overall effect: Z = 0.34 (P = 0.73)							

Analysis 6.8. Comparison 6 Methods of vascular occlusion, Outcome 8 Blood loss.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 6 Methods of vascular occlusion

Outcome: 8 Blood loss



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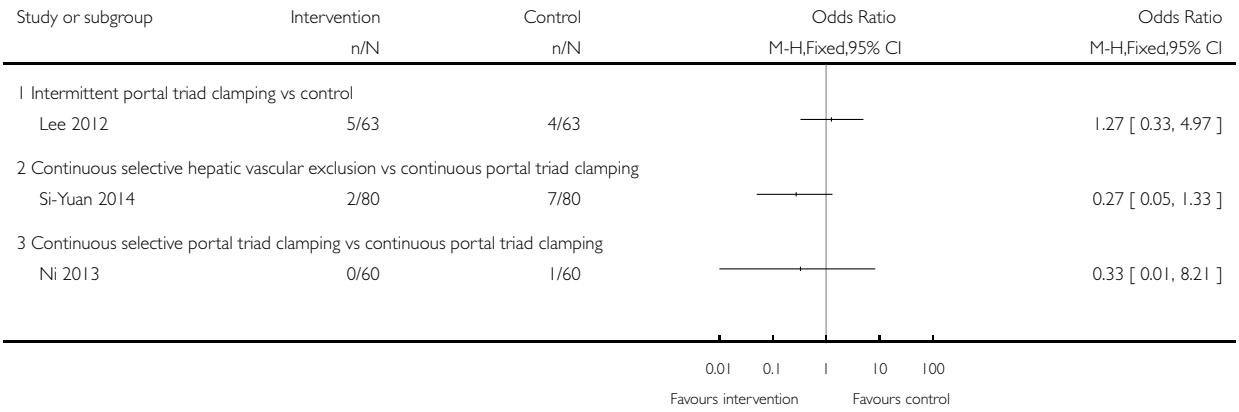
Study or subgroup	Intervention N	Mean(SD)[litres]	Control N	Mean(SD)[litres]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
6 Intermittent portal triad clamping vs continuous portal triad clamping							
Belghiti 1999	44	1.29 (0.9)	42	1.18 (0.8)		53.8 %	0.11 [-0.25, 0.47]
Capussotti 2003	17	0.732 (0.64)	18	0.73 (0.52)		46.2 %	0.00 [-0.39, 0.39]
Subtotal (95% CI)	**61**		**60**			**100.0 %**	**0.06 [-0.20, 0.32]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.17$, df = 1 (P = 0.68); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.44 (P = 0.66)							
7 Intermittent portal triad clamping vs continuous selective portal triad clamping							
Liang 2009	40	0.57 (0.29)	40	0.65 (0.28)		100.0 %	-0.08 [-0.20, 0.05]
Subtotal (95% CI)	**40**		**40**			**100.0 %**	**-0.08 [-0.20, 0.05]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.24 (P = 0.22)							
8 Intermittent selective portal triad clamping vs intermittent portal triad clamping							
Figueras 2005	41	0.735 (0.4)	39	0.67 (0.53)		59.6 %	0.06 [-0.14, 0.27]
Wu 2002	30	1.159 (1.21)	28	1.69 (0.9)		40.4 %	-0.53 [-1.07, 0.02]
Subtotal (95% CI)	**71**		**67**			**100.0 %**	**-0.17 [-0.74, 0.39]**
Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 3.92$, df = 1 (P = 0.05); $I^2 = 74\%$							
Test for overall effect: Z = 0.60 (P = 0.55)							

Analysis 6.9. Comparison 6 Methods of vascular occlusion, Outcome 9 Major blood loss (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 6 Methods of vascular occlusion

Outcome: 9 Major blood loss (proportion)

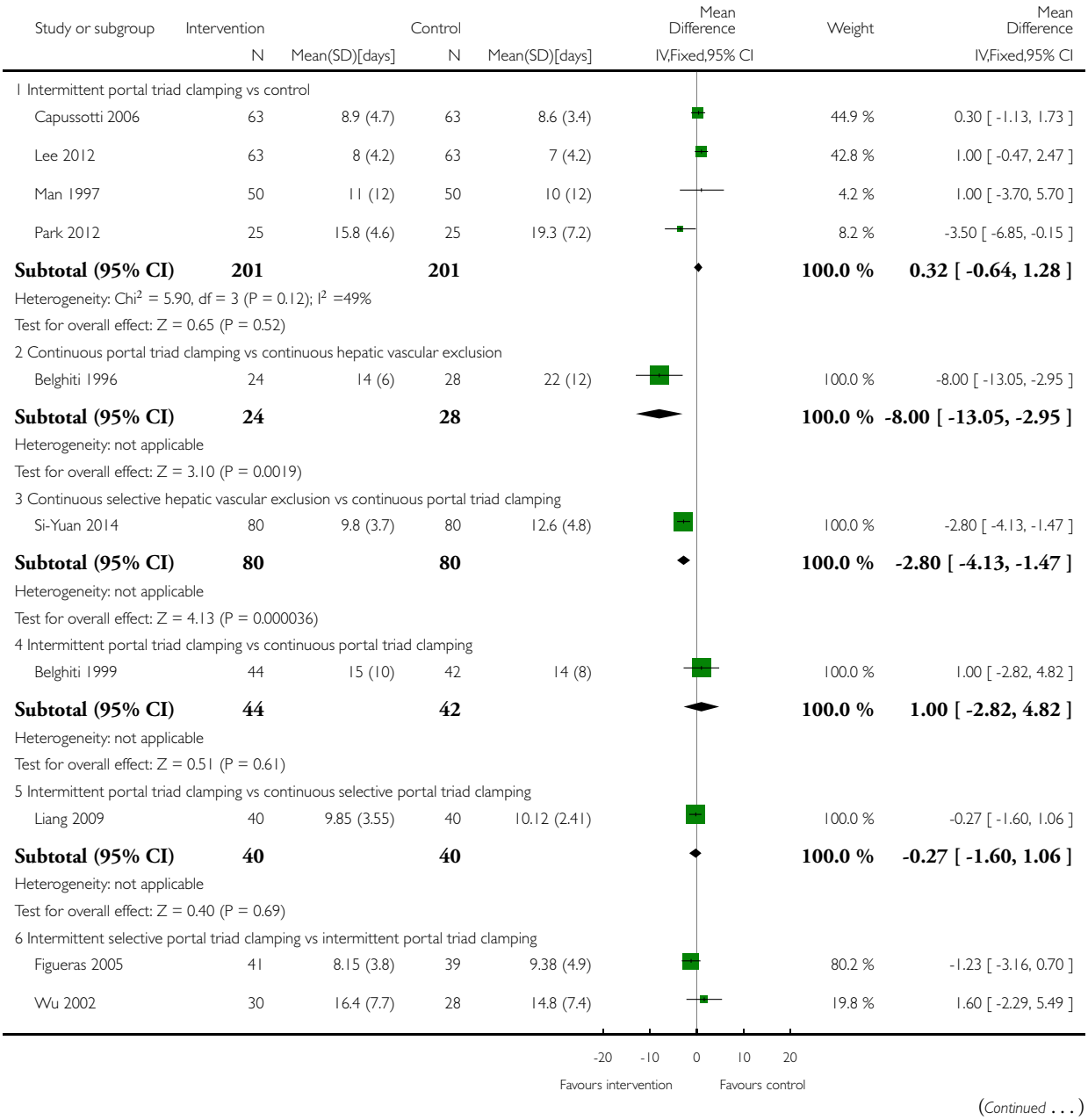


Analysis 6.10. Comparison 6 Methods of vascular occlusion, Outcome 10 Total hospital stay.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 6 Methods of vascular occlusion

Outcome: 10 Total hospital stay



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Study or subgroup	Intervention N	Mean(SD)[days]	Control N	Mean(SD)[days]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Subtotal (95% CI)	**71**		**67**			**100.0 %**	**-0.67 [-2.40, 1.06]**
Heterogeneity: Chi^2 = 1.63, df = 1 (P = 0.20); I^2 =39%							
Test for overall effect: Z = 0.76 (P = 0.45)							

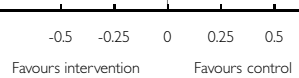
Analysis 6.11. Comparison 6 Methods of vascular occlusion, Outcome 11 ITU stay.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 6 Methods of vascular occlusion

Outcome: 11 ITU stay

Study or subgroup	Intervention N	Mean(SD)[days]	Control N	Mean(SD)[days]	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Continuous selective hepatic vascular exclusion vs continuous portal triad clamping						
Si-Yuan 2014	80	1.2 (0.5)	80	1.5 (1)		-0.30 [-0.54, -0.06]

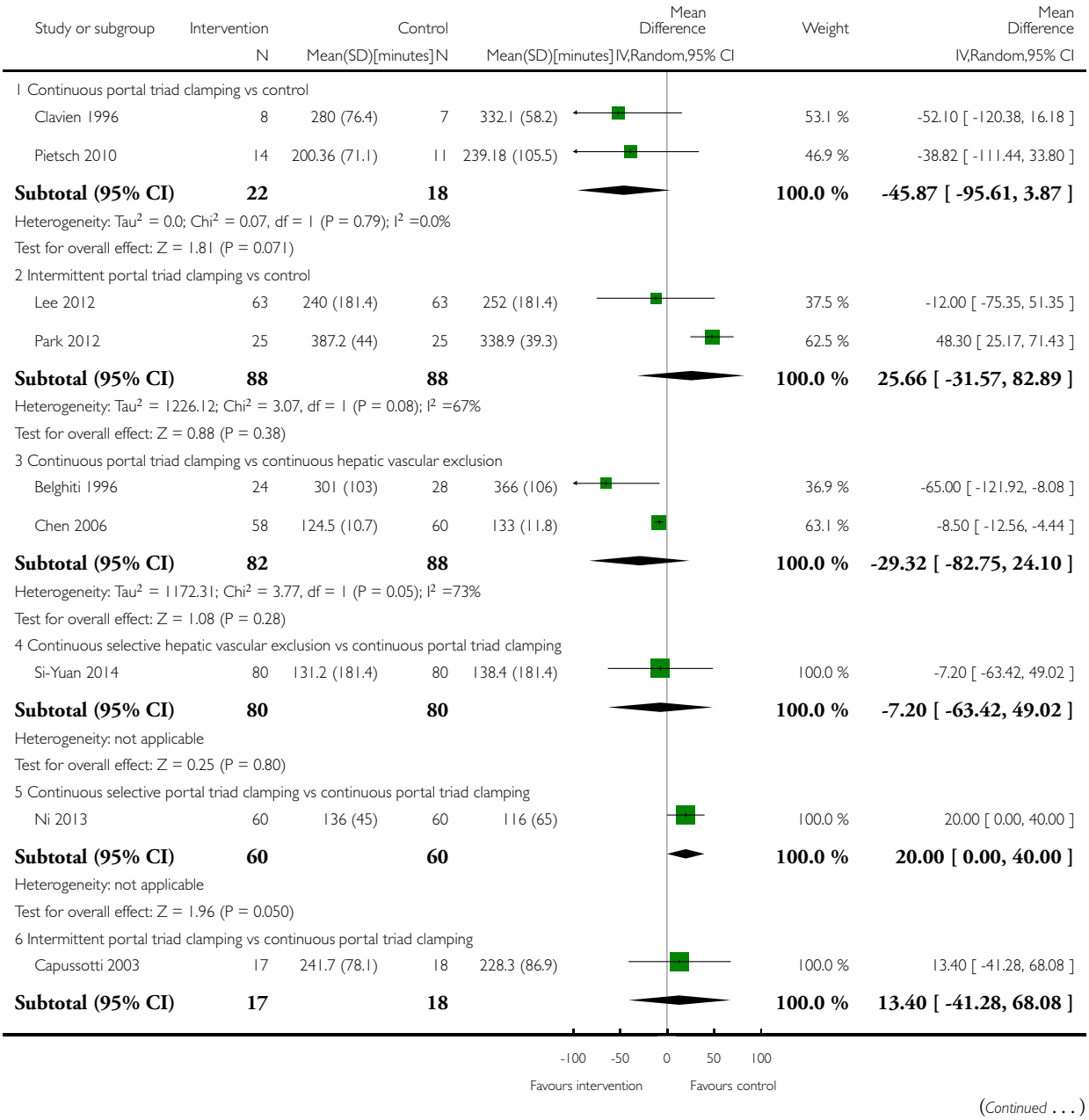


Analysis 6.12. Comparison 6 Methods of vascular occlusion, Outcome 12 Operating time.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 6 Methods of vascular occlusion

Outcome: 12 Operating time



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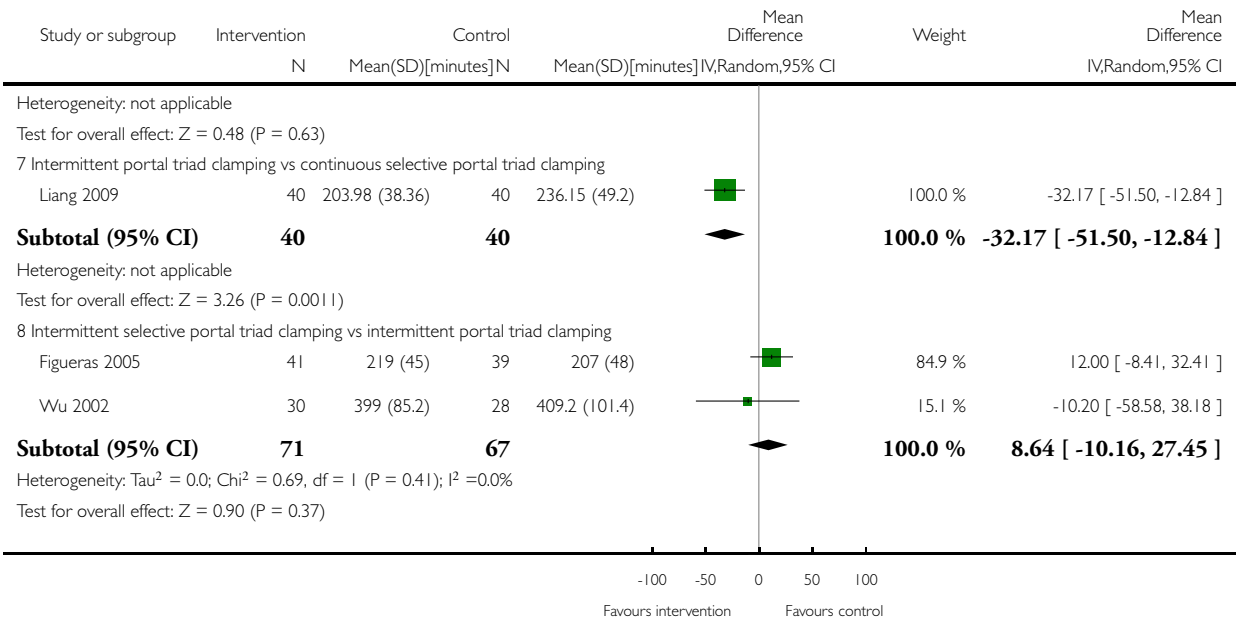
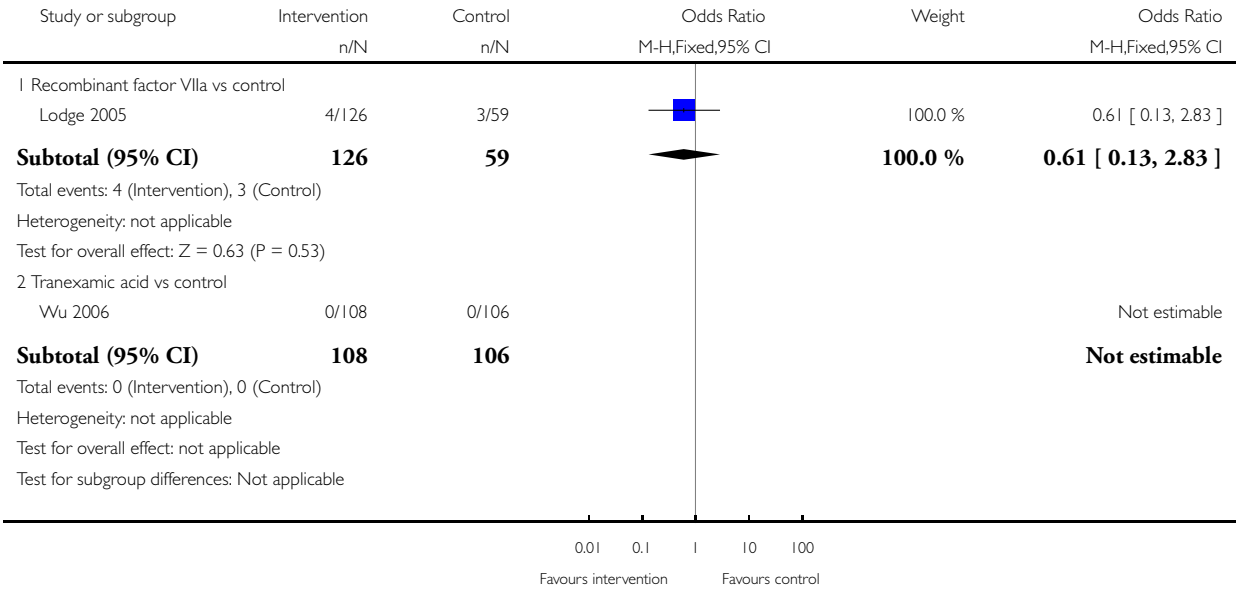


Analysis 7.1. Comparison 7 Pharmacological interventions, Outcome 1 Mortality (perioperative).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 7 Pharmacological interventions

Outcome: 1 Mortality (perioperative)

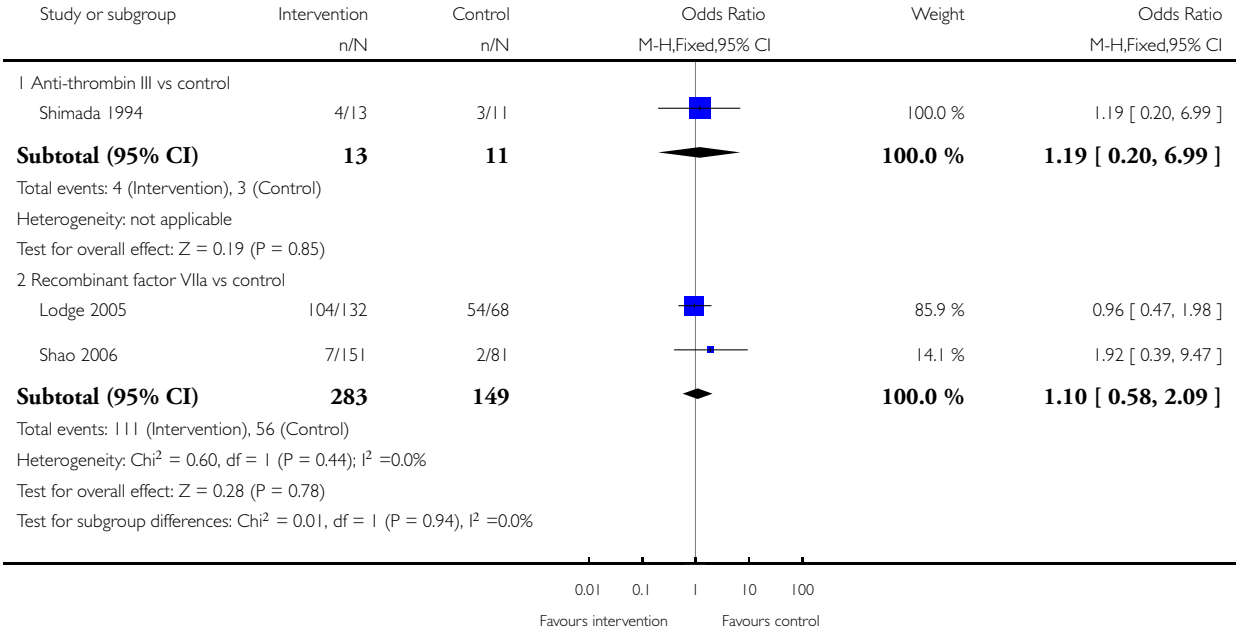


Analysis 7.2. Comparison 7 Pharmacological interventions, Outcome 2 Serious adverse events (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 7 Pharmacological interventions

Outcome: 2 Serious adverse events (proportion)

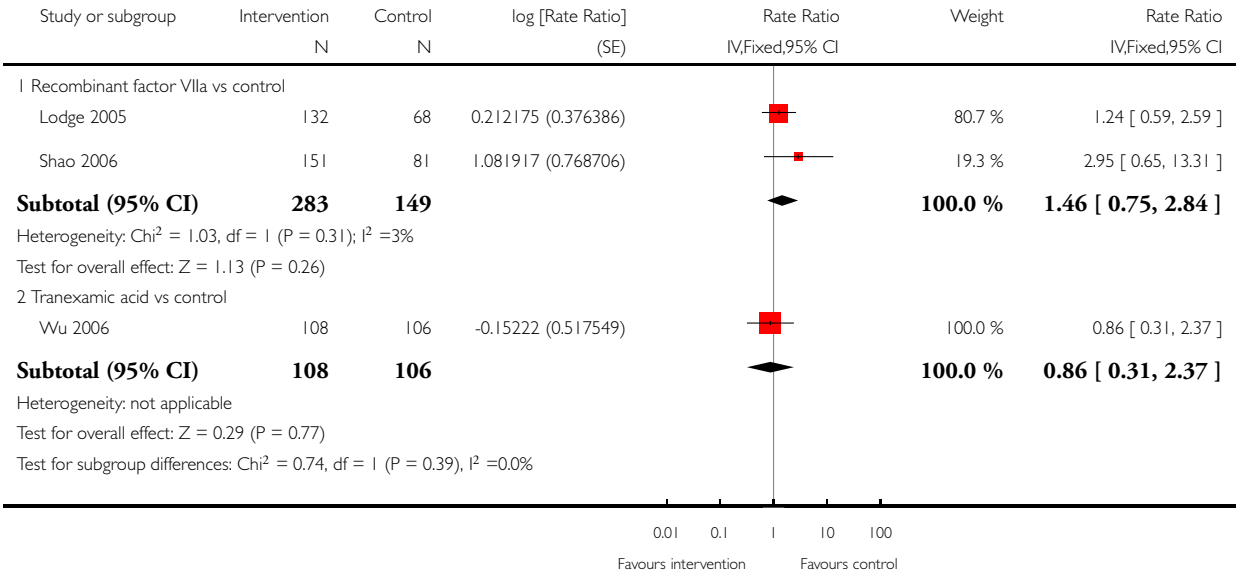


Analysis 7.3. Comparison 7 Pharmacological interventions, Outcome 3 Serious adverse events (number).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 7 Pharmacological interventions

Outcome: 3 Serious adverse events (number)

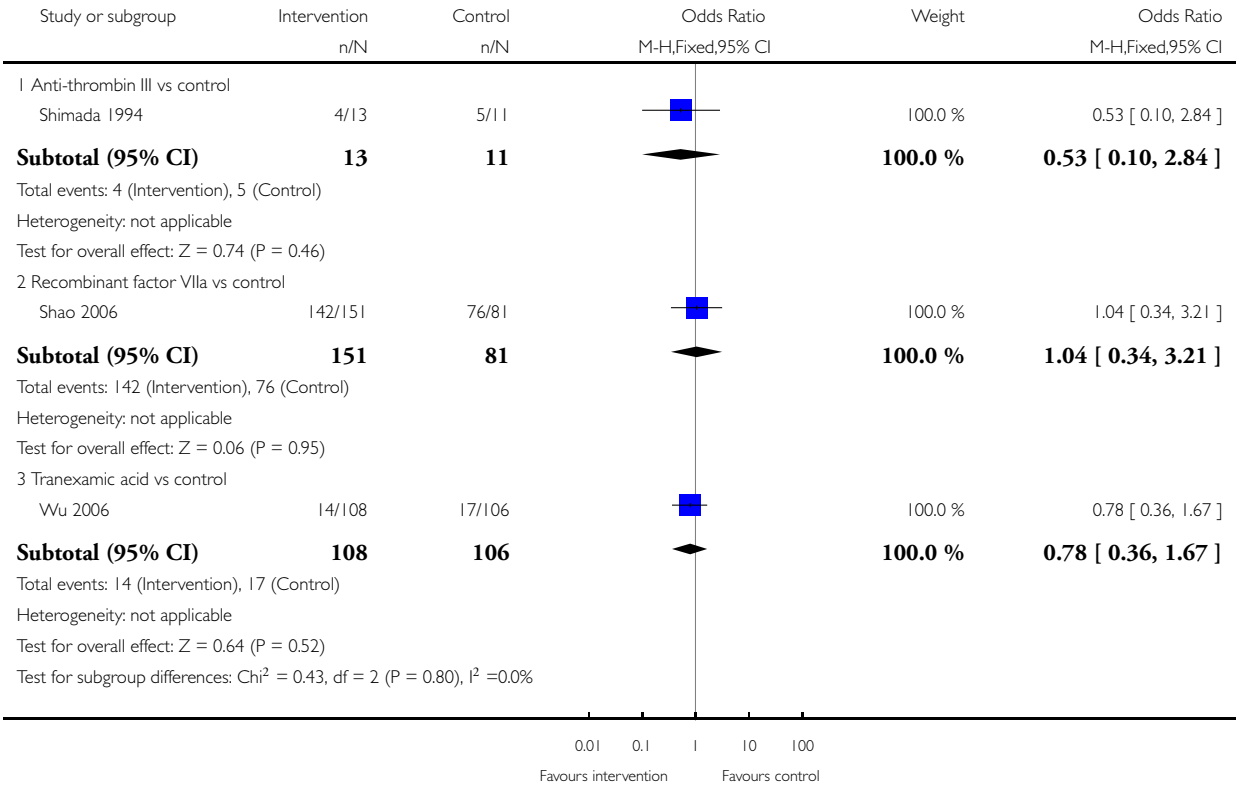


Analysis 7.4. Comparison 7 Pharmacological interventions, Outcome 4 Adverse events (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 7 Pharmacological interventions

Outcome: 4 Adverse events (proportion)

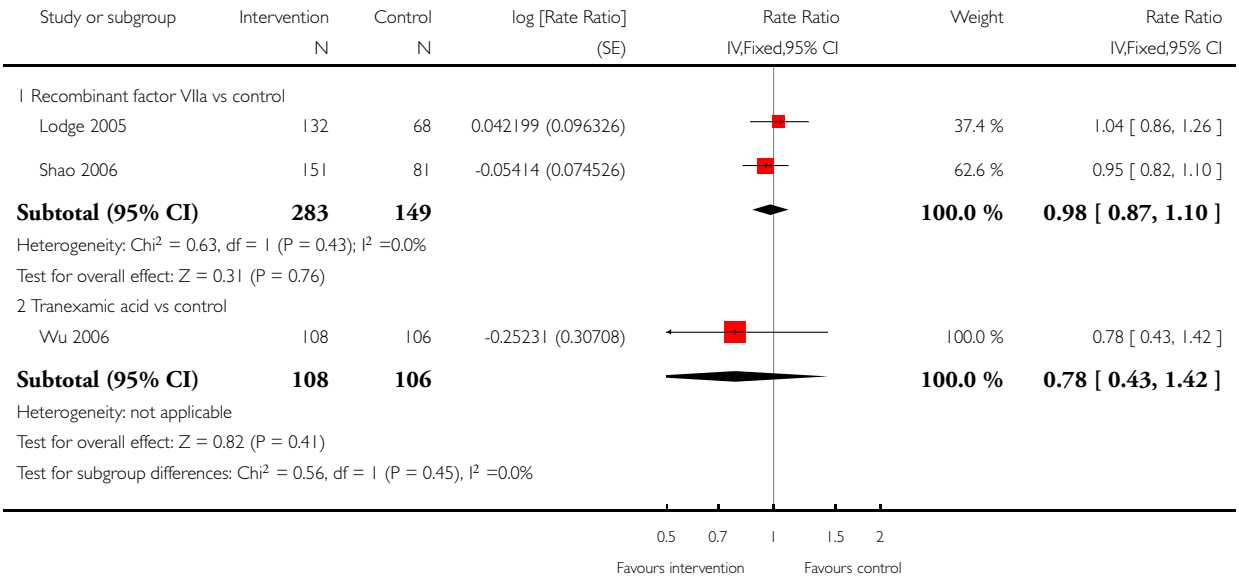


Analysis 7.5. Comparison 7 Pharmacological interventions, Outcome 5 Adverse events (number).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 7 Pharmacological interventions

Outcome: 5 Adverse events (number)

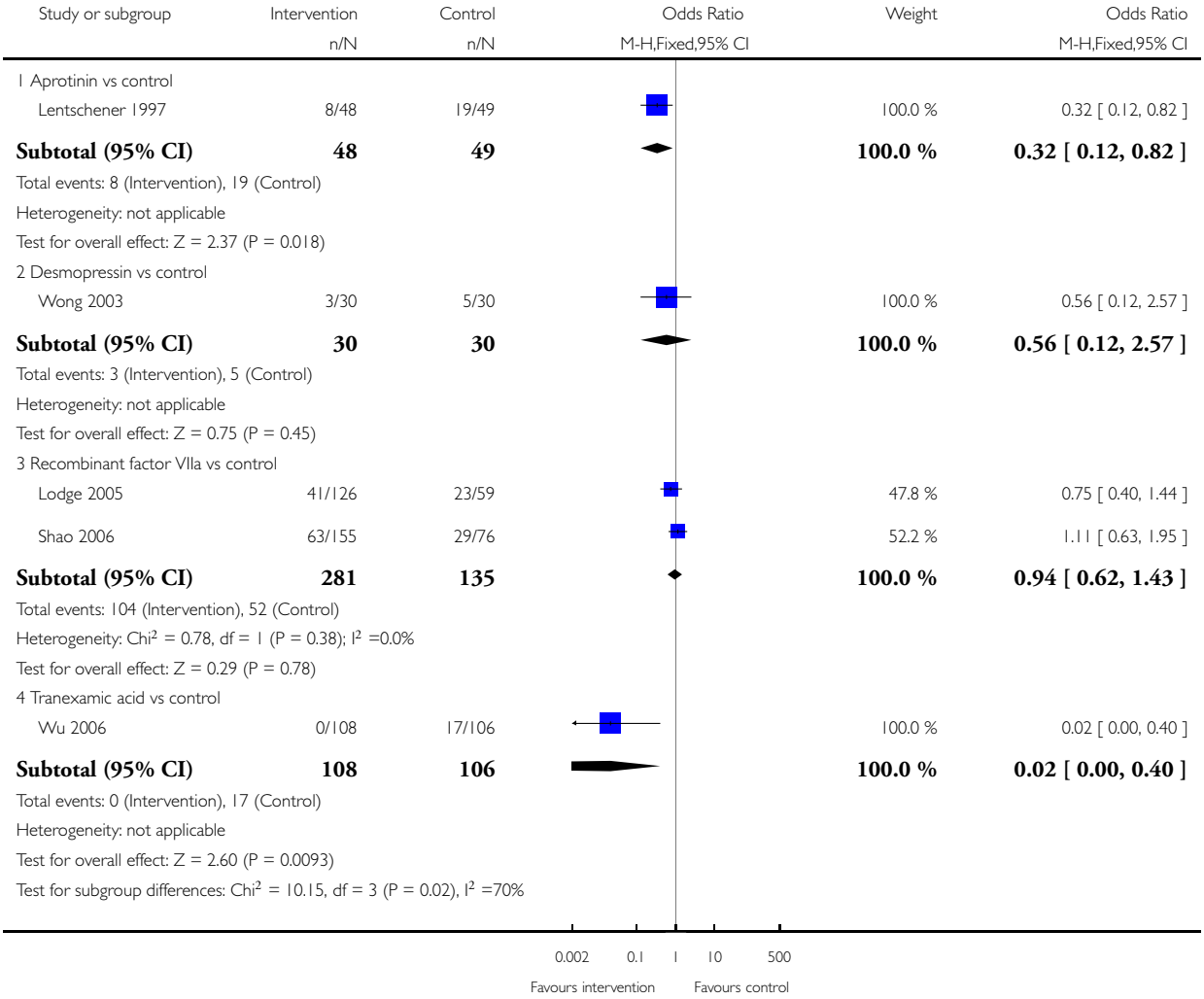


Analysis 7.6. Comparison 7 Pharmacological interventions, Outcome 6 Blood transfusion (proportion).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 7 Pharmacological interventions

Outcome: 6 Blood transfusion (proportion)

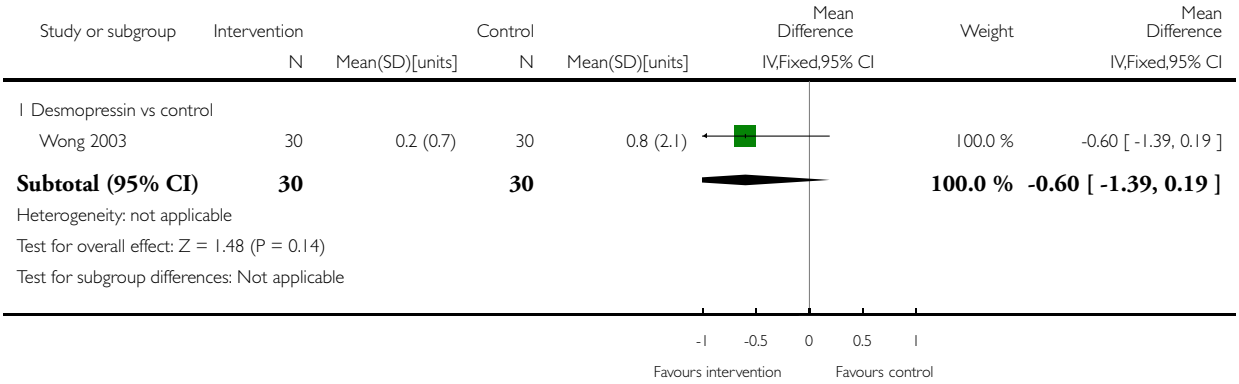


Analysis 7.7. Comparison 7 Pharmacological interventions, Outcome 7 Blood transfusion (fresh frozen plasma).

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 7 Pharmacological interventions

Outcome: 7 Blood transfusion (fresh frozen plasma)

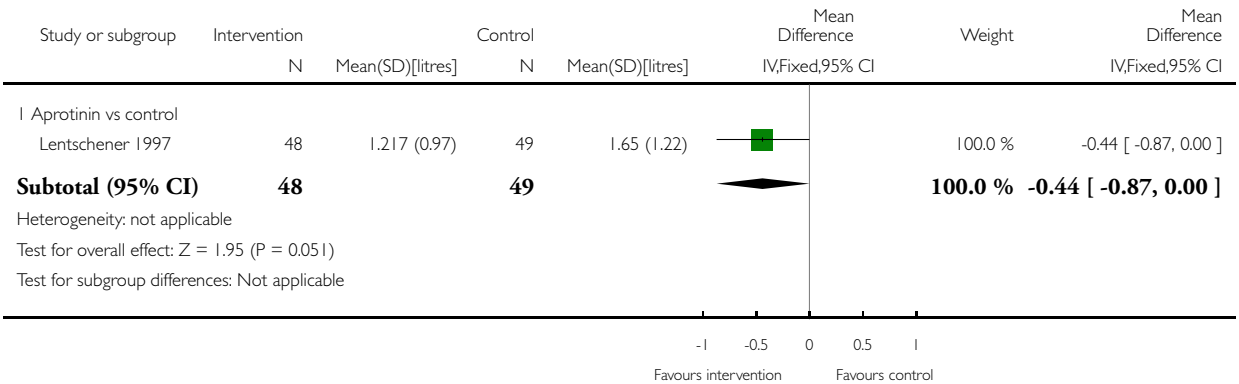


Analysis 7.8. Comparison 7 Pharmacological interventions, Outcome 8 Blood loss.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 7 Pharmacological interventions

Outcome: 8 Blood loss

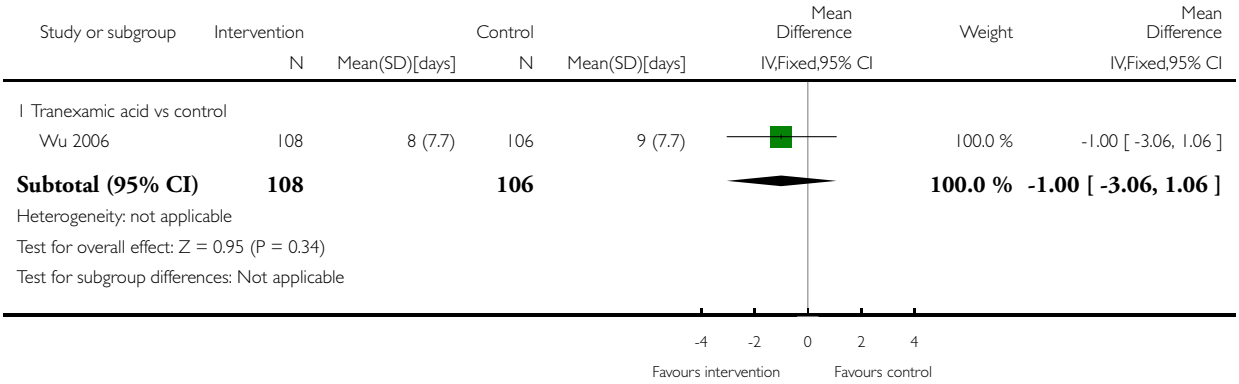


Analysis 7.9. Comparison 7 Pharmacological interventions, Outcome 9 Hospital stay.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 7 Pharmacological interventions

Outcome: 9 Hospital stay

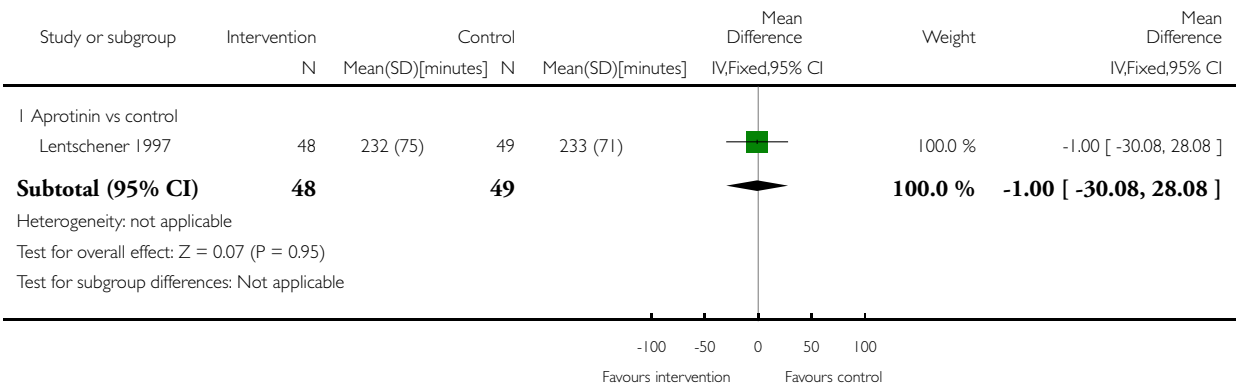


Analysis 7.10. Comparison 7 Pharmacological interventions, Outcome 10 Operating time.

Review: Methods to decrease blood loss during liver resection: a network meta-analysis

Comparison: 7 Pharmacological interventions

Outcome: 10 Operating time



ADDITIONAL TABLES

Table 1. Different methods of cardiopulmonary interventions

Acute normovolemic haemodilution (ANH)
Low central venous pressure (central venous pressure)
Hypoventilation
Combination of ANH with central venous pressure or hypotension

Table 2. Different methods of parenchymal transection

Finger-fracture method
Clamp-crush method
Cavitron ultrasonic surgical aspirator
Sharp dissection
Radiofrequency dissecting sealer
Ultrasonic shears
Stapler
Waterjet (Hydrojet)

Table 3. Different methods of dealing with raw surface

Suturing for large and medium vessels and ducts and performing electrocauterisation of small vessels and ducts
Suturing for large vessels and performing ultrasonic shears for medium-sized and small vessels and ducts
Suturing and argon beam coagulator
Suturing and fibrin sealant
Suturing and collagen
Suturing and oxidised cellulose
Suturing and cyanoacrylate
Suturing and combination of fibrin sealant with collagen or oxidised cellulose

Table 4. Different methods of vascular occlusion

No vascular occlusion
Portal triad clamping (continuous) (occlusion of inflow alone)
Portal triad clamping (intermittent) (occlusion of inflow alone)
Hepatic vascular exclusion (occlusion of inflow and outflow) (continuous or intermittent)
Selective portal trial clamping (occlusion of inflow to the hemi-liver that is being resected) (continuous or intermittent)
Selective hepatic vascular exclusion (occlusion of inflow to the hemi-liver and outflow from the hemi-liver that is being resected) (continuous or intermittent)

Table 5. Clavien-Dindo classification of postoperative complications

Grades	Definitions	Examples
I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, or radiological interventions	Drugs such as antiemetics, antipyretics, analgesics, diuretics, and electrolytes; physiotherapy; wound infections opened at the bedside
II	Requiring pharmacological treatment with drugs other than those allowed for grade I complications	Blood transfusions, total parenteral nutrition
III	Requiring surgical, endoscopic, or radiological intervention	Bile leak requiring endoscopic stent; re-operation for any cause; drainage of infected intra-abdominal collection
IV	Life-threatening complication requiring high dependency or intensive care management	Dialysis
V	Death of patient	-
Suffix d	If the patient suffers from a complication at the time of discharge and needs further follow-up to evaluate the complication fully	-

Adapted from Dindo 2004; Clavien 2009.

Table 6. Cardiopulmonary interventions: choice of model results

Blood transfusion (red blood cell) (units)	
Treatment number	**Treatment name**
1	Control

Table 6. Cardiopulmonary interventions: choice of model results (*Continued*)

2	Acute normovolemic haemodilution		
3	Acute normovolemic haemodilution plus hypotension		
4	Acute normovolemic haemodilution plus low central venous pressure		
5	Low central venous pressure		
	Fixed-effect model	**Random-effects model**	**Inconsistency model**
Dbar[a]	2.68	−8.90	−9.80
pD[b]	10.05	12.67	11.96
DIC[c]	12.73	3.77	2.17
d[2][d]	−1.23 (95% CrI −1.74 to −0.73)	−1.26 (95% CrI −4.92 to 2.39)	-
d[3][e]	−1.65 (95% CrI −2.06 to −1.25)	−1.68 (95% CrI −5.33 to 1.98)	-
d[4][f]	0.15 (95% CrI −0.10 to 0.40)	−0.57 (95% CrI −3.35 to 1.88)	-
d[5][g]	−0.81 (95% CrI −1.33 to −0.30)	−1.08 (95% CrI −3.43 to 1.13)	-
Between-study standard deviation	-	1.446	
Model used	Random-effects model		
Evidence of inconsistency	There is no evidence of inconsistency since the difference in DIC between consistency and inconsistency models was not significant		
Blood loss (litres)			
Treatment number	**Treatment name**		
1	Control		
2	Acute normovolemic haemodilution		
3	Acute normovolemic haemodilution plus hypotension		
4	Acute normovolemic haemodilution plus low central venous pressure		

Table 6. Cardiopulmonary interventions: choice of model results (*Continued*)

5	Hypoventilation		
6	Low central venous pressure		
	Fixed-effect model	**Random-effects model**	**Inconsistency model**
Dbar[a]	−24.73	−36.06	−36.65
pD[b]	14.00	17.77	18.26
DIC[c]	−10.73	−18.29	−18.39
d[2][d]	0.00 (95% CrI −0.10 to 0.10)	0.00 (95% CrI −0.95 to 0.96)	-
d[3][e]	−0.25 (95% CrI −0.37 to −0.13)	−0.25 (95% CrI −1.20 to 0.71)	-
d[4][f]	0.01 (95% CrI −0.04 to 0.07)	−0.10 (95% CrI −0.88 to 0.46)	-
d[5][g]	0.00 (95% CrI −1.12 to 1.12)	−0.01 (95% CrI −1.44 to 1.43)	-
d[6][h]	−0.29 (95% CrI −0.40 to −0.18)	−0.32 (95% CrI −0.86 to 0.09)	-
Between-study standard deviation	-	0.3734	-
Model used	Random-effects model		
Evidence of inconsistency	There is no evidence of inconsistency since the difference in DIC between consistency and inconsistency models was not significant		

[a] Dbar = posterior mean of deviance.
[b] pD = effective number of parameters.
[c] DIC = deviance information criterion.
[d] d[2] indicates effect estimate (mean difference) of treatment 2 versus treatment 1.
[e] d[3] indicates effect estimate (mean difference) of treatment 3 versus treatment 1.
[f] d[4] indicates effect estimate (mean difference) of treatment 4 versus treatment 1.
[g] d[5] indicates effect estimate (mean difference) of treatment 5 versus treatment 1.
[h] d[6] indicates effect estimate (mean difference) of treatment 6 versus treatment 1.

Table 7. Parenchymal transection methods: choice of model results

Adverse events (proportion)			
Treatment number	**Treatment name**		
1	Clamp-crush method		
2	Cavitron ultrasonic surgical aspirator		
3	Hydrojet		
4	Radiofrequency dissecting sealer		
5	Sharp transection method		
6	Stapler		
	Fixed-effect model	**Random-effects model**	**Inconsistency model***
Dbar[a]	95.62	80.26	81.67
pD[b]	13.05	17.04	16.71
DIC[c]	108.67	97.30	98.37
d[2][d]	0.32 (95% CrI −0.28 to 0.92)	0.76 (95% CrI −2.18 to 4.69)	-
d[3][e]	−0.99 (95% CrI −2.76 to 0.54)	−0.56 (95% CrI −6.84 to 6.60)	-
d[4][f]	0.11 (95% CrI −0.46 to 0.68)	0.19 (95% CrI −2.95 to 3.50)	-
d[5][g]	0.10 (95% CrI −0.79 to 1.00)	0.1 (95% CrI −5.59 to 5.80)	-
d[6][h]	0.06 (95% CrI −0.63 to 0.76)	0.06 (95% CrI −5.59 to 5.76)	-
Between-study standard deviation	-	2.436	-
Model used	Random-effects model		
Evidence of inconsistency	There is no evidence of inconsistency since the difference in DIC between consistency and inconsistency models was not significant		
Adverse events (number)			
Treatment number	**Treatment name**		
1	Clamp-crush method		

Table 7. Parenchymal transection methods: choice of model results (*Continued*)

2	Cavitron ultrasonic surgical aspirator		
3	Hydrojet		
4	Radiofrequency dissecting sealer		
5	Sharp transection method		
6	Stapler		
	Fixed-effect model	**Random-effects model**	**Inconsistency model***
Dbar[a]	80.99	80.94	79.59
pD[b]	11.93	11.88	14.76
DIC[c]	92.92	92.83	94.35
d[2][d]	0.47 (95% CrI −0.08 to 1.03)	0.47 (95% CrI −0.08 to 1.03)	-
d[3][e]	0.34 (95% CrI −0.71 to 1.29)	0.33 (95% CrI −0.71 to 1.28)	-
d[4][f]	0.61 (95% CrI 0.12 to 1.12)	0.61 (95% CrI 0.12 to 1.11)	-
d[5][g]	0.12 (95% CrI −0.56 to 0.81)	0.12 (95% CrI −0.56 to 0.81)	-
d[6][h]	0.62 (95% CrI −0.21 to 1.48)	0.62 (95% CrI −0.20 to 1.45)	-
Between-study standard deviation	-	2.499	-
Model used	Fixed-effect model		-
Evidence of inconsistency	There is no evidence of inconsistency since the difference in DIC between consistency and inconsistency models was not significant		
Blood transfusion (proportion)			
Treatment number	**Treatment name**		
1	Clamp-crush method		
2	Cavitron ultrasonic surgical aspirator		
3	Hydrojet		
4	Radiofrequency dissecting sealer		

Table 7. Parenchymal transection methods: choice of model results (*Continued*)

5	Sharp transection method		
	Fixed-effect model	**Random-effects model**	**Inconsistency model***
Dbar[a]	72.41	71.86	72.23
pD[b]	11.91	13.99	14.98
DIC[c]	84.33	85.85	87.21
d[2][d]	0.39 (95% CrI −0.62 to 1.42)	0.42 (95% CrI −1.09 to 1.96)	-
d[3][e]	0.55 (95% CrI −0.75 to 1.83)	0.60 (95% CrI −1.47 to 2.83)	-
d[4][f]	0.09 (95% CrI −0.50 to 0.68)	0.14 (95% CrI −0.77 to 1.32)	-
d[5][g]	−0.22 (95% CrI −1.16 to 0. 71)	−0.22 (95% CrI −2.21 to 1. 75)	-
Between-study standard deviation	-	0.6464	-
Model used	Fixed-effect model		-
Evidence of inconsistency	There is no evidence of inconsistency since the difference in DIC between consistency and inconsistency models was not significant		

[a] DBar = posterior mean of deviance.
[b] pD = effective number of parameters.
[c] DIC = deviance information criterion.
[d] d[2] indicates log transformed effect estimate (odds ratio or rate ratio) of treatment 2 versus treatment 1.
[e] d[3] indicates log transformed effect estimate (odds ratio or rate ratio) of treatment 3 versus treatment 1.
[f] d[4] indicates log transformed effect estimate (odds ratio or rate ratio) of treatment 4 versus treatment 1.
[g] d[5] indicates log transformed effect estimate (odds ratio or rate ratio) of treatment 5 versus treatment 1.
[h] d[6] indicates log transformed effect estimate (odds ratio or rate ratio) of treatment 6 versus treatment 1.

Table 8. Vascular occlusion methods: choice of model results

Serious adverse events (proportion)	
Treatment number	**Treatment name**
1	Control
2	ConHVE
3	ConPTC

Table 8. Vascular occlusion methods: choice of model results (*Continued*)

4	ConSelectiveHVE		
5	ConSelectivePTC		
6	IntPTC		
	Fixed-effect model	**Random-effects model**	**Inconsistency model**
Dbar[a]	64.25	63.57	64.03
pD[b]	12.54	14.37	14.83
DIC[c]	76.79	77.95	78.86
d[2][d]	0.82 (95% CrI −1.70 to 3.50)	0.62 (95% CrI −5.00 to 5.89)	-
d[3][e]	0.35 (95% CrI −1.26 to 1.96)	0.16 (95% CrI −3.87 to 3.71)	-
d[4][f]	−1.98 (95% CrI −8.24 to 1.48)	−2.25 (95% CrI −9.99 to 3.38)	-
d[5][g]	−0.63 (95% CrI −2.29 to 0.97)	−1.01 (95% CrI −5.35 to 2.36)	-
d[6][h]	0.15 (95% CrI −0.61 to 0.92)	−0.07 (95% CrI −2.53 to 1.85)	-
Between-study standard deviation	-	1.216	-
Model used	Fixed-effect model		
Evidence of inconsistency	There is no evidence of inconsistency since the difference in DIC between consistency and inconsistency models was not significant		
Adverse events (proportion)			
Treatment number	**Treatment name**		
1	Control		
2	ConHVE		
3	ConPTC		
4	ConSelectiveHVE		

Table 8. Vascular occlusion methods: choice of model results (*Continued*)

5	ConSelectivePTC		
6	IntPTC		
7	IntSelectivePTC		
	Fixed-effect model	**Random-effects model**	**Inconsistency model**
Dbar[a]	120.82	118.76	119.07
pD[b]	18.10	21.01	21.93
DIC[c]	138.92	139.77	141.00
d[2][d]	0.95 (95% CrI −0.21 to 2.12)	0.90 (95% CrI −1.12 to 2.84)	-
d[3][e]	0.83 (95% CrI 0.00 to 1.69)	0.78 (95% CrI −0.58 to 2.09)	-
d[4][f]	0.05 (95% CrI −1.19 to 1.27)	0.00 (95% CrI −2.05 to 1.96)	-
d[5][g]	0.10 (95% CrI −0.81 to 1.01)	0.07 (95% CrI −1.42 to 1.50)	-
d[6][h]	0.24 (95% CrI −0.19 to 0.68)	0.18 (95% CrI −0.66 to 0.88)	-
d[7][i]	0.09 (95% CrI −0.75 to 0.93)	0.04 (95% CrI −1.37 to 1.35)	-
Between-study standard deviation	-	0.4825	-
Model used	Fixed-effect model		
Evidence of inconsistency	There is no evidence of inconsistency since the difference in DIC between consistency and inconsistency models was not significant		
Blood transfusion (proportion)			
Treatment number	**Treatment name**		
1	Control		
2	ConHVE		
3	ConPTC		
4	ConSelectiveHVE		
5	ConSelectivePTC		
6	IntPTC		

Table 8. Vascular occlusion methods: choice of model results (*Continued*)

7	IntSelectivePTC		
	Fixed-effect model	**Random-effects model**	**Inconsistency model**
Dbar[a]	139.87	120.00	120.10
pD[b]	19.04	25.25	25.72
DIC[c]	158.91	145.25	145.82
d[2][d]	−2.55 (95% CrI −3.80 to −1.36)	−2.88 (95% CrI −7.47 to 1.47)	-
d[3][e]	−0.77 (95% CrI −1.56 to 0.01)	−1.11 (95% CrI −3.72 to 1.28)	-
d[4][f]	−1.46 (95% CrI −2.58 to −0.36)	−1.79 (95% CrI −6.38 to 2.53)	-
d[5][g]	−0.26 (95% CrI −1.18 to 0.67)	−0.48 (95% CrI −3.83 to 2.72)	-
d[6][h]	−0.34 (95% CrI −0.84 to 0.16)	−0.47 (95% CrI −2.32 to 1.28)	-
d[7][i]	−0.92 (95% CrI −1.96 to 0.08)	−0.97 (95% CrI −4.24 to 2.24)	-
Between study standard deviation	-	1.613	-
Model used	Random-effects model		
Evidence of inconsistency	There is no evidence of inconsistency since the difference in DIC between consistency and inconsistency models was not significant		

Blood transfusion (red blood cell) (units)

Treatment number	**Treatment name**
1	Control
2	ConHVE
3	ConPTC
4	ConSelectiveHVE
5	ConSelectivePTC

Table 8. Vascular occlusion methods: choice of model results (*Continued*)

6	IntPTC		
7	IntSelectivePTC		
	Fixed-effect model	**Random-effects model**	**Inconsistency model**
Dbar[a]	−1.55	−1.05	0.24
pD[b]	15.99	17.36	19.34
DIC[c]	14.44	16.32	19.58
d[2][d]	−1.65 (95% CrI −3.96 to 0.67)	−1.56 (95% CrI −4.18 to 1.14)	-
d[3][e]	−1.25 (95% CrI −2.39 to −0.10)	−1.18 (95% CrI −2.54 to 0.31)	-
d[4][f]	−2.45 (95% CrI −4.08 to −0.82)	−2.37 (95% CrI −4.33 to −0.30)	-
d[5][g]	−1.45 (95% CrI −2.59 to −0.31)	−1.41 (95% CrI −2.86 to 0.12)	-
d[6][h]	−1.36 (95% CrI −2.48 to −0.23)	−1.35 (95% CrI −2.69 to 0.01)	-
d[7][i]	−1.43 (95% CrI −2.61 to −0.24)	−1.43 (95% CrI −3.01 to 0.08)	-
Between-study standard deviation	-	0.3149	-
Model used	Fixed-effect model		
Evidence of inconsistency	There is no evidence of inconsistency since the difference in DIC between consistency and inconsistency models was not significant		
Blood loss (litres)			
Treatment number	**Treatment name**		
1	Control		
2	ConHVE		
3	ConPTC		
4	ConSelectiveHVE		

Table 8. Vascular occlusion methods: choice of model results (*Continued*)

5	ConSelectivePTC		
6	IntPTC		
7	IntSelectivePTC		
	Fixed-effect model	**Random-effects model**	**Inconsistency model**
Dbar[a]	−45.73	−61.66	−63.13
pD[b]	22.01	29.37	30.58
DIC[c]	−23.72	−32.29	−32.55
d[2][d]	−0.36 (95% CrI −0.50 to −0.23)	−0.37 (95% CrI −0.94 to 0.22)	-
d[3][e]	−0.02 (95% CrI −0.12 to 0.07)	−0.14 (95% CrI −0.52 to 0.14)	-
d[4][f]	−0.27 (95% CrI −0.54 to −0.01)	−0.39 (95% CrI −1.16 to 0.27)	-
d[5][g]	0.09 (95% CrI −0.04 to 0.21)	0.00 (95% CrI −0.57 to 0.45)	-
d[6][h]	0.01 (95% CrI −0.05 to 0.07)	−0.06 (95% CrI −0.39 to 0.17)	-
d[7][i]	0.00 (95% CrI −0.21 to 0.2)	−0.18 (95% CrI −0.84 to 0.30)	-
Between-study standard deviation	-	0.2539	-
Model used	Random-effects model		
Evidence of inconsistency	There is no evidence of inconsistency since the difference in DIC between consistency and inconsistency models was not significant		

Con: continuous; **Int**: intermittent; **HVE**: hepatic vascular exclusion; **PTC:** portal triad clamping.

[a] DBar = posterior mean of deviance.
[b] pD = effective number of parameters.
[c] DIC = deviance information criterion.
[d] d[2] indicates effect estimate (mean difference) of treatment 2 versus treatment 1.
[e] d[3] indicates effect estimate (mean difference) of treatment 3 versus treatment 1.
[f] d[4] indicates effect estimate (mean difference) of treatment 4 versus treatment 1.
[g] d[5] indicates effect estimate (mean difference) of treatment 5 versus treatment 1.
[h] d[6] indicates effect estimate (mean difference) of treatment 6 versus treatment 1.

[i] d[7] indicates effect estimate (mean difference) of treatment 7 versus treatment 1.

Table 9. Cardiopulmonary interventions: pair-wise comparisons[a,b]

Blood transfusion (red blood cell) (units)				
	Acute normovolemic haemodilution	**Acute normovolemic haemodilution plus hypotension**	**Acute normovolemic haemodilution plus low central venous pressure**	**Low central venous pressure**
Control	MD −1.26; 95% CrI −4.92 to 2.39	MD −1.68; 95% CrI −5.33 to 1.98	MD −0.57; 95% CrI −3.35 to 1.88	MD −1.08; 95% CrI −3.43 to 1.13
Acute normovolemic haemodilution	-	MD −0.42; 95% CrI −5.59 to 4.75	MD 0.69; 95% CrI −3.80 to 5.18	MD 0.18; 95% CrI −4.12 to 4.49
Acute normovolemic haemodilution plus hypotension	-	-	MD 1.11; 95% CrI −3.39 to 5.60	MD 0.60; 95% CrI −3.71 to 4.91
Acute normovolemic haemodilution plus low central venous pressure	-	-	-	MD −0.51; 95% CrI −3.97 to 2.96
Blood loss (litres)				
	Acute normovolemic haemodilution	**Acute normovolemic haemodilution plus hypotension**	**Acute normovolemic haemodilution plus low central venous pressure**	**Hypoventilation**
Control	MD 0.00; 95% CrI −0.95 to 0.96	MD −0.25; 95% CrI −1.20 to 0.71	MD −0.10; 95% CrI −0.88 to 0.46	MD −0.01; 95% CrI −1.44 to 1.43
Acute normovolemic haemodilution	-	MD −0.25; 95% CrI −1.60 to 1.10	MD −0.11; 95% CrI −1.27 to 1.06	MD −0.01; 95% CrI −1.73 to 1.71
Acute normovolemic haemodilution plus hypotension	-	-	MD 0.14; 95% CrI −1.02 to 1.31	MD 0.24; 95% CrI −1.48 to 1.96
Acute normovolemic haemodilution plus low central venous pressure	-	-	-	MD 0.10; 95% CrI −1.49 to 1.68
Hypoventilation	-	-	-	-

[a] The table provides the effect estimate of each pair-wise comparison. To identify the effect estimate of a comparison (e.g. A versus B), look at the cell that occupies the column corresponding to treatment A and the row corresponding to treatment B. This gives the information directly. If that cell is empty (indicated by a '-', you have to look at column corresponding to treatment B and row corresponding to treatment A. You will have to take the inverse of this number (i.e. 1/number) to get the treatment effect.
[b] Treatment effects with evidence of difference are shown by italics (not applicable).

Table 10. Parenchymal transection methods: pair-wise comparisons[a,b]

Adverse events (proportion)				
	Cavitron ultrasonic surgical aspirator	**Hydrojet**	**Radiofrequency dissecting sealer**	**Sharp transection method**
Clamp-crush method	OR 2.15; 95% CrI 0.11 to 108.74	OR 0.57; 95% CrI 0.00 to 732.89	OR 1.20; 95% CrI 0.05 to 33.05	OR 1.11; 95% CrI 0.00 to 331.29
Cavitron ultrasonic surgical aspirator	-	OR 0.27; 95% CrI 0.00 to 501.34	OR 0.56; 95% CrI 0.01 to 62.38	OR 0.52; 95% CrI 0.00 to 398.54
Hydrojet	-	-	OR 2.12; 95% CrI 0.00 to 3638.36	OR 1.94; 95% CrI 0.00 to 12959.09
Radiofrequency dissecting sealer	-	-	-	OR 0.92; 95% CrI 0.00 to 638.06
Sharp transection method	-	-	-	-
Adverse events (number)				
	Cavitron ultrasonic surgical aspirator	**Hydrojet**	**Radiofrequency dissecting sealer**	**Sharp transection method**
Clamp-crush method	rate ratio 1.60; 95% CrI 0.92 to 2.79	rate ratio 1.40; 95% CrI 0.49 to 3.63	rate ratio 1.84; 95% CrI 1.13 to 3.06	rate ratio 1.13; 95% CrI 0.57 to 2.24
Cavitron ultrasonic surgical aspirator	-	rate ratio 0.88; 95% CrI 0.28 to 2.75	rate ratio 1.15; 95% CrI 0.54 to 2.42	rate ratio 0.71; 95% CrI 0.29 to 1.71
Hydrojet	-	-	rate ratio 1.31; 95% CrI 0.43 to 4.01	rate ratio 0.81; 95% CrI 0.24 to 2.71
Radiofrequency dissecting sealer	-	-	-	rate ratio 0.62; 95% CrI 0.26 to 1.44
Sharp transection method	-	-	-	-
Blood transfusion (proportion)				

Table 10. Parenchymal transection methods: pair-wise comparisons[a,b] (*Continued*)

	Cavitron ultrasonic surgical aspirator	Hydrojet	Radiofrequency dissecting sealer	Sharp transection method
Clamp-crush method	OR 1.48; 95% CrI 0.54 to 4.13	OR 1.73; 95% CrI 0.47 to 6.25	OR 1.09; 95% CrI 0.61 to 1.97	OR 0.80; 95% CrI 0.31 to 2.03
Cavitron ultrasonic surgical aspirator	-	OR 1.17; 95% CrI 0.23 to 6.05	OR 0.74; 95% CrI 0.23 to 2.39	OR 0.54; 95% CrI 0.14 to 2.15
Hydrojet	-	-	OR 0.63; 95% CrI 0.15 to 2.61	OR 0.46; 95% CrI 0.09 to 2.27
Radiofrequency dissecting sealer	-	-	-	OR 0.73; 95% CrI 0.24 to 2.21

[a] The table provides the effect estimate of each pair-wise comparison. To identify the effect estimate of a comparison (e.g. A versus B), look at the cell that occupies the column corresponding to treatment A and the row corresponding to treatment B. This gives the information directly. If that cell is empty (indicated by a '-', you have to look at column corresponding to treatment B and row corresponding to treatment A. You will have to take the inverse of this number (i.e. 1/number) to get the treatment effect.

[b] Treatment effects with evidence of difference are shown by italics (not applicable).

Table 11. Vascular occlusion methods: pair-wise comparisons[a,b]

Serious adverse events (proportion)					
	ConHVE	**ConPTC**	**ConSelectiveHVE**	**ConSelectivePTC**	**IntPTC**
Control	OR 2.27; 95% CrI 0.18 to 33.05	OR 1.42; 95% CrI 0.28 to 7.09	OR 0.14; 95% CrI 0.00 to 4.37	OR 0.53; 95% CrI 0.10 to 2.65	OR 1.16; 95% CrI 0.54 to 2.51
ConHVE	-	OR 0.63; 95% CrI 0.03 to 13.31	OR 0.06; 95% CrI 0.00 to 15.06	OR 0.23; 95% CrI 0.01 to 5.02	OR 0.51; 95% CrI 0.03 to 7.68
ConPTC	-	-	OR 0.10; 95% CrI 0.00 to 16.28	OR 0.37; 95% CrI 0.04 to 3.70	OR 0.82; 95% CrI 0.14 to 4.86
ConSelectiveHVE	-	-	-	Not estimable	Not estimable
ConSelectivePTC	-	-	-	-	OR 2.19; 95% CrI 0.36 to 13.26
Adverse events (proportion)					
	ConHVE	**ConPTC**	**ConSelectiveHVE**	**ConSelectivePTC**	**IntPTC**
Control	OR 2.58; 95% CrI 0.81 to 8.30	OR 2.30; 95% CrI 1.00 to 5.41	OR 1.06; 95% CrI 0.31 to 3.58	OR 1.11; 95% CrI 0.45 to 2.75	OR 1.28; 95% CrI 0.83 to 1.97

Table 11. Vascular occlusion methods: pair-wise comparisons[a,b] (*Continued*)

ConHVE	-	OR 0.89; 95% CrI 0.21 to 3.75	OR 0.41; 95% CrI 0.08 to 2.22	OR 0.43; 95% CrI 0.10 to 1.88	OR 0.49; 95% CrI 0.14 to 1.71
ConPTC	-	-	OR 0.46; 95% CrI 0.10 to 2.04	OR 0.48; 95% CrI 0.14 to 1.67	OR 0.55; 95% CrI 0.21 to 1.43
ConSelectiveHVE	-	-	-	OR 1.05; 95% CrI 0.23 to 4.84	OR 1.21; 95% CrI 0.33 to 4.45
ConSelectivePTC	-	-	-	-	OR 1.15; 95% CrI 0.42 to 3.16
IntPTC	-	-	-	-	-

Blood transfusion (proportion)

	ConHVE	**ConPTC**	**ConSelectiveHVE**	**ConSelectivePTC**	**IntPTC**
Control	OR 0.06; 95% CrI 0.00 to 4.33	OR 0.33; 95% CrI 0.02 to 3.59	OR 0.17; 95% CrI 0.00 to 12.59	OR 0.62; 95% CrI 0.02 to 15.18	OR 0.63; 95% CrI 0.10 to 3.59
ConHVE	-	Not estimable	Not estimable	Not estimable	Not estimable
ConPTC	-	-	OR 0.51; 95% CrI 0.00 to 83.52	Not estimable	OR 1.89; 95% CrI 0.09 to 41.17
ConSelectiveHVE	-	-	-	Not estimable	Not estimable
ConSelectivePTC	-	-	-	-	OR 1.01; 95% CrI 0.02 to 42.32
IntPTC	-	-	-	-	-

Blood transfusion (red blood cell)

	ConHVE	**ConPTC**	**ConSelectiveHVE**	**ConSelectivePTC**	**IntPTC**
Control	MD −1.65; 95% CrI −3.96 to 0.67	MD −1.25; 95% CrI −2.39 to −0.10	MD −2.45; 95% CrI −4.08 to −0.82	MD −1.45; 95% CrI −2.59 to −0.31	MD −1.36; 95% CrI −2.48 to −0.23
ConHVE	-	MD 0.40; 95% CrI −2.18 to 2.98	MD −0.80; 95% CrI −3.64 to 2.03	MD 0.20; 95% CrI −2.39 to 2.78	MD 0.29; 95% CrI −2.29 to 2.86
ConPTC	-	-	MD −1.20; 95% CrI −3.20 to 0.79	MD −0.20; 95% CrI −1.82 to 1.42	MD −0.11; 95% CrI −1.72 to 1.50
ConSelectiveHVE	-	-	-	MD 1.00; 95% CrI −0.99 to 2.99	MD 1.09; 95% CrI −0.89 to 3.07

Table 11. Vascular occlusion methods: pair-wise comparisons[a,b] (*Continued*)

ConSelectivePTC	-	-	-	-	MD 0.09; 95% CrI −1.51 to 1.70
IntPTC	-	-	-	-	-

Blood loss

-	**ConHVE**	**ConPTC**	**ConSelectiveHVE**	**ConSelectivePTC**	**IntPTC**
Control	MD −0.37; 95% CrI −0.94 to 0.22	MD −0.14; 95% CrI −0.52 to 0.14	MD −0.39; 95% CrI −1.16 to 0.27	MD 0.00; 95% CrI −0.57 to 0.45	MD −0.06; 95% CrI −0.39 to 0.17
ConHVE	-	MD 0.23; 95% CrI −0.44 to 0.90	MD −0.02; 95% CrI −0.94 to 0.90	MD 0.37; 95% CrI −0.41 to 1.14	MD 0.31; 95% CrI −0.34 to 0.95
ConPTC	-	-	MD −0.25; 95% CrI −1.04 to 0.54	MD 0.14; 95% CrI −0.47 to 0.74	MD 0.08; 95% CrI −0.35 to 0.52
ConSelectiveHVE	-	-	-	MD 0.39; 95% CrI −0.49 to 1.26	MD 0.33; 95% CrI −0.44 to 1.10
ConSelectivePTC	-	-	-	-	MD −0.06; 95% CrI −0.64 to 0.52
IntPTC	-	-	-	-	-

Con: continuous; **Int**: intermittent; **HVE**: hepatic vascular exclusion; **PTC**: portal triad clamping.

[a] The table provides the effect estimate of each pair-wise comparison. To identify the effect estimate of a comparison (e.g. A versus B), look at the cell that occupies the column corresponding to treatment A and the row corresponding to treatment B. This gives the information directly. If that cell is empty (indicated by a ' -', you have to look at column corresponding to treatment B and row corresponding to treatment A. You will have to take the inverse of this number (i.e. 1/number) to get the treatment effect.

[b] Treatment effects with evidence of difference are shown by italics.

Table 12. Intervention and control (ordered by category and comparisons)

Study	Intervention				Co-interventions					
	Intervention	**Control**	**Other information**	**Type of intervention**	**Vascular occlusion**	**Parenchymal transection method**	**Raw surface**	**Pharmacological methods**	**Cardiopulmonary methods**	**Autologous transfusion**
Capussotti 2012	Anterior approach	Control	-	Anterior approach	Not stated	Clamp-crush, bipolar dissecting	Not stated	Not stated	Not stated	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

						sealer				
Liu 2006	Anterior approach	Control	-	Anterior approach	Not stated	Cavitron ultrasonic surgical aspirator	Not stated	Not stated	Not stated	Not stated
Kajikawa 1994	Autologous blood donation	Control	Note: autologous blood donation group was further randomised to recombinant erythropoietin and no erythropoietin	Autologous transfusion	Not stated	Not stated	Not stated	Not stated	Not stated	Factor being randomised
Kostopanagiotou 2007	Autologous blood donation	Control	Autologous blood donation: 2 units of blood were withdrawn before surgery	Autologous transfusion	Hepatic vascular exclusion	Not stated	Not stated	Not stated	Not stated	Factor being randomised
Guo 2013	Acute normovolemic haemodilution plus low central venous pressure	Control	Acute normovolemic dilution plus low central venous pressure: blood withdrawn to a target	Cardiopulmonary methods	Not stated	Not stated	Not stated	Not stated	Factor being randomised	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

			of 28% haematocrit and replaced with fluid. Target for central venous pressure was not reported							
Jarnagin 2008	Acute normovolemic haemodilution plus low central venous pressure	Low central venous pressure	Acute normovolemic haemodilution: blood was withdrawn and replaced by colloids and crystalloids to reach a haematocrit target of 8 gm/dL. Low central venous pressure was maintained < 5 H_20 using fluid restriction and pharmacologic manipulation	Cardiopulmonary methods	Intermittent portal triad clamping	Not stated	Not stated	Not stated	Factor being randomised	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

Matot 2002	Acute normovolemic haemodilution plus low central venous pressure	Low central venous pressure	Acute normovolemic haemodilution: blood was withdrawn and replaced by colloids to reach a haematocrit target of 24%. Low central venous pressure was achieved by fluid restriction	Cardiopulmonary methods	Not stated	Not stated	Not stated	Not stated	Factor being randomised	Not stated
Yao 2006	Acute normovolemic haemodilution	Acute normovolemic haemodilution with hypotension 3rd group: control	Acute normovolemic haemodilution: withdrawal of blood and replacement with fluids to maintain a target haematocrit of 30%. Acute normovolemic haemod-	Cardiopulmonary methods	Not stated	Not stated	Not stated	Not stated	Factor being randomised	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

			ilution with controlled hypotension: in addition to acute normovolemic haemodilution, sodium nitroprusside was used. Target blood pressure not known							
Hasegawa 2002	Hypoventilation	Control	-	Cardiopulmonary methods	Intermittent portal triad clamping or selective occlusion	Clamp crush or cavitron ultrasonic surgical aspirator	Not stated	Not stated	Factor being randomised	None
Choi 2007	Low central venous pressure	Control	Low central venous pressure: by restricting flow from legs	Cardiopulmonary methods	Not stated	Not stated	Not stated	Not stated	Factor being randomised	Not stated
El-Kharboutly 2004	Low central venous pressure	Control	Low central venous pressure: nitroglycerine	Cardiopulmonary intervention	Intermittent portal triad clamping	Not stated	Not stated	Not stated	Factor being randomised	Not stated
Kato 2008	Low central venous pressure	Control	Low central venous pressure: by infe-	Cardiopulmonary methods	Intermittent portal triad clamping	Cavitron ultrasonic surgical aspi-	Fibrin glue used	Not stated	Factor being randomised	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

			rior IVC clamping			rator				
Wang 2006	Low central venous pressure	Control	Low central venous pressure: by limiting fluid, nitroglycerine, and furosemide	Cardiopulmonary methods	Varied	Clamp-crush	Not stated	Not stated	Factor being randomised	Not stated
Guo 2014	Low central venous pressure	Low central venous pressure + acute normovolemic haemodilution. 3rd group: control	Low central venous pressure: fluid restriction and nitroglycerine. Acute normovolemic haemodilution plus low central venous pressure: withdrawal of blood to a target haematocrit of 30% and replacement with colloids	Cardiopulmonary methods	Not stated	Not stated	Not stated	Not stated	Factor being randomised	Not stated
Rahbari 2014	Stapler	Clamp-crush method	Stapler: Autosuture Endo-GIA stapler (Covidien)	Parenchumal transection	Variable	Factor being randomised	Variable	Not stated	Low central venous pressure	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

Koo 2005	Cavitron ultrasonic surgical aspirator	Clamp-crush method	-	Parenchymal transection	No vascular occlusion	Factor being randomised	Not stated	Not stated	Not stated	Not stated
Takayama 2001	Cavitron ultrasonic surgical aspirator	Clamp-crush method	-	Parenchymal transection	Intermittent total or selective portal triad clamping	Factor being randomised	Fibrin glue used	Not stated	Not stated	Not stated
Doklestic 2012	Cavitron ultrasonic surgical aspirator	Clamp-crush method 3rd group: radiofrequency dissecting sealer	Ultrasonic dissector: cavitron ultrasonic surgical aspirator. Radiofrequency dissecting sealer: Ligasure	Parenchymal transection	Intermittent portal triad clamping	Factor being randomised	Not stated	Not stated	Low central venous pressure	Not stated
Rau 2001	Cavitron ultrasonic surgical aspirator	Hydrojet	Hydrojet: Jet Cutter	Parenchymal transection	Portal triad clamping	Factor being randomised	Variable	Not stated	Not stated	Not stated
Savlid 2013	Cavitron ultrasonic surgical aspirator	Stapler	Stapler: Endostapler (Covidien)	Parenchymal transection	Variable	Factor being randomised	Not stated	Not stated	Not stated	Not stated
Lesurtel 2005	Cavitron ultrasonic surgical aspirator	Radiofrequency dissecting sealer. 3rd group: hydrojet	Radiofrequency dissecting sealer: Tissue Link Hydrojet: Helix Hydro-Jet A	Parenchymal transection	No vascular occlusion	Factor being randomised	Not stated	Not stated	Not stated	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

			4th group with clamp-crush and vascular occlusion was excluded since there was difference in the co-intervention between the groups							
Ikeda 2009	Radiofrequency dissecting sealer	Clamp-crush method	Radiofrequency dissecting sealer: Ligasure	Parenchymal transection	Intermittent portal triad clamping or hemihepatic occlusion	Factor being randomised	Not stated	Not stated	Not stated	No
Lupo 2007	Radiofrequency dissecting sealer	Clamp-crush method	Radiofrequency dissecting sealer: Radionics needles	Parenchymal transection	No vascular occlusion	Factor being randomised	Not stated	Not stated	Not stated	Not stated
Muratore 2014	Radiofrequency dissecting sealer	Clamp-crush method	Radiofrequency dissecting sealer: Ligasure (Covidien)	Parenchymal transection	Not stated	Factor being randomised	No fibrin glue used	Not stated	Low central venous pressure	Not stated
Arita 2005	Radiofrequency dissecting sealer	Clamp-crush method	Radiofrequency dissecting sealer: Tissue Link (Valley Lab)	Parenchymal transection	Variable	Factor being randomised	Not stated	Not stated	Not stated	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

Smyrniotis 2005	Sharp transection	Clamp-crush method	Sharp transection: using scalpel	Parenchymal transection	Selective hepatic vascular exclusion	Factor being randomised	Not stated	Not stated	Low central venous pressure	Not stated
Shimada 1994	Antithrombin III concentrate	Control	Antithrombin concentrate: 1500 IU IV over 30 min: immediately before the operation, just before hepatic division, and immediately after operation	Pharmacological methods	Not stated	Not stated	Not stated	Factor being randomised	Not stated	Not stated
Lentschener 1997	Aprotinin	Control	Aprotinin: Loading dose: 2 X 10^6 kIU of aprotinin over a 20 min period after induction of anaesthesia. Continuous infusion: 5 x 10^5 kIU per hour administered by an infusion	Pharmacological methods	Intermittent portal triad clamping	Kelly clamp	Fibrin glue used	Factor being randomised	None	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

			pump until skin closure Additional bolus: 5 X 10^5 KIU of aprotinin was infused every three transfused red b10od cell (red blood cell) packs Control: placebo							
Wong 2003	Desmopressin	Control	Desmopressin: 30 mcg/kg shortly after induction Control: placebo	Pharmacological methods	Varied	Cavitron ultrasonic surgical aspirator	Not stated	Factor being randomised	Not stated	Not stated
Lodge 2005	Recombinant factor VIIa	Control	Recombinant factor VIIa: 1st dose: slow intravenous injection (20 mcg/kg or 80 mcg/kg) within 5 min before incision. 2nd dose: identical dose was	Pharmacological methods	Mixture of methods	Not stated	No fibrin glue used	Factor being randomised	Not stated	No

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

			given 5 h after incision if the surgery time was anticipated to exceed 6 hours Control: placebo							
Shao 2006	Recombinant factor VIIa	Control	Recombinant factor VIIa: brand not stated Dose: 50 or 100 mcg/kg before skin incision over 2 minutes and repeated every 2 hours until a maximum of 4 doses Control: placebo	Pharmacological methods	Not stated	Not stated	Not stated	Factor being randomised	Not stated	Not stated
Wu 2006	Tranexamic acid	Control	Tranexamic acid: 500 mg just before the surgery followed by 250 mg 4x/day for 3 days	Pharmacological methods	Varied	Clamp-crush method	Not stated	Factor being randomised	Not stated	Not stated
Chapman 2000	Collagen	Fibrin sealant	Collagen: Instat (Johnson	Raw surface	Not stated	Not stated	Factor being randomised	Not stated	Not stated	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

			& Johnson) Fibrin sealant: Costasis (Cohesion Technologies) - bovine thrombin and collagen combined with patient's own plasma							
Franceschi 2006	Collagen	Fibrin sealant	Collagen: Instat (Ethicon) Fibrin sealant: CryoSeal FS	Raw surface	Not stated	Not stated	Factor being randomised	Not stated	Not stated	Not stated
Kohno 1992	Collagen	Fibrin sealant	Collagen: Avitene (Alcon Inc). Fibrin sealant: Beriplast P (Beringwerke AB)	Raw surface	Not stated	Not stated	Factor being randomised	Not stated	Not stated	Not stated
Moench 2014	Collagen	Fibrin sealant	Collagen: Sangustop fleece (Aesculap AG). Fibrin-based haemostat:	Raw surface	Not stated	A number of parenchymal transection techniques	Factor being randomised	None	Not stated	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

			Tachosil (Nycomed)							
Fischer 2011	Fibrin sealant	Argon beam coagulator	Fibrin sealant: Tacchosil (Nycomed)	Raw surface	A mixture of approaches	A mixture of approaches	Factor being randomised	Not stated	Not stated	Not stated
Frilling 2005	Fibrin sealant	Argon beam coagulator	Fibrin sealant: Tacchosil	Raw surface	Not stated	A mixture of approaches	Factor being randomised	Not stated	Not stated	Not stated
Bektas 2014	Fibrin sealant	Control	Fibrin sealant: TISSEEL (Baxter Health Corporation) Spray; 5 mL of fibrinogen with synthetic aprotinin and 5 mL of thrombin (500 IU/mL)	Raw surface	Intermittent portal triad clamping	Different types of liver resection	Factor being randomised	Not stated	Not stated	Not stated
De Boer 2012	Fibrin sealant	Control	Fibrin sealant: Quixil (Johnson & Johnson Medical) spray; 5 mL of fibrinogen and tranexamic acid and 5 mL of thrombin	Raw surface	With and without inflow occlusion	Clamp-crush, cavitron ultrasonic surgical aspirator, electric coagulation based, combined	Factor being randomised	Not stated	Not stated	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

Liu 1993	Fibrin sealant	Control	Fibrin sealant: name not available	Raw surface	Not stated	Not stated	Factor being randomised	Not stated	Not stated	Not stated
Noun 1996	Fibrin sealant	Control	Fibrin sealant: Biocol	Raw surface	Varied	Clamp-crush method or cavitron ultrasonic surgical aspirator	Factor being randomised	Not stated	Not stated	Not stated
Porte 2012	Fibrin sealant	Gelatin	Fibrin sealant: Fibrocaps (ProFibrix)	Raw surface	Not stated	Not stated	Factor being randomised	Not stated	Not stated	Not stated
Genyk 2014	Fibrin sealant	Oxidised cellulose	Fibrin sealant: Tacchosil Oxidised cellulose: Surgicel	Raw surface	Not stated	Not stated	Factor being randomised	Not stated	Not stated	Not stated
Koea 2013	Fibrin sealant	Oxidised cellulose	Fibrin sealant: Fibrin Pad Oxidised cellulose: no further details	Raw surface	Not stated	Not stated	Factor being randomised	Not stated	Not stated	Not stated
Ollinger 2013	Fibrin sealant	Oxidised cellulose	Fibrin sealant: Tachosil (Nycomed) Oxidised cellulose: Veriset (Covidien)	Raw surface	Varied	Not stated	Factor being randomised	Not stated	Not stated	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

Kakaei 2013	Fibrin sealant	Oxidised cellulose 3rd group: cyanoacrylate	Oxidised cellulose: Surgicel (Ethicon Inc) Cyanoacrylate: Glubran 2 (GEM SRL) Fibrin sealant: Tachosil (Takeda Pharmaceuticals)	Raw surface	Not stated	Clamp-crush method	Factor being randomised	Not stated	Not stated	Not stated
Gugenheim 2011	Fibrin sealant	Plasma-Jet coagulator	Fibrin sealant: fibrin glue (no further details)	Raw surface	Not stated	Cavitron ultrasonic surgical aspirator	Factor being randomised	Not stated	Not stated	Not stated
Figueras 2007	Fibrin sealant plus collagen	Control	Fibrin sealant spray: Tissucol Collagen: collagen sponge (Johnson & Johnson) Note: In both groups, bleeding from raw surface was controlled using argon beam coagulator or Tissuelink	Raw surface	Intermittent portal triad or selective clamping	Cavitron ultrasonic surgical aspirator	Factor being randomised	Not stated	Not stated	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

Belghiti 1996	Continuous portal triad clamping	Continuous hepatic vascular exclusion	Hepatic vascular exclusion by encircling the entire retrohepatic inferior vena cava	Vascular occlusion	Factor being randomised	Clamp-crush or cavitron ultrasonic surgical aspirator	Fibrin glue used	Not stated	Not stated	Not stated
Chen 2006	Continuous portal triad clamping	Continuous hepatic vascular exclusion	Hepatic vascular exclusion by encircling the entire infrahepatic inferior vena cava	Vascular occlusion	Factor being randomised	Clamp-crush method	Not stated	Not stated	Not stated	Not stated
Si-Yuan 2014	Continuous portal triad clamping	Continuous selective hepatic vascular exclusion	-	Vascular occlusion	Factor being randomised	Not stated	Not stated	Not stated	Low central venous pressure	Not stated
Ni 2013	Continuous portal triad clamping	Continuous selective portal triad clamping	-	Vascular occlusion	Factor being randomised	Clamp-crush method	Not stated	Not stated	Low central venous pressure	Not stated
Chouker 2004	Continuous portal triad clamping	Control	-	Vascular occlusion	Factor being randomised	Not stated	Not stated	Not stated	Not stated	Not stated
Clavien 1996	Continuous portal triad clamping	Control	Note: After every 1 hour of continuous portal triad clamping (or 30 minutes	Vascular occlusion	Factor being randomised	Not stated	Not stated	Not stated	Not stated	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

			for cirrhotic patients), the clamp was released for 10 minutes before reclamping							
Dayangac 2010	Continuous portal triad clamping	Control	-	Vascular occlusion	Factor being randomised	Not stated	Not stated	Not stated	Not stated	Not stated
Pietsch 2010	Continuous portal triad clamping	Control	-	Vascular occlusion	Factor being randomised	Not stated	Not stated	Not stated	Not stated	Not stated
Belghiti 1999	Continuous portal triad clamping	Intermittent portal triad clamping	Continuous portal triad clamping: until end of transection Intermittent portal triad clamping: 15 minutes on and 5 minutes off until hepatectomy	Vascular occlusion	Factor being randomised	Cavitron ultrasonic surgical aspirator	Not stated	Not stated	Low central venous pressure	Not stated
Capussotti 2003	Continuous portal triad clamping	Intermittent portal triad clamping	Intermittent portal triad clamping: 15 minutes on and	Vascular occlusion	Factor being randomised	Clamp-crush	Fibrin glue used	Not stated	Not stated	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

			5 minutes off							
Liang 2009	Continuous selective portal triad clamping	Intermittent portal triad clamping	Intermittent portal triad clamping: 20 minutes on and 5 minutes off	Vascular occlusion	Factor being randomised	Clamp crush	Not stated	None	Not stated	Not stated
Capussotti 2006	Intermittent portal triad clamping	Control	Intermittent portal triad clamping: 15 minutes on and 5 minutes off	Vascular occlusion	Factor being randomised	Clamp-crush or bipolar dissecting sealer	Not stated	Not stated	Low central venous pressure	Not stated
Lee 2012	Intermittent portal triad clamping	Control	Intermittent portal triad clamping: 15 minutes on and 5 minutes off	Vascular occlusion	Factor being randomised	Cavitron ultrasonic surgical aspirator	Fibrin glue used	Not stated	Low central venous pressure	Not stated
Man 1997	Intermittent portal triad clamping	Control	Intermittent portal triad clamping: 20 minutes on and 5 minutes off	Vascular occlusion	Factor being randomised	Cavitron ultrasonic surgical aspirator	Not stated	Not stated	Not stated	Not stated
Man 2003	Intermittent portal triad clamping	Control	Intermittent portal triad clamping: 20 minutes on and	Vascular occlusion	Factor being randomised	Not stated	Not stated	Not stated	Not stated	Not stated

Table 12. Intervention and control (ordered by category and comparisons) (*Continued*)

			5 minutes off (until resection is completed or a maximum of 6 cycles)							
Park 2012	Intermittent portal triad clamping	Control	Intermittent portal triad clamping: 15 minutes on and 5 minutes off	Vascular occlusion	Factor being randomised	Not stated	Not stated	Not stated	Not stated	Not stated
Figueras 2005	Intermittent portal triad clamping	Intermittent selective portal triad clamping	Intermittent clamping: 15 minutes on and 5 minutes off	Vascular occlusion	Factor being randomised	Not stated	Not stated	Not stated	Not stated	Not stated
Wu 2002	Intermittent portal triad clamping	Intermittent selective portal triad clamping	Intermittent portal triad clamping: 15 minutes on and 5 minutes off Intermittent selective portal triad clamping: 30 minutes on and 5 minutes off	Vascular occlusion	Factor being randomised	Clamp-crush method	Not stated	Not stated	Not stated	Not stated

Table 13. Risk of bias (ordered by category and comparisons)

Study	Intervention	Control	Sequence generation	Allocation concealment	Blinding of participants and healthcare providers	Blinding of outcome assessors	Missing outcome bias	Selective reporting bias	Source of funding bias	Other bias	Overall risk of bias
Capussotti 2012	Anterior approach	Control	Low	Unclear	Unclear	Unclear	High	Low	Low	Low	Unclear or high
Liu 2006	Anterior approach	Control	Unclear	Unclear	High	High	High	High	Low	Low	Unclear or high
Kajikawa 1994	Autologous blood donation	Control	Unclear	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low	Unclear or high
Kostopanagiotou 2007	Autologous blood donation	Control	Unclear	Unclear	Unclear	Unclear	High	High	Unclear	Low	Unclear or high
Guo 2013	Acute normovolemic haemodilution plus low central venous pressure	Control	Unclear	Unclear	Unclear	Unclear	Unclear	High	Low	Low	Unclear or high
Jarnagin 2008	Acute normovolemic haemodilution plus low central venous pressure	Low central venous pressure	Unclear	Unclear	Unclear	Unclear	High	Low	Unclear	Low	Unclear or high

Table 13. Risk of bias (ordered by category and comparisons) (*Continued*)

Matot 2002	Acute normo-volemic haemod-ilution plus low central venous pressure	Low central venous pressure	Low	Unclear	High	Unclear	Low	High	Low	Low	Unclear or high
Yao 2006	Acute normo-volemic haemod-ilution	Acute normo-volemic haemod-ilution with hy-poten-sion 3rd group: control	Unclear	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low	Unclear or high
Hasegawa 2002	Hy-poventi-lation	Control	Low	Low	Low	High	Low	High	Low	Low	Unclear or high
Choi 2007	Low central venous pressure	Control	Unclear	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low	Unclear or high
El-Khar-boutly 2004	Low central venous pressure	Control	Unclear	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low	Unclear or high
Kato 2008	Low central venous pressure	Control	Low	Low	Unclear	Unclear	Low	High	Unclear	Low	Unclear or high
Wang 2006	Low central venous pressure	Control	Unclear	Unclear	Unclear	Unclear	High	High	Unclear	Low	Unclear or high
Guo 2014	Low central venous	Low central venous	Unclear	Unclear	Unclear	Unclear	Unclear	High	Low	Low	Unclear or high

Table 13. Risk of bias (ordered by category and comparisons) (*Continued*)

	pressure	pressure + acute normo-volemic haemod-ilution. 3rd group: control									
Rahbari 2014	Stapler	Clamp-crush method	Low	Low	High	Low	Low	Low	High	Low	Unclear or high
Koo 2005	Cav-itron ul-trasonic surgical aspirator	Clamp-crush method	Unclear	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low	Unclear or high
Takayama 2001	Cav-itron ul-trasonic surgical aspirator	Clamp-crush method	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear	Low	Unclear or high
Dok-lestic 2012	Cav-itron ul-trasonic surgical aspirator	Clamp-crush method. 3rd group: radiofre-quency dissect-ing sealer	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Unclear or high
Rau 2001	Cav-itron ul-trasonic surgical aspirator	Hydro-jet	Unclear	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low	Unclear or high
Savlid 2013	Cav-itron ul-trasonic surgical aspirator	Stapler	Low	Low	Unclear	Unclear	Low	Low	High	Low	Unclear or high

Table 13. Risk of bias (ordered by category and comparisons) (*Continued*)

Lesurtel 2005	Cavitron ultrasonic surgical aspirator	Radiofrequency dissecting sealer. 3rd group: hydrojet	Unclear	Unclear	Unclear	Unclear	Low	Low	High	Low	Unclear or high
Ikeda 2009	Radiofrequency dissecting sealer	Clamp-crush method	Low	Unclear	High	High	Low	Low	Low	Low	Unclear or high
Lupo 2007	Radiofrequency dissecting sealer	Clamp-crush method	Low	Unclear	Unclear	Unclear	Low	High	Low	Low	Unclear or high
Muratore 2014	Radiofrequency dissecting sealer	Clamp-crush method	Low	Low	Unclear	High	Low	Low	Low	Low	Unclear or high
Arita 2005	Radiofrequency dissecting sealer	Clamp-crush method	Low	Low	High	High	Low	Low	Low	Low	Unclear or high
Smyrniotis 2005	Sharp transection	Clamp-crush method	Unclear	Unclear	Unclear	Unclear	Low	High	Unclear	Low	Unclear or high
Shimada 1994	Antithrombin III concentrate	Control	Unclear	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low	Unclear or high

Table 13. Risk of bias (ordered by category and comparisons) (*Continued*)

Lentschener 1997	Aprotinin	Control	Low	Unclear	Unclear	Low	High	High	High	Low	Unclear or high
Wong 2003	Desmopressin	Control	Unclear	Unclear	Low	Low	High	High	Low	Low	Unclear or high
Lodge 2005	Recombinant factor VIIa	Control	Low	Low	Low	Low	High	Low	High	Low	Unclear or high
Shao 2006	Recombinant factor VIIa	Control	Unclear	Unclear	Unclear	Unclear	High	High	High	Low	Unclear or high
Wu 2006	Tranexamic acid	Control	Unclear	Unclear	Low	Low	Low	High	Unclear	Low	Unclear or high
Chapman 2000	Collagen	Fibrin sealant	Low	Unclear	Unclear	Unclear	High	High	High	Low	Unclear or high
Franceschi 2006	Collagen	Fibrin sealant	Unclear	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low	Unclear or high
Kohno 1992	Collagen	Fibrin sealant	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear	Low	Unclear or high
Moench 2014	Collagen	Fibrin sealant	Low	Low	High	High	High	Low	High	Low	Unclear or high
Fischer 2011	Fibrin sealant	Argon beam coagulator	Unclear	Low	High	High	High	Low	High	Low	Unclear or high
Frilling 2005	Fibrin sealant	Argon beam coagulator	Unclear	Unclear	High	High	Low	Low	Unclear	Low	Unclear or high
Bektas 2014	Fibrin sealant	Control	Low	Low	High	High	Low	Low	High	Low	Unclear or high

Table 13. Risk of bias (ordered by category and comparisons) (*Continued*)

De Boer 2012	Fibrin sealant	Control	Low	Low	High	High	Low	Low	High	Low	Unclear or high
Liu 1993	Fibrin sealant	Control	Unclear	Unclear	Unclear	Unclear	Low	High	Unclear	Low	Unclear or high
Noun 1996	Fibrin sealant	Control	Unclear	Unclear	Unclear	Unclear	High	High	Unclear	Low	Unclear or high
Porte 2012	Fibrin sealant	Gelatin	Unclear	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low	Unclear or high
Genyk 2014	Fibrin sealant	Oxidised cellulose	Unclear	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low	Unclear or high
Koea 2013	Fibrin sealant	Oxidised cellulose	Low	Low	High	High	High	High	High	Low	Unclear or high
Ollinger 2013	Fibrin sealant	Oxidised cellulose	Unclear	Unclear	High	High	Low	Low	High	Low	Unclear or high
Kakaei 2013	Fibrin sealant	Oxidised cellulose 3rd group: cyanoacrylate	Low	Unclear	High	Unclear	Unclear	High	Low	Low	Unclear or high
Gugenheim 2011	Fibrin sealant	Plasma-Jet coagulator	Unclear	Unclear	Unclear	Unclear	Low	High	Unclear	Low	Unclear or high
Figueras 2007	Fibrin sealant plus collagen	Control	Low	Low	Unclear	Unclear	Low	Low	Low	Low	Unclear or high
Belghiti 1996	Continuous portal triad clamping	Continuous hepatic vascular exclusion	Unclear	Unclear	Unclear	Unclear	High	High	Unclear	Low	Unclear or high

Table 13. Risk of bias (ordered by category and comparisons) (*Continued*)

Chen 2006	Continuous portal triad clamping	Continuous hepatic vascular exclusion	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Unclear or high
Si-Yuan 2014	Continuous portal triad clamping	Continuous selective hepatic vascular exclusion	Unclear	Low	Unclear	Unclear	Low	High	Unclear	Low	Unclear or high
Ni 2013	Continuous portal triad clamping	Continuous selective portal triad clamping	Unclear	Low	Unclear	Unclear	Low	Low	Low	Low	Unclear or high
Chouker 2004	Continuous portal triad clamping	Control	Unclear	Unclear	High	Unclear	High	High	Unclear	Low	Unclear or high
Clavien 1996	Continuous portal triad clamping	Control	Unclear	Unclear	Unclear	Unclear	High	High	Low	Low	Unclear or high
Dayangac 2010	Continuous portal triad clamping	Control	Low	Low	High	Low	Low	High	Low	Low	Unclear or high
Pietsch 2010	Continuous portal triad clamp-	Control	Unclear	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low	Unclear or high

Table 13. Risk of bias (ordered by category and comparisons) (*Continued*)

	ing										
Belghiti 1999	Continuous portal triad clamping	Intermittent portal triad clamping	Unclear	Unclear	Unclear	Unclear	Low	High	Unclear	Low	Unclear or high
Capussotti 2003	Continuous portal triad clamping	Intermittent portal triad clamping	Low	Unclear	Unclear	Unclear	Low	Low	Unclear	Low	Unclear or high
Liang 2009	Continuous selective portal triad clamping	Intermittent portal triad clamping	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low	Unclear or high
Capussotti 2006	Intermittent portal triad clamping	Control	Low	Unclear	Unclear	Unclear	Low	High	Unclear	Low	Unclear or high
Lee 2012	Intermittent portal triad clamping	Control	Low	Low	High	High	Low	Low	Low	Low	Unclear or high
Man 1997	Intermittent portal triad clamping	Control	Unclear	Unclear	Unclear	Unclear	Low	High	Low	Low	Unclear or high
Man 2003	Intermittent portal triad	Control	Unclear	Unclear	Unclear	Unclear	Low	High	Unclear	Low	Unclear or high

Table 13. Risk of bias (ordered by category and comparisons) (*Continued*)

	clamping										
Park 2012	Intermittent portal triad clamping	Control	Low	Low	Unclear	Unclear	High	High	Low	Low	Unclear or high
Figueras 2005	Intermittent portal triad clamping	Intermittent selective portal triad clamping	Unclear	Unclear	Unclear	Unclear	Low	High	Low	Low	Unclear or high
Wu 2002	Intermittent portal triad clamping	Intermittent selective portal triad clamping	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low	Unclear or high

Table 14. Detailed 'Summary of findings' table: anterior approach vs conventional approach

Outcomes	**Illustrative comparative risks* (95% CrI)**		**Relative effect (95% CrI)**	**No of participants (studies)**	**Quality of the evidence (GRADE)**
	Assumed risk	**Corresponding risk**			
	Control	**Intervention**			
Mortality (perioperative)	**76 per 1000**	**19 per 1000** (2 to 82)	**OR 0.23** (0.03 to 1.08)	**185** (2 studies)	⊕◯◯◯ **Very low**[1,2,3]
Mortality (longest follow-up)	None of the trials reported this outcome.				
Serious adverse events (proportion)	**125 per 1000**	**154 per 1000** (40 to 457)	**OR 1.27** (0.29 to 5.89)	**65** (1 study)	⊕◯◯◯ **Very low**[1,2,3]

Table 14. Detailed 'Summary of findings' table: anterior approach vs conventional approach (*Continued*)

Serious adverse events (number)	None of the trials reported this outcome.
Health-related quality of life (30 days, 3 months)	None of the trials reported this outcome.
Health-related quality of life (maximal follow-up)	None of the trials reported this outcome.

*The basis for the **assumed risk** is the mean control group proportion. The **corresponding risk** (and its 95% credible interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CrI).
Network meta-analysis was not performed for any of the outcomes since there were only two treatments
CrI: credible intervals; **OR**: odds ratio.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).
[2] Sample size was low (total number of participants fewer than 400 for continuous outcomes and fewer than 300 events in total in both groups for other outcomes) (downgraded by 1 point).
[3] Credible intervals spanned no effect and clinically significant effect (20% relative risk reduction for binary outcomes; standardised mean difference of 0.5 for health-related quality of life) (downgraded by 1 point).

Table 15. Detailed 'Summary of findings' table: autologous blood donation vs control

Outcomes	**Illustrative comparative risks* (95% CrI)**		**Relative effect (95% CrI)**	**No of participants (studies)**	**Quality of the evidence (GRADE)**
	Assumed risk	**Corresponding risk**			
	Control	**Intervention**			
Mortality (perioperative)	There was no mortality in either group.			28 (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Mortality (longest follow-up): reported at 1	There was no mortality in either group.			28 (1 study)	⊕◯◯◯ **Very low**[1,2,3]

Table 15. Detailed 'Summary of findings' table: autologous blood donation vs control (*Continued*)

year			
Serious adverse events (proportion)	None of the trials reported this outcome.		
Serious adverse events (number)	None of the trials reported this outcome.		
Health-related quality of life (30 days, 3 months)	None of the trials reported this outcome.		
Health-related quality of life (longest follow-up)	None of the trials reported this outcome.		

*The basis for the **assumed risk** is the mean control group proportion. The **corresponding risk** (and its 95% credible interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CrI).
Network meta-analysis was not performed for any of the outcomes since there were only two treatments
CrI: credible intervals; **OR**: odds ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).
[2] Sample size was low (total number of participants fewer than 400 for continuous outcomes and fewer than 300 events in total in both groups for other outcomes) (downgraded by 1 point).
[3]Credible intervals spanned no effect and clinically significant effect (20% relative risk reduction for binary outcomes; standardised mean difference of 0.5 for health-related quality of life) (downgraded by 1 point).

Table 16. Detailed 'Summary of findings' table: cardiopulmonary interventions

Outcomes	**Illustrative comparative risks* (95% CrI)**		**Relative effect (95% CrI)**	**No of participants (studies)**	**Quality of the evidence (GRADE)**
	Assumed risk	**Corresponding risk**			
	Control	**Intervention**			

Table 16. Detailed 'Summary of findings' table: cardiopulmonary interventions *(Continued)*

Mortality (perioperative)					
Hypoventilation vs control	There was no mortality in either group.			**79** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Low central venous pressure vs control	There was no mortality in either group.			**85** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Mortality (longest follow-up)	None of the trials reported this outcome.				
Serious adverse events (proportion)					
Hypoventilation vs control	**26 per 1000**	**60 per 1000** (5 to 679)	**OR 2.41** (0.18 to 80.4)	**79** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Low central venous pressure vs acute normovolemic haemodilution plus low CVP	**302 per 1000**	**284 per 1000** (157 to 460)	**OR 0.92** (0.43 to 1.97)	**63** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Serious adverse events (number)					
Low central venous pressure vs control	**100 per 1000**	**0 per 1000** (0 to 2)	**Rate ratio 0.00** (0 to 0.02)	**42** (1 study)	⊕◯◯◯ **Very low**[a,b,c]
Low central venous pressure vs acute normovolemic haemodilution plus low central venous pressure	**103 per 1000**	**77 per 1000** (15 to 287)	**Rate ratio 0.73** (0.13 to 3.53)	**78** (1 study)	⊕◯◯◯ **Very low**[a,b,c]
Health-related quality of life (30 days, 3 months)	None of the trials reported this outcome.				
Health-related quality of life (longest follow-up)	None of the trials reported this outcome.				

*The basis for the **assumed risk** is the mean control group proportion. The **corresponding risk** (and its 95% credible interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CrI).
Network meta-analysis was not performed for any of the outcomes because of the lack of availability of direct and indirect comparisons in the network
CrI: credible intervals; **OR**: odds ratio.

Table 16. Detailed 'Summary of findings' table: cardiopulmonary interventions (*Continued*)

GRADE Working Group grades of evidence **High quality:** Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality:** We are very uncertain about the estimate.

[1a] Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).
[2] Sample size was low (total number of participants fewer than 400 for continuous outcomes and fewer than 300 events in total in both groups for other outcomes) (downgraded by 1 point).
[3] Credible intervals spanned no effect and clinically significant effect (20% relative risk reduction for binary outcomes; standardised mean difference of 0.5 for health-related quality of life) (downgraded by 1 point).

Table 17. Detailed 'Summary of findings' table: methods of parenchymal transection

Outcomes	**Illustrative comparative risks* (95% CrI)**		**Relative effect (95% CrI)**	**No of participants (studies)**	**Quality of the evidence (GRADE)**
	Assumed risk	**Corresponding risk**			
	Control	**Intervention**			
Mortality (perioperative)					
CUSA vs clamp-crush method	**23 per 1000**	**6 per 1000** (0 to 54)	**OR 0.24** (0.01 to 2.41)	**172** (2 studies)	⊕◯◯◯ **Very low**[1,2,3]
Radiofrequency dissecting sealer vs clamp-crush method	**10 per 1000**	**16 per 1000** (4 to 65)	**OR 1.60** (0.43 to 6.7)	**390** (5 studies)	⊕◯◯◯ **Very low**[1,2,3]
Sharp transection method vs clamp-crush method	There was no mortality in either group.			**82** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Stapler vs clamp-crush method	**31 per 1000**	**67 per 1000** (12 to 375)	**OR 2.26** (0.39 to 18.93)	**130** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Hydrojet vs CUSA	**55 per 1000**	**54 per 1000** (9 to 258)	**OR 0.98** (0.16 to 6.04)	**111** (2 studies)	⊕◯◯◯ **Very low**[1,2,3]
Radiofrequency dissecting sealer vs CUSA	**44 per 1000**	**28 per 1000** (3 to 166)	**OR 0.61** (0.07 to 4.28)	**90** (2 studies)	⊕◯◯◯ **Very low**[1,2,3]

Table 17. Detailed 'Summary of findings' table: methods of parenchymal transection (*Continued*)

Stapler vs CUSA	There was no mortality in either group.			**79** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Radiofrequency dissecting sealer vs hydrojet	**80 per 1000**	**9 per 1000** (0 to 145)	**OR 0.10** (0 to 1.95)	**50** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Mortality (longest follow-up)	None of the trials reported this outcome.				
Serious adverse events (proportion)					
CUSA vs clamp-crush method	**93 per 1000**	**31 per 1000** (6 to 110)	**OR 0.31** (0.06 to 1.2)	**172** (2 studies)	⊕◯◯◯ **Very low**[1,2,3]
Radiofrequency dissecting sealer vs clamp-crush method	**58 per 1000**	**49 per 1000** (15 to 145)	**OR 0.83** (0.24 to 2.74)	**240** (3 studies)	⊕◯◯◯ **Very low**[1,2,3]
Sharp transection method vs clamp-crush method	**49 per 1000**	**106 per 1000** (20 to 502)	**OR 2.31** (0.39 to 19.69)	**82** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Hydrojet vs CUSA	**100 per 1000**	**124 per 1000** (61 to 238)	**OR 1.27** (0.58 to 2.81)	**61** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Radiofrequency dissecting sealer vs CUSA	**50 per 1000**	**30 per 1000** (3 to 180)	**OR 0.58** (0.06 to 4.16)	**40** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Stapler vs CUSA	**246 per 1000**	**246 per 1000** (6 to 931)	**OR 1.00** (0.02 to 41.22)	**130** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Serious adverse events (number)					
CUSA vs clamp-crush method	**45 per 1000**	**29 per 1000** (3 to 166)	**Rate ratio 0.63** (0.07 to 4.17)	**132** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Radiofrequency dissecting sealer vs clamp-crush method	**61 per 1000**	**190 per 1000** (75 to 474)	**Rate ratio 3.64** (1.25 to 13.97)	**130** (2 studies)	⊕⊕◯◯ **Low**[1,2]
Hydrojet vs CUSA	**80 per 1000**	**121 per 1000** (20 to 546)	**Rate ratio 1.59** (0.24 to 13.83)	**50** (1 study)	⊕◯◯◯ **Very low**[1,2,3]

Table 17. Detailed 'Summary of findings' table: methods of parenchymal transection (*Continued*)

Radiofrequency dissecting sealer vs CUSA	**80 per 1000**	**121 per 1000** (20 to 546)	**Rate ratio 1.59** (0.24 to 13.83)	**50** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Stapler vs CUSA	**180 per 1000**	**230 per 1000** (109 to 424)	**Rate ratio 1.36** (0.56 to 3.36)	**100** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Radiofrequency dissecting sealer vs hydrojet	**120 per 1000**	**120 per 1000** (23 to 445)	**Rate ratio 1.00** (0.17 to 5.88)	**50** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Health-related quality of life (30 days, 3 months)	None of the trials reported this outcome.				
Health-related quality of life (maximal follow-up)	None of the trials reported this outcome.				

*The basis for the **assumed risk** is the mean control group proportion. The **corresponding risk** (and its 95% credible interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CrI).
Network meta-analysis was not performed for any of the outcomes because of the lack of availability of direct and indirect comparisons in the network
CrI: credible intervals; **CUSA**: cavitron ultrasonic surgical aspirator; **OR**: odds ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).
[2] Sample size was low (total number of participants fewer than 400 for continuous outcomes and fewer than 300 events in total in both groups for other outcomes) (downgraded by 1 point).
[3] Credible intervals spanned no effect and clinically significant effect (20% relative risk reduction for binary outcomes; standardised mean difference of 0.5 for health-related quality of life) (downgraded by 1 point).

Table 18. Detailed 'Summary of findings' Table: methods of dealing with cut surface

Outcomes	Illustrative comparative risks* (95% CrI)	Relative effect (95% CrI)	No of participants (studies)	Quality of the evidence (GRADE)

Table 18. Detailed 'Summary of findings' Table: methods of dealing with cut surface (*Continued*)

	Assumed risk	Corresponding risk			
	Control	**Intervention**			
Mortality (perioperative)					
Fibrin sealant vs control	**11 per 1000**	**41 per 1000** (10 to 253)	**OR 4.03** (0.9 to 31.72)	**380** (2 studies)	⊕○○○ **Very low**[1,2,3]
Fibrin sealant and collagen vs control	**13 per 1000**	**45 per 1000** (10 to 268)	**OR 3.48** (0.74 to 27.03)	**300** (1 study)	⊕○○○ **Very low**[1,2,3]
Fibrin sealant vs argon beam	**53 per 1000**	**72 per 1000** (25 to 198)	**OR 1.39** (0.46 to 4.45)	**227** (2 studies)	⊕○○○ **Very low**[1,2,3]
Fibrin sealant vs collagen	**33 per 1000**	**30 per 1000** (7 to 123)	**OR 0.91** (0.2 to 4.14)	**256** (3 studies)	⊕○○○ **Very low**[1,2,3]
Oxidised cellulose vs fibrin sealant	**56 per 1000**	**31 per 1000** (1 to 565)	**OR 0.54** (0.01 to 22.09)	**50** (1 study)	⊕○○○ **Very low**[1,2,3]
Plasmajet vs fibrin sealant	**103 per 1000**	**65 per 1000** (7 to 332)	**OR 0.60** (0.06 to 4.31)	**58** (1 study)	⊕○○○ **Very low**[1,2,3]
Mortality (longest follow-up)	None of the trials reported this outcome.				
Serious adverse events (proportion)					
Fibrin sealant vs control	**186 per 1000**	**191 per 1000** (128 to 275)	**OR 1.03** (0.64 to 1.66)	**457** (3 studies)	⊕○○○ **Very low**[1,2,3]
Fibrin sealant vs argon beam	**269 per 1000**	**183 per 1000** (78 to 360)	**OR 0.61** (0.23 to 1.53)	**106** (1 study)	⊕○○○ **Very low**[1,2,3]
Fibrin sealant vs collagen	**258 per 1000**	**356 per 1000** (205 to 547)	**OR 1.59** (0.74 to 3.47)	**127** (1 study)	⊕○○○ **Very low**[1,2,3]
Oxidised cellulose vs fibrin sealant	**444 per 1000**	**309 per 1000** (113 to 603)	**OR 0.56** (0.16 to 1.9)	**50** (1 study)	⊕○○○ **Very low**[1,2,3]
Plasmajet vs fibrin sealant	**207 per 1000**	**25 per 1000** (0 to 165)	**OR 0.10** (0 to 0.76)	**58** (1 study)	⊕○○○ **Very low**[1,2,3]
Serious adverse events (number)					

Table 18. Detailed 'Summary of findings' Table: methods of dealing with cut surface (*Continued*)

Fibrin sealant vs control	**486 per 1000**	**470 per 1000** (307 to 640)	**Rate ratio 0.94** (0.47 to 1.88)	**70** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Fibrin sealant & collagen vs control	**147 per 1000**	**186 per 1000** (116 to 286)	**Rate ratio 1.33** (0.76 to 2.33)	**300** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Fibrin sealant vs argon beam	**65 per 1000**	**249 per 1000** (107 to 547)	**Rate ratio 4.81** (1.73 to 17.5)	**121** (1 study)	⊕⊕◯◯ **Low**[1,2]
Fibrin sealant vs collagen	**323 per 1000**	**369 per 1000** (266 to 488)	**Rate ratio 1.23** (0.76 to 2)	**189** (2 studies)	⊕◯◯◯ **Very low**[1,2,3]
Fibrin sealant vs cyanoacrylate	**67 per 1000**	**67 per 1000** (2 to 733)	**Rate ratio 1.01** (0.03 to 38.36)	**30** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Oxidised cellulose vs cyanoacrylate	**67 per 1000**	**277 per 1000** (46 to 921)	**Rate ratio 5.37** (0.67 to 163.2)	**30** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Oxidised cellulose vs fibrin sealant	**67 per 1000**	**278 per 1000** (46 to 926)	**Rate ratio 5.40** (0.67 to 174.86)	**30** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Health-related quality of life (30 days, 3 months)	None of the trials reported this outcome.				
Health-related quality of life (longest follow-up)	None of the trials reported this outcome.				

*The basis for the **assumed risk** is the mean control group proportion. The **corresponding risk** (and its 95% credible interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CrI).
Network meta-analysis was not performed for any of the outcomes because of the lack of availability of direct and indirect comparisons in the network
CrI: credible intervals; **OR**: odds ratio.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).
[2] Sample size was low (total number of participants fewer than 400 for continuous outcomes and fewer than 300 events in total in both groups for other outcomes) (downgraded by 1 point).

[3]Credible intervals spanned no effect and clinically significant effect (20% relative risk reduction for binary outcomes; standardised mean difference of 0.5 for health-related quality of life) (downgraded by 1 point).

Table 19. Detailed 'Summary of findings' table: methods of vascular occlusion

Outcomes	Illustrative comparative risks* (95% CrI)		Relative effect (95% CrI)	No of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	Intervention			
Mortality (perioperative)					
Continuous portal triad clamping vs control	There was no mortality in either group.			**15** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Intermittent portal triad clamping vs control	**26 per 1000**	**15 per 1000** (3 to 60)	**OR 0.60** (0.13 to 2.42)	**392** (4 studies)	⊕◯◯◯ **Very low**[1,2,3]
Continuous portal triad clamping vs continuous hepatic vascular exclusion	**1 per 1000**	**5 per 1000** (4 to 15)	**OR 4.91** (3.68 to 15.64)	**170** (2 studies)	⊕◯◯◯ **Very low**[1,2,3]
Continuous selective hepatic vascular exclusion vs continuous portal triad clamping	There was no mortality in either group.			**160** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Continuous selective portal triad clamping vs continuous portal triad clamping	There was no mortality in either group.			**120** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Intermittent portal triad clamping vs continuous portal triad clamping	**67 per 1000**	**10 per 1000** (0 to 70)	**OR 0.14** (0 to 1.05)	**121** (2 studies)	⊕◯◯◯ **Very low**[1,2,3]
Intermittent portal triad clamping vs continuous selective portal triad clamp-	There was no mortality in either group.			**80** (1 study)	⊕◯◯◯ **Very low**[1,2,3]

Table 19. Detailed 'Summary of findings' table: methods of vascular occlusion (*Continued*)

ing					
Intermittent selective portal triad clamping vs intermittent portal triad clamping	**1 per 1000**	**2 per 1000** (0 to 69)	**OR 2.27** (0.17 to 74)	**138** (2 studies)	⊕◯◯◯ **Very low**[1,2,3]
Mortality (longest follow-up)	None of the trials reported this outcome.				
Serious adverse events (proportion)*					
Continuous hepatic vascular exclusion vs control	**99 per 1000**	**200 per 1000** (19 to 785)	**Rate ratio 2.27** (0.18 to 33.05)	**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Continuous portal triad clamping vs control	**99 per 1000**	**135 per 1000** (30 to 439)	**Rate ratio** 1.42 (0.28 to 7.09)	**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Continuous selective hepatic vascular exclusion vs control	**99 per 1000**	**15 per 1000** (0 to 325)	**Rate ratio 0.14** (0 to 4.37)	**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Continuous selective portal triad clamping vs control	**99 per 1000**	**55 per 1000** (11 to 226)	**Rate ratio 0.53** (0.1 to 2.65)	**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Intermittent portal triad clamping vs control	**99 per 1000**	**113 per 1000** (56 to 217)	**Rate ratio 1.16** (0.54 to 2.51)	**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Continuous portal triad clamping vs continuous hepatic vascular exclusion	**50 per 1000**	**32 per 1000** (2 to 412)	**Rate ratio 0.63** (0.03 to 13.31)	**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Continuous selective hepatic vascular exclusion vs continuous hepatic vascular exclusion	**50 per 1000**	**3 per 1000** (0 to 442)	**Rate ratio 0.06** (0 to 15.06)	**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Continuous selective portal triad clamping vs continuous hepatic vascular exclusion	**50 per 1000**	**12 per 1000** (1 to 209)	**Rate ratio 0.23** (0.01 to 5.02)	**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]

Table 19. Detailed 'Summary of findings' table: methods of vascular occlusion (*Continued*)

Intermittent portal triad clamping vs continuous hepatic vascular exclusion	**50 per 1000**	**26 per 1000** (2 to 288)	**Rate ratio 0.51** (0.03 to 7.68)	**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Continuous selective hepatic vascular exclusion vs continuous portal triad clamping	**139 per 1000**	**16 per 1000** (0 to 724)	**Rate ratio 0.10** (0 to 16.28)	**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Continuous selective portal triad clamping vs continuous portal triad clamping	**139 per 1000**	**56 per 1000** (6 to 374)	**Rate ratio 0.37** (0.04 to 3.7)	**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Intermittent portal triad clamping vs continuous portal triad clamping	**139 per 1000**	**117 per 1000** (22 to 439)	**Rate ratio 0.82** (0.14 to 4.86)	**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Continuous selective portal triad clamping vs continuous selective hepatic vascular exclusion	As there were no serious adverse events in either group, the credible intervals were extremely wide. This is equivalent to not estimable in direct comparisons			**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Intermittent portal triad clamping vs continuous selective hepatic vascular exclusion	As there were no serious adverse events in either group, the credible intervals were extremely wide. This is equivalent to not estimable in direct comparisons			**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Intermittent portal triad clamping vs continuous selective portal triad clamping	**130 per 1000**	**247 per 1000** (51 to 665)	**Rate ratio 2.19** (0.36 to 13.26)	**815** (6 studies)	⊕◯◯◯ **Very low**[1,2,3]
Serious adverse events (number)					
Intermittent portal triad clamping vs control	**80 per 1000**	**119 per 1000** (36 to 358)	**Rate ratio 1.55** (0.43 to 6.4)	**100** (1 study)	⊕◯◯◯ **Very low**[a,b,c]

Table 19. Detailed 'Summary of findings' table: methods of vascular occlusion (*Continued*)

Continuous portal triad clamping vs continuous hepatic vascular exclusion	**179 per 1000**	**36 per 1000** (2 to 218)	**Rate ratio 0.17** (0.01 to 1.28)	**52** (1 study)	⊕◯◯◯ **Very low**[a,b,c]
Intermittent portal triad clamping vs continuous portal triad clamping	**190 per 1000**	**21 per 1000** (0 to 116)	**Rate ratio 0.09** (0 to 0.56)	**86** (1 study)	⊕⊕◯◯ **Low**[a,b]
Intermittent selective portal triad clamping vs intermittent portal triad clamping	**134 per 1000**	**165 per 1000** (76 to 328)	**Rate ratio 1.27** (0.53 to 3.15)	**138** (2 studies)	⊕◯◯◯ **Very low**[a,b,c]
Health-related quality of life (30 days, 3 months)	None of the trials reported this outcome.				
Health-related quality of life (longest follow-up)	None of the trials reported this outcome.				

*The basis for the **assumed risk** is the mean control group proportion. The **corresponding risk** (and its 95% credible interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CrI).
Network meta-analysis was not performed for any of the outcomes other than serious adverse events (proportion) because of the lack of availability of direct and indirect comparisons in the network
CrI: credible intervals; **OR**: odds ratio.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).
[2] Sample size was low (total number of participants fewer than 400 for continuous outcomes and fewer than 300 events in total in both groups for other outcomes) (downgraded by 1 point).
[3] Credible intervals spanned no effect and clinically significant effect (20% relative risk reduction for binary outcomes; standardised mean difference of 0.5 for health-related quality of life) (downgraded by 1 point).

Table 20. Detailed 'Summary of findings' table: pharmacological interventions

Outcomes	Illustrative comparative risks* (95% CrI)		Relative effect (95% CrI)	No of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	Intervention			
Mortality (perioperative)					
Recombinant factor VIIa vs control	**51 per 1000**	**33 per 1000** (7 to 158)	**OR 0.63** (0.13 to 3.51)	**185** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Tranexamic acid vs control	There was no mortality in either group.			**214** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Mortality (longest follow-up)	None of the trials reported this outcome.				
Serious adverse events (proportion)					
Anti-thrombin III vs control	**273 per 1000**	**312 per 1000** (67 to 761)	**OR 1.21** (0.19 to 8.49)	**24** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Recombinant Factor VIIa vs control	**376 per 1000**	**396 per 1000** (256 to 555)	**OR 1.09** (0.57 to 2.07)	**432** (2 studies)	⊕◯◯◯ **Very low**[1,2,3]
Serious adverse events (number)					
Recombinant Factor VIIa vs control	**81 per 1000**	**120 per 1000** (68 to 217)	**Rate ratio 1.55** (0.83 to 3.16)	**432** (2 studies)	⊕◯◯◯ **Very low**[1,2,3]
Tranexamic acid vs control	**75 per 1000**	**65 per 1000** (23 to 164)	**Rate ratio 0.85** (0.29 to 2.41)	**214** (1 study)	⊕◯◯◯ **Very low**[1,2,3]
Health-related quality of life (30 days, 3 months)	None of the trials reported this outcome.				
Health-related quality of life (maximal follow-up)	None of the trials reported this outcome.				

*The basis for the **assumed risk** is the mean control group proportion. The **corresponding risk** (and its 95% credible interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CrI).
Network meta-analysis was not performed for any of the outcomes because of the lack of availability of direct and indirect comparisons

Table 20. Detailed 'Summary of findings' table: pharmacological interventions (*Continued*)

in the network **CrI**: credible intervals; **OR**: odds ratio
GRADE Working Group grades of evidence **High quality:** Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality:** We are very uncertain about the estimate.

[1] Risk of bias was unclear or high in the trial(s) (downgraded by 1 point).
[2] Sample size was low (total number of participants fewer than 400 for continuous outcomes and fewer than 300 events in total in both groups for other outcomes) (downgraded by 1 point).
[3] Credible intervals spanned no effect and clinically significant effect (20% relative risk reduction for binary outcomes; standardised mean difference of 0.5 for health-related quality of life) (downgraded by 1 point).

APPENDICES

Appendix 1. Search strategies

Database	Time span	Search strategy
The Central Register of Controlled Trials (CENTRAL)	2015, Issue 9	1. Blood loss OR bleeding OR hemorrhage OR haemorrhage OR hemorrhages OR haemorrhages OR hemostasis OR haemostasis OR transfusion 2. MeSH descriptor Hemorrhage explode all trees 3. MeSH descriptor Blood Transfusion explode all trees 4. (#1 OR #2 OR #3) 5. Liver OR hepatic OR hepato* 6. MeSH descriptor Liver explode all trees 7. (5 OR 6) 8. Resection OR resections OR segmentectomy OR segmentectomies 9. (7 AND 8) 10. Hepatectomy OR hepatectomies 11. MeSH descriptor Hepatectomy explode all trees 12. (9 OR 10 OR 11) 13. (4 AND 12)

(*Continued*)

MEDLINE (PubMed)	January 1947 to September 2015	(Blood loss OR bleeding OR hemorrhage OR haemorrhage OR hemorrhages OR haemorrhages OR hemostasis OR haemostasis OR transfusion OR "Hemorrhage" [MeSH] OR "Blood Transfusion" [MeSH]) AND (((liver OR hepatic OR hepato* OR "liver" [MeSH]) AND (resection OR resections OR segmentectomy OR segmentectomies)) OR hepatectomy OR hepatectomies OR "hepatectomy" [MeSH]) AND ((randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab]) NOT (animals [mh] NOT humans [mh]))
Embase (OvidSP)	January 1974 to September 2015	1. (Blood loss or bleeding or hemorrhage or haemorrhage or hemorrhages or haemorrhages or hemostasis or haemostasis or transfusion).af 2. Exp bleeding/or exp blood transfusion/ 3 .1 or 2 4. (Liver or hepatic or hepato*).af 5. (Resection or resections or segmentectomy or segmentectomies).af 6. 4 and 5 7. (Hepatectomy or hepatectomies).af 8. Exp Liver Resection/ 9. 6 or 7 or 8 10. 3 and 9 11. Exp crossover-procedure/or exp double-blind procedure/or exp randomized controlled trial/or single-blind procedure/ 12. (Random* OR factorial* OR crossover* OR cross over* OR cross-over* OR placebo* OR double* adj blind* OR single* adj blind* OR assign* OR allocat* OR volunteer*).af 13. 11 OR 12 14. 10 AND 13
Science Citation Index Expanded (Web of Science)	January 1945 to September 2015	1. TS=(Blood loss OR bleeding OR hemorrhage OR haemorrhage OR hemorrhages OR haemorrhages OR hemostasis OR haemostasis OR transfusion) 2. TS=((liver OR hepatic OR hepato*) AND (resection OR resections OR segmentectomy OR segmentectomies) OR hepatectomy OR hepatectomies) 3. TS=(random* OR rct* OR crossover OR masked OR blind* OR placebo* OR meta-analysis OR systematic review* OR meta-analys*) 4. 1 AND 2 AND 3

(*Continued*)

World Health Organization International Clinical Trials Registry Platform Search Portal (www.who.int/ictrp)	September 2015	Liver resection OR hepatectomy

Appendix 2. WinBUGS code

Binary outcome

Binary outcome - fixed-effect model

```
# Binomial likelihood, logit link
# Fixed effects model
model{ # *** PROGRAM STARTS
for(i in 1:ns){ # LOOP THROUGH trials
mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
for (k in 1:na[i]) { # LOOP THROUGH ARMS
r[i,k] ~ dbin(p[i,k],n[i,k]) # binomial likelihood
# model for linear predictor
logit(p[i,k]) <- mu[i] + d[t[i,k]] - d[t[i,1]]
# expected value of the numerators
rhat[i,k] <- p[i,k] * n[i,k]
#Deviance contribution
dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))
+ (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
}
# summed residual deviance contribution for this trial
resdev[i] <- sum(dev[i,1:na[i]])
}
totresdev <- sum(resdev[]) # Total Residual Deviance
d[1]<-0 # treatment effect is zero for reference treatment
# vague priors for treatment effects
for (k in 2:nt){ d[k] ~ dnorm(0,.0001) }

# pair wise ORs and LORs for all possible pair-wise comparisons, if nt>2
for (c in 1:(nt-1)) {
for (k in (c+1):nt) {
or[c,k] <- exp(d[k] - d[c])
lor[c,k] <- (d[k]-d[c])
}
}
# ranking on relative scale
for (k in 1:nt) {
# rk[k] <- nt+1-rank(d[],k) # assumes events are “good”
rk[k] <- rank(d[],k) # assumes events are “bad”
best[k] <- equals(rk[k],1) #calculate probability that treat k is best
for (h in 1:nt){ prob[h,k] <- equals(rk[k],h) } # calculates probability that treat k is h-th best
}
```

```
} # *** PROGRAM ENDS
```

Binary outcome - random-effects model

```
# Binomial likelihood, logit link
# Random effects model
model{ # *** PROGRAM STARTS
for(i in 1:ns){ # LOOP THROUGH trials
w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
delta[i,1] <- 0 # treatment effect is zero for control arm
mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
for (k in 1:na[i]) { # LOOP THROUGH ARMS
r[i,k] ~ dbin(p[i,k],n[i,k]) # binomial likelihood
logit(p[i,k]) <- mu[i] + delta[i,k] # model for linear predictor
rhat[i,k] <- p[i,k] * n[i,k] # expected value of the numerators
#Deviance contribution
dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))
+ (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k]))) }
# summed residual deviance contribution for this trial
resdev[i] <- sum(dev[i,1:na[i]])
for (k in 2:na[i]) { # LOOP THROUGH ARMS
# trial-specific LOR distributions
delta[i,k] ~ dnorm(md[i,k],taud[i,k])
# mean of LOR distributions (with multi-arm trial correction)
md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]
# precision of LOR distributions (with multi-arm trial correction)
taud[i,k] <- tau *2*(k-1)/k
# adjustment for multi-arm randomised clinical trialss
w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])
# cumulative adjustment for multi-arm trials
sw[i,k] <- sum(w[i,1:k-1])/(k-1)
}
}
totresdev <- sum(resdev[]) # Total Residual Deviance
d[1]<-0 # treatment effect is zero for reference treatment
# vague priors for treatment effects
for (k in 2:nt){ d[k] ~ dnorm(0,.0001) }
sd ~ dunif(0,5) # vague prior for between-trial SD
tau <- pow(sd,-2) # between-trial precision = (1/between-trial variance)

# pair wise ORs and LORs for all possible pair-wise comparisons, if nt>2
for (c in 1:(nt-1)) {
for (k in (c+1):nt) {
or[c,k] <- exp(d[k] - d[c])
lor[c,k] <- (d[k]-d[c])
}
}
# ranking on relative scale
for (k in 1:nt) {
# rk[k] <- nt+1-rank(d[],k) # assumes events are “good”
rk[k] <- rank(d[],k) # assumes events are “bad”
best[k] <- equals(rk[k],1) #calculate probability that treat k is best
for (h in 1:nt){ prob[h,k] <- equals(rk[k],h) } # calculates probability that treat k is h-th best
```

```
}

} # *** PROGRAM ENDS
```

Binary outcome - inconsistency model (random-effects)

```
# Binomial likelihood, logit link, inconsistency model
# Random effects model
model{ # *** PROGRAM STARTS
for(i in 1:ns){ # LOOP THROUGH trials
delta[i,1]<-0 # treatment effect is zero in control arm
mu[i] ~ dnorm(0,.0001) # vague priors for trial baselines
for (k in 1:na[i]) { # LOOP THROUGH ARMS
r[i,k] ~ dbin(p[i,k],n[i,k]) # binomial likelihood
logit(p[i,k]) <- mu[i] + delta[i,k] # model for linear predictor
#Deviance contribution
rhat[i,k] <- p[i,k] * n[i,k] # expected value of the numerators
dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))
+ (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
}
# summed residual deviance contribution for this trial
resdev[i] <- sum(dev[i,1:na[i]])
for (k in 2:na[i]) { # LOOP THROUGH ARMS
# trial-specific LOR distributions
delta[i,k] ~ dnorm(d[t[i,1],t[i,k]] ,tau)
}
}
totresdev <- sum(resdev[]) # Total Residual Deviance
for (c in 1:(nt-1)) { # priors for all mean treatment effects
for (k in (c+1):nt) { d[c,k] ~ dnorm(0,.0001) }
}
sd ~ dunif(0,5) # vague prior for between-trial standard deviation
var <- pow(sd,2) # between-trial variance
tau <- 1/var # between-trial precision
} # *** PROGRAM ENDS
```

Continuous outcome (mean difference)

Continuous outcome (mean difference) - fixed-effect model

```
# Normal likelihood, identity link
# Fixed effect model
model{ # *** PROGRAM STARTS
for(i in 1:ns){ # LOOP THROUGH trials
mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
for (k in 1:na[i]) { # LOOP THROUGH ARMS
var[i,k] <- pow(se[i,k],2) # calculate variances
prec[i,k] <- 1/var[i,k] # set precisions
y[i,k] ~ dnorm(theta[i,k],prec[i,k])
# model for linear predictor
theta[i,k] <- mu[i] + d[t[i,k]] - d[t[i,1]]
#Deviance contribution
```

```
dev[i,k] <- (y[i,k]-theta[i,k])*(y[i,k]-theta[i,k])*prec[i,k]
}
# summed residual deviance contribution for this trial
resdev[i] <- sum(dev[i,1:na[i]])
}
totresdev <- sum(resdev[]) #Total Residual Deviance
d[1]<-0 # treatment effect is zero for control arm
# vague priors for treatment effects
for (k in 2:nt){ d[k] ~ dnorm(0,.0001) }
# ranking on relative scale
for (k in 1:nt) {
rk[k] <- rank(d[],k) # assumes lower is better
# rk[k] <- nt+1-rank(d[],k) # assumes lower outcome is worse
best[k] <- equals(rk[k],1) #calculate probability that treat k is best
for (h in 1:nt){ prob[h,k] <- equals(rk[k],h) } # calculates probability that treat k is h-th best
}
} # *** PROGRAM ENDS
```

Continuous outcome (mean difference) - random-effects model

```
# Normal likelihood, identity link
# Random effects model for multi-arm trials
model{ # *** PROGRAM STARTS
for(i in 1:ns){ # LOOP THROUGH trials
w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
delta[i,1] <- 0 # treatment effect is zero for control arm
mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
for (k in 1:na[i]) { # LOOP THROUGH ARMS
var[i,k] <- pow(se[i,k],2) # calculate variances
prec[i,k] <- 1/var[i,k] # set precisions
y[i,k] ~ dnorm(theta[i,k],prec[i,k])
theta[i,k] <- mu[i] + delta[i,k] # model for linear predictor
#Deviance contribution
dev[i,k] <- (y[i,k]-theta[i,k])*(y[i,k]-theta[i,k])*prec[i,k]
}
# summed residual deviance contribution for this trial
resdev[i] <- sum(dev[i,1:na[i]])
for (k in 2:na[i]) { # LOOP THROUGH ARMS
# trial-specific MD distributions
delta[i,k] ~ dnorm(md[i,k],taud[i,k])
# mean of MD distributions, with multi-arm trial correction
md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]
# precision of MD distributions (with multi-arm trial correction)
taud[i,k] <- tau *2*(k-1)/k
# adjustment, multi-arm randomised clinical trialss
w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])
# cumulative adjustment for multi-arm trials
sw[i,k] <- sum(w[i,1:k-1])/(k-1)
}
}
totresdev <- sum(resdev[]) #Total Residual Deviance
d[1]<-0 # treatment effect is zero for control arm
# vague priors for treatment effects
```

```
for (k in 2:nt){ d[k] ~ dnorm(0,.0001) }
sd ~ dunif(0,5) # vague prior for between-trial SD
tau <- pow(sd,-2) # between-trial precision = (1/between-trial variance)
# ranking on relative scale
for (k in 1:nt) {
rk[k] <- rank(d[],k) # assumes lower is better
# rk[k] <- nt+1-rank(d[],k) # assumes lower outcome is worse
best[k] <- equals(rk[k],1) #calculate probability that treat k is best
for (h in 1:nt){ prob[h,k] <- equals(rk[k],h) } # calculates probability that treat k is h-th best
}
} # *** PROGRAM ENDS
```

Continuous outcome (mean difference) - inconsistency model (random-effects)

```
# Normal likelihood, identity link
# Random effects model for multi-arm trials
model{ # *** PROGRAM STARTS
for(i in 1:ns){ # LOOP THROUGH trials
delta[i,1] <- 0 # treatment effect is zero for control arm
mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
for (k in 1:na[i]) { # LOOP THROUGH ARMS
var[i,k] <- pow(se[i,k],2) # calculate variances
prec[i,k] <- 1/var[i,k] # set precisions
y[i,k] ~ dnorm(theta[i,k],prec[i,k]) # binomial likelihood
theta[i,k] <- mu[i] + delta[i,k] # model for linear predictor
#Deviance contribution
dev[i,k] <- (y[i,k]-theta[i,k])*(y[i,k]-theta[i,k])*prec[i,k]
}
# summed residual deviance contribution for this trial
resdev[i] <- sum(dev[i,1:na[i]])
for (k in 2:na[i]) { # LOOP THROUGH ARMS
# trial-specific MD distributions
delta[i,k] ~ dnorm(d[t[i,1],t[i,k]] ,tau)
}
}
totresdev <- sum(resdev[]) # Total Residual Deviance
for (c in 1:(nt-1)) { # priors for all mean treatment effects
for (k in (c+1):nt) { d[c,k] ~ dnorm(0,.0001) }
}
sd ~ dunif(0,5) # vague prior for between-trial standard deviation
tau <- pow(sd,-2) # between-trial precision
} # *** PROGRAM ENDS
```

Continuous outcome (standardised mean difference)

We will calculate the standardised mean difference and its standard error for each treatment comparison using the statistical algorithms used by RevMan 2014.

Continuous outcome (standardised mean difference) - fixed-effect model

```
# Normal likelihood, identity link
# Trial-level data given as treatment differences
# Fixed effects model
```

```
model{ # *** PROGRAM STARTS
for(i in 1:ns2) { # LOOP THROUGH 2-ARM trials
y[i,2] ~ dnorm(delta[i,2],prec[i,2]) # normal likelihood for 2-arm trials
#Deviance contribution for trial i
resdev[i] <- (y[i,2]-delta[i,2])*(y[i,2]-delta[i,2])*prec[i,2]
}
for(i in (ns2+1):(ns2+ns3)) { # LOOP THROUGH THREE-ARM trials
for (k in 1:(na[i]-1)) { # set variance-covariance matrix
for (j in 1:(na[i]-1)) {
Sigma[i,j,k] <- V[i]*(1-equals(j,k)) + var[i,k+1]*equals(j,k)
}
}
Omega[i,1:(na[i]-1),1:(na[i]-1)] <- inverse(Sigma[i,,]) #Precision matrix
# multivariate normal likelihood for 3-arm trials
y[i,2:na[i]] ~ dmnorm(delta[i,2:na[i]],Omega[i,1:(na[i]-1),1:(na[i]-1)])
#Deviance contribution for trial i
for (k in 1:(na[i]-1)){ # multiply vector & matrix
ydiff[i,k]<- y[i,(k+1)] - delta[i,(k+1)]
z[i,k]<- inprod2(Omega[i,k,1:(na[i]-1)], ydiff[i,1:(na[i]-1)])
}
resdev[i]<- inprod2(ydiff[i,1:(na[i]-1)], z[i,1:(na[i]-1)])
}
for(i in 1:(ns2+ns3)){ # LOOP THROUGH ALL trials
for (k in 2:na[i]) { # LOOP THROUGH ARMS
var[i,k] <- pow(se[i,k],2) # calculate variances
prec[i,k] <- 1/var[i,k] # set precisions
delta[i,k] <- d[t[i,k]] - d[t[i,1]]
}
}
totresdev <- sum(resdev[]) #Total Residual Deviance
d[1]<-0 # treatment effect is zero for reference treatment
# vague priors for treatment effects
for (k in 2:nt){ d[k] ~ dnorm(0,.0001) }
# ranking on relative scale
for (k in 1:nt) {
rk[k] <- nt+1-rank(d[],k) # assumes higher HRQoL is "good"
#rk[k] <- rank(d[],k) # assumes higher outcome is "bad"
best[k] <- equals(rk[k],1) #calculate probability that treat k is best
for (h in 1:nt){ prob[h,k] <- equals(rk[k],h) } # calculates probability that treat k is h-th best
}
} # *** PROGRAM ENDS
```

Continuous outcome (standardised mean difference) - random-effects model

```
# Normal likelihood, identity link
# Trial-level data given as treatment differences
# Random effects model
model{ # *** PROGRAM STARTS
for(i in 1:ns2) { # LOOP THROUGH 2-ARM trials
y[i,2] ~ dnorm(delta[i,2],prec[i,2]) # normal likelihood for 2-arm trials
#Deviance contribution for trial i
resdev[i] <- (y[i,2]-delta[i,2])*(y[i,2]-delta[i,2])*prec[i,2]
}
```

```
for(i in (ns2+1):(ns2+ns3)) { # LOOP THROUGH THREE-ARM trials
for (k in 1:(na[i]-1)) { # set variance-covariance matrix
for (j in 1:(na[i]-1)) {
Sigma[i,j,k] <- V[i]*(1-equals(j,k)) + var[i,k+1]*equals(j,k)
}
}
Omega[i,1:(na[i]-1),1:(na[i]-1)] <- inverse(Sigma[i,,]) #Precision matrix
# multivariate normal likelihood for 3-arm trials
y[i,2:na[i]] ~ dmnorm(delta[i,2:na[i]],Omega[i,1:(na[i]-1),1:(na[i]-1)])
#Deviance contribution for trial i
for (k in 1:(na[i]-1)){ # multiply vector & matrix
ydiff[i,k]<- y[i,(k+1)] - delta[i,(k+1)]
z[i,k]<- inprod2(Omega[i,k,1:(na[i]-1)], ydiff[i,1:(na[i]-1)])
}
resdev[i]<- inprod2(ydiff[i,1:(na[i]-1)], z[i,1:(na[i]-1)])
}
for(i in 1:(ns2+ns3)){ # LOOP THROUGH ALL trials
w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
delta[i,1] <- 0 # treatment effect is zero for control arm
for (k in 2:na[i]) { # LOOP THROUGH ARMS
var[i,k] <- pow(se[i,k],2) # calculate variances
prec[i,k] <- 1/var[i,k] # set precisions
}
for (k in 2:na[i]) { # LOOP THROUGH ARMS
# trial-specific SMD distributions
delta[i,k] ~ dnorm(md[i,k],taud[i,k])
# mean of random effects distributions, with multi-arm trial correction
md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]
# precision of random effects distributions (with multi-arm trial correction)
taud[i,k] <- tau *2*(k-1)/k
# adjustment, multi-arm randomised clinical trialss
w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])
# cumulative adjustment for multi-arm trials
sw[i,k] <- sum(w[i,1:k-1])/(k-1)
}
}
totresdev <- sum(resdev[]) #Total Residual Deviance
d[1]<-0 # treatment effect is zero for reference treatment
# vague priors for treatment effects
for (k in 2:nt){ d[k] ~ dnorm(0,.0001) }
sd ~ dunif(0,5) # vague prior for between-trial SD
tau <- pow(sd,-2) # between-trial precision = (1/between-trial variance)
# ranking on relative scale
for (k in 1:nt) {
rk[k] <- nt+1-rank(d[],k) # assumes higher HRQoL is "good"
# rk[k] <- rank(d[],k) # assumes higher outcome is "bad"
best[k] <- equals(rk[k],1) #calculate probability that treat k is best
for (h in 1:nt){ prob[h,k] <- equals(rk[k],h) } # calculates probability that treat k is h-th best
}
} # *** PROGRAM ENDS
```

Continuous outcome (standardised mean difference) - inconsistency model (random-effects)

```
# Normal likelihood, identity link
# Trial-level data given as treatment differences
# Random effects model
model{ # *** PROGRAM STARTS
for(i in 1:ns2) { # LOOP THROUGH 2-ARM trials
y[i,2] ~ dnorm(delta[i,2],prec[i,2]) # normal likelihood for 2-arm trials
#Deviance contribution for trial i
resdev[i] <- (y[i,2]-delta[i,2])*(y[i,2]-delta[i,2])*prec[i,2]
}
for(i in (ns2+1):(ns2+ns3)) { # LOOP THROUGH THREE-ARM trials
for (k in 1:(na[i]-1)) { # set variance-covariance matrix
for (j in 1:(na[i]-1)) {
Sigma[i,j,k] <- V[i]*(1-equals(j,k)) + var[i,k+1]*equals(j,k)
}
}
Omega[i,1:(na[i]-1),1:(na[i]-1)] <- inverse(Sigma[i,,]) #Precision matrix
# multivariate normal likelihood for 3-arm trials
y[i,2:na[i]] ~ dmnorm(delta[i,2:na[i]],Omega[i,1:(na[i]-1),1:(na[i]-1)])
#Deviance contribution for trial i
for (k in 1:(na[i]-1)){ # multiply vector & matrix
ydiff[i,k]<- y[i,(k+1)] - delta[i,(k+1)]
z[i,k]<- inprod2(Omega[i,k,1:(na[i]-1)], ydiff[i,1:(na[i]-1)])
}
resdev[i]<- inprod2(ydiff[i,1:(na[i]-1)], z[i,1:(na[i]-1)])
}
for(i in 1:(ns2+ns3)){ # LOOP THROUGH ALL trials
for (k in 2:na[i]) { # LOOP THROUGH ARMS
var[i,k] <- pow(se[i,k],2) # calculate variances
prec[i,k] <- 1/var[i,k] # set precisions
}
for (k in 2:na[i]) { # LOOP THROUGH ARMS
# trial-specific SMD distributions
delta[i,k] ~ dnorm(md[i,k],taud[i,k])
# mean of random effects distributions
md[i,k] <- d[t[i,k]] - d[t[i,1]]
# precision of random effects distributions
taud[i,k] <- tau *2*(k-1)/k
}
}
totresdev <- sum(resdev[]) #Total Residual Deviance
d[1]<-0 # treatment effect is zero for reference treatment
# vague priors for treatment effects
for (k in 2:nt){ d[k] ~ dnorm(0,.0001) }
sd ~ dunif(0,5) # vague prior for between-trial SD
tau <- pow(sd,-2) # between-trial precision = (1/between-trial variance)
} # *** PROGRAM ENDS
```

Count outcome

Count outcome - fixed-effect model

```
# Poisson likelihood, log link
```

```
# Fixed effects model
model{ # *** PROGRAM STARTS
for(i in 1:ns){ # LOOP THROUGH trials
mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
for (k in 1:na[i]) { # LOOP THROUGH ARMS
r[i,k] ~ dpois(theta[i,k]) # Poisson likelihood
theta[i,k] <- lambda[i,k]*E[i,k] # failure rate * exposure
# model for linear predictor
log(lambda[i,k]) <- mu[i] + d[t[i,k]] - d[t[i,1]]
#Deviance contribution
dev[i,k] <- 2*((theta[i,k]-r[i,k]) + r[i,k]*log(r[i,k]/theta[i,k])) }
# summed residual deviance contribution for this trial
resdev[i] <- sum(dev[i,1:na[i]])
}
totresdev <- sum(resdev[]) #Total Residual Deviance
d[1]<-0 # treatment effect is zero reference treatment
# vague priors for treatment effects
for (k in 2:nt){ d[k] ~ dnorm(0,.0001) }

# pair wise RRs and LRRs for all possible pair-wise comparisons, if nt>2
for (c in 1:(nt-1)) {
for (k in (c+1):nt) {
rater[c,k] <- exp(d[k] - d[c])
lrater[c,k] <- (d[k]-d[c])
}
}
# ranking on relative scale
for (k in 1:nt) {
# rk[k] <- nt+1-rank(d[],k) # assumes events are "good"
rk[k] <- rank(d[],k) # assumes events are "bad"
best[k] <- equals(rk[k],1) #calculate probability that treat k is best
for (h in 1:nt){ prob[h,k] <- equals(rk[k],h) } # calculates probability that treat k is h-th best
}
} # *** PROGRAM ENDS
```

Count outcome - random-effects model

```
# Poisson likelihood, log link
# Random effects model
model{ # *** PROGRAM STARTS
for(i in 1:ns){ # LOOP THROUGH trials
w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
delta[i,1] <- 0 # treatment effect is zero for control arm
mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
for (k in 1:na[i]) { # LOOP THROUGH ARMS
r[i,k] ~ dpois(theta[i,k]) # Poisson likelihood
theta[i,k] <- lambda[i,k]*E[i,k] # failure rate * exposure
# model for linear predictor
log(lambda[i,k]) <- mu[i] + d[t[i,k]] - d[t[i,1]]
#Deviance contribution
dev[i,k] <- 2*((theta[i,k]-r[i,k]) + r[i,k]*log(r[i,k]/theta[i,k])) }
# summed residual deviance contribution for this trial
resdev[i] <- sum(dev[i,1:na[i]])
```

```
for (k in 2:na[i]) { # LOOP THROUGH ARMS
# trial-specific LOR distributions
delta[i,k] ~ dnorm(md[i,k],taud[i,k])
# mean of LOR distributions (with multi-arm trial correction)
md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]
# precision of LOR distributions (with multi-arm trial correction)
taud[i,k] <- tau *2*(k-1)/k
# adjustment for multi-arm randomised clinical trialss
w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])
# cumulative adjustment for multi-arm trials
sw[i,k] <- sum(w[i,1:k-1])/(k-1)
}
}
totresdev <- sum(resdev[]) # Total Residual Deviance
d[1]<-0 # treatment effect is zero for reference treatment
# vague priors for treatment effects
for (k in 2:nt){ d[k] ~ dnorm(0,.0001) }
sd ~ dunif(0,5) # vague prior for between-trial SD
tau <- pow(sd,-2) # between-trial precision = (1/between-trial variance)

# pair wise ORs and LORs for all possible pair-wise comparisons, if nt>2
for (c in 1:(nt-1)) {
for (k in (c+1):nt) {
or[c,k] <- exp(d[k] - d[c])
lor[c,k] <- (d[k]-d[c])
}
}
# ranking on relative scale
for (k in 1:nt) {
# rk[k] <- nt+1-rank(d[],k) # assumes events are “good”
rk[k] <- rank(d[],k) # assumes events are “bad”
best[k] <- equals(rk[k],1) #calculate probability that treat k is best
for (h in 1:nt){ prob[h,k] <- equals(rk[k],h) } # calculates probability that treat k is h-th best
}

} # *** PROGRAM ENDS
```

Count outcome - inconsistency model (random-effects)

```
# Poisson likelihood, log link
# Random effects model
model{ # *** PROGRAM STARTS
for(i in 1:ns){ # LOOP THROUGH trials
delta[i,1] <- 0 # treatment effect is zero for control arm
mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
for (k in 1:na[i]) { # LOOP THROUGH ARMS
r[i,k] ~ dpois(theta[i,k]) # Poisson likelihood
theta[i,k] <- lambda[i,k]*E[i,k] # failure rate * exposure
# model for linear predictor
log(lambda[i,k]) <- mu[i] + d[t[i,k]] - d[t[i,1]]
#Deviance contribution
dev[i,k] <- 2*((theta[i,k]-r[i,k]) + r[i,k]*log(r[i,k]/theta[i,k])) }
# summed residual deviance contribution for this trial
```

```
resdev[i] <- sum(dev[i,1:na[i]])
for (k in 2:na[i]) { # LOOP THROUGH ARMS
# trial-specific LOR distributions
delta[i,k] ~ dnorm(md[i,k],taud[i,k])
# mean of LRR distributions (without multi-arm trial correction)
md[i,k] <- d[t[i,k]] - d[t[i,1]]
# precision of LOR distributions (without multi-arm trial correction)
taud[i,k] <- tau *2*(k-1)/k
}
}
totresdev <- sum(resdev[]) # Total Residual Deviance
d[1]<-0 # treatment effect is zero for reference treatment
# vague priors for treatment effects
for (k in 2:nt){ d[k] ~ dnorm(0,.0001) }
sd ~ dunif(0,5) # vague prior for between-trial SD
tau <- pow(sd,-2) # between-trial precision = (1/between-trial variance)
} # *** PROGRAM ENDS
```

Appendix 3. Raw data

Legend

Binary outcomes

ns= number of studies; nt=number of treatments; t[,1] indicates control and t[,2] indicates intervention. In a three-arm trial, t[,3] indicates the second intervention. r[,1] indicates the number with events in the control group; n[,1] indicates the total number of people in the control group. r[,2], n[,2], r[,3], and n[,3] indicate the corresponding numbers for intervention and second intervention. In two-arm trials, r[,3] and n[,3] will be entered as 'NA' to indicate empty cells. na[] indicates the number of arms in the trial. Study indicates the study name and is for reference only.

Continuous outcomes

ns= number of studies; nt=number of treatments; t[,1] indicates control and t[,2] indicates intervention. In a three-arm trial, t[,3] indicates the second intervention. y[,1] indicates the mean in the control group; se[,1] indicates the standard error in the control group. y[,2], se[,2], y[,3], and se[,3] indicate the corresponding numbers for intervention and second intervention. In two-arm trials, y[,3] and se[,3] will be entered as 'NA' to indicate empty cells. na[] indicates the number of arms in the trial. Study indicates the study name and is for reference only.

Count outcomes

ns= number of studies; nt=number of treatments; t[,1] indicates control and t[,2] indicates intervention. In a three-arm trial, t[,3] indicates the second intervention. r[,1] indicates the number of events in the control group; E[,1] indicates the total number of people in the control group. r[,2], E[,2], r[,3], and E[,3] indicate the corresponding numbers for intervention and second intervention. In two-arm trials, r[,3] and E[,3] will be entered as 'NA' to indicate empty cells. na[] indicates the number of arms in the trial. Study indicates the study name and is for reference only.

Cardiopulmonary interventions

#Blood_transfusion_red blood cell; treatment codes: 1 = Control; 2 = ANH; 3 = ANH_Hypotension; 4 = ANH_Lowcentral venous pressure; 5 = Lowcentral venous pressure

list(nt=5,ns=6)

y[,1]	se[,1]	y[,2]	se[,2]	y[,3]	se[,3]	t[,1]	t[,2]	t[,3]	na[]	#study
1.6625	0.2	0.4175	0.16	0	0.01	1	2	3	3	#Yao 2006
0.8775	0.05	1.145	0.12	NA	NA	1	4	NA	2	#Guo 2013
2.75	0.4	1.3	0.075	NA	NA	1	5	NA	2	#El-Kharboutly 2004
3.215	0.58	1.3125	0.12	NA	NA	1	5	NA	2	#Wang 2006
0.44	0.37	0.7	0.35	NA	NA	4	5	NA	2	#Jarnagin 2008
0	0.47	0	0.47	NA	NA	4	5	NA	2	#Matot 2002

END

#Blood_loss; treatment codes: 1 = Control; 2 = ANH; 3 = ANH_Hypotension; 4 = ANH_Lowcentral venous pressure; 5 = Hypoventilation; 6 = Lowcentral venous pressure

list(nt=6,ns=9)

y[,1]	se[,1]	y[,2]	se[,2]	y[,3]	se[,3]	t[,1]	t[,2]	t[,3]	na[]	#study
0.651	0.01	0.654	0.05	0.404	0.06	1	2	3	3	#Yao 2006
0.711	0.02	0.735	0.02	NA	NA	1	4	NA	2	#Guo 2013
0.63	0.41	0.63	0.4	NA	NA	1	5	NA	2	#Hasegawa 2002
0.783	0.08	0.589	0.07	NA	NA	1	6	NA	2	#Choi 2007
1.021	0.07	0.49	0.06	NA	NA	1	6	NA	2	#El-Kharboutly 2004
0.584	0.1	0.499	0.1	NA	NA	1	6	NA	2	#Kato 2008
2.329	0.51	0.904	0.04	NA	NA	1	6	NA	2	#Wang 2006
0.8	0.09	0.7	0.09	NA	NA	4	6	NA	2	#Jarnagin 2008
0.75	0.41	0.89	0.41	NA	NA	4	6	NA	2	#Matot 2002

(*Continued*)

END										
Methods of parenchymal transection										
#Adverse_events_proportion; treatment codes: 1 = ClampCrush; 2 = cavitron ultrasonic surgical aspirator; 3 = Hydrojet; 4 = RFDS; 5 = SharpTransection; 6 = Stapler										
list(nt=6,ns=8)										
r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	t[,1]	t[,2]	t[,3]	na[]	#study
15	20	7	20	10	20	1	2	4	3	#Doklestic 2012
17	25	25	25	NA	NA	1	2	NA	2	#Koo 2005
14	66	20	66	NA	NA	1	2	NA	2	#Takayama 2001
7	40	9	40	NA	NA	1	4	NA	2	#Arita 2005
17	50	18	50	NA	NA	1	4	NA	2	#Muratore 2014
16	41	17	41	NA	NA	1	5	NA	2	#Smyrniotis 2005
30	65	31	65	NA	NA	1	6	NA	2	#Rahbari 2014
8	30	3	31	NA	NA	2	3	NA	2	#Rau 2001
END										
#Adverse_events_number; treatment codes: 1 = ClampCrush; 2 = Cavitron ultrasonic surgical aspirator; 3 = Hydrojet; 4 = RFDS; 5 = SharpTransection; 6 = Stapler										
list(nt=6,ns=7)										
r[,1]	E[,1]	r[,2]	E[,2]	r[,3]	E[,3]	t[,1]	t[,2]	t[,3]	na[]	#study
16	66	25	66	NA	NA	1	2	NA	2	#Takayama 2001
7	40	9	40	NA	NA	1	4	NA	2	#Arita 2005
11	60	15	60	NA	NA	1	4	NA	2	#Ikeda 2009
2	26	12	24	NA	NA	1	4	NA	2	#Lupo 2007
16	41	18	41	NA	NA	1	5	NA	2	#Smyrniotis 2005

(*Continued*)

8	25	7	25	9	25	2	3	4	3	#Lesurtel 2005
19	50	22	50	NA	NA	2	6	NA	2	#Savlid 2013
END										
#Blood_transfusion_proportion; treatment codes: 1 = ClampCrush; 2 = Cavitron ultrasonic surgical aspirator; 3 = Hydrojet; 4 = RFDS; 5 = SharpTransection										
list(nt=5,ns=8)										
r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	t[,1]	t[,2]	t[,3]	na[]	#study
2	20	3	20	4	20	1	2	4	3	#Doklestic 2012
1	66	1	66	NA	NA	1	2	NA	2	#Takayama 2001
0	40	2	40	NA	NA	1	4	NA	2	#Arita 2005
2	60	2	60	NA	NA	1	4	NA	2	#Ikeda 2009
13	26	8	24	NA	NA	1	4	NA	2	#Lupo 2007
13	50	16	50	NA	NA	1	4	NA	2	#Muratore 2014
15	41	13	41	NA	NA	1	5	NA	2	#Smyrniotis 2005
8	25	8	25	5	25	2	3	4	3	#Lesurtel 2005
END										
Methods of vascular occlusion										
#Serious_adverse_events_proportion; treatment codes: 1 = Control; 2 = ConHVE; 3 = ConPTC; 4 = ConSelectiveHVE; 5 = ConSelectivePTC; 6 = IntPTC										
list(nt=6,ns=8)										
r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	t[,1]	t[,2]	t[,3]	na[]	#study
4	63	2	63	NA	NA	1	6	NA	2	#Capussotti 2006
9	63	14	63	NA	NA	1	6	NA	2	#Lee 2012
2	25	1	25	NA	NA	1	6	NA	2	#Park 2012

(*Continued*)

3	60	2	58	NA	NA	2	3	NA	2	#Chen 2006
2.5	81	0.5	81	NA	NA	3	4	NA	2	#Si-Yuan 2014
22	60	12	60	NA	NA	3	5	NA	2	#Ni 2013
4	18	2	17	NA	NA	3	6	NA	2	#Capussotti 2003
1	40	4	40	NA	NA	5	6	NA	2	#Liang 2009
END										
#Adverse_events_proportion; treatment codes: 1 = Control; 2 = ConHVE; 3 = ConPTC; 4 = ConSelectiveHVE; 5 = ConSelectivePTC; 6 = IntPTC; 7 = IntSelectivePTC										
list(nt=7,ns=12)										
r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	t[,1]	t[,2]	t[,3]	na[]	#study
16	63	21	63	NA	NA	1	6	NA	2	#Capussotti 2006
15	63	26	63	NA	NA	1	6	NA	2	#Lee 2012
15	50	13	50	NA	NA	1	6	NA	2	#Man 1997
9	20	5	20	NA	NA	1	6	NA	2	#Man 2003
19	60	17	58	NA	NA	2	3	NA	2	#Chen 2006
17	80	9	80	NA	NA	3	4	NA	2	#Si-Yuan 2014
24	60	13	60	NA	NA	3	5	NA	2	#Ni 2013
13	42	11	44	NA	NA	3	6	NA	2	#Belghiti 1999
4	18	2	17	NA	NA	3	6	NA	2	#Capussotti 2003
9	40	8	40	NA	NA	5	6	NA	2	#Liang 2009
15	39	12	41	NA	NA	6	7	NA	2	#Figueras 2005
8	28	10	30	NA	NA	6	7	NA	2	#Wu 2002
END										

(*Continued*)

#Blood_transfusion_proportion; treatment codes: 1 = Control; 2 = ConHVE; 3 = ConPTC; 4 = ConSelectiveHVE; 5 = ConSelectivePTC; 6 = IntPTC; 7 = IntSelectivePTC

list(nt=7,ns=13)

r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	t[,1]	t[,2]	t[,3]	na[]	#study
6	15	1	19	NA	NA	1	3	NA	2	#Chouker 2004
1	63	8	63	NA	NA	1	6	NA	2	#Capussotti 2006
9	63	14	63	NA	NA	1	6	NA	2	#Lee 2012
29	50	18	50	NA	NA	1	6	NA	2	#Man 1997
19	20	12	20	NA	NA	1	6	NA	2	#Man 2003
8	60	27	58	NA	NA	2	3	NA	2	#Chen 2006
22	80	13	80	NA	NA	3	4	NA	2	#Si-Yuan 2014
4	60	6	60	NA	NA	3	5	NA	2	#Ni 2013
12	42	14	44	NA	NA	3	6	NA	2	#Belghiti 1999
5	18	5	17	NA	NA	3	6	NA	2	#Capussotti 2003
15	40	14	40	NA	NA	5	6	NA	2	#Liang 2009
4	39	6	41	NA	NA	6	7	NA	2	#Figueras 2005
12	28	5	30	NA	NA	6	7	NA	2	#Wu 2002

END

#Blood_transfusion_red blood cell; treatment codes: 1 = Control; 2 = ConHVE; 3 = ConPTC; 4 = ConSelectiveHVE; 5 = ConSelectivePTC; 6 = IntPTC; 7 = IntSelectivePTC

list(nt=7,ns=10)

y[,1]	se[,1]	y[,2]	se[,2]	y[,3]	se[,3]	t[,1]	t[,2]	t[,3]	na[]	#study
1.9	1.02	1.3	0.85	NA	NA	1	3	NA	2	#Clavien 1996
1.5	0.45	0	0.45	NA	NA	1	6	NA	2	#Man 1997
2.5	0.64	2.9	0.8	NA	NA	2	3	NA	2	#Belghiti 1996

(*Continued*)

2.2	0.42	1	0.42	NA	NA	3	4	NA	2	#Si-Yuan 2014
1.4	0.05	1.2	0.03	NA	NA	3	5	NA	2	#Ni 2013
3	0.4	2.3	0.39	NA	NA	3	6	NA	2	#Belghiti 1999
0.5	0.02	0.5	0.27	NA	NA	3	6	NA	2	#Capussotti 2003
1.3675	0.09	1.4825	0.15	NA	NA	5	6	NA	2	#Liang 2009
0.36	0.16	0.34	0.14	NA	NA	6	7	NA	2	#Figueras 2005
2.5425	0.26	2.24	0.4	NA	NA	6	7	NA	2	#Wu 2002
END										
#Blood_loss; treatment codes: 1 = Control; 2 = ConHVE; 3 = ConPTC; 4 = ConSelectiveHVE; 5 = ConSelectivePTC; 6 = IntPTC; 7 = IntSelectivePTC										
list(nt=7,ns=16)										
y[,1]	se[,1]	y[,2]	se[,2]	y[,3]	se[,3]	t[,1]	t[,2]	t[,3]	na[]	#study
2.17	0.22	1.38	0.16	NA	NA	1	3	NA	2	#Chouker 2004
0.32	0.05	0.328	0.02	NA	NA	1	3	NA	2	#Dayangac 2010
0.671	0.32	0.65	0.16	NA	NA	1	3	NA	2	#Pietsch 2010
0.204	0.02	0.184	0.03	NA	NA	1	6	NA	2	#Capussotti 2006
0.489	0.06	0.488	0.07	NA	NA	1	6	NA	2	#Lee 2012
1.99	0.18	1.28	0.18	NA	NA	1	6	NA	2	#Man 1997
0.324	0.03	0.486	0.06	NA	NA	1	6	NA	2	#Park 2012
1.195	0.21	0.989	0.26	NA	NA	2	3	NA	2	#Belghiti 1996
0.42	0.03	0.77	0.04	NA	NA	2	3	NA	2	#Chen 2006
0.777	0.09	0.529	0.09	NA	NA	3	4	NA	2	#Si-Yuan 2014
0.2	0.1	0.3	0.1	NA	NA	3	5	NA	2	#Ni 2013
1.18	0.12	1.29	0.14	NA	NA	3	6	NA	2	#Belghiti 1999

(*Continued*)

0.733	0.12	0.732	0.15	NA	NA	3	6	NA	2	#Capussotti 2003
0.649	0.04	0.57	0.05	NA	NA	5	6	NA	2	#Liang 2009
0.671	0.09	0.735	0.06	NA	NA	6	7	NA	2	#Figueras 2005
1.685	0.17	1.159	0.22	NA	NA	6	7	NA	2	#Wu 2002
END										

Appendix 4. Technical details of network meta-analysis

The posterior probabilities (effect estimates or values) of the treatment contrast (i.e., log odds ratio or mean difference) may vary depending upon the priors and initial values to start the simulations.

We used non-informative priors for all distributions. For distributions of effect estimates for different studies and different treatments, normal distribution with mean = 0 and variance = 10,000 were used. For between-study standard deviation in random-effects models, a uniform distribution with limits of 0 and 5 was used for all analyses. The only exception was adverse events proportion in the comparison of parenchymal transection methods, where we chose the random-effects model based on the fit, but the posterior distribution was determined by the prior distribution. For this comparison, the distribution for between-study standard deviation was changed to a uniform distribution with limits of 0 and 2.

In order to control the random error due to the choice of initial values, we performed the network analysis for three different initial values (priors) as per the guidance from the National Institute for Health and Care Excellence (NICE) Decision Support Unit (DSU) documents (Dias 2013a). If the results from three different initial values ('chains') are similar (convergence), then the results are reliable. It is important to discard the results of the initial simulations as they can be significantly affected by the choice of the initial values and only include the results of the simulations obtained after the convergence. The discarding of the initial simulations is called 'burn in'. We ran the models for all outcomes for 30,000 simulations for 'burn in' for three different chains (a set of initial values). We ran the models for another 100,000 simulations to obtain the effect estimates. We obtained the effect estimates from the results of all the three chains (different initial values). We ensured that the results in the three different chains were similar in order to control for random error due to the choice of initial values. This was done in addition to the visual inspection of convergence obtained after simulations in the burn in. The mean effect estimate and 95% credible intervals were the median and 2.5% percentile and 97.5% credible intervals.

We ran three different models for each outcome. Fixed-effect model assumes that the treatment effect is the same across studies. The random-effects consistency model assumes that the treatment effect is distributed normally across the studies but assumes that the transitivity assumption is satisfied (i.e., the population studied, the definition of outcomes, and the methods used were similar across studies and that there is consistency between the direct comparison and indirect comparison). A random-effects inconsistency model does not assume transitivity assumption. If the inconsistency model resulted in a better model fit than the consistency model, the results of the network meta-analysis can be unreliable and so should be interpreted with extreme caution. If there was evidence of inconsistency, we planned to identify areas in the network where substantial inconsistency might be present in terms of clinical and methodological diversities between trials and, when appropriate, limit network meta-analysis to a more compatible subset of trials.

The choice of the model between fixed-effect model and random-effects model was based on the model fit as per the guidelines of the NICE TSU (Dias 2013a). The model fit was assessed by deviance residuals and Deviance Information Criteria (DIC) according to NICE TSU guidelines (Dias 2013a). A difference of three or five in the DIC is not generally considered important (Dias 2012b). We used the simpler model, that is, fixed-effect model was used if the DIC were similar between the fixed-effect model and random-effects model. We used the random-effects model if it resulted in a better model fit as indicated by a DIC lower than that of fixed-effect model by at least three.

We have calculated the effect estimates of the treatment and the 95% credible intervals using the formulae for calculating the effect estimates in indirect comparisons (Bucher 1997):

$\ln(OR_{AC}) = \ln(OR_{AB}) - \ln(OR_{CB})$ and

$Var(\ln OR_{AC}) = Var(\ln OR_{AB}) + Var(\ln OR_{CB})$

where ln indicates natural logarithm; OR indicates odds ratio; Var indicates variance; and A, B, and C are three different treatments.

Appendix 5. Simulated data

#Simulation used for analysis; treatments 1,2,3,4; ln effect estimates: 2 vs 1 = 0, 3 vs 1 = 0.1, 4 vs 1 =- 0.15, 3 vs 2 = 0.1, 4 vs 2 = -0.15; 4 vs 3 = 0.25)

Methods of simulating data: We have simulated the data using Excel. For this purpose, we have fixed the ln (natural logarithm) odds of the comparisons at the predetermined values. We have then added or subtracted a random value between -0.25 and 0.25 from the resulting odds ratio to determine the odds ratio of the individual study. We simulated the odds ratio for 15 studies. We then performed the network meta-analysis using the codes provided in Appendix 2. We also performed a meta-analysis of the simulated data using frequentist meta-analysis in RevMan; this showed the effect estimates obtained by the frquentist estimates included the predetermined effect estimate and was close but not the same to the predetermined effect estimate

list(nt=4,ns=15)										
r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	t[,1]	t[,2]	t[,3]	na[]	#study
22	23	22	23	NA	NA	1	2	NA	2	#1
12	30	20	60	NA	NA	1	2	NA	2	#2
4	20	7	40	NA	NA	1	2	NA	2	#3
12	22	13	22	NA	NA	1	2	NA	2	#4
20	24	19	24	NA	NA	1	3	NA	2	#5
24	26	24	26	NA	NA	1	3	NA	2	#6
16	20	16	20	NA	NA	1	4	NA	2	#7
9	22	9	22	NA	NA	1	4	NA	2	#8
5	26	6	26	NA	NA	1	4	NA	2	#9
27	28	27	28	NA	NA	1	4	NA	2	#10
9	21	9	21	NA	NA	1	4	NA	2	#11
4	20	4	20	NA	NA	2	3	NA	2	#12
18	22	18	22	NA	NA	2	4	NA	2	#13
5	27	11	54	NA	NA	3	4	NA	2	#14
5	27	13	54	NA	NA	3	4	NA	2	#15
END										

Appendix 6. Results of simulation

Frequentist direct[1]	Network (fixed-effect model)[2]	Network (random-effects model)[2]
0.89 [0.48, 1.66]	0.90 [0.51,1.58]	0.90 [0.49,1.67]
0.83 [0.26, 2.72]	0.83 [0.40,1.69]	0.84 [0.39,1.81]
1.05 [0.56, 1.99]	1.04 [0.60,1.81]	1.05 [0.58,1.92]
1.00 [0.21, 4.71]	0.93 [0.41,2.08]	0.93 [0.39,2.20]
1.00 [0.22, 4.63]	1.16 [0.57,2.36]	1.16 [0.53,2.54]
1.26 [0.55, 2.86]	1.25 [0.65,2.48]	1.25 [0.60,2.56]

Footnotes:
[1]Mean estimate and 95% confidence intervals
[2]Mean estimate and 95% credible intervals

Appendix 7. Sample size calculation

The overall mortality in the control groups (conventional approach in the comparison 'anterior approach versus conventional approach'; no autologous blood transfusion in the comparison autologous blood transfusion in the comparison 'autologous blood transfusion versus control'; no active intervention or control group in the 'cardiopulmonary interventions'; 'clamp-crush method' for 'parenchymal transection methods'; no active intervention or control group in the 'methods of dealing with raw surface'; no vascular occlusion in the 'methods of vascular occlusion'; and no active intervention or control group in the 'pharmacological interventions'), in which mortality was reported, was 1.8% (21/1196). Based on this control group proportion, a relative risk reduction of 20% in the experimental group, type I error of 5%, and type II error of 20%, the required information size for the outcome measure of perioperative mortality was 38,614 participants. This is the sample size required in a meta-analysis if there was no heterogeneity. In the presence of I^2 of 25%, the required sample size is 38,614/(1-0.25) = 51,485; In the presence of I^2 of 50%, the required sample size is 38,614/(1-0.5) = 77,228.
Network analyses may be more prone to the risk of random errors than direct comparisons (Del Re 2013). Accordingly, a greater sample size is required in indirect comparisons than direct comparisons (Thorlund 2012). The power and precision in indirect comparisons depends upon various factors such as the number of participants included under each comparison and the heterogeneity between the trials (Thorlund 2012). If there were no heterogeneity across the trials, the sample size in indirect comparisons would be equivalent to the sample size in direct comparisons. The effective indirect sample size can be calculated using the number of participants included in each direct comparison (Thorlund 2012). For example, a sample size of 2500 participants in the direct comparison A versus C (n_{AC}) and a sample size of 7500 participants in the direct comparison B versus C (n_{BC}) results in an effective indirect sample size of 1876 participants. However, in the presence of heterogeneity within the comparisons, the sample size required is higher. In the above scenario, for an I^2 statistic for each of the comparisons A versus C (I_{AC}^2) and B versus C (I_{BC}^2) of 25%, the effective indirect sample size is 1407 participants. For an I^2 statistic for each of the comparisons A versus C and B versus C of 50%, the effective indirect sample size is 938 participants (Thorlund 2012). We planned to calculate the effective indirect sample size using the following generic formula (Thorlund 2012):
$((n_{AC} \times (1 - I_{AC}^2)) \times (n_{BC} \times (1-I_{BC}^2))/((n_{AC} \times (1 - I_{AC}^2)) + (n_{BC} \times (1-I_{BC}^2))$.
However, we did not perform this as the number of participants included in this network analysis is less than that needed in a direct comparison. In addition, there is currently no method to calculate the effective indirect sample size for a network analysis involving more than three treatment groups.
Sample size calculations for serious adverse events and blood transfusion (proportion) for a relative risk reduction of 20% in the experimental group, type I error of 5%, and type II error of 20% are shown below.
Control group proportion for serious adverse events = 16.7% (151/905)

Required information size for serious adverse events = 3592
Required information size for serious adverse events with I^2 of 25% = 3592/(1-0.25) = 4789
Required information size for serious adverse events with I^2 of 50% = 3592/(1-0.5) = 7184
Control group proportion for blood transfusion = 21.8% (327/1500)
Required information size for blood transfusion = 2602
Required information size for blood transfusion with I^2 of 25% = 3592/(1-0.25) = 3469
Required information size for blood transfusion with I^2 of 50% = 3592/(1-0.5) = 5204

Appendix 8. WinBUGS code for subgroup analysis

We have only shown the code for the random-effects model for a binary outcome. The differences in the code are underlined. We planned to make similar changes for other outcomes.

```
# Binomial likelihood, logit link, subgroup
# Random effects model for multi-arm trials
model{ # *** PROGRAM STARTS
for(i in 1:ns){ # LOOP THROUGH trials
w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
delta[i,1] <- 0 # treatment effect is zero for control arm
mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
for (k in 1:na[i]) { # LOOP THROUGH ARMS
r[i,k] ~ dbin(p[i,k],n[i,k]) # binomial likelihood
# model for linear predictor, covariate effect relative to treat in arm 1
logit(p[i,k]) <- mu[i] + delta[i,k] + (beta[t[i,k]]-beta[t[i,1]]) * x[i]
rhat[i,k] <- p[i,k] * n[i,k] # expected value of the numerators
#Deviance contribution
dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))
+ (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k]))) }
# summed residual deviance contribution for this trial
resdev[i] <- sum(dev[i,1:na[i]])
for (k in 2:na[i]) { # LOOP THROUGH ARMS
# trial-specific LOR distributions
delta[i,k] ~ dnorm(md[i,k],taud[i,k])
# mean of LOR distributions (with multi-arm trial correction)
md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]
# precision of LOR distributions (with multi-arm trial correction)
taud[i,k] <- tau *2*(k-1)/k
# adjustment for multi-arm randomised clinical trialss
w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])
# cumulative adjustment for multi-arm trials
sw[i,k] <- sum(w[i,1:k-1])/(k-1)
}
}
totresdev <- sum(resdev[]) # Total Residual Deviance
d[1]<-0 # treatment effect is zero for reference treatment
beta[1] <- 0 # covariate effect is zero for reference treatment
for (k in 2:nt){ # LOOP THROUGH TREATMENTS
d[k] ~ dnorm(0,.0001) # vague priors for treatment effects
beta[k] <- B # common covariate effect
}
B ~ dnorm(0,.0001) # vague prior for covariate effect
sd ~ dunif(0,5) # vague prior for between-trial SD
tau <- pow(sd,-2) # between-trial precision = (1/between-trial variance)
```

```
# treatment effect when covariate = z[j]
for (k in 1:nt){ # LOOP THROUGH TREATMENTS
for (j in 1:nz) { dz[j,k] <- d[k] + (beta[k]-beta[1])*z[j] }
}
# *** PROGRAM ENDS
```

Appendix 9. Summary of findings (secondary outcomes): blood transfusion requirements

Methods to decrease blood loss during liver resection: a network meta-analysis: blood transfusion requirements

Patient or population: people undergoing liver resection
Settings: secondary or tertiary setting
Intervention and control: various treatments
Follow-up: perioperative period

Outcomes	Anterior approach versus conventional approach	Autologous blood donation versus control	Cardiopulmonary interventions	Methods of parenchymal transection	Methods of dealing with raw surface	Methods of vascular occlusion	Pharmacological interventions
Treatments The first treatment listed is the control. The remaining are interventions	1. Conventional approach 2. Anterior approach	1. Control 2. Autologous blood donation	1. Control 2. Acute normovolemic haemodilution plus low central venous pressure 3. Hypoventilation 4. Low central venous pressure	1. Clamp-crush method 2. Cavitron ultrasonic surgical aspirator 3. Hydrojet 4. Radiofrequency dissecting sealer 5. Sharp transection method 6. Stapler	1. Control 2. Argon beam 3. Collagen 4. Cyanoacrylate 5. Fibrin sealant 6. Fibrin sealant plus collagen 7. Oxidised cellulose 8. Plasmajet	1. Control 2. Continuous hepatic vascular exclusion 3. Continuous portal triad clamping 4. Continuous selective hepatic vascular exclusion 5. Continuous selective portal triad clamping 6. Intermittent portal triad clamping	1. Control 2. Antithrombin III 3. Recombinant factor VIIa 4. Tranexamic acid

(*Continued*)

					7. Intermittent selective portal triad clamping		
Blood transfusion (proportion)	There was no evidence of differences in blood transfusion (proportion) between the 2 groups (quality of evidence = very low)[1,2,3,4].	The blood transfusion (proportion) was lower in autologous blood donation than control. Proportion requiring blood transfusion in control group: 619 per 1000 Proportion requiring blood transfusion in autologous blood donation group: 111 per 1000 (25 to 409) Relative effect: OR 0.18, 95% CrI 0.04 to 0.66 42 participants; 1. Quality of evidence = low [1,2].	The blood transfusion (proportion) was higher in low central venous pressure than acute normovolemic haemodilution plus low central venous pressure. Proportion requiring blood transfusion in acute normovolemic haemodilution plus low central venous pressure: 118 per 1000 Proportion requiring blood transfusion in low central venous pressure group: 376 per 1000 (184 to 820) Relative effect: OR 3.19, 95% CrI 1.56 to 6.95 208 participants; 2. Quality of evidence = low [1,2]. There was no evidence of	*There was no evidence of differences in blood transfusion (proportion) for any of the comparisons (quality of evidence = very low)[1,2,3,4].	There was no evidence of differences in blood transfusion (proportion) for any of the comparisons (quality of evidence = very low)[1,2,3,4].	* The blood transfusion (proportion) was lower in continuous portal triad clamping than control. Proportion requiring blood transfusion in control group: 300 per 1000 Proportion requiring blood transfusion in continuous portal triad clamping: 18 per 1000 (0 to 148) Relative effect: OR 0.06, 95% CrI 0.00 to 0.49 34 participants; 1. Quality of evidence = low [1,2]. The blood transfusion (proportion) was higher in continuous portal triad clamping than continuous hepatic vascular exclu-	The blood transfusion (proportion) was lower in aprotinin than control. Proportion requiring blood transfusion in control group: 291 per 1000 Proportion requiring blood transfusion in aprotinin group: 90 per 1000 (32 to 227) Relative effect: OR 0.31, 95% CrI 0.11 to 0.78. 97 participants; 1. Quality of evidence = low [1,2]. The blood transfusion (proportion) was lower in tranexamic acid than control Proportion requiring blood transfusion in tranexamic

(*Continued*)

			differences in other comparisons (quality of evidence = very low)[1,2,3].			sion Proportion requiring blood transfusion in continuous hepatic vascular exclusion: 133 per 1000 Proportion requiring blood transfusion in continuous portal triad clamping group: 785 per 1000 (326 to 2072) Relative effect: OR 5.90, 95% CrI 2.45 to 15.58 118 participants; 1. Quality of evidence = low[1,2]. There was no evidence of differences in other comparisons (quality of evidence = very low)[1,2,3,4].	acid group: 3 per 1000 (0 to 38) Relative effect: OR 0.01, 95% CrI 0.00 to 0.13. 214 participants; 1. Quality of evidence = low[1,2]. There was no evidence of differences in other comparisons (quality of evidence = very low)[1,2,3].
Blood transfusion (red blood cells)	None of the trials reported this outcome.	There was no evidence of differences in blood transfusion quantity (red blood cells) between the groups (quality of evidence = very low)[1,2,3].	* The blood transfusion quantity (red blood cells) was lower in acute normovolemic haemodilution. The mean blood transfusion quantity (red blood cells)	The blood transfusion quantity (red blood cells) was lower in hydrojet than cavitron ultrasonic surgical aspirator. The mean blood transfusion quantity (red blood	The blood transfusion quantity (red blood cells) was lower in fibrin sealant than control. The mean blood transfusion quantity (red blood cells) in the	* The blood transfusion quantity (red blood cells) was lower in continuous portal triad clamping than control. The mean blood transfusion quantity (red blood	The blood transfusion quantity (red blood cells) was lower in aprotinin than control. The mean blood transfusion quantity (red blood cells)

(*Continued*)

			in the control group was 1. 38 units. The mean blood transfusion quantity (red blood cells) in the acute normovolemic haemodilution was 1. 25 lower (1.74 to 0.75 lower) . 20 participants; 1. Quality of evidence: very low)[1,2,3]. The mean blood transfusion quantity (red blood cells) in the acute normovolemic haemodilution plus hypotension was 1.66 lower (2.06 to 1.32 lower). 20 participants; 1. Quality of evidence: low[1,2]. The mean blood transfusion quantity (red blood cells) in the acute normovolemic haemodilution plus low central venous	cell) in the cavitron ultrasonic surgical aspirator group was 2. 48 units. The mean blood transfusion quantity (red blood cells) in the hydrojet group was 0. 98 lower (1.90 to 0.06 lower) . 61 participants; 1. Quality of evidence = very low[1,2,3]. There was no evidence of difference in blood transfusion quantity (red blood cells) in the remaining comparisons (quality of evidence = very low)[1,2,3].	control group was 3.5 units. The mean blood transfusion quantity (red blood cells) in the fibrin sealant group was 0. 53 lower (1.00 to 0.07 lower) . 122 participants; 2. Quality of evidence = very low[1,2,3]. The blood transfusion quantity (red blood cells) was higher in fibrin sealant than cyanoacrylate. The mean blood transfusion quantity (red blood cells) in the cyanoacrylate group was 2.13 units. The mean blood transfusion quantity (red blood cells) in the fibrin sealant group was 2. 20 higher (1.59 to 2.81 higher). 30 participants; 1.	cells) in the control group was 1.7 units. The mean blood transfusion quantity (red blood cells) in the intermittent portal triad clamping was 1.25 lower (2.39 to 0.10 lower). (network meta-analysis) 786 participants; 10. Quality of evidence = very low[1,2,3]. The blood transfusion quantity (red blood cells) was lower in intermittent portal triad clamping than control. The mean blood transfusion quantity (red blood cells) in the intermittent portal triad clamping was 1.50 lower (2.75 to 0.26 lower). 100 participants; 1. Quality of evidence = very	in the control group was 2. 10 units. The mean blood transfusion quantity (red blood cells) in the aprotinin group was 0. 94 lower (no information to calculate confidence intervals; P = 0. 015). 97 participants; 1. Quality of evidence = very low[a,b,c]. There was no evidence of difference in blood transfusion quantity (red blood cells) in the remaining comparisons (quality of evidence = very low)[1,2,3].

(*Continued*)

			pressure was 0.27 higher (0.01 to 0.52 higher). 30 participants; 1. Quality of evidence: very low[1,2,3]. There was no evidence of differences in other comparisons (quality of evidence = very low)[1,2,3].		Quality of evidence = low [1,2]. There was no evidence of difference in blood transfusion quantity (red blood cells) in the remaining comparisons (quality of evidence =very low)[1,2,3,4].	low[1,2,3]. The blood transfusion quantity (red blood cells) was lower in continuous selective hepatic vascular exclusion than continuous portal triad clamping. The mean blood transfusion quantity (red blood cells) in the continuous portal triad clamping group was 1.125 units. The mean blood transfusion quantity (red blood cells) in the continuous selective hepatic vascular exclusion was 1.20 lower (2.37 to 0.04 lower). 160 participants; 1. Quality of evidence = very low[1,2,3]. The blood transfusion quantity (red blood cells)	

(*Continued*)

						was lower in continuous selective portal triad clamping than continuous portal triad clamping. The mean blood transfusion quantity (red blood cells) in the continuous selective portal triad clamping was 0.20 lower (0.31 to 0.09 lower). 120 participants; 1. Quality of evidence = very low[1,2,3]. There was no evidence of difference in blood transfusion quantity (red blood cells) in the remaining comparisons (quality of evidence = very low)[1,2,3,4].	
Blood transfusion (platelets)	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.	There was no evidence of differences in blood transfusion quantity (platelets) between the groups (quality of evidence = very low)[1,2,3].

(*Continued*)

Blood transfusion (fresh frozen plasma)	None of the trials reported this outcome.	None of the trials reported this outcome.	The blood transfusion quantity (fresh frozen plasma) was lower in low central venous pressure than control The mean blood transfusion quantity (fresh frozen plasma) in the control group was 4.23 units. The mean blood transfusion quantity (red blood cells) in the low central venous pressure was 2.48 lower (3.58 to 1.37 lower). 50 participants; 1. Quality of evidence = low [1,2]. There was no evidence of differences in the other comparison (quality of evidence = very low) [1,2,3].	There was no evidence of differences in blood transfusion quantity (fresh frozen plasma) between the groups (quality of evidence = very low) [1,2,3].	The blood transfusion quantity (fresh frozen plasma) was lower in fibrin sealant than cyanoacrylate. The mean blood transfusion quantity (fresh frozen plasma) in the cyanoacrylate group was 0.8 units. The mean blood transfusion quantity (fresh frozen plasma) in the fibrin sealant group was 0.81 lower (1.04 to 0.62 lower). 30 participants; 1. Quality of evidence = very low [1,2,3]. The blood transfusion quantity (fresh frozen plasma) was higher in oxidised cellulose than fibrin sealant. The mean blood transfusion quantity (fresh frozen plasma)	None of the trials reported this outcome.	There was no evidence of differences in blood transfusion quantity (fresh frozen plasma) between the groups (quality of evidence = very low) [1,2,3].

(*Continued*)

					in the fibrin sealant group was 8.8 units. The mean blood transfusion quantity (fresh frozen plasma) in the oxidised cellulose group was 0.53 higher (0.36 to 0.71 higher). 80 participants; 2. Quality of evidence = very low[1,2,3]. There was no evidence of difference in blood transfusion quantity (fresh frozen plasma) in the remaining comparisons (quality of evidence = very low)[1,2,3].		
Blood transfusion (cryoprecipitate)	None of the trials reported this outcome.	None of the trials reported this outcome.	There was no evidence of differences in blood transfusion quantity (cryoprecipitate) between the groups (quality of evidence = very low)[1,2,3].	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.
Blood loss	There was no evidence of differences in blood loss between the groups (qual-	There was no evidence of differences in blood loss between the groups (qual-	* The blood loss was lower in acute normovolemic haemodilution plus hy-	There was no evidence of differences in blood loss between the groups (qual-	There was no evidence of differences in blood loss between the groups (qual-	There was no evidence of differences in blood loss between the groups (qual-	The blood loss was lower in tranexamic acid than control (difference in me-

(*Continued*)

	ity of evidence = very low)[1,2,3].	ity of evidence = very low)[1,2,3].	potension than control The mean blood loss in the control group was 0.71 litres. The mean blood loss in the acute normovolemic haemodilution plus hypotension was 0.25 lower (0.37 to 0.13 lower). 20 participants; 1. Quality of evidence = very low[1,2,3]. The mean blood loss in the low central venous pressure was 0.34 lower (0.46 to 0.22 lower). 237 participants; 4. Quality of evidence = very low[1,2,3]. The mean blood loss in the acute normovolemic haemodilution group was 0.65 litres. The blood loss in acute normovolemic haemodilution plus hy-	ity of evidence = very low)[1,2,3].	ity of evidence = very low)[1,2,3].	ity of evidence = very low)[1,2,3,4].	dian: -0.30 litres, P < 0.001; 214 participants; 1 study). The mean blood loss in the control group was 0.45 litres. The mean blood loss in the tranexamic acid was 0.30 lower (no information to calculate confidence intervals; P < 0.001). 214 participants; 1. Quality of evidence = low[1,2]. There was no evidence of difference in blood transfusion quantity (red blood cells) in the remaining comparisons (quality of evidence = very low)[1,2,3].

(*Continued*)

			potension was 0.25 lower (0.40 to 0.10 lower) 20 participants; 1. Quality of evidence = very low[1,2,3]. There was no evidence of differences in other comparisons (quality of evidence = very low)[1,2,3].				
Major blood loss (proportion)	There was no evidence of differences in major blood loss (proportion) between the 2 groups (quality of evidence = very low)[1,2,3,4].	There was no evidence of differences in major blood loss (proportion) between the 2 groups (quality of evidence = very low)[1,2,3].	There was no evidence of differences in major blood loss (proportion) between the groups (quality of evidence = very low)[1,2,3].	None of the trials reported this outcome.	None of the trials reported this outcome.	There was no evidence of differences in major blood loss (proportion) between the groups (quality of evidence = very low)[1,2,3].	None of the trials reported this outcome.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[1] Risk of bias was unclear or high in the trial[s] (downgraded by 1 point).
[2] Sample size was low (total number of participants fewer than 400 for continuous outcomes and fewer than 300 events in total in both groups for other outcomes) (downgraded by 1 point).
[3] Credible intervals overlapped no effect and clinically significant effect (20% relative risk reduction for binary outcomes;1 unit of transfusion quantity; 500 ml blood loss) (downgraded by 1 point)
[4] There was considerable or substantial heterogeneity in the pair-wise comparison or at least 1 of the comparisons in the network (downgrade by 2 points)
*Network meta-analysis was performed for these outcome because of the availability of direct and indirect comparisons in the network. The remaining outcomes were analysed by direct comparisons
CrI: credible intervals; **MD**: mean difference; **OR**: odds ratio.

Appendix 10. Summary of findings (secondary outcomes): operating time, hospital stay, and time needed to return to work

Methods to decrease blood loss during liver resection: a network meta-analysis: operating time, hospital stay, and time-to-return to work

Patient or population: people undergoing liver resection
Settings: secondary or tertiary setting
Intervention and control: various treatments
Follow-up: peri-operative period

Outcomes	Anterior approach versus conventional approach	Autologous blood donation versus control	Cardiopulmonary interventions	Methods of parenchymal transection	Methods of dealing with raw surface	Methods of vascular occlusion	Pharmacological interventions
Treatments The first treatment listed is the control. The remaining are interventions	1. Conventional approach 2. Anterior approach	1. Control 2. Autologous blood donation	1. Control 2. Acute normovolemic haemodilution plus low central venous pressure 3. Hypoventilation 4. Low central venous pressure	1. Clamp-crush method 2. Cavitron ultrasonic surgical aspirator 3. Hydrojet 4. Radiofrequency dissecting sealer 5. Sharp transection method 6. Stapler	1. Control 2. Argon beam 3. Collagen 4. Cyanoacrylate 5. Fibrin sealant 6. Fibrin sealant plus collagen 7. Oxidised cellulose 8. Plasmajet	1. Control 2. Continuous hepatic vascular exclusion 3. Continuous portal triad clamping 4. Continuous selective hepatic vascular exclusion 5. Continuous selective portal triad clamping 6. Intermittent portal triad clamping 7. Intermittent selective portal triad clamping	1. Control 2. Antithrombin III 3. Recombinant factor VIIa 4. Tranexamic acid
Total hospital stay	There was no evidence of differ-	There was no evidence of differ-	The total hospital stay was lower in low	There was no evidence of differ-	There was no evidence of differ-	The total hospital stay was lower in con-	There was no evidence of differ-

(*Continued*)

	ences in hospital stay between the groups (quality of evidence = very low) [1,2,3].	ences in hospital stay between the groups (quality of evidence = very low) [1,2,3].	central venous pressure than control. The mean hospital stay in the control group was 20. 75 days. The mean hospital stay in the low central venous pressure was 2. 42 lower (3.91 to 0.94 lower) . 197 participants; 3. Quality of evidence = very low[1,2,3]. There were no evidence of differences in the remaining comparisons (quality of evidence = very low)[a,b,c].	ences in hospital stay between the groups (quality of evidence = very low) [1,2,3].	ences in hospital stay between the groups (quality of evidence = very low) [1,2,3].	tinuous portal triad clamping than continuous hepatic vascular exclusion. The mean hospital stay in the continuous hepatic vascular exclusion group was 22 days. The mean hospital stay in the continuous portal triad clamping was 8.00 lower (13.03 to 2.95 lower). 52 participants; 1. Quality of evidence = low [1,2]. The mean hospital stay in the continuous portal triad clamping group was 14 days. The mean hospital stay in the continuous selective hepatic vascular exclusion was 2.80 lower (4.13 to 1.47 lower). 160 participants; 1. Quality of ev-	ences in hospital stay between the groups (quality of evidence = very low) [1,2,3].

(*Continued*)

						idence = low [1,2]. There were no evidence of differences in the remaining comparisons (quality of evidence = very low)[1,2,3].	
ITU stay	There was no evidence of differences in ITU stay between the 2 groups (quality of evidence = very low) [1,2,3].	None of the trials reported this outcome.	None of the trials reported this outcome.	There was no evidence of differences in ITU stay between the 2 groups (quality of evidence = very low) [1,2,3].	There was no evidence of differences in ITU stay between the 2 groups (quality of evidence = very low) [1,2,3].	The ITU stay was lower in continuous selective hepatic vascular exclusion than continuous portal triad clamping. The mean ITU stay in the continuous portal triad clamping group was 1.5 days. The mean ITU stay in the continuous selective hepatic vascular exclusion group was 0.3 lower (0.55 to 0.06 lower). 160 participants; 1. Quality of evidence = very low[1,2,3]. There was no evidence of differences in other comparisons (quality of evidence = very low)[1,2,3].	None of the trials reported this outcome.

(*Continued*)

Operating time	There was no evidence of differences in operating time between the 2 groups (quality of evidence = very low) [1,2,3].	There was no evidence of differences in operating time between the 2 groups (quality of evidence = very low) [1,2,3].	The operating time was lower in low central venous pressure than control. The mean operating time in the control group was 246 minutes. The mean operating time in the low central venous pressure was 15.32 lower (29.03 to 1.69 lower). 192 participants; 4. Quality of evidence = very low[1,2,3]. There was no evidence of differences in other comparisons (quality of evidence = very low)[1,2,3].	There was no evidence of differences in operating time between the groups (quality of evidence = very low) [1,2,3].	The operating time was higher in fibrin sealant & collagen than control. The mean operating time in the control group was 263 minutes. The mean operating time in the fibrin sealant & collagen was 19. 72 higher (2. 93 to 36.57 higher). 300 participants; 1. Quality of evidence = very low[1,2,3]. There was no evidence of differences in other comparisons (quality of evidence = very low)[1,2,3].	The operating time was lower in intermittent portal triad clamping than continuous selective portal triad clamping. The mean operating time in the continuous selective portal triad clamping group was 236 minutes. The mean operating time in the intermittent portal triad clamping group was 30. 53 lower (49. 68 to 11.29 lower). 80 participants; 1. Quality of evidence = very low[1,2,3]. There was no evidence of differences in other comparisons (quality of evidence = very low)[1,2,3,4].	The operating time was lower in tranexamic acid than control. The mean operating time in the control group was 261 minutes. The mean operating time in the tranexamic acid was 52.20 lower (no information to calculate confidence intervals; P = 0. 003). 214 participants; 1. Quality of evidence = low [1,2]. There was no evidence of differences in other comparisons (quality of evidence = very low)[1,2,3].
Time needed to return to work	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.	None of the trials reported this outcome.

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to

(*Continued*)

change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[1] Risk of bias was unclear or high in the trial[s] (downgraded by 1 point).
[2] Sample size was low (total number of participants fewer than 400 for continuous outcomes and fewer than 300 events in total in both groups for other outcomes) (downgraded by 1 point).
[3] Credible intervals overlapped no effect and clinically significant effect (20% relative risk reduction for binary outcomes; 1 day of hospital stay, intensive therapy unit stay, and time-to-return to work; 15 minutes of operating time) (downgraded by 1 point)
[4] There was considerable or substantial heterogeneity in the pair-wise comparison or at least 1 of the comparisons in the network (downgrade by 2 points)
* Network meta-analysis was not performed for any of the outcomes because of the lack of availability of direct and indirect comparisons in the network
CrI:credible intervals; **ITU**: intensive therapy unit;**MD**: mean difference; **OR**: odds ratio.

WHAT'S NEW

Last assessed as up-to-date: 23 September 2015.

Date	Event	Description
18 July 2016	New citation required and conclusions have changed	The conclusions changed from "Very low quality evidence suggested that liver resection using a radiofrequency dissecting sealer without vascular occlusion or fibrin sealant may increase serious adverse events, and this should be evaluated in further randomised clinical trials. The risk of serious adverse events with liver resection using no special equipment compared with more complex methods requiring special equipment was uncertain due to the very low quality of the evidence. The credible intervals were wide and considerable benefit or harm with a specific method of liver resection cannot be ruled out" into "Low-quality evidence suggests that liver resection using a radiofrequency dissecting sealer may be associated with more adverse events than with the clamp-crush method. Low-quality evidence also suggests that the proportion of participants requiring a blood transfusion was higher in the groups receiving low central venous pressure than in those receiving acute normovolemic haemodilution plus low central venous pressure; very low-quality evidence suggests that blood transfusion quantity (red blood cells) was lower in the fibrin sealant group than in the control; blood transfusion quantity (fresh frozen plasma) was higher in the oxidised cellulose group than in the fibrin sealant group; and blood loss, total hospital stay, and operating time were lower with low central venous pressure than control. There is no

(*Continued*)

		evidence to suggest that using special equipment for liver resection is of any benefit in decreasing the mortality, morbidity, or blood transfusion requirements (very low-quality evidence). Radiofrequency dissecting sealer should not be used outside the clinical trial setting since there is low-quality evidence for increased harm without any evidence of benefits. In addition, it should be noted that the sample size was small and the credible intervals were wide, and considerable benefit or harm with a specific method of liver resection cannot be ruled out."
18 July 2016	New search has been performed	We performed a new search on 23 September 2015. Because of the revised inclusion criteria, we could include 67 trials, compared to 9 trials in the previous version
16 July 2016	Amended	We revised the inclusion criteria and methods. This allowed the inclusion of 67 trials, compared to 9 trials in the previous version. This also led to changes in the conclusions

CONTRIBUTIONS OF AUTHORS

Elisabetta Moggia identified the studies, extracted the data, and completed sections of the review.

Benjamin Rousse re-analysed the network meta-analysis and revised the errors in the analysis.

Constantinos Simillis identified the studies, extracted the data, performed part of the analysis, and drafted the previous version of review (Simillis 2014).

Tianjing Li critically reviewed the content, particularly in relation to the network meta-analysis.

Brian R Davidson critically commented on the review.

Kurinchi S Gurusamy performed the analysis and revised the review.

All review authors agreed on this review version before publication.

DECLARATIONS OF INTEREST

Review authors perform research related to decreasing blood loss in liver resection. This includes clinical studies. No other conflicts of interest.

SOURCES OF SUPPORT

Internal sources

- University College London, UK.

External sources

- National Institute for Health Research, UK.

National Institute for Health Research, the health research wing of the UK Government Department of Health funds K Gurusamy to complete this review.
Award number: Directly commissioned Incentive Award 15/65/01

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

1. We calculated the odds ratios (OR) rather than the risk ratios (RR) since it is easier to model the OR for network meta-analysis. Although ORs are more difficult to interpret than RRs, we overcame this problem by presenting the results as illustrative comparative risks for mortality, serious adverse events, and proportion of people requiring blood transfusion.

2. We calculated the mean difference (MD) and 95% credible interval (CrI) for quantity of blood transfused rather than the standardised mean difference (SMD) and 95% CrI. We expected some authors to report quantity of blood transfused in litres transfused and others to report this as number of units transfused. However, all the trials included in this review reported the quantity of blood transfused in units enabling us to calculate the MD and 95% CrI, which is easier to interpret than SMD.

3. We planned to calculate the rate ratio with 95% CrI. However, the trials reported the proportion of people with serious adverse events. So we calculated the OR with 95% CrI rather than the rate ratio with 95% CrI.

4. We used the residual deviance and Deviance Information Criteria (DIC) for assessing between-study heterogeneity as per the guidance from the National Institute for Health and Care Excellence (NICE) Decision Support Unit (DSU) Technical Support Documents (Dias 2012b; Dias 2013a).

5. We reported the network meta-analysis on all the outcomes although we planned to perform the network analysis for the primary outcomes and one secondary outcome on blood transfusion requirements. This was to obtain and report the maximum information from the available data.

6. We planned to report the random-effects model for network meta-analysis. However, we decided to report the fixed-effects model or random-effects model based on residual deviance and DIC statistics as recommended by the NICE DSU Technical Support Documents (Dias 2013a).

7. We did not fit the inconsistency model that uses the design-by-treatment approach proposed by Higgins and White (Higgins 2012; White 2012), since we used the assessment of inconsistency using the approach suggested by NICE DSU.

8. We did not first calculate all pair-wise meta-analysis estimates and then compare them with indirect comparison estimates (Bucher 1997) for each loop, as the method that we used is an extension of the Bucher et al. (Bucher 1997) method to assess inconsistency (Dias 2012c; Dias 2013e).

9. We did not perform the direct comparison. This was because of the exclusion of many trials that might have been suitable for direct comparison but were unsuitable for the overview.

Differences between first version and second version (current version)

1. We included all the interventions aimed at limiting blood loss and blood transfusion requirements. This was because of requests for this information by stakeholders, which resulted in a directly commissioned report that included all interventions aimed at decreasing blood loss and blood transfusion requirements.
2. We included the outcome 'any adverse event' in addition to the serious adverse events since it was not possible to assess the severity of the outcomes in many trials, for example, bile leak could be a mild adverse event or a serious adverse event depending upon whether an additional intervention was needed to resolve it.
3. Unlike in the previous version, where we considered a combination of one method from each of Table 2, Table 3, and Table 4 as a treatment strategy, in this review, we considered each of these interventions (different methods of cardiopulmonary interventions, parenchymal transection methods, methods of dealing with raw surface, vascular occlusion methods, and pharmacological interventions) as separate networks. This approach was in response to the lack of information on the details of co-interventions in the trials and the design of the trials, which limited the number of trials included in the previous analysis. In many of the trials, the surgeons involved in the trial were allowed to choose their method of liver resection apart from the factor being randomised. This is based on an assumption that the factors are independent of each other, that is, there is no interaction between the factors, or the choice of one factor is not dependent on the choice of another factor. There is no evidence to support or refute this assumption. However, if we planned to include only trials in which all the intervention variables were adequately reported and none were left to the choice of the surgeons, we would not even have been able to include as many trials as we did in the previous version, as we have now included all the interventions aimed at decreasing blood loss and blood transfusion requirements during liver resection.
4. We performed a network meta-analysis only when it was possible to compare the direct and indirect estimates because one cannot assess consistency between the direct and indirect estimates unless both are available.
5. We presented the direct estimates as those performed using Bayesian and frequentist analyses. For frequentist analysis, we presented the results of the model that was used for Bayesian analysis (which was determined by the model fit).
6. We planned to perform subgroup analysis using WinBUGS rather than RevMan.
7. We did not perform sensitivity analysis considering some adverse events as serious and mild, since we included 'any adverse events' as an outcome. This captured the adverse events for which we were unable to assess the severity.
8. We modified the 'Summary of findings' table from the original format because of the presence of many comparisons and many outcomes. We presented only the comparisons in which there was evidence of differences with the illustrative examples. For other comparisons, we simply mentioned that there was no evidence of differences. This is to ensure that the most important information is available in the 'Summary of findings' table.
9. We have provided links in the 'Summary of findings' table to tables with a more traditional 'Summary of findings' format.
10. In addition to this 'Summary of findings' table, we also provided the 'Summary of findings' table for network meta-analysis in a graphical format (in the form of forest plots along with the quality of evidence), in which we used the methodology of grading the quality of evidence in network meta-analysis suggested by the GRADE Working group (Puhan 2014). The first step is to estimate the evidence from direct and indirect effect estimates. Further steps included rating the quality of evidence from direct and indirect effect estimates, presenting the estimate combined from the direct estimate and indirect estimate, and rating the quality of the network meta-analysis effect estimates (Puhan 2014). Although codes are available for node splitting, they resulted in numerical errors because of the data,so we calculated the direct estimates (including only the trials that compared the specific intervention and control) and indirect estimates (after removing the trials that compared the specific intervention and control).
11. We provided the minimal clinically important differences that we used or planned to use in an explicit manner. We considered a 20% relative risk reduction as minimal clinically important differences for binary outcomes and count outcomes. For continuous outcomes, we used or planned to use the following minimal clinically important differences: a standardised mean difference of 0.5 for health-related quality of life, a mean difference of one unit for blood transfusion quantity, a mean difference of 500 mL for blood loss, a mean difference of one day of hospital stay and time-to-return to activity, and a mean difference of 15 min for operating time.

NOTES

Considerable overlap is evident in the Background and Methods sections of this review and those of several other reviews written by the same group of authors.

Author order was changed in August 2013 as follows: Constantinos Simillis, Tianjing Li, Jessica Vaughan, Lorne Becker, Brian Davidson, Kurinchi Gurusamy.

Author order was changed in October 2016 as follows: Elisabetta Moggia, Benjamin Rouse, Constantinos Simillis, Tianjing Li, Jessica Vaughan, Brian Davidson, Kurinchi Gurusamy.

INDEX TERMS

Medical Subject Headings (MeSH)

Bayes Theorem; Blood Loss, Surgical [*prevention & control]; Blood Transfusion [utilization]; Catheter Ablation [methods]; Fibrin Tissue Adhesive [administration & dosage]; Hemostasis, Surgical [*methods]; Hepatectomy [adverse effects; *methods]; Randomized Controlled Trials as Topic; Suction [instrumentation; methods]

MeSH check words

Humans