Surgical management of pediatric inguinal hernia: A systematic review and guideline from the European Pediatric Surgeons' Association Evidence- and Guideline Committee.

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Abstract

Introduction

Inguinal hernia repair represents the most common operation in infancy; however, consensus about the optimal management, from surgical timing to the best technique is lacking. Hence, recommendations for clinical practice are needed. This study assesses the available evidence and compiles recommendations on pediatric inguinal hernia.

Materials and Methods

The European Pediatric Surgeons' Association Evidence- and Guideline Committee addressed six questions on pediatric inguinal hernia repair with the following topics (1) open versus laparoscopic and (2) extra-peritoneal versus trans-peritoneal repair, (3) contralateral exploration, (4) surgical timing and (5) anesthesia technique in preterm infants and (6) operation urgency in girls with irreducible ovarian hernia. Systematic literature searches were performed querying PubMed, MEDLINE, Embase (Ovid) and The Cochrane Library. Reviews and meta-analyses were conducted according to the PRISMA statement.

Results

Seventy-two out of 5173 articles were included, 27 in the meta-analyses. Laparoscopic repair shortens operation time compared to open repair. In preterm infants, hernia repair after NICU/hospital discharge is associated with less respiratory difficulties and recurrences, regional anesthesia decreases postoperative apnea and pain. The review regarding operation urgency for irreducible ovarian hernia gained insufficient evidence of low quality.

Conclusions

Laparoscopic repair may be beneficial for children with inguinal hernia and preterm infants may benefit using regional anesthesia and postponing surgery. However, no definite superiority was found and

available evidence was of moderate to low quality. Evidence for other topics was less conclusive. For the optimal management of inguinal hernia repair a tailored approach is recommended considering the local facilities, sources and the expertise of the medical team involved.

Keywords: Hernia, Inguinal; Laparoscopy; Anesthesia, General; Child; Ovary.

Introduction

Inguinal hernia is one of the most common pediatric surgical disorders, characterized by protrusion of intra-abdominal contents, e.g. omentum, intestines or ovary, through the patent processus vaginalis in the inguinal region. The incidence of inguinal hernia during childhood is estimated between 8 to 50 of every 1000 live births, rising to almost 20% in premature or very low birth weight infants[1,2]. The risk for incarceration in term and preterm children is reported to be 12% and 39%, respectively[3]. In some children, inguinal hernia may be asymptomatic; however surgical repair is always necessary because of the risk of incarceration. Over the past decade, there is increasing evidence regarding the best treatment options for pediatric inguinal hernia. Nevertheless, there are still controversies about the optimal timing for hernia repair in premature infants and girls with irreducible ovarian hernia, whether the operation should be done as an open repair or laparoscopically, and whether contralateral exploration should be performed at the time of unilateral hernia repair or not. In adults, several international guidelines have already been proposed for the treatment of inguinal hernia[4,5]. Although pediatric surgeons will inevitably face numerous cases of inguinal hernia in their professional careers, there are no (international) guidelines for the management of inguinal hernias in infants and children.

The aim of this systematic review is to collect all currently available evidence and to compile recommendations for future treatment of inguinal hernia in the pediatric population.

Materials and Methods

Research questions

The members of the European Pediatric Surgeons' Association (EUPSA) Evidence Based Practice Committee drafted and iteratively refined six questions regarding the management of pediatric inguinal hernia, including primary and secondary outcomes for each question. These questions guided this systematic review and Evidence-Based guideline (**Table 1**).

1. Is laparoscopic inguinal hernia repair associated with better outcome compared to open repair?

2. Which laparoscopic technique is associated with better outcome: the extra-peritoneal approach or trans-peritoneal approach?
3. Should contralateral inguinal exploration be performed at the time of open unilateral inguinal hernia repair?
4. In preterm infants, should hernia repair be performed before or after hospital discharge or discharge from the neonatal intensive care unit (NICU)?
5. In preterm infants, is regional anesthesia associated with better outcome compared to general anesthesia?
6. Should hernia repair in girls with irreducible ovary without symptoms of incarceration or ischemia be performed as an emergency surgery?

Protocol and registration

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement[6]. The pre-specified protocol was registered in PROSPERO (CRD42019124799). Institutional Review Board approval and informed consent were not required for execution of this review.

Search strategy

A comprehensive literature search was conducted in March 2019 using PubMed, MEDLINE, Embase (Ovid) and The Cochrane Library databases using Medical Subject Headings (MeSH) and text words that were specific to each research question (Appendix 1. Search strategy). Reference lists of included articles were screened for identification of additional studies. Selection of studies was restricted to full-text articles available in English, without any limits to the year of publication.

Study selection

For each question, two review authors independently screened and reviewed all articles that were identified for their specific research question based on title, key words and abstract, and full-text for final selection. Randomized controlled trials, case-control studies, case-series and retrospective studies were considered eligible for inclusion. Review articles, letters to the editor, conference abstracts, poster presentations and case reports were excluded. If the full text of articles was not available from one of the libraries, it was retrieved by contacting the authors. Any discrepancies in the selection process were resolved by second joint review of the literature to reach mutual consensus or by consulting a third independent review author if necessary.

Quality assessment

Risk of bias assessment of the included studies was performed using Risk of Bias 2.0 (RoB 2.0) for randomized clinical trials, as recommended by members of the Cochrane collaboration. RoB 2.0 assessed the bias of studies in the following domains: randomization process, deviations from intended interventions, missing data, measurement of the outcome and selection of the reported results. Each domain was scored as "*low risk*", "*some concerns*" or "*high risk*" and the overall risk of bias was determined. In addition, for non-randomized studies, Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) was used. ROBINS-I assessed the bias of studies in the following domains: confounding, selection of participants into the study, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes and selection of the reported result. Each of the domains was scored as "*low*", "*moderate*", "*serious*", "*critical risk*" or "NI, no information" and an overall risk of bias was determined.

Data extraction and review process

Two review authors systematically extracted all relevant study information and patient characteristics pertinent to their review question from studies included in their part of the review. Primary and secondary outcome measures for each review question are presented in **Table 1**. Missing data were

calculated or retrieved from the author(s) if necessary. The Oxford Centre for Evidence-Based Medicine Classification of levels of evidence and grades of recommendation was used to assess the level of evidence of the included studies and grade the strength of the recommendations (**Table 2**)[7]. In June 2019, the results of this systematic review together with the corresponding recommendations were presented at the EUPSA annual conference in Belgrade, Serbia, and subsequently opened for discussion.

Statistical analysis

Statistical analyses were performed using Review Manager (RevMan), version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2014) and MedCalc, version 18.5. Weighted mean differences (WMD) and pooled estimates of proportion (%) or odds ratios (OR) with their corresponding 95% confidence intervals (CI) were calculated for the analysis of continuous and dichotomous variables, respectively. Meta-analyses were performed using a random-effects model according to the Mantel-Haenszel method. Heterogeneity between the included studies was assessed using the inconsistency (I^2) score and was considered substantial if above 50%.

Results

Search strategy

Literature search and manual reference analysis showed 5173 articles after duplicates were removed. After the initial screening and exclusion of 5016 articles, 157 full-text articles were assessed for eligibility. In total, 72 articles were included in the qualitative synthesis of the six review questions (**Figure 1**). Twenty-seven articles were finally included in the meta-analyses.

Quality assessment

Quality assessment was performed on all different outcomes using the Cochrane RoB 2.0 tool for randomized clinical trials and the ROBINS-I tool for non-randomized studies of interventions (Appendix

2). The overall risk of bias using the RoB 2.0 tool for randomized studies that were included in the meta-analysis for review question 1 and 2 was considered low. Overall risk of bias for randomized studies included for review question 5 was considered high, except for one study. Risk of bias assessment using the ROBINS-I tool for non-randomized studies that were included for review questions 2, 3, 4 and 6 showed that there was a serious or critical risk of bias concerning several domains.

Question 1. Is laparoscopic hernia repair associated with better outcome compared to open repair?

Recommendation (Level 1 evidence; Grade B): Based on the currently available evidence there is no definite superiority of either the laparoscopic or open treatment strategy regarding perioperative (i.e. spermatic cord/vessel injury, ovarian lesion and bleeding) and postoperative (i.e. hematoma, edema, hydrocele, wound infection and testicular atrophy) complications, recurrence rate and development of metachronous contralateral inguinal hernia (MCIH). Laparoscopic inguinal hernia repair might be advantageous in children with bilateral inguinal hernia in terms of reduced operation time.

Background

Hernia repair can be performed either with the traditional open, or the increasingly used laparoscopic approach. Laparoscopic hernia repair is believed to result in shorter operation time for children with bilateral inguinal hernia and less postoperative complications compared to open hernia repair[8,9]. Thereby, laparoscopic repair allows for contralateral exploration and simultaneous repair of the processus vaginalis if it remains to be patent. However, no differences in long-term outcome after laparoscopic repair of a contralateral patent processus vaginalis could yet be identified[9].

Results

Eight randomized controlled trials that compared laparoscopic (*n*=375 patients) to open pediatric hernia repair (*n*=375 patients) could be included in the meta-analysis[10–17]. Patients' age at the time of

surgery and mean follow-up time in the included studies ranged from 0 to 18 years and 24 hours to 30 months, respectively (Appendix 3).

There were no differences between the complication and recurrence rates. Perioperative complications including injury to spermatic cord or spermatic vessels, ovarian lesion or bleeding (OR 3.16 [95% CI 0.34 to 29.60], I^2=0%, p=0.31)[10,12,15,16] and postoperative complications including hematoma, edema, hydrocele, wound infection and testicular atrophy (OR 0.37 [95% CI 0.10 to 1.32], I^2=55%, p=0.13)[10–12,14–16,18] between laparoscopic and open hernia repair were similar. Recurrence rates after laparoscopic and open hernia repair were reported to be 1.1% and 1.2%, respectively (OR 0.88 [95% CI 0.20 to 3.88], I^2=0%, p=0.87)[10–12,14–16,18].

This meta-analysis demonstrated no differences regarding development of MCIH after laparoscopic versus open hernia repair (OR 0.28 [95% CI 0.04 to 1.86], I^2=52%, p=0.19)[11,14,15,18]. Unilateral operation time (in minutes)(WMD 0.62 [95% CI -5.70 to 6.95], I^2=97%, p=0.85)[11–16,18], length of hospital stay (in hours)(WMD 0.74 [95% CI -0.38 to 1.87], I^2=59%, p=0.20)[11,12,14,16,18] and time to full recovery (in hours)(WMD 2.05 [95% CI -11.13 to 15.23], I^2=67%, p=0.76)[10–12,14] were also not different between the groups. Bilateral operation time (in minutes) was shown to be reduced after laparoscopic repair (WMD -7.19 [95% CI -10.04 to -4.34], I^2=73%, p<0.001)(**Table 3** and Appendix 4)[10–12,16,18].

Discussion and summary

The results of this meta-analysis on open versus laparoscopic hernia repair indicates that the laparoscopic approach results in shorter operation time for children with bilateral hernia compared to open inguinal hernia repair. Complication and recurrence rates were not different between both techniques. Additionally, it has recently been demonstrated that in particular the laparoscopic hernia repair technique with extracorporeal suturing is likely to be associated with less complications and shorter operation time compared to intracorporeal suturing[19]. The recurrence rate was potentially found to be higher after laparoscopic repair[20], whereas two recent meta-analyses could not demonstrate any differences between open and laparoscopic repair with respect to recurrence

rates[8,21]. It is believed that laparoscopic surgery with simultaneous repair of the contralateral patent processus might be advantageous to prevent development of MCIH, although based on the currently available evidence no difference in MCIH development could be demonstrated. Still, there is great variety among the laparoscopic techniques that are currently used for repair of inguinal hernias in children and long-term follow-up results are lacking. Therefore, no definite recommendation on the superiority of either the laparoscopic or open treatment strategy can be made.

Question 2. Which laparoscopic technique is associated with better outcome: the extra-peritoneal approach or trans-peritoneal approach?

Recommendation (Level 2 evidence; Grade B): Based on the currently available evidence there is no definite superiority for either the laparoscopic extra-peritoneal or trans-peritoneal approach regarding the occurrence of intraoperative (i.e. vessel injury and conversion to open surgery) or postoperative (i.e. hydrocele, wound infection and testicular atrophy) complications and recurrence rate. In comparison with the trans-peritoneal approach, the laparoscopic (unilateral and bilateral) extra-peritoneal approach may result in reduced operation time in children with inguinal hernia.

Background

Minimally invasive surgery for the repair of pediatric inguinal hernia is often performed, and innovations in laparoscopic hernia techniques evolve alongside its increasing popularity. Speck and Smith previously described the evolution of laparoscopic hernia repair techniques and demonstrated the different methods of minimally invasive closure of pediatric inguinal hernias for the Society of American Gastrointestinal and Endoscopic Surgeons[22]. The techniques can be roughly categorized by the number of ports and the suturing technique that is used to close the internal inguinal ring: extra-corporeal suturing through the pre-peritoneal plane or intra-corporeal suturing through the trans-peritoneal approach. Compared to the open technique, laparoscopic extracorporeal suturing is

considered to result in fewer complications and shorter unilateral operation time, whereas intracorporeal suturing potentially shortens the time interval between surgery and discharge[21].

Results

Shalaby et al. directly compared the extra-peritoneal approach (*n*=75 patients) to the trans-peritoneal approach (*n*=75 patients) in a randomized trial and showed that there were no differences between the study groups in postoperative development of hydrocele (2.7% versus 4%) or recurrence rate (1.3% versus 4%, p=0.61)[23]. Intraoperative injury to the spermatic vessels and conversion to the open approach were not reported in either study group. None of the patients developed a postoperative wound infection or testicular atrophy. Mean (SD) duration (in minutes) of bilateral hernia repair was shorter in patients who underwent extra-peritoneal hernia repair compared to trans-peritoneal repair (11.4 ± 2.7 versus 21.9 ± 7.2, p<0.001).

Three retrospective cohort studies including 833 patients compared the extra-peritoneal and trans-peritoneal approach and were included in the meta-analysis for the second review question (Appendix 3)[24–27]. No difference was found between the extra-peritoneal and trans-peritoneal approach in recurrence rate (OR 1.22 [95% CI 0.33 to 4.47], I^2=0%, p=0.77). Both unilateral (WMD -9.84 [95% CI -16.33 to -3.03], I^2=97%, p=0.005)[24–26] and bilateral (WMD -13.54 [95% CI -16.08 to -11.01], I^2=54% p<0.001)[24–27] operation times were shorter in patients who underwent extra-peritoneal hernia repair. Conversion to open surgery (OR 2.88 [95% CI 0.29 to 28.28], I^2=0%, p=0.36)[24–27], intra-operative vessel injury (OR 0.55 [95% CI 0.09 to 3.38], I^2=41%, p=0.52), and postoperative complications including wound infection (OR 3.29 [95% CI 0.17 to 64.65], I^2=NA, p=0.43)[MJL1][MF2][KD3], hydrocele (OR 1.04 [95% CI 0.32 to 3.30], I^2=0%, p=0.95), and testicular atrophy (OR 0.15 [95% CI 0.01 to 3.76], I^2=NA, p=0.25) did not differ[24–27] (**Table 3** and Appendix 4).

Discussion and summary

In 2009, the International Pediatric Endosurgery Group Evidence-Based Review Committee was not yet able to make clear recommendations on a specific method for minimally invasive hernia repair in children since level 1a evidence comparing different laparoscopic techniques was lacking[9]. Based on low-quality evidence from retrospective studies that were included in this meta-analysis, the extra-peritoneal approach is believed to reduce the operation time of both unilateral and bilateral laparoscopic hernia repair in children. Moderate quality evidence from a single randomized controlled trial considers only bilateral inguinal hernia repair in children to be shorter using the extra-peritoneal technique. Additional high-level evidence is required before definite conclusions can be drawn.

Question 3. Should contralateral inguinal exploration be performed at the time of open unilateral inguinal hernia repair?

Recommendation (Level 2 and 3 evidence): Since high-level evidence comparing contralateral exploration to unilateral repair without contralateral exploration is lacking and there is extensive heterogeneity among the currently available evidence, no clear recommendation can be made.

Background

In children who present with unilateral inguinal hernia, a second contralateral hernia (i.e. metachronous inguinal hernia, MCIH) occurs in 10-15% after unilateral repair[28]. No definite risk factors could be identified for MCIH development and accurate diagnostic modalities (e.g. preoperative ultrasonography) to detect or predict development of MCIH are lacking[29,30]. For several decades, routine exploration of the contralateral groin during unilateral surgery and simultaneous repair of an existing contralateral patent processus vaginalis (CPPV) has been believed to potentially prevent development of MCIH. However, as not all CPPVs necessarily develop into clinically relevant MCIH, and contralateral exploration also increases the risk for (potentially unnecessary) operative complications, controversy still exists whether to perform contralateral exploration or not[28,31–33]. This is especially

intriguing in light of a recent warning on the potentially harmful impact of repeated anesthesia on the child's brain, that was recently released by the US Food and Drug Administration[34].

Results

Twenty-four studies retrospectively evaluated the use of contralateral exploration of which 23 studies (*n*=9063 patients) could be included in the data-analysis[35–58]. Age at surgical repair and duration of follow-up ranged from 1 week to 16 years and 3 months to 10 years, respectively (Appendix 3).

Twenty-three studies (*n*=5726 patients) performed contralateral exploration and assessed its results. Pooled estimate of positive contralateral exploration rates showed that the processus vaginalis was found to be patent in 63.49% ([95% CI 56.88 to 69.87], I^2=95.76%)[36,37,39–59]. Pooled estimates of eleven studies (*n*=3008 patients) evaluating the results of patients who did not undergo contralateral exploration, showed that MCIH developed in 8.4% ([95% CI 5.48 to 11.90], I^2=85.88%)(**Table 4**)[36,37,39,40,42,43,49,50,57–59].

Complications including testicular atrophy, hydrocele, hematoma, wound infection, apnea and recurrence were described by thirteen studies and reported to be found in 1.97% ([95% CI 0.98 to 3.29; I^2=81.03) of 3230 patients[36,37,40–42,44,48,50,51,53,55–57]. Six studies (*n*=1096 patients) reported that contralateral exploration increases the total anesthesia time by on average 15-20 minutes[40,41,45,47,51,55]. Mean values with the corresponding standard deviations of both unilateral repair and unilateral repair with contralateral exploration were not reported. Furthermore, in patients who underwent unilateral hernia repair and subsequent second surgery following development of MCIH, the duration of surgery was not reported.

Discussion and summary

Based on the results of this review, the contralateral processus vaginalis is found to be patent in 63.5% of the children with unilateral inguinal hernia, whereas on the contrary only 8.4% of the children who underwent unilateral hernia repair without contralateral exploration actually develop a MCIH. The

345 average complication rate of contralateral exploration is 1.97%, although no study directly compared
346 the complications of contralateral exploration to the complications of unilateral hernia repair and
347 subsequent development of MCIH. Contralateral exploration appears to increase anesthesia time by
348 15-20 minutes; however, unilateral hernia repair with subsequent second anesthesia and surgery if
349 MCIH develops, will probably increase anesthesia time even more.

350 In 2011, Nataraja et al. performed a systematic review on the evidence for routine
351 contralateral exploration during open hernia repair and reported an overall risk for MCIH development
352 of 5.76% (95% CI 5.55 to 5.97). They also found that patients younger than six months (12.4%) and
353 patients with an initial left-sided inguinal hernia (12.1%) were more likely to develop a MCIH[28].
354 Laparoscopic evaluation of the contralateral processus during open or laparoscopic hernia repair is
355 increasingly performed as the laparoscopic technique or the use of a laparoscope through the
356 ipsilateral hernia sac allows clear visualization of the contralateral ring. Chong et al. recently assessed
357 the long term follow-up results of open (*n*=1156 patients) and laparoscopic (*n*=541) hernia repair in
358 children and found that the use of laparoscopy to visualize the contralateral side resulted in a
359 significantly lower rate of MCIH repair (3.8% versus 0.8%)[60]. This corresponds to the results of a recent
360 systematic review by Muensterer et al. who found that a CPPV was concomitantly found during
361 laparoscopic inguinal hernia repair in 38.5% of 19,188 pediatric patients, and prophylactic closure of
362 the CPPV resulted in a risk reduction of 5.7% (95% CI 3.6 to 7.7; $p<0.001$)[61]. More specifically, Li et al.
363 recommended laparoscopic contralateral repair in patients younger than three years old with initial
364 left-sided inguinal hernia[62].

365 To summarize, low-quality evidence from retrospective cohort studies suggests that open
366 contralateral exploration with repair of a CPPV may prevent development of MCIH in children who
367 present with a unilateral inguinal hernia. Though no firm conclusions can yet be drawn since high-level
368 evidence comparing contralateral exploration to unilateral repair without contralateral exploration is
369 lacking and there is extensive heterogeneity among the currently available evidence.

370

Question 4. In preterm infants, should hernia repair be performed before or after hospital discharge or discharge from the NICU?

Recommendation (Level 2 evidence; Grade B): Postponing hernia repair until after discharge may be beneficial in terms of preventing respiratory difficulties and hernia recurrence. No significant differences were found for incarceration and reoperation rate.

Background

Controversy still exists about the timing of inguinal hernia repair in the premature population, in which the incidence of inguinal hernia rises to almost 20%[63]. Early hernia repair (i.e. before discharge from the NICU) potentially prevents complications including the risk of incarceration, whereas late repair (i.e. after discharge from the NICU) potentially decreases the risk for operative and postoperative anesthetic and surgical complications[64]. The timing of inguinal hernia repair in preterm infants should therefore represent a balance of the risks of hernia incarceration against postoperative respiratory complications[64]. In 2005, the majority (63%) of pediatric surgeons that were surveyed preferred to perform hernia repair before hospital discharge[65]. However, the risk of postoperative apnea is inversely related to gestational age and postconceptional age, and it is believed that postponing hernia repair surgery decreases the risk of postoperative apnea without increasing the risk of incarceration[66,67].

Results

Seven retrospective cohort studies (*n*=2024 patients) assessed the optimal timing of inguinal hernia repair in preterm infants (Appendix 3)[68–74]. Within these studies, 1176 patients were operated on before NICU discharge and 848 patients underwent hernia repair after NICU discharge. Average gestational age and birth weight of the included patients ranged from 26.2 to 32.2 weeks and 740 to 1460 grams, respectively. The average waiting time from diagnosis to surgery ranged from 2.8 to 10.7 weeks, and surgical repair was performed at an average postconceptional age of 11.3 to 62.9 weeks.

The meta-analysis indicated no difference in incarceration rates between patients undergoing hernia repair before (18.1%) and after (11.3%) discharge (OR 1.42 [95% CI 0.87 to 2.34], I2=0%, p=0.16)[74–79].

Recurrence and reoperation[78,80] rates occurred in 5.7% and 5.1% of the patients with early repair and 1.8% and 3.3% of the patients with hernia repair after discharge[74,75,77–80]. Respiratory difficulties were reported in 5.1% and 3.3% of the patients with early and late repair, respectively[74–78,80]. Statistical analysis showed that there were more recurrences (OR 3.52 [95% CI 1.28 to 9.70], I^2=0%, p=0.01)[74,75,77–79] and respiratory difficulties (OR 4.90 [95% CI 2.69 to 8.93], I^2=24%, p<0.001)[74–78,80] in patients that were operated before versus after discharge. The reoperation rate was not different between the groups (OR 1.60 [95% CI 0.91 to 2.82], I^2=0%, p=0.10)(**Table 3** and Appendix 4)[78,80]. Testicular atrophy was described in three studies, in which zero events were recorded among any of the patients[74,77,78]. These data could therefore not be pooled. Duration of surgery was only investigated by Khan et al. who reported an average (SD) duration of 114 (52) minutes before discharge, compared to 95 (29) minutes after discharge[75]. None of the included studies reported on the length of hospital stay.

Discussion and summary

Moderate-quality evidence from meta-analysis of retrospective cohort studies suggests that inguinal hernia repair performed after NICU discharge may reduce the risk of respiratory difficulties and hernia recurrence compared to repair before discharge. No differences could be demonstrated for incarceration and reoperation rate. However, the currently available evidence is limited and among the included studies, the patients' age at the time of inguinal hernia repair varied largely (11.3-62.9 weeks). Furthermore, follow-up duration was sometimes poorly reported[74,77] or varied among the studies included for the outcome recurrence[75,78,79]. For the outcome reoperation, two studies were included: Sulkowski et al. reported reoperation as being either ipsilateral recurrence of inguinal hernia or occurrence of metachronous hernia[80]; The outcome reoperation in the study of Takahashi et al.

included any complication requiring surgery. In both of the cases the indication for reoperation was cryptorchism instead of hernia recurrence[78].

The results for this topic are in line with the results of a previous meta-analysis by Masoudian et al., who also demonstrated a significant increase in the odds of respiratory difficulty (OR 3.59 [95% CI 1.10 to 11.75], I^2=42%) and recurrence (OR 4.12 [95% CI 1.17 to 14.45], I^2=0%) if hernia repair was performed before NICU discharge. They also found no significant differences regarding incarceration rate, surgical complications and reoperation rate[81].

Question 5. In preterm infants, is regional anesthesia associated with better outcome compared to general anesthesia?

Recommendation (Level 1 evidence; Grade B): Central regional anesthesia instead of general anesthesia may be considered in preterm infants requiring surgery for inguinal hernia repair, since it is associated with some decrease in the occurrence of postoperative apnea and decreased postoperative pain among this population.

Background

Preterm infants undergoing surgery with general anesthesia are susceptible to apneic episodes, with or without bradycardia, in the postoperative period. Alterations caused by apnea and bradycardia include a reduced cerebral blood flow and significant oxygen desaturations, yielding an increased risk of affecting neurodevelopmental outcome[82,83]. Additionally, there are increasing concerns that general anesthetics and sedative agents have a potential harmful effect on the child's developing brain[34]. According to the results of a systematic review by Jones et al., spinal anesthesia was initially not found to reduce the overall incidence of postoperative morbidity in preterm infants undergoing inguinal hernia repair. However, after exclusion of infants receiving ketamine from the analysis, spinal anesthesia rather than general anesthesia in preterm infants without receiving any sedatives reduced the risk of postoperative apnea by 47%. In former preterm infants without preoperative apnea, spinal

anesthesia may even reduce the risk of postoperative apnea by up to 66%. In order to prevent one infant from having an episode of post-operative apnea, four infants needed to be treated with spinal anesthesia[84].

Results

Thirteen articles describing eight randomized controlled trials were included in the meta-analysis for the fifth review question (Appendix 3)[59,85–95]. A recent randomized controlled trial in which children were randomly assigned to receive either awake-regional or sevoflurane-based general anesthesia for inguinal hernia repair in early infancy was included. Data of this General Anesthesia compared to Spinal anesthesia (GAS) trial, which reports both term and preterm patients, was extrapolated on preterm patients for some outcomes. The overall failure rate of regional anesthesia was reported to be 20%, none of the studies reported failure rates of general anesthesia.

In preterm infants undergoing surgical hernia repair, the risk of apnea was not different between central regional anesthesia and general anesthesia (OR 0.68 [95% CI 0.37 to 1.23], I^2=6%, p=0.20)[88,91,96–99]. Results of the per-protocol analysis, in which patients from the regional anesthesia group that required sedation or switched to general anesthesia were included in the general anesthesia group, showed that regional anesthesia was associated with a reduced risk of postoperative apnea (OR 0.46 [95% CI 0.22 to 0.96], I^2=11%, p=0.04)[88,96–99]. Subgroup analysis including only preterm infants with early (within one hour postoperative) postoperative apnea (OR 0.60 [95% CI 0.18 to 1.98], I^2=31%, p=0.41)[91,97–99] or preterm infants with preoperative apnea's (OR 0.52 [95% CI 0.11 to 2.45], I^2=3%, p=0.40)[88,96,97] indicated no differences between regional and general anesthesia. The risk of postoperative apnea episodes requiring intervention (e.g. stimulation, assisted ventilation, continuous positive airway pressure, endo-tracheal intubation or administration of methylxanthine) was reduced after regional anesthesia (OR 0.11 [95% CI 0.00 to 2.51], I^2=77%, p=0.17), although not reaching statistical significance[88,96,99].

The risk of bradycardia (OR 0.75 [95% CI 0.29 to 1.90], I^2=21%, p=0.54)[88,96–98,100] and that of postoperative hypotension (OR 0.83 [95% CI 0.01 to 95.94], I^2=90%, p=0.94)[88,101] was not different between the regional versus general anesthesia group. Postoperative pain was significantly lower in patients who had central regional anesthesia (OR 0.44 [95% CI 0.31 to 0.63], I^2=0%, p<0.001)[59,88] (**Table 3** and Appendix 4)[59]. The GAS trial was the only study reporting neurodevelopmental outcome and they demonstrated that there was no difference in neurodevelopmental outcome between the awake-regional anesthesia and general anesthesia group in terms of the mean composite cognitive score (0.169 [95% CI -2.30 to 2.64]) at two years of follow-up [95].

Discussion and summary

Moderate–quality evidence from meta-analysis of RCTs indicates that central regional anesthesia, without additional sedatives, may reduce the risk of postoperative apnea in premature infants undergoing inguinal hernia repair. It also suggests that central regional anesthesia is associated with a better postoperative pain control in premature infants undergoing inguinal hernia repair. However, central regional anesthesia is also reported to be associated with a 20% failure rate.

There are some concerns on the quality of various studies included in the meta-analysis. Thereby, considerable variation in the classification to define postoperative apnea and subsequently the duration of apnea existed among the included studies, which complicated the comparison of this outcome. However, for most outcomes included, the majority of the evidence originates from the GAS study, which was judged as having a good quality and a low risk of bias. The GAS study defined postoperative apnea as “an unexplained episode of cessation of breathing for 20 seconds or longer, or a shorter respiratory pause associated with bradycardia, cyanosis, pallor, and/or marked hypotonia requiring intervention”[99,102].

Question 6. Should hernia repair in girls with irreducible ovary without symptoms of incarceration or ischemia be performed as an emergency surgery?

Recommendation (Level 4 evidence; Grade C): Since high-level evidence comparing emergency and elective repair of asymptomatic irreducible ovarian hernias in girls is lacking and there is extensive heterogeneity among the currently available evidence, no clear recommendation can be made.

Background

Ovarian inguinal hernias comprise 13-22% of all hernias in female children[103–106] and are most common in infants before one year of age[104,107–109]. Incarcerated inguinal hernias in girls involve the ovary in 58-82%[110,111]. Irreducible ovarian inguinal hernias are believed to potentially be at risk for ovarian torsion and it is assumed that ovarian torsion causes ovarian injury in girls with ovarian inguinal hernias[112,113]. In 1991, Boley et al. showed that in 27% of the girls with an ovarian inguinal hernia the ovary was twisted or infarcted at the time of surgery. Based on these findings, they suggested that asymptomatic irreducible ovarian hernias should be considered as any other incarceration, and emergency surgery should be performed if non-operative reduction was unsuccesful[112]. In 1993, the American Academy of Pediatrics Section of Surgery performed a survey in which 27% of the pediatric surgeons responded that they repair reducible ovarian hernias electively, 59% at the next available opportunity and 10% performed emergent repair. In 2003, these results were 49%, 36% and 5%, respectively. Irreducible asymptomatic ovaries were reported to be operated at the next available opportunity by 42% in 1993 and 50% in 2005, while 44% and 32% operated urgently[65,114].

Results

Twelve retrospective case series (*n*=506 patients) were included in the systematic review, whereas none could be included for quantitative analysis of the results (Appendix 3)[103,104,106,107,110–112,115–119]. Several authors suggest that both reducible and irreducible asymptomatic ovarian inguinal hernias should be repaired within a few days following diagnosis[104,108,109], whereas others state that asymptomatic irreducible ovaries should be treated with urgent manual, or if unsuccessful, operative reduction[112,116]. The reported incidence of ovarian strangulation in girls with irreducible hernias among

the included studies was between 0-36% (**Table 5**)[104,108,109,112]. Turk et al. operated on 7 girls with irreducible hernias within 24-72 hours after their presentation (semi-elective) and reported no strangulations[109]. Esposito et al. performed surgical repair in 16 patients that presented with asymptomatic irreducible hernias within 1-4 days after diagnosis and also reported no cases of strangulation or torsion. All patients underwent follow-up ultrasonography one year after surgery and none of the ovaries atrophied[108]. In contrast, Hirabayashi et al. evaluated 71 girls who were diagnosed as having asymptomatic ovarian hernias at a median age of 1.5 months, of whom 58 underwent surgery at a median age of 11 months, as their policy was to postpone surgery until 9 months of age. By that time the ovary had already reduced spontaneously into the abdomen in 35 (60%) girls. In 22 (38%) girls, and also in 13 girls who had not been preoperatively diagnosed with ovarian hernias, ovary was found in the hernia sac during surgery. There were no reports of ovarian torsion, yet in one patient the hernia sac including the fallopian tube and ovary was ligated[107]. Marinkovic et al. reported ovarian torsion in 35 girls (14%) who presented with incarcerated hernia and subsequently performed salphingo-oophorectomy twice[116]. Lee et al. reported that ovaries were ischemic in 4.5% of incarcerated hernias[110]. In girls with ovarian torsion, the ovary was found to be strangulated in 55%[113]. Chen at al. reported ovarian strangulation in 9/32 female patients (<1 year old) that presented with incarcerated ovarian hernias, and found that a larger ovary (≥5 cm^3) was more likely for ovarian torsion. As the ovarian volume decreases with inclining age, female infants therefore have an increased risk for developing ovarian strangulation[115].

Discussion and summary

All included studies were retrospective case series with low level of evidence. The studies were heterogeneous with respect to inclusion criteria, especially regarding the type of ovarian hernia (e.g. reducible/irreducible and symptomatic or asymptomatic), timing of surgery and outcome measures. Moreover, follow-up data were very limited.

In addition to the studies that were included in this review, Dreuning et al. recently evaluated a large cohort (*n*=1084) of female patients who underwent inguinal hernia repair. Their reported incidences of ovarian herniation and ovarian strangulation were 21.7% and 6%, respectively. In girls with ovarian strangulation, the median time interval between diagnosis and surgery was 11.5 (1.3-20.5) days, and three patients underwent an emergency operation within 24 hours after diagnosis. No firm conclusions on the timing of surgery could be drawn because the exact time of occurrence of the inguinal hernia was unknown[120].

Although repair within a few days may reduce the risk for ovarian torsion and strangulation, based on the currently available low quality evidence, no recommendation can be made regarding the timing of repair for asymptomatic irreducible ovarian inguinal hernias.

Conclusion

In this systematic review and Evidence-Based guideline, all currently available evidence pertinent to six pre-specified review questions, was assessed by the members of the EUPSA Evidence and Guidelines Committee. Based on the evidence included in this review, laparoscopic repair may be beneficial for children with inguinal hernia and preterm infants may benefit using central regional anesthesia and postponing surgery. However, no definite superiority was found and available evidence was of moderate to low quality. As inguinal hernia repair in children is a widely performed surgery, local circumstances may differ and recommendations may not apply to every clinical setting. For the optimal management of inguinal hernia repair a tailored approach is therefore recommended taking into consideration the local facilities, sources and expertise of the medical team involved.

Summary of recommendations

- Based on the currently available evidence there is no definite superiority of either the laparoscopic or open treatment strategy regarding perioperative (i.e. spermatic cord/vessel injury, ovarian lesion and bleeding) and postoperative (i.e. hematoma, edema, hydrocele,

wound infection and testicular atrophy) complications, recurrence rate and development of metachronous contralateral inguinal hernia (MCIH). Laparoscopic inguinal hernia repair might be advantageous in children with bilateral inguinal hernia in terms of reduced operation time (Level 1 evidence; Grade B).

- Based on the currently available evidence there is no definite superiority for either the laparoscopic extra-peritoneal or trans-peritoneal approach regarding the occurrence of intraoperative (i.e. vessel injury and conversion to open surgery) or postoperative (i.e. hydrocele, wound infection and testicular atrophy) complications and recurrence rate. In comparison with the trans-peritoneal approach, the laparoscopic (unilateral and bilateral) extra-peritoneal approach may result in reduced operation time in children with inguinal hernia (Level 2 evidence; Grade B).
- Since high-level evidence comparing contralateral exploration to unilateral repair without contralateral exploration is lacking and there is extensive heterogeneity among the currently available evidence, no clear recommendation can be made (Level 2 and 3 evidence).
- Postponing hernia repair until after discharge may be beneficial in terms of preventing respiratory difficulties and hernia recurrence. No significant differences were found for incarceration and reoperation rate. (Level 2 evidence; Grade B).
- Central regional anesthesia instead of general anesthesia may be considered in preterm infants requiring surgery for inguinal hernia repair, since it is associated with some decrease in the occurrence of postoperative apnea and decreased postoperative pain among this population (Level 1 evidence; Grade B).
- Since high-level evidence comparing emergency and elective repair of asymptomatic irreducible ovarian hernias in girls is lacking and there is extensive heterogeneity among the currently available evidence, no clear recommendation can be made (Level 4 evidence; Grade C).

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Figure 1. PRISMA flow chart of the study selection for all questions (Q1-Q6).

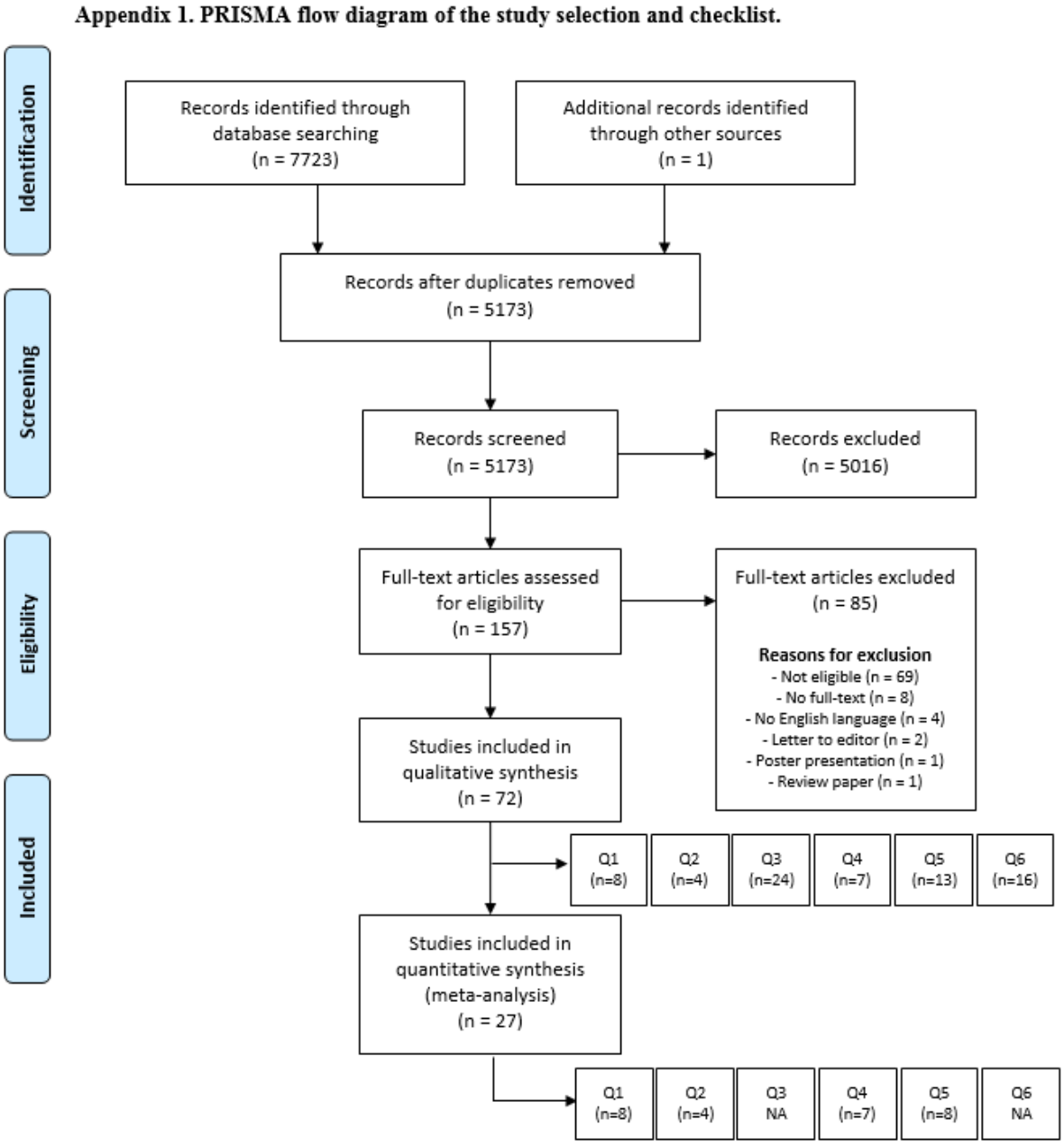

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Table 1. Outcome measures for the six review questions

Review questions	Primary outcome measure(s)	Secondary outcome measure(s)
1. Is laparoscopic hernia repair associated with better outcome compared to open repair?	1.1 Complications [a] 1.2 recurrence rate	1.3 Incidence of MCIH 1.4 Duration of surgery (including anesthesia) 1.5 Length of hospital stay 1.6 Time to full recovery
2. Which laparoscopic technique is associated with better outcome: the extra-peritoneal approach or trans-peritoneal approach?	2.1 Recurrence rate	2.2 Duration of surgery (including anesthesia) 2.3 Conversion to open surgery 2.4 Complications [a]
3. Should contralateral inguinal exploration be performed at the time of open unilateral inguinal hernia repair?	3.1 Incidence of MCIH	3.2 Complications [a] 3.3 Duration of surgery (including anesthesia) 3.4 Recurrence rate
4. In preterm infants, should hernia repair be performed before or after hospital discharge or discharge from the Neonatal Intensive Care Unit (NICU)?	4.1 Incarceration rate	4.2 Recurrence 4.3 Reoperation rate 4.4 Postoperative complications 4.5 Respiratory difficulties 4.6 Duration of surgery 4.7 Length of hospital stay
5. In preterm infants, is regional anesthesia associated with better outcome compared to general anesthesia?	5.1 Postoperative apnea's	5.2 Postoperative complications (bradycardia and hypotension) 5.3 Postoperative pain 5.4 Failure of regional anesthesia 5.5 Neurodevelopmental outcome at two years of age
6. Should hernia repair in girls with irreducible ovary without symptoms of incarceration or ischemia be performed as an emergency surgery?	6.1 Ovarian complications [b]	6.2 Recurrence rate

MCIH, metachronous contralateral inguinal hernia

[a] Complications included both operative and postoperative complications: vessel injury, bleeding, anesthetic complications, hematoma, hydrocele, apnea, wound infection and testicular ascent/atrophy

[b] Defined as ovarian torsion, strangulation, ischemia or atrophy

Table 2. Oxford Centre for Evidence-Based Medicine 2011 Classification of levels of evidence and grades of recommendation (adapted from www.cebm.net).

Level of evidence	Grade of Recommendation
1. Systematic review of randomized trials or *n*-of -1 trials	A. Consistent Level 1 studies
2. Randomized trial or observational study	B. Consistent Level 2 or 3 studies or extrapolation from Level 1 studies
3. Non-randomized controlled cohort/follow-up study	C. Level 4 studies or extrapolations from Level 2 or 3 studies
4. Case-series, case-control studies or historically controlled studies	D. Level 5 evidence or inconsistent or inconclusive studies of any level
5. Mechanism-based reasoning (expert opinion)	

Table 3. Results of the meta-analysis for all outcomes for research question 1, 2, 4 and 5.

Outcome measures	Patients (n)	OR (95% CI)	Mean difference (95% CI)	p-value	Favors
Question 1. Is laparoscopic hernia repair (LH) associated with better outcome compared to open repair (OH)?					
Primary					
1.1 Complications: intraoperative	419	3.16 (0.34 to 29.60)	N/A	0.31	-
1.1 Complications: postoperative	622	0.37 (0.10 to 1.32)	N/A	0.13	-
1.2 Recurrence rate	693	0.88 (0.20 to 3.88)	N/A	0.87	-
Secondary					
1.3 Incidence of MCIH	343	0.28 (0.04 to 1.86)	N/A	0.19	-
1.4 Operation time (unilateral), *min*	434	N/A	0.62 (-5.70 to 6.95)	0.85	-
1.4 Operation time (bilateral), *min*	194	N/A	-7.19 (-10.04 to -4.34)	<0.001	LH
1.5 Length of hospital stay, *h*	565	N/A	0.74 (-0.38 to 1.87)	0.20	-
1.6 Time to full recovery, *h*	272	N/A	2.05 (-11.13 to 15.23)	0.76	-
Question 2. Which laparoscopic technique is associated with better outcome: the extra-peritoneal approach (EPA) or trans-peritoneal approach (TPA)?					
Primary					
2.1 Recurrence rate	833	1.22 (0.33 to 4.47)	N/A	0.77	-
Secondary					
2.2 Operation time (unilateral), *min*	93	N/A	-13.54 (-16.08 to -11.01)	<0.001	EPA
2.2 Operation time (bilateral), *min*	740	N/A	-9.84 (-16.66 to -3.03)	0.005	EPA
2.3 Conversion to open surgery	833	2.88 (0.29 to 28.28)	N/A	0.36	-
2.4 Complications: intraoperative vessel injury	833	0.55 (0.09 to 3.38)	N/A	0.52	-
2.4 Complications: postoperative wound infection	833	3.29 (0.17 to 64.65)	N/A	0.43	-
2.4 Complications: postoperative hydrocele	833	1.04 (0.32 to 3.30)	N/A	0.95	-
2.4 Complications: postoperative testicular atrophy	833	0.15 (0.01 to 3.76)	N/A	0.25	-
Question 4. In preterm infants, should hernia repair be performed before (early) or after (late) hospital discharge/discharge from the Neonatal Intensive Care Unit (NICU)?					
Primary					
4.1 Incarceration rate	604	1.42 (0.87 to 2.34)	N/A	0.16	-
Secondary					
4.2 Recurrence rate	519	3.52 (1.28 to 9.70)	N/A	0.01	Late
4.3 Reoperation rate	1468	1.60 (0.91 to 2.82)	N/A	0.10	-
4.4 Postoperative complications: testicular atrophy	165	N/A	N/A	N/A	
4.4 Respiratory difficulties	1930	4.90 (2.69 to 8.93)	N/A	<0.001	Late

Question 5. In preterm infants, is regional anesthesia associated with better outcome compared to general anesthesia?					
Primary					
5.1 Postoperative apnea's (overall)	571	0.68 (0.37 to 1.23)	N/A	0.20	-
5.1 Postoperative apnea [a]	541	0.46 (0.22 to 0.96)	N/A	0.04	Regional
5.1 Postoperative apnea within the first postoperative hour	465	0.60 (0.18 to 1.98)	N/A	0.41	-
5.1 Postoperative apnea in infants with preoperative apnea's	32	0.52 (0.11 to 2.45)	N/A	0.32	-
5.1 Postoperative apnea requiring intervention	470	0.11 (0.00 to 2.51)	N/A	0.17	-
5.2 Postoperative complications: bradycardia	135	0.75 (0.29 to 1.90)	N/A	0.54	-
5.2 Postoperative complications: hypotension	749	0.83 (0.01 to 95.94)	N/A	0.94	-
5.3 Postoperative pain	781	0.44 (0.31 to 0.63)	N/A	<0.001	Regional

CI, confidence interval; min, minutes; h, hours

[a] Pure regional anesthesia versus general anesthesia and sedation

Table 4. Outcome results for question 3: should contralateral exploration be performed at the time of unilateral hernia repair or not?

	Patients *n*	**Weighted average %**	**95% CI**
Intervention group (unilateral hernia repair <u>with</u> contralateral exploration)			
Positive contralateral exploration (i.e. PPV)	5726	63.49	56.88, 69.86
Complications	3230	1.97[a]	0.98, 3.29
Duration of surgery, *min*	-	-	-
Control group (unilateral hernia repair <u>without</u> contralateral exploration)			
Development of MCIH after unilateral hernia repair	3008	8.41	5.48, 11.90
Complications	30	16.67	NA
Duration of surgery, *min*	-	-	-

CI, confidence interval; min, minutes; MCIH, metachronous contralateral inguinal hernia repair

[a] Five studies assessed complications in the total study population, which also included patients who only underwent unilateral hernia repair

Question 1. Is laparoscopic hernia repair associated with better outcome compared to open repair?

Outcomes

1. Primary
   - Operative and post-operative complications
   - Recurrence rate

2. Secondary
   - MCIH
   - Duration of surgery (both operation and anesthesia)
   - Duration of hospital admission (time to full recovery)
   - Postoperative pain

Search strategy

Pubmed:

("hernia, inguinal"[MeSH] OR (("hernia"[tw] OR "hernias"[tw]) OR "herniorrhaphy"[tw] OR "herniotomy"[tw] AND "inguinal"[tw])) AND ("Child"[MeSH] OR "Child, preschool"[MeSH] OR "Young Adult"[MeSH] OR "Infant"[MeSH] OR "child"[tw] OR "children"[tw] OR "childhood"[tw] OR "schoolchild"[tw] OR "schoolchildren"[tw] OR "infant"[tw] OR "infants"[tw] OR "infancy"[tw] OR "boy"[tw] OR "boys"[tw] OR "boyhood"[tw] OR "girl"[tw] OR "girls"[tw] OR "girlhood"[tw] OR "youth"[tw] OR "youths"[tw] OR "toddler"[tw] OR "toddlers"[tw] OR "teen"[tw] OR "teens"[tw] OR "teenager"[tw] OR "Puberty"[Mesh] OR "puberty"[tw] OR "preschool"[tw] OR "pre school"[tiab] OR "pre-school"[tw] OR "juvenile"[tw] OR "young"[tw] OR "youngster"[tw] OR "youngsters"[tw] OR "schoolchild"[tw] OR "schoolchildren"[tw] OR "kid"[tw] OR "kids"[tw] OR "underage"[tw] OR "under age"[tw] OR "under aged"[tw] OR "puberal"[tw] OR "pubescent"[tw] OR "prepubescent"[tw] OR "prepuberty"[tw] OR "school age"[tw] OR "schoolage"[tw] OR "school ages"[tw] OR "Pediatrics"[Mesh] OR "Pediatrics"[tw] OR "Pediatric"[tw] OR "Paediatrics"[tw] OR "Paediatric"[tw]) AND ("laparoscopy"[MeSH] OR "laparoscopy"[tw] OR "laparoscopies"[tw] OR "laparoscopic"[tw] OR "minilaparoscopy"[tw] OR "minilaparoscopic"[tw]) AND ("Comparative Study" [Publication Type] OR compar*[tw] OR "open"[tw] OR "versus"[tw])

Embase:

(exp inguinal hernia/ OR (("hernia".mp. OR "hernias".mp.) OR "herniorrhaphy".mp. OR "herniotomy".mp. AND "inguinal".mp.)) AND (Exp Child/ OR exp young adult/ OR exp Infant/ OR "child".mp. OR "children".mp. OR "childhood".mp. OR "schoolchild".mp. OR "schoolchildren".mp. OR "infant".mp. OR "infants".mp. OR "infancy".mp. OR "boy".mp. OR "boys".mp. OR "boyhood".mp. OR "girl".mp. OR "girls".mp. OR "girlhood".mp. OR "youth".mp. OR "youths".mp. OR "toddler".mp. OR "toddlers".mp. OR "teen".mp. OR "teens".mp. OR "teenager".mp. OR exp Puberty/ OR "puberty".mp. OR "preschool".mp. OR "pre school".ti,ab. OR "pre-school".mp. OR "juvenile".mp. OR "young".mp. OR "youngster".mp. OR "youngsters".mp. OR "schoolchild".mp. OR "schoolchildren".mp. OR "kid".mp. OR "kids".mp. OR "underage".mp. OR "under age".mp. OR "under aged".mp. OR "puberal".mp. OR "pubescent".mp. OR "prepubescent".mp. OR "prepuberty".mp. OR "school age".mp. OR "schoolage".mp. OR "school ages".mp. OR exp Pediatrics/ OR "Pediatrics".mp. OR "Pediatric".mp. OR "Paediatrics".mp. OR "Paediatric".mp.) AND (exp laparoscopy/ OR "laparoscopy".mp. OR "laparoscopies".mp. OR "laparoscopic".mp. OR "minilaparoscopy".mp. OR

"minilaparoscopic".mp.) AND (exp Comparative Study/ OR compar*.mp. OR "open".mp. OR "versus".mp.)

Cochrane:

(("hernia" OR "hernias" OR "herniorrhaphy" OR "herniotomy") AND "inguinal") AND ("Adolescent" OR "Young Adult" OR "Infant" OR "child" OR "children" OR "childhood" OR "schoolchild" OR "schoolchildren" OR "infant" OR "infants" OR "infancy" OR "boy" OR "boys" OR "boyhood" OR "girl" OR "girls" OR "girlhood" OR "youth" OR "youths" OR "toddler" OR "toddlers" OR "teen" OR "teens" OR "teenager" OR "Puberty" OR "puberty" OR "preschool" OR "pre school" OR "pre-school" OR "juvenile" OR "young" OR "youngster" OR "youngsters" OR "schoolchild" OR "schoolchildren" OR "kid" OR "kids" OR "underage" OR "under age" OR "under aged" OR "puberal" OR "pubescent" OR "prepubescent" OR "prepuberty" OR "school age" OR "schoolage" OR "school ages" OR "Pediatrics" OR "Pediatric" OR "Paediatrics" OR "Paediatric") AND ("laparoscopy" OR "laparoscopies" OR "laparoscopic" OR "minilaparoscopy" OR "minilaparoscopic") AND ("Comparative Study" OR compar* OR "open" OR "versus")

Question 1. Is laparoscopic hernia repair associated with better outcome compared to open repair?

Table 1. Risk of bias assessment in randomized controlled studies using ROB 2.0

Domains	Chan et al.	Celebi et al.	Gause et al.	Koivusalo et al.	Saranga et al.	Shalaby et al.	Inal et al.	Zhu et al.
	O1-O6	O1|O2|O4|O6	O1|O2|O4-O6	O1-O6	O1|O2|O4	O1|O2|O4|O5	O4	O1-O5
Bias arising from the randomization process	Low	Low	Low	Low	High	Low	Unclear	Low
Bias due to deviations from intended interventions	Low	Low	Low	Low	Unclear	Unclear	Unclear	Unclear
Bias due to missing outcome data	Low	Low	Low	Low	Low	Low	Low	Low
Bias in measurement of the outcome	Low	Low	Low	Low	Unclear	Unclear	Unclear	Unclear
Bias in selection of the reported result	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Overall	**Low**	**Low**	**Low**	**Low**	**Some concerns**	**Low**	**Low**	**Low**

The risk of bias is scored as “low”, “some concerns”, or “high”

O1 outcome 1 (complications), *O2* outcome 2 (recurrence rate), *O3* outcome 3 (incidence of metachronous contralateral inguinal hernia), *O4* outcome 4 (duration of surgery (including anesthesia)), *O5* outcome 5 (length of hospital stay), *O6* outcome 6 (time to full recovery)

Question 2. Which laparoscopic technique is associated with better outcome: the extra-peritoneal approach or trans-peritoneal approach?

Table 2 Risk of bias assessment in non-randomized studies using ROBINS-I

Domain	Bharathi et al.	Korkmaz et al.	Wang et al.
	O1-O7	O1-O7	O1-O7
Bias due to confounding	Serious	Serious	Serious
Bias in selection of participants into the study	Low	Low	Low
Bias in classification of interventions	Low	Low	Low
Bias due to deviations from intended interventions	Low	Low	Low
Bias due to missing data	Low	Low	Low
Bias in measurement of outcomes	Low	Low	Low
Bias in selection of the reported result	Low	Low	Low
Overall	**Serious**	**Serious**	**Serious**

The risk of bias is scored as "low", "moderate", "serious", "critical" or "NI: no information"

O1 outcome 1 (postoperative hernial recurrence), *O2* outcome 2 (intra-operative vessel injury), *O3* outcome 3 (intra-operative conversion to open), *O4* outcome 4 (postoperative hydrocele), *O5* outcome 5 (Postoperative testicular atrophy), *O6* outcome 6 (postoperative wound infection), *O7* outcome 7 (operation time (bilateral & unilateral))

Table 3 Risk of bias assessment in the randomized controlled study using ROB 2.0

Domain	Shalaby et al.
	O1-O7
Bias arising from the randomization process	Low
Bias due to deviations from intended interventions	Low
Bias due to missing outcome data	Low
Bias in measurement of the outcome	Low
Bias in selection of the reported result	Low
Overall	**Low**

The risk of bias is scored as "low", "some concerns", or "high"

O1 outcome 1 (postoperative hernial recurrence), *O2* outcome 2 (intra-operative vessel injury), *O3* outcome 3 (intra-operative conversion to open), *O4* outcome 4 (postoperative hydrocele), *O5* outcome 5 (Postoperative testicular atrophy), *O6* outcome 6 (postoperative wound infection), *O7* outcome7 (operation time (bilateral))

Question 3. Should contralateral inguinal exploration be performed at the time of open unilateral inguinal hernia repair?

Table 4 Risk of bias assessment in non-randomized studies using ROBINS-I

A.

Domain	Clausen et al.	Disma et al.	Gilbert et al.	Gunnlaugsson et al.		Holcomb et al.	Jona et al. (II)	Kalani et al.	Kling et al.	Laufer et al.
	O1	O1	O3	O1-O3	O4	O1-O3	O1|O2|O4	O1|O2|O4	O1	O2
Bias due to confounding	Serious	Moderate	Serious	Serious	Serious	Serious	Moderate	Serious	Critical	Serious
Bias in selection of participants into the study	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Bias in classification of interventions	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Bias due to deviations from intended interventions	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Bias due to missing data	NI	Low	NI	NI	NI	NI	NI	NI	NI	NI
Bias in measurement of outcomes	Low	Low	Low	Serious	Serious	Low	Serious	Low	Low	Low
Bias in selection of the reported result	NI	Low	NI	NI	NI	NI	NI	NI	NI	NI
Overall	**Serious**	**Moderate**	**Serious**	**Serious**	**Serious**	**Serious**	**Serious**	**Serious**	**Critical**	**Serious**

The risk of bias is scored as “low”, “moderate”, “serious”, “critical” or “NI: no information”

B.

Domain	Lugo Vincente et al.	Maillet et al.	Martin et al.	McLaughlin et al.	Moss et al.	Rescorla et al.	Rothenberg et al.	Simpson et al.
	O2-O4	O1|O2|O4	O3	O1-O4	O2	O1|O2|O4	O2	O2-O4
Bias due to confounding	Moderate	Serious	Serious	Critical	Serious	Serious	Serious	Serious
Bias in selection of participants into the study	Low	Low	Moderate	Moderate	Low	Low	Low	Moderate
Bias in classification of interventions	Low	Low	Low	Low	Low	Low	Low	Low
Bias due to deviations from intended interventions	Low	Low	Low	Low	Low	Low	Low	Low
Bias due to missing data	NI	NI	NI	NI	NI	NI	NI	NI
Bias in measurement of outcomes	Low	Low	NI	NI	Serious	Serious	Low	Serious
Bias in selection of the reported result	NI	Low	NI	NI	NI	NI	NI	NI
Overall	**NI**	**Serious**	**Serious**	**Critical**	**Serious**	**Serious**	**serious**	**Serious**

The risk of bias is scored as “low”, “moderate”, “serious”, “critical” or “NI: no information”

C.

Domain	Solomon et al.	Surana et al.	Tepas et al.	Wright et al.	Zampieri et al.
	O2	O1	O1	O1	O2 | O4
Bias due to confounding	Serious	Serious	Critical	Critical	Serious
Bias in selection of participants into the study	Low	Moderate	Low	Low	Serious
Bias in classification of interventions	Low	Low	Low	Low	Low
Bias due to deviations from intended interventions	Low	Low	Low	Low	Low
Bias due to missing data	NI	NI	NI	NI	NI
Bias in measurement of outcomes	Low	Serious	Low	Low	Low
Bias in selection of the reported result	NI	NI	NI	NI	NI
Overall	**Serious**	**Serious**	**Critical**	**Critical**	**Serious**

The risk of bias is scored as “low”, “moderate”, “serious”, “critical” or “NI: no information”

O1 outcome 1 (incidence of metachronous contralateral inguinal hernia), *O2* outcome 2 (complications), *O3* outcome 3 (duration of surgery), *O4* outcome 4 (recurrence rate)

Question 4. In preterm infants, should the hernia repair be performed before or after hospital discharge or discharge from the Neonatal Intensive Care Unit (NICU)?

Table 5 Risk of bias assessment in non-randomized studies using ROBINS-I

Domain	Crankson et al. 2015		Khan et al. 2018		Lee et al. 2011	Pandey et al. 2016	Sulkowski et al. 2015	Takahashi et al. 2012	Young et al. 2018	
	O1-O2	O3	O1-O2	O3	O1 | O3	O1-O3	O1-O3	O1-O3	O1-O2	O3
Bias due to confounding	Serious	Serious	Serious	Serious	Serious	Serious	Serious	Serious	Serious	NA
Bias in selection of participants into the study	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	NA
Bias in classification of interventions	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	NA
Bias due to deviations from intended interventions	Low	Moderate	Moderate	Moderate	Low	Low	Moderate	Low	Low	NA
Bias due to missing data	Low	Low	Low	Low	Low	Low	Moderate	Low	Low	NA
Bias in measurement of outcomes	Moderate	Serious	Moderate	Serious	Moderate	Moderate	Moderate	Moderate	Moderate	NA
Bias in selection of the reported result	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	NA
Overall	**Serious**	**Serious**	**Serious**	**Serious**	**Serious**	**Serious**	**Serious**	**Serious**	**Serious**	**NA**

The risk of bias is scored as “low”, “moderate”, “serious”, “critical” or “NI: no information”

O1 outcome 1 (incarceration rate), *O2* outcome 2 (recurrence rate/reoperation rate), *O3* outcome 3 (respiratory difficulties)

Question 5. In preterm infants, is regional anesthesia associated with better outcome compared to general anesthesia?

Table 6. Risk of bias assessment in randomized controlled studies using ROB 2.0

Domain	Welborn et al. 1990	Krane et al. 1995	Somri et al. 1998	Kunst et al. 1999	Williams et al. 2001	El-Gohari et al. 2004	Das et al. 2005	GAS trials 2015-2019
	O1-2	O2-3	O1-4	O1-2	O1|O2|O4	O1|O4	O1|O3|O4	O1-5
Bias arising from the randomization process	High	High	High	Some concerns	Some concerns	High	Low	Low
Bias due to deviations from intended interventions	Some concerns	NI	NI	NI	Some concerns	Some concerns	Low	Low
Bias due to missing outcome data	Low	Low	High	Low	High	High	Low	Low
Bias in measurement of the outcome	Low	Low	Some concerns	High	Some concerns	High	Some concerns	Low
Bias in selection of the reported result	Some concerns	Some concerns	High	High	Some concerns	NI	Some concerns	Low
Overall	**Some concerns**	**Some concerns**	**High**	**High**	**Some concerns**	**High**	**Some concerns**	**Low**

The risk of bias is scored as “low”, “some concerns”, “high” or “NI”: no information

O1 outcome 1 (Postoperative apneas), *O2* outcome 2 (Postoperative complications : bradycardia/hypotension), *O3* outcome 3 (Postoperative pain), *O4* outcome 4 (Incidence of failure of regional analgesia), *O5* outcome 5 (Neurodevelopmental outcome at 2 years of age).

Question 6. Should the hernia repair in girls with irreducible ovary without symptoms of incarceration or ischemia be performed as an emergency surgery?

Table 7. Risk of bias assessment in non-randomized studies using ROBINS-I

Domain	Boley et al.	Stylianos et al.	Merriman et al.	Huang et al.	Takehara et al.	Houben et al.	Hirabayashi et al.	Lee et al.	Chen et al.	Esposito et al.	Marinkovic et al.	Turk et al.
	O1	O1	O1	O1	O1	O1 I O2	O1	O1 I O2	O1	O1 I O2	O1	O1
Bias arising from the randomization process	Serious	Serious	Serious	Serious	Serious	Serious	Serious	Serious	Serious	Moderate	Moderate	Moderate
Bias due to deviations from intended interventions	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Bias due to missing outcome data	moderate	Serious	Moderate	Moderate	Moderate	Low	Low	Low	Low	Low	Serious	NI
Bias in measurement of the outcome	Low	Serious	Moderate	Moderate	Low	Low	Low	Moderate	Moderate	Low	Serious	NI
Bias in selection of the reported result	NI	NI	NI	NI	Ni	Moderate	Low	NI	Low	Low	NI	Moderate
Overall	**Serious**	**Serious**	**Serious**	**Serious**	**Serious**	**Serious**	**Serious**	**Serious**	**Serious**	**Moderate**	**Serious**	**Serious**

The risk of bias is scored as “low”, “moderate”, “serious”, “critical” or “NI: no information”

O1 outcome 1 (complications); *O2* outcome 2 (recurrence rate)

Table 1. Study characteristics and patient demographics of studies comparing laparoscopic and open hernia repair in children (review question 1).

Table 2. Table 1. Study characteristics and patient demographics of studies comparing extra-peritoneal (EPA) versus trans-peritoneal (TPA) laparoscopic hernia repair in children (review question 2).

							Laterality		Approach		
Author	**Year**	**Country**	**Study design**	**Patients, *n***	**Male, *n* (%)**	**Age range**	**Unilateral, *n***	**Bilateral, *n***	**EPA, *n* (%)**	**TPA, *n* (%)**	**Follow-up, mean**
Bharati et al.	2008	India	Retrospective cohort	163	143 (87.7)	1-14 yr	146	17	112 (68.7)	51 (31.3)	3 mo
Shalaby et al.	2010	Egypt	RCT	150	120 (80)	2-96 mo	Unclear	Unclear	75 (50)	75 (50)	24 mo
Korkmaz et al.	2018	Turkey	Retrospective cohort	71	31 (43.7)	3.5-60 mo	64	7	24 (33.8)	47 (66.2)	-
Wang et al.	2019	China	Retrospective cohort	599	533 (89)	40.5 ±31.6 mo	530	69	412 (68.8)	187 (31.2)	26 mo
EPA, extra-peritoneal approach; TPA, trans-peritoneal approach; RCT, randomized clinical trial; yr, year; mo, months											

Table 3. Study characteristics, patient demographics and hernia characteristics of patients with unilateral inguinal hernia who underwent contralateral inguinal exploration or not (i.e. control group)(review question 3).

Study	**Year**	**Study design**	**Patients, *n***	**Male, *n*(%)**	**Age range**	**Positive CE, *n* (%)**	**Control group, *n*[a]**	**Development of MCIH, *n* (%)**	**Follow-up, mean (range)**
Rothenberg et al.	1955	Retrospective cohort	50	3 (6)	1 mo - 12 yr	37 (74)	-	-	-
Clausen et al.	1958	Retrospective cohort	164	Unclear	0-2 yr, >2 yr	79 (48.2)	708	36 (7.6)	3yr
McLaughlin et al.	1960	Retrospective cohort	108	Unclear	0-3 yr	60 (55.6)	-	-	-
Gilbert et al.	1960	Prospective cohort	100	13 (13)	0-4 yr, >4 yr	59 (59)	-	-	-
Laufer et al.	1961	Prospective cohort	120	16 (13.3)	0-9 yr	76 (63.4)	-	-	-
Martin et al.	1961	Prospective cohort	55	10 (18.2)	1 mo - 12 yr	46 (83.6)	-	-	-
Kling et al.	1963	Retrospective cohort	33	1 (3)	0-10 yr	22 (66.6)	530	54 (10.1)	>4yr
Holcomb et al.	1965	Prospective cohort	433	62 (14.3)	10 h – 12 yr	242 (56)	-	-	-
Solomon et al.	1967	Prospective cohort	100	13 (13)	0-14 yr	40 (40)	-	-	-
Gunnlaugsson et al.	1967	Retrospective cohort	174	Unclear	0-15 yr	153 (88)	11	2 (18)	-
Simpson et al.	1968	Retrospective cohort	218	Unclear	0-15 yr	188 (86)	-	-	-
Rowe et al.	1969	Retrospective cohort	1,965	Unclear	0-16 yr	946 (48)	-	-	-

Kalani et al.	1972	Prospective cohort	100	Unclear	0-10 yr	61 (61)	30	3 (10)	3yr
Wright et al.	1982	Retro- and prospective cohort	100	100 (100)	0-12 yr	39 (39)	8	2 (25)	-
Resclorla et al.	1984	Retrospective cohort	92	85/100*	0-2 mo	81 (88)	8	3 (37.5)	-
Tepas et al.	1985	Prospective cohort	121	0 (0)	0-6 mo	75 (61)	179[b]	2 (1.1)	3-6yr
Moss et al.	1991	Retrospective cohort	300	Unclear	0-2 mo	255 (85)	-	-	27 mo
Surana et al.	1992	Retrospective cohort	390	53 (13.6)	0-2 yr	191 (49)	551	54 (9.8)	-
Gupta et al.	1993	Retrospective cohort	9	7 (77.8)	0-12 yr	Unclear	-	-	-
Lugo Vincente et al.	1995	Retrospective cohort	116	89/161*	0-6 yr, >6 yr	85 (73)	-	-	6 yr
Jona et al.	1996	Retrospective cohort	320	252 (78.8)	3 wk – 6 yr	Unclear	-	-	-
		Prospective cohort	331	265 (80.1)	<6 yr	183 (55)	41	6 (14)	10 yr
Zampieri et al.	2008	Retrospective cohort	118	0 (0)	1 mo – 8 yr	56 (47.5)	-	-	3 mo
Maillet et al.	2014	Retrospective cohort	407	407 (100)	12 dy – 492 dy	204 (50.1)	575	60 (11)	12 mo
Disma et al.	2018	RCT with cohort	131	Unclear	Unclear	90 (68.9)	367	10 (2.7)	24 mo

CE, contralateral exploration; RCT, randomized controlled trial; dy, day; wk, weeks; mo, months; yr, year

[a] Control group existed of patients who only underwent unilateral inguinal hernia repair without contralateral exploration

[b] Patients in the unilateral hernia repair group were all male aged between 6-24 months

* Total study population also comprised patients with unilateral inguinal hernia who did not undergo contralateral exploration

Table 4. Study characteristics, patient demographics and hernia characteristics of preterm infants undergoing hernia repair before and after discharge from the hospital or neonatal intensive care unit (NICU)(review question 4).

					Timing of surgery				Laterality, *%*
Author	**Year**	**Country**	**Study design**	**Patients, *n***	**Before discharge**	**After discharge**	**Male, *n* (%)**	**PCA at surgery, mean (SD) / (range), weeks**	**Right, left, bilateral hernia**
Crankson et al.	2015	Saudi Arabia	Retrospective cohort	84	23	61	74 (88)	B: 39.5 ± 3.1 A: 62.9 ± 32.6	B: 40.1, 30.4, 30.4 A: 39.3, 31.1, 29.5
Khan et al.	2018	USA	Retrospective cohort	263	115	148	(male : female) 3.3 : 1	B: 39.5 (4) A: 40.8 (7.4)	Unclear
Lee et al.	2011	USA	Retrospective cohort	80	45	35	65 (81%)	B: 37.0 ± 6.7 A: 44.1 ± 7.9	85% bilateral
Pandey et al.	2017	USA	Retrospective cohort	39	23	16	B: 17 (74) A: 11 (69)	B: 41.6 ± 3.9 A: 45.4 ± 4.6	B: 13, 8.6, 78.3 A: 31.3, 25, 43.7
Sulkowski et al.	2015	USA	Retrospective cohort	1,421	938	483	B: 776 (82.7) A: 430 (89)	B: 38 (36, 41) A: 49 (43, 55)	Unclear

Takahashi et al.	2012	Japan	Retrospective cohort	47	14	33	B: 7 (50) A: 21 (64)	B: 42.2 ± 5.7 A: 48.8 ± 3.7	Unclear
Youn et al.	2018	South Korea	Retrospective cohort	90	18	72	B: 13 (82.2) A: 59 (81.9)	13 (2.7–58)	25.5, 26.7, 47.8
PCA, post conceptional age; SD, standard deviation; B, before discharge; A, after discharge									

Table 5. Study characteristics and patient demographics of preterm infants undergoing hernia repair under general or regional anesthesia (review question 5).

					Type of anesthesia			
Author	**Year**	**Country**	**Study design**	**Patients, *n***	**Central regional**	**General**	**GA at birth mean/median(*); ±SD / (range), weeks**	**PCA at surgery, mean/median(*); ±SD / (range), weeks**
Welborn et al.	1990	USA	RCT	36	20	16	C: 31.4 (25-36) G: 31.8 (25-36)	C: 40.8 (35-46) G: 43.3 (38-51)
Krane et al.	1995	USA	RCT	18	9	9	C: 29.2 ± 3.6 G: 29.9 ± 3.9	C: 42.3 ± 4.1 G: 40.9 ± 2.1
Somri et al.	1998	Israel	RCT	40	20	20	C: 33.1 ± 4.0 G: 32.7 ± 3.2	C: 43.7 ± 5.3 G: 44.2 ± 5.4
Kunst et al.	1999	Germany	RCT	17	8	9	C: 26.9 ± 2.0 G: 29.7 ± 3.7	
Williams et al.	2001	UK	RCT	24	10	14	C: 28* (26, 33) G: 30* (23, 35)	C: 40* (36, 44) G: 38* (32-46)
El Gohari et al.	2004	Egypt	RCT	30	15	15	Not specified	Not specified
Das et al.	2005	India	RCT	30	15	15	Not specified	Not specified
GAS Study	2015	Multicenter	RCT	711	355	356	C: 35.5 ± 4.1 G: 35.5 ± 3.9	C: 45.5 ± 4.7 G: 45.6 ± 4.6
RCT, randomized controlled trial; GA, gestational age; PCA, post-conceptional age; SD, standard deviation; C, central regional; G, general								

Table 6. Study characteristics, patient demographics and hernia characteristics of girls with irreducible hernias (review question 6).

Author	*Year*	*Country*	*Study design*	*Patients n*	*Age, median (range)*	*Hernia characteristics*	*Ovarian complications*		*Oophorectomy*	*Follow-up (range)*
						Irreducible / incarcerated hernia	*Ischemia n (%)*	*Torsion n (%)*		
Boley et al.	1991	USA	Retrospective cohort	15	Unclear	Irreducible ovarian hernia	0	4 (27)		-
Stylianos et al.	1993	USA	Retrospective cohort	85	Unclear	Incarcerated hernia	Unclear	Unclear[b]		-
Merriman et al.	2000	USA	Retrospective cohort	71	8 wk (2 wk-3 yr)	Irreducible hernias (n=71) Ovarian hernias (n=58/71)	4[a]	11/58 (15.5)	3	-
Huang et al.	2003	Taiwan	Retrospective cohort	32	1-18 mo	Asymptomatic movable palpable mass over the labium major	Unclear	Unclear		-
Takehara et al.	2009	Japan	Retrospective cohort	15	(4 wk – 4 yr)	Irreducible ovarian hernia (n=11) / Incarcerated hernia (n=4)	0	**4**	1	-
Houben et al.	2015	China	Retrospective cohort	3	12 mo (2 wk-16 yr)	Irreducible ovarian hernia	1	0	1	-
Hirabayashi et al.	2017	Japan	Retrospective cohort	71	1.5 mo	Ovarian hernias	1/58[c]	0 (0)		-
Lee et al.	2018	Korea	Retrospective cohort	66	Mean 3.8 mo ± 3.9	PO: Incarcerated inguinal hernia (n=66) IO: ovarian hernia (n=51/66)	3	0	1	29.2 mo (2–64)
Chen et al.	2018	China	Retrospective cohort	32	< 1 yr	Incarcerated ovarian hernias (n=32)	3	6		-
Esposito et al.	2019	Italy	Retrospective cohort	37	0-7 yr	Preoperative asymptomatic irreducible hernias (n=16) Intraoperative ovarian hernias (n=37)	0 (0)	0 (0)		36 mo (1–60)
Marinkovic et al.	1998	Serbia	Retrospective cohort	93	Mean 6 wk	PO: Incarcerated inguinal hernias (n=93) IO: Irreducible ovaries (n=35)	0	5 (14)	2	-
Turk et al.	2013	Turkey	Retrospective cohort	7	0-2 mo	Irreducible hernias	0 (0)	0 (0)		-

NFS, not further specified; PO, preoperative; IO, intraoperative; wk, week; yr, year; mo, months

[a] *mildly swollen and bruised*

[b] *It was only reported that infarction of the testis or ovary occurred in 17 (20%) patients, though not further specified.*

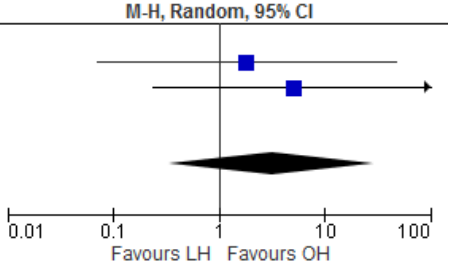
[c] *In one patient the hernia sac containing fallopian tube and ovary was ligated by accident. In 58 out of 71 patients with ovarian hernias surgical repair was performed.*

Meta-analysis of primary and secondary outcomes between laparoscopic and open hernia repair in children.

1.1A Perioperative complications

Study or Subgroup	LH Events	LH Total	OH Events	OH Total	Weight	Odds Ratio M-H, Random, 95% CI
Celebi 2014	0	28	0	31		Not estimable
Gause 2016	1	26	0	15	47.0%	1.82 [0.07, 47.61]
Saranga 2008	2	35	0	34	53.0%	5.15 [0.24, 111.30]
Shalaby 2012	0	125	0	125		Not estimable
Total (95% CI)		**214**		**205**	**100.0%**	**3.16 [0.34, 29.60]**
Total events	3		0			

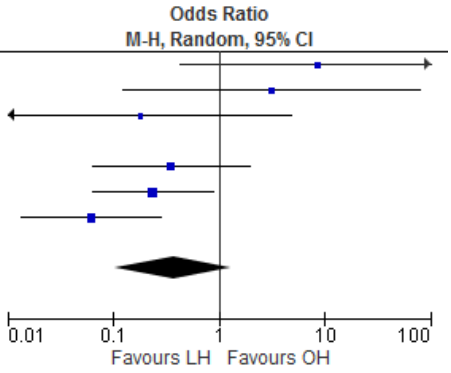
Heterogeneity: Tau² = 0.00; Chi² = 0.21, df = 1 (P = 0.65); I² = 0%
Test for overall effect: Z = 1.01 (P = 0.31)



1.1B Postoperative complications

Study or Subgroup	LH Events	LH Total	OH Events	OH Total	Weight	Odds Ratio M-H, Random, 95% CI
Celebi 2014	3	28	0	31	11.6%	8.65 [0.43, 175.22]
Chan 2005	1	41	0	42	10.5%	3.15 [0.12, 79.54]
Gause 2016	0	26	1	15	10.4%	0.18 [0.01, 4.77]
Koivusalo 2008	0	47	0	42		Not estimable
Saranga 2008	2	35	5	34	20.6%	0.35 [0.06, 1.95]
Shalaby 2012	3	87	12	92	24.5%	0.24 [0.06, 0.88]
Zhu 2015	2	53	19	49	22.4%	0.06 [0.01, 0.28]
Total (95% CI)		**317**		**305**	**100.0%**	**0.37 [0.10, 1.32]**
Total events	11		37			

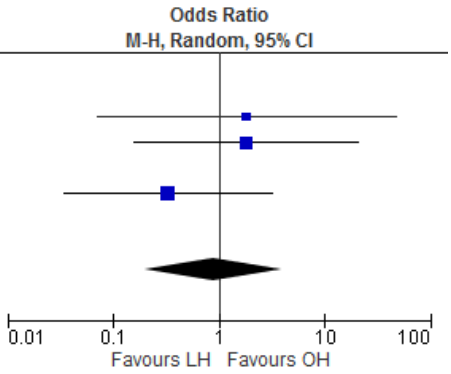
Heterogeneity: Tau² = 1.28; Chi² = 11.14, df = 5 (P = 0.05); I² = 55%
Test for overall effect: Z = 1.53 (P = 0.13)



1.2 Recurrence rate

Study or Subgroup	LH Events	LH Total	OH Events	OH Total	Weight	Odds Ratio M-H, Random, 95% CI
Celebi 2014	0	28	0	31		Not estimable
Chan 2005	0	41	0	42		Not estimable
Gause 2016	1	26	0	15	20.6%	1.82 [0.07, 47.61]
Koivusalo 2008	2	47	1	42	37.0%	1.82 [0.16, 20.85]
Saranga 2008	0	35	0	34		Not estimable
Shalaby 2012	1	125	3	125	42.4%	0.33 [0.03, 3.20]
Zhu 2015	0	53	0	49		Not estimable
Total (95% CI)		**355**		**338**	**100.0%**	**0.88 [0.20, 3.88]**
Total events	4		4			

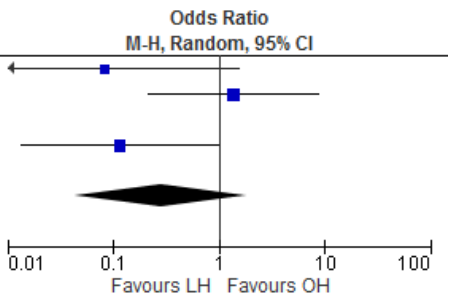
Heterogeneity: Tau² = 0.00; Chi² = 1.26, df = 2 (P = 0.53); I² = 0%
Test for overall effect: Z = 0.17 (P = 0.87)



1.3 Incidence of metachronous contralateral inguinal hernia (MCIH)

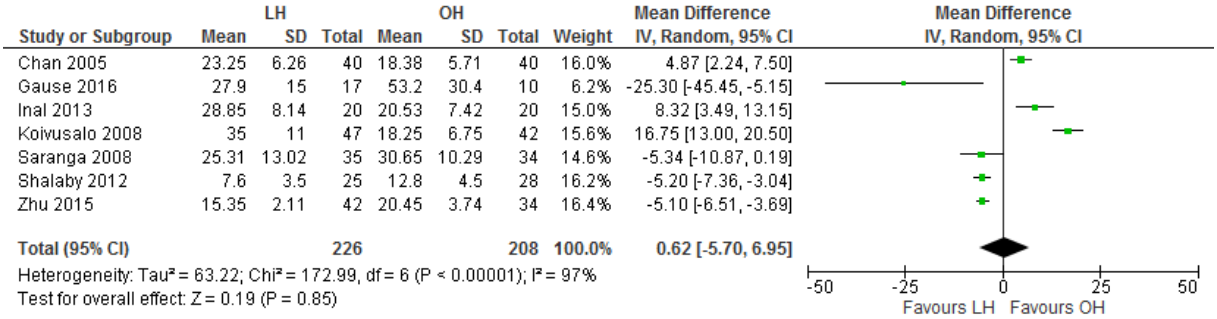
Study or Subgroup	LH Events	LH Total	OH Events	OH Total	Weight	Odds Ratio M-H, Random, 95% CI
Chan 2005	0	41	5	42	25.1%	0.08 [0.00, 1.54]
Koivusalo 2008	3	47	2	42	39.7%	1.36 [0.22, 8.58]
Saranga 2008	0	35	0	34		Not estimable
Zhu 2015	1	53	7	49	35.1%	0.12 [0.01, 0.98]
Total (95% CI)		**176**		**167**	**100.0%**	**0.28 [0.04, 1.86]**
Total events	4		14			

Heterogeneity: Tau² = 1.45; Chi² = 4.21, df = 2 (P = 0.12); I² = 52%
Test for overall effect: Z = 1.31 (P = 0.19)

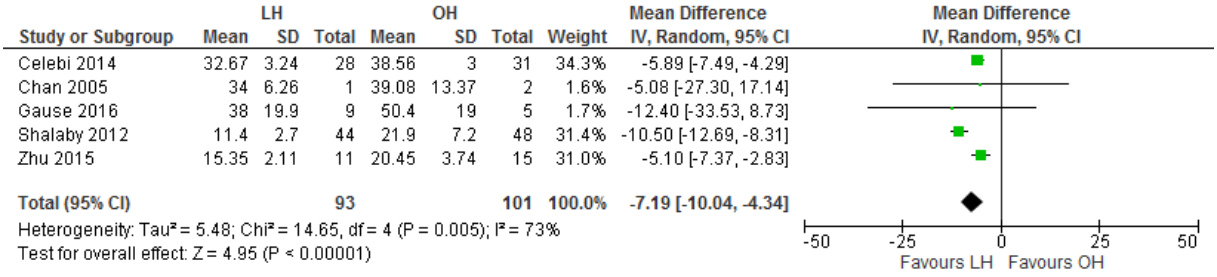


Meta-analysis of secondary outcomes between laparoscopic and open hernia repair in children (continued)

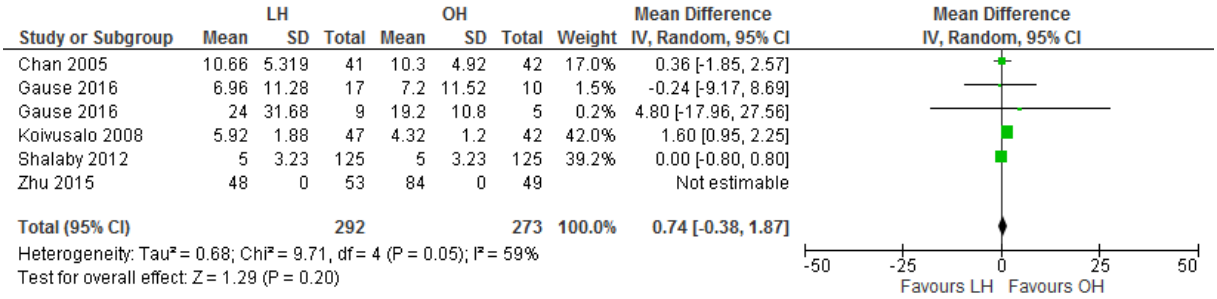
1.4A Unilateral operation time (in minutes)



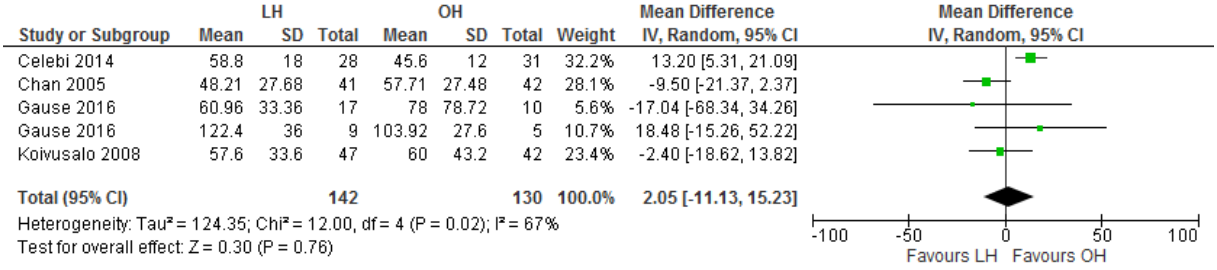
1.4B Bilateral operation time (in minutes)



1.5 Length of hospital stay (in hours)



1.6 Time to full recovery (in hours)



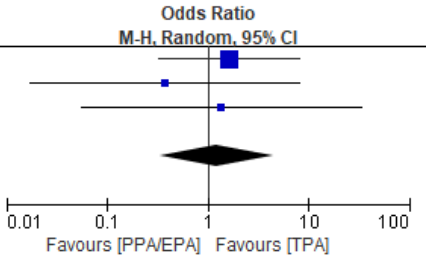
Question 2

Meta-analysis of primary and secondary outcomes between the pre-peritoneal approach and trans-peritoneal approach for inguinal hernia repair in children.

2.1 Recurrence rate

	EPA		TPA			Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
Bharathi 2008	7	112	2	51	65.6%	1.63 [0.33, 8.15]	2008
Korkmaz 2018	0	24	2	47	17.9%	0.37 [0.02, 8.05]	2018
Wang 2019	1	412	0	187	16.5%	1.37 [0.06, 33.71]	2019
Total (95% CI)		**548**		**285**	**100.0%**	**1.22 [0.33, 4.47]**	
Total events	8		4				

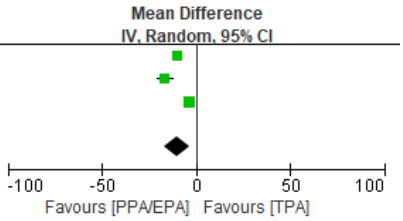
Heterogeneity: Tau² = 0.00; Chi² = 0.71, df = 2 (P = 0.70); I² = 0%
Test for overall effect: Z = 0.29 (P = 0.77)



2.2A Unilateral operation time (in minutes)

	EPA			TPA				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Bharathi 2008	15	3	101	25	7.5	45	33.8%	-10.00 [-12.27, -7.73]	2008
Korkmaz 2018	18.41	6.05	22	35.12	10.8	42	31.1%	-16.71 [-20.84, -12.58]	2018
Wang 2019	9.72	4.27	353	13.31	2.73	177	35.0%	-3.59 [-4.19, -2.99]	2019
Total (95% CI)			**476**			**264**	**100.0%**	**-9.84 [-16.66, -3.03]**	

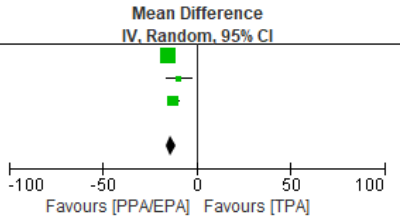
Heterogeneity: Tau² = 34.41; Chi² = 64.30, df = 2 (P < 0.00001); I² = 97%
Test for overall effect: Z = 2.83 (P = 0.005)



2.2B Bilateral operation time (in minutes)

	EPA			TPA				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Bharathi 2008	25	1.25	11	40	1.25	6	54.8%	-15.00 [-16.24, -13.76]	2008
Korkmaz 2018	32.5	3.54	2	42	5.7	5	10.9%	-9.50 [-16.50, -2.50]	2018
Wang 2019	13	1.32	59	25.5	4.7	10	34.3%	-12.50 [-15.43, -9.57]	2019
Total (95% CI)			**72**			**21**	**100.0%**	**-13.54 [-16.08, -11.01]**	

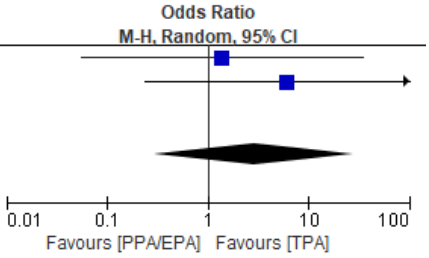
Heterogeneity: Tau² = 2.66; Chi² = 4.37, df = 2 (P = 0.11); I² = 54%
Test for overall effect: Z = 10.45 (P < 0.00001)



2.3 Conversion rate to open surgery

	EPA		TPA			Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
Bharathi 2008	1	112	0	51	50.3%	1.39 [0.06, 34.60]	2008
Korkmaz 2018	1	24	0	47	49.7%	6.06 [0.24, 154.61]	2018
Wang 2019	0	616	0	283		Not estimable	2019
Total (95% CI)		**752**		**381**	**100.0%**	**2.88 [0.29, 28.28]**	
Total events	2		0				

Heterogeneity: Tau² = 0.00; Chi² = 0.40, df = 1 (P = 0.53); I² = 0%
Test for overall effect: Z = 0.91 (P = 0.36)

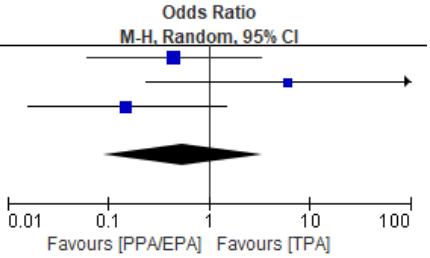


Meta-analysis of primary and secondary outcomes between the pre-peritoneal approach and trans-peritoneal approach for inguinal hernia repair in children (continued)

2.4A Intraoperative vessel injury

Study or Subgroup	EPA Events	EPA Total	TPA Events	TPA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Bharathi 2008	2	146	2	67	41.4%	0.45 [0.06, 3.27]	2008
Korkmaz 2018	1	24	0	47	22.7%	6.06 [0.24, 154.61]	2018
Wang 2019	1	616	3	283	35.9%	0.15 [0.02, 1.47]	2019
Total (95% CI)		**786**		**397**	**100.0%**	**0.55 [0.09, 3.38]**	
Total events	4		5				

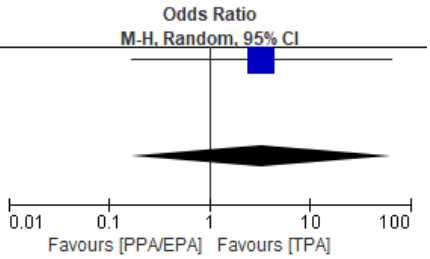
Heterogeneity: Tau² = 1.05; Chi² = 3.37, df = 2 (P = 0.19); I² = 41%
Test for overall effect: Z = 0.64 (P = 0.52)



2.4B Postoperative wound infection

Study or Subgroup	EPA Events	EPA Total	TPA Events	TPA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Bharathi 2008	3	146	0	67	100.0%	3.29 [0.17, 64.65]	2008
Korkmaz 2018	0	24	0	47		Not estimable	2018
Wang 2019	0	616	0	283		Not estimable	2019
Total (95% CI)		**786**		**397**	**100.0%**	**3.29 [0.17, 64.65]**	
Total events	3		0				

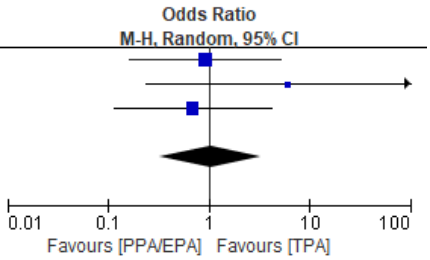
Heterogeneity: Not applicable
Test for overall effect: Z = 0.78 (P = 0.43)



2.4C Postoperative hydrocele

Study or Subgroup	EPA Events	EPA Total	TPA Events	TPA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Bharathi 2008	4	146	2	67	45.4%	0.92 [0.16, 5.13]	2008
Korkmaz 2018	1	24	0	47	12.8%	6.06 [0.24, 154.61]	2018
Wang 2019	3	616	2	283	41.8%	0.69 [0.11, 4.14]	2019
Total (95% CI)		**786**		**397**	**100.0%**	**1.04 [0.32, 3.30]**	
Total events	8		4				

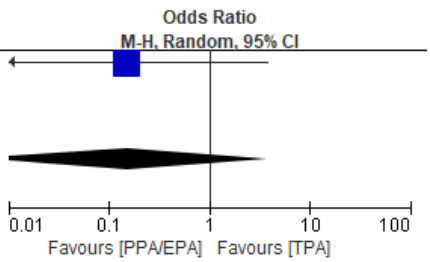
Heterogeneity: Tau² = 0.00; Chi² = 1.37, df = 2 (P = 0.50); I² = 0%
Test for overall effect: Z = 0.06 (P = 0.95)



2.4D Postoperative testicular atrophy

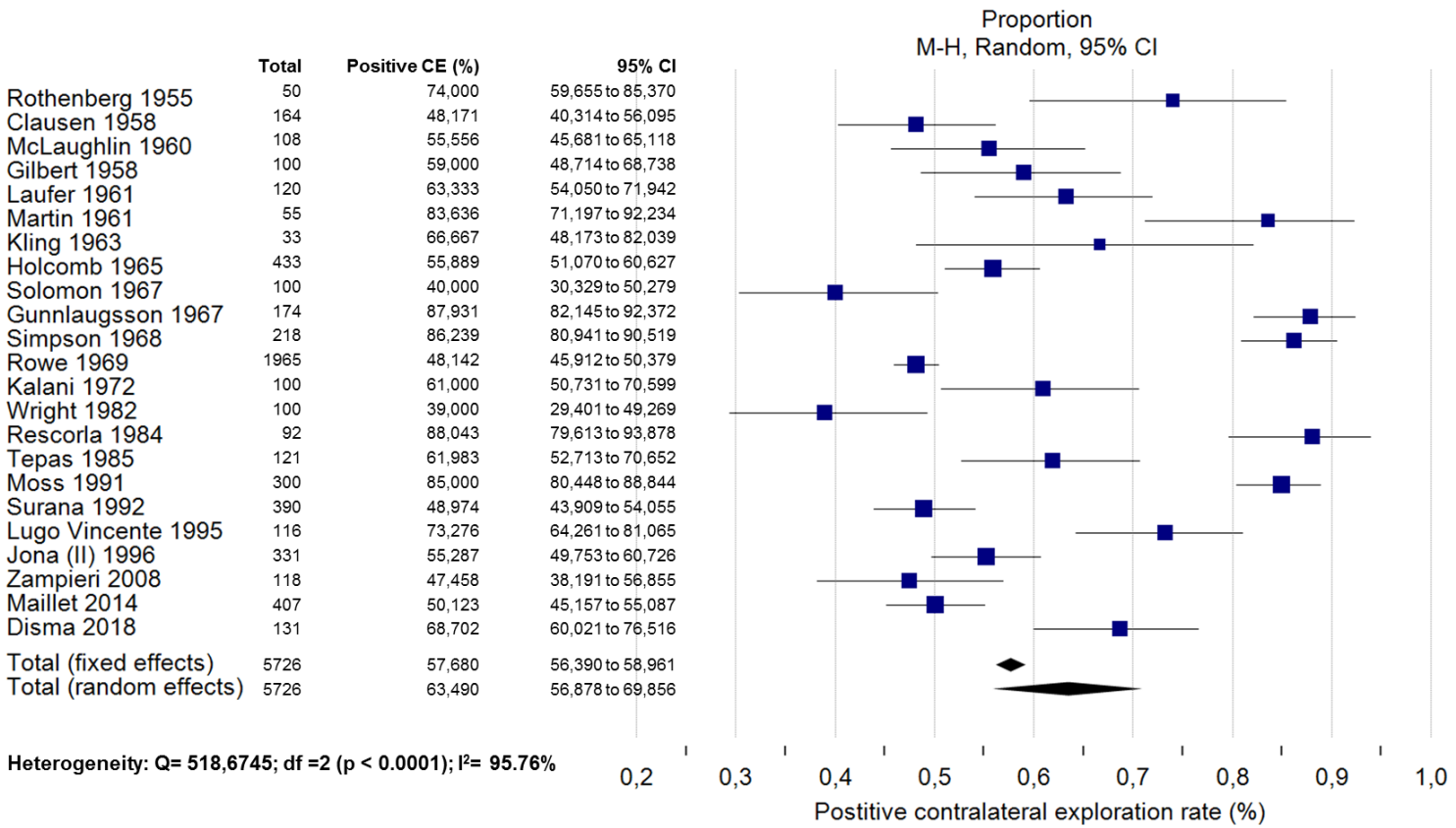
Study or Subgroup	EPA Events	EPA Total	TPA Events	TPA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Bharathi 2008	0	146	1	67	100.0%	0.15 [0.01, 3.76]	2008
Korkmaz 2018	0	24	0	47		Not estimable	2018
Wang 2019	0	616	0	283		Not estimable	2019
Total (95% CI)		**786**		**397**	**100.0%**	**0.15 [0.01, 3.76]**	
Total events	0		1				

Heterogeneity: Not applicable
Test for overall effect: Z = 1.15 (P = 0.25)

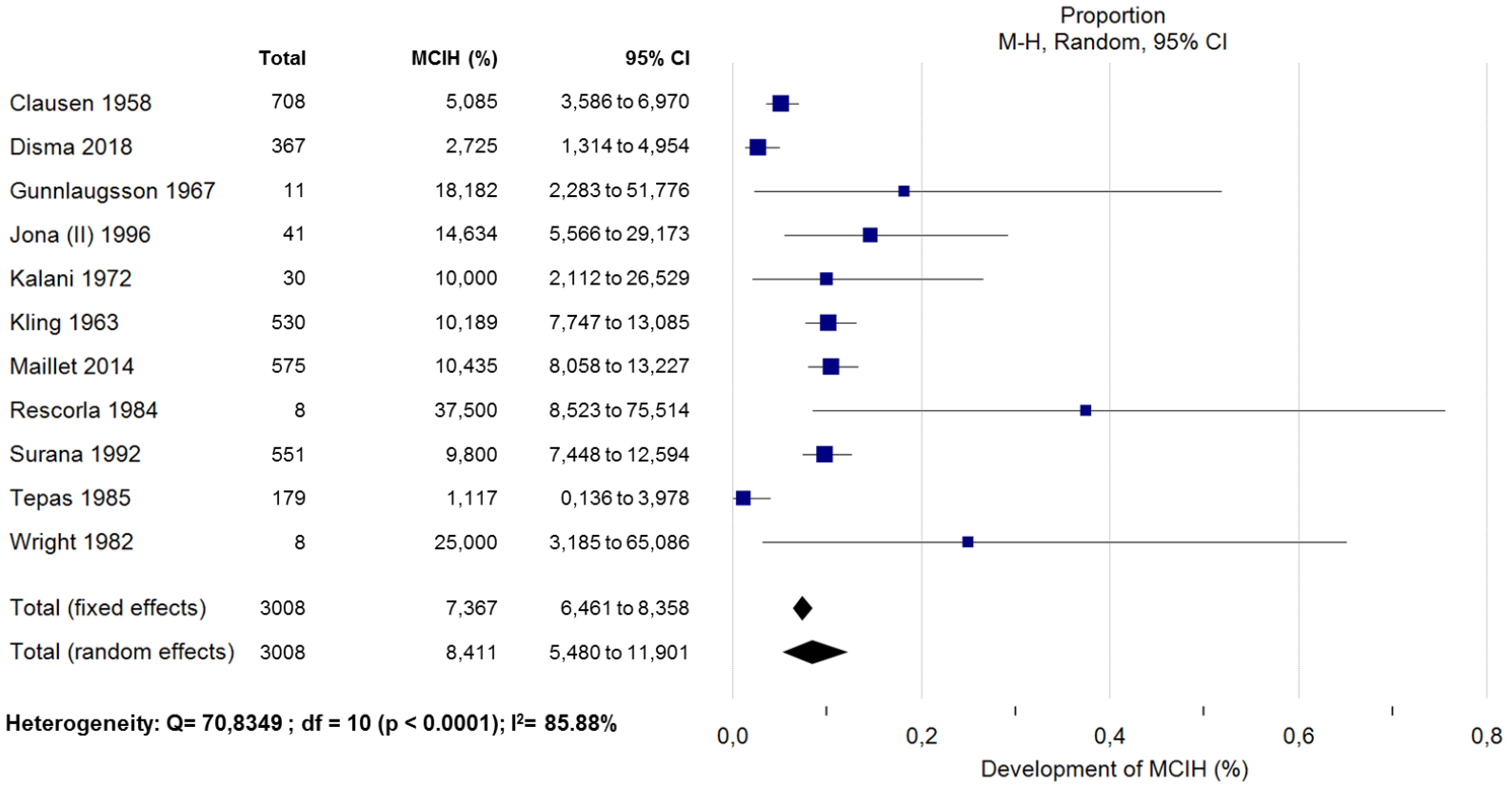


Question 3

A. Positive contralateral exploration rate (intervention group).



B. Development of MCIH in control group.



Heterogeneity: Q= 70,8349 ; df = 10 (p < 0.0001); I^2= 85.88%

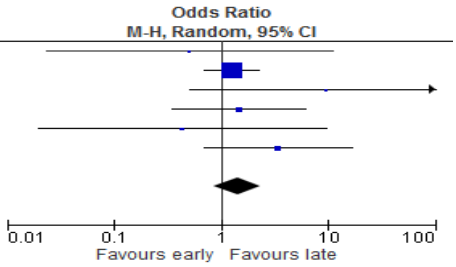
Question 4

Meta-analysis on primary and secondary outcomes between hernia repair before or after hospital discharge from the Neonatal Intensive Care Unit (NICU).

4.1 Incarceration

Study or Subgroup	Early Events	Early Total	Late Events	Late Total	Weight	Odds Ratio M-H, Random, 95% CI
Crankson 2015	0	23	2	61	2.6%	0.51 [0.02, 10.95]
Khan 2018	27	115	29	148	70.3%	1.26 [0.70, 2.28]
Lee 2011	5	45	0	35	2.9%	9.64 [0.51, 180.56]
Pandey 2017	8	23	4	15	12.0%	1.47 [0.35, 6.13]
Takahashi 2012	0	14	2	33	2.6%	0.43 [0.02, 9.64]
Youn 2018	3	18	4	72	9.6%	3.40 [0.69, 16.81]
Total (95% CI)		**238**		**364**	**100.0%**	**1.42 [0.87, 2.34]**
Total events	43		41			

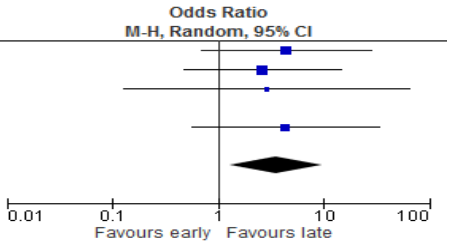
Heterogeneity: Tau² = 0.00; Chi² = 3.95, df = 5 (P = 0.56); I² = 0%
Test for overall effect: Z = 1.39 (P = 0.16)



4.2 Recurrence

Study or Subgroup	Early Events	Early Total	Late Events	Late Total	Weight	Odds Ratio M-H, Random, 95% CI
Crankson 2015	3	23	2	61	29.7%	4.42 [0.69, 28.42]
Khan 2018	4	115	2	148	34.9%	2.63 [0.47, 14.62]
Pandey 2017	2	23	0	12	10.6%	2.91 [0.13, 65.53]
Takahashi 2012	0	14	0	33		Not estimable
Youn 2018	2	18	2	72	24.8%	4.38 [0.57, 33.44]
Total (95% CI)		**193**		**326**	**100.0%**	**3.52 [1.28, 9.70]**
Total events	11		6			

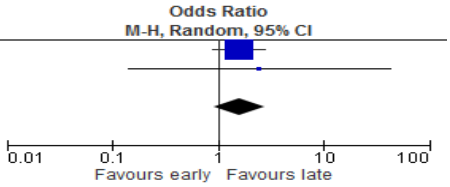
Heterogeneity: Tau² = 0.00; Chi² = 0.23, df = 3 (P = 0.97); I² = 0%
Test for overall effect: Z = 2.43 (P = 0.01)



4.3 Reoperation rate

Study or Subgroup	Early Events	Early Total	Late Events	Late Total	Weight	Odds Ratio M-H, Random, 95% CI
Sulkowski 2015	48	938	16	483	96.1%	1.57 [0.88, 2.80]
Takahashi 2012	1	14	1	33	3.9%	2.46 [0.14, 42.38]
Total (95% CI)		**952**		**516**	**100.0%**	**1.60 [0.91, 2.82]**
Total events	49		17			

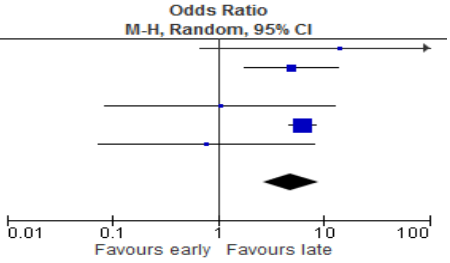
Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.76); I² = 0%
Test for overall effect: Z = 1.63 (P = 0.10)



4.4. Respiratory difficulties

Study or Subgroup	Early Events	Early Total	Late Events	Late Total	Weight	Odds Ratio M-H, Random, 95% CI
Crankson 2015	2	23	0	61	3.6%	14.30 [0.66, 309.90]
Khan 2018	17	115	5	148	23.0%	4.96 [1.77, 13.89]
Lee 2011	0	45	0	35		Not estimable
Pandey 2017	2	23	1	12	5.3%	1.05 [0.09, 12.88]
Sulkowski 2015	494	938	73	483	62.1%	6.25 [4.72, 8.27]
Takahashi 2012	1	14	3	33	5.9%	0.77 [0.07, 8.11]
Total (95% CI)		**1158**		**772**	**100.0%**	**4.90 [2.69, 8.93]**
Total events	516		82			

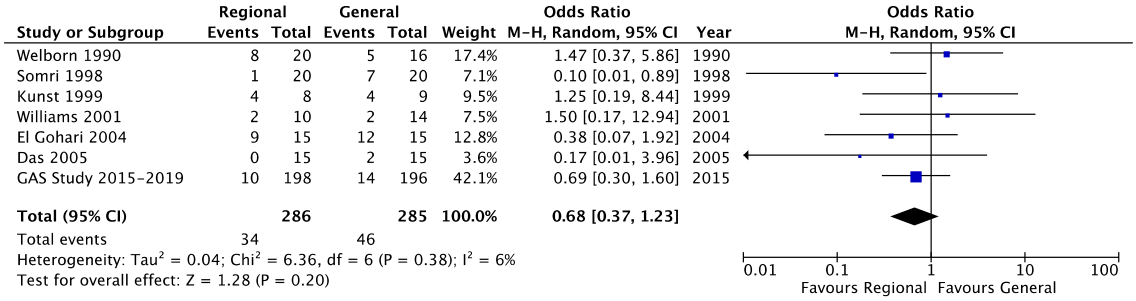
Heterogeneity: Tau² = 0.13; Chi² = 5.29, df = 4 (P = 0.26); I² = 24%
Test for overall effect: Z = 5.20 (P < 0.00001)



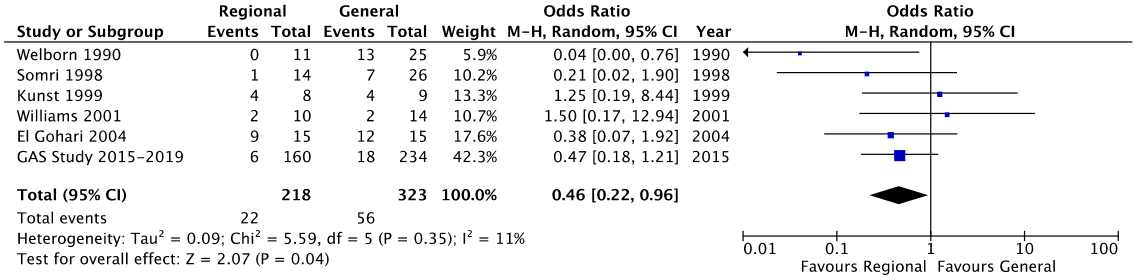
Question 5

Meta-analysis on the primary outcome between regional and general anesthesia in preterm infants.

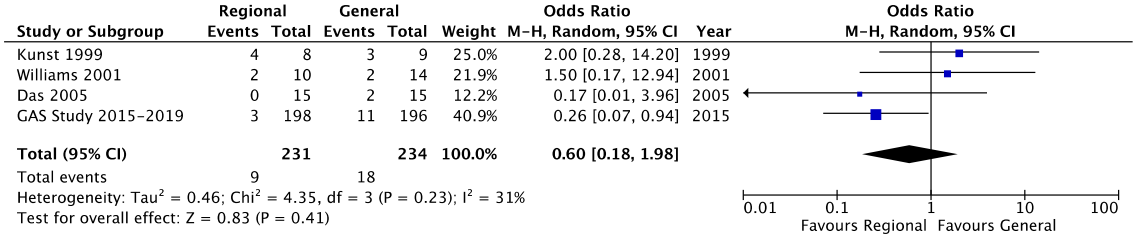
5.1A. Postoperative apnea in preterm infants (overall)



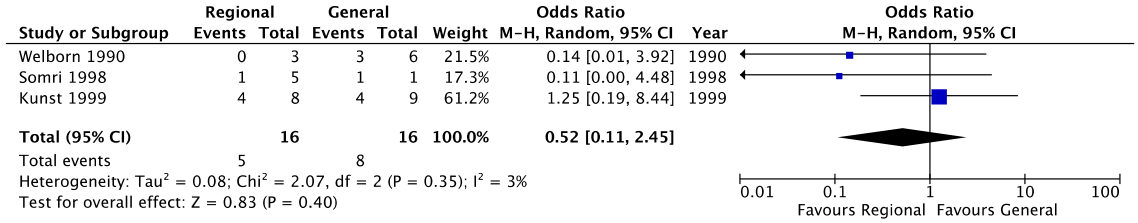
5.1B. Postoperative apnea in preterm infants : "pure" regional anesthesia vs general anesthesia and sedation



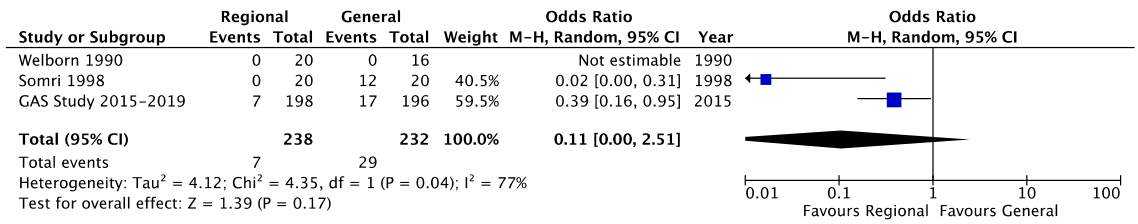
5.1C. Postoperative (early) apnea in preterm infants (within the first postoperative hour)



5.1D. Postoperative apnea in preterm infants with pre-operative apnea episodes



5.1E. Postoperative apnea requiring intervention (preterm infants)

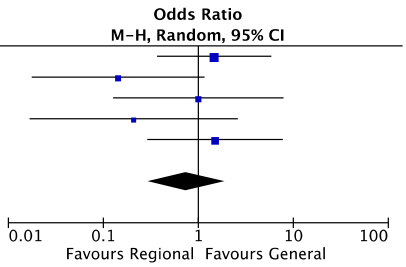


Meta-analysis on the secondary outcomes between regional and general anesthesia in preterm infants (continued)

5.2A. Postoperative bradycardia (preterm infants)

Study or Subgroup	Regional Events	Regional Total	General Events	General Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Welborn 1990	8	20	5	16	30.8%	1.47 [0.37, 5.86]	1990
Krane 1995	3	9	7	9	16.4%	0.14 [0.02, 1.16]	1995
Somri 1998	2	20	2	20	16.8%	1.00 [0.13, 7.89]	1998
Kunst 1999	5	8	8	9	11.9%	0.21 [0.02, 2.60]	1999
Williams 2001	6	10	7	14	24.1%	1.50 [0.29, 7.75]	2001
Total (95% CI)		**67**		**68**	**100.0%**	**0.75 [0.29, 1.90]**	
Total events	24		29				

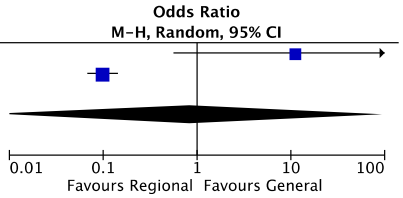
Heterogeneity: $Tau^2 = 0.24$; $Chi^2 = 5.04$, df = 4 (P = 0.28); $I^2 = 21\%$
Test for overall effect: Z = 0.61 (P = 0.54)



5.2B. Postoperative hypotension (preterm and term infants)

Study or Subgroup	Regional Events	Regional Total	General Events	General Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Somri 1998	4	20	0	20	45.2%	11.18 [0.56, 222.98]	1998
GAS Study 2015-2019	141	354	309	355	54.8%	0.10 [0.07, 0.14]	2015
Total (95% CI)		**374**		**375**	**100.0%**	**0.83 [0.01, 95.94]**	
Total events	145		309				

Heterogeneity: $Tau^2 = 10.65$; $Chi^2 = 9.99$, df = 1 (P = 0.002); $I^2 = 90\%$
Test for overall effect: Z = 0.07 (P = 0.94)



5.3 Postoperative pain (preterm and term infants)

Study or Subgroup	Regional Events	Regional Total	General Events	General Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Somri 1998	4	20	8	20	6.2%	0.38 [0.09, 1.54]	1998
Das 2005	15	15	15	15		Not estimable	2005
GAS Study 2015-2019	57	355	107	356	93.8%	0.45 [0.31, 0.64]	2015
Total (95% CI)		**390**		**391**	**100.0%**	**0.44 [0.31, 0.63]**	
Total events	76		130				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.05$, df = 1 (P = 0.82); $I^2 = 0\%$
Test for overall effect: Z = 4.57 (P < 0.00001)