

Outcomes of Visceral Arterial Reconstruction – A Systematic Review

Abstract

Aims: Review of synthetic grafts (SG) and autologous vein grafts (AVG) in visceral arterial reconstruction (VAR) in chronic visceral ischemia.

Methods: Systematic review methodology was employed.

Results: Six studies were included (218 patients and 281 vessels). Two studies had data about AVG only, three had data about SG only and one had both AVG and SG data. Three studies reported outcomes for AVG (117 patients, 132 vessels revascularised). One-year primary patency was 87% (95% CI 71%, 97%). Graft thrombosis rate was 6% (95% CI 0%, 16%). Pooled stenosis rate at one-year was 11% (95% CI 1%, 28%). Graft dilatation occurred in 20.5% in one series and aneurysmal dilatation occurred only in 2/29 vein grafts. 30-day (n=96), one-year (n=72) and five-year mortality (n=30) were 0%, 0% and 12% respectively. Four studies reported outcomes for synthetic grafts (106 patients, 147 vessels). The pooled primary patency at one year was 100% (95% CI 99%, 100%). Pooled primary 5-year patency rate was 88% (95% CI 69%, 100%). There was no graft infection in two of the three studies. Overall pooled percentage of graft thrombosis and stenosis at one year was 0%. Jimenez et al (2002) reported one graft thrombosis at 20 months and graft stenosis in two patients at 46 and 49 months. Illuminati et al (2017) reported graft thrombosis in 2/24 patients at 22 and 52 months. Thirty days, one-year and 5-year mortality was 1% (95% CI 0%, 6), 7% (95% CI 0%, 20%) and 39% (95% CI 11%) respectively.

Conclusion: Patency was better with SG compared with AVG. Mortality was higher in the SG group. Graft dilatation does occur with vein grafts, but in this review no intervention was found necessary. Poorly designed studies, incomplete reporting and absence of morbidity and mortality indices preclude emphatic conclusions.

Keywords: Chronic mesenteric ischaemia, chronic visceral ischaemia, visceral arterial reconstruction, mesenteric artery ischaemia, renal artery stenosis, renal artery obstruction, superior mesenteric artery, coeliac artery, systematic review.

Introduction

Visceral arteries include the celiac axis and its branches, superior and inferior mesenteric arteries, and the renal arteries. Reconstruction of these arteries is performed when they are significantly diseased causing end-organ symptoms. Reconstruction include endovascular procedures such as angioplasties with or without stent, surgical procedures, namely, thrombectomy or embolectomy in acute cases, endarterectomy with or without patch closure, bypass using synthetic conduits or vein graft, segmental reconstruction and re-implantation of the diseased artery. Historically, open bypass procedures have been preferred to endovascular procedures using various techniques [1]. The topic of interest in this review is the use of autologous vein graft (AVG) and synthetic graft (SG) in visceral arterial reconstruction and their outcomes.

Among the vein grafts, autologous reversed saphenous vein graft is the commonest used conduit for arterial bypass. Synthetic grafts such as dacron, polytetrafluoroethylene (PTFE), polyester, and polyurethane grafts and homografts such as the Dradik umbilical vein graft or cryopreserved arterial graft have all been used in arterial bypass surgery. The hypogastric artery is also used occasionally. There are advantages and disadvantages with the use of autologous vein graft and synthetic grafts [2]. Graft infection and stenosis secondary to intimal hyperplasia are the main concerns with synthetic grafts [2]. Most authors report using synthetic graft except in patients with high risk of infection. Vein grafts have a propensity to dilate over time [3-5]. There are reports of its occurrence in Aorto-coronary grafts. However, the exact incidence is not clear with a wide range of incidence rates being reported [3,5].

Neitzel et al [3] have reported an incidence of 14% and Dieteret et al [5] report an incidence of 0.07%. Similar concerns have been expressed with visceral arterial bypass originating from the aorta to the target visceral vessel. Controversy in this aspect exists with no documented cumulative evidence available supporting the use of either conduit in visceral arterial reconstruction. Hence, a systematic review was undertaken to study the individual outcomes of autologous vein graft and synthetic graft in visceral arterial reconstruction originating from the aorta.

Methods

The methodology of the current review was according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [6]. The study is registered with Centre for Reviews and Dissemination, University of York, PROSPERO 2017: CRD42017083572

Inclusion and exclusion criteria

All studies in which patients undergoing visceral arterial bypass procedure utilizing autologous vein graft or synthetic graft as a primary intervention in chronic visceral ischaemia were included irrespective of study design. Studies were excluded if data of acute mesenteric ischaemia and chronic mesenteric ischaemia or autologous and synthetic grafts could not be separated. We also excluded studies in which data of bypass procedures could not be separated from interventions such as angioplasty or stenting, endarterectomies with or without patch and re-implantation, re-interventions and combined aortic aneurysm repair with visceral artery reconstruction. Studies which included patients with Takayasu's arteritis were also excluded so that outcomes due to the disease process will not affect the graft outcome. Non-English language articles when English translation was not available, case series of less than 10 cases and case reports were also excluded.

Outcome measures

Outcome measures included primary patency, secondary patency, complications such as graft thrombosis, dilatation, infection, aneurysm (true and false/pseudo), anastomotic stenosis and all-cause mortality (30 day, one-year and 5-years).

Search methods for identification of studies

The electronic databases searched to identify potential studies were Ovid-Embase and PubMed Medline. No limits or filters were applied to any of the databases. The keywords used for the search were "Mesenteric vascular disease", "acute mesenteric ischaemia", "mesenteric artery, superior", "mesenteric artery, inferior", "celiac artery", "renal artery", "saphenous vein" and "vein". A detailed search strategy is included in supplementary file 1. The reference lists of relevant papers were also checked to search for potential studies for inclusion.

Selection of studies

With the specified search strategy, each database was explored by two authors (GG and RD) independently. The search results were merged to remove duplication. Title screening was done for all the articles obtained through initial hit. Articles were rejected on initial screen when the review authors determined from the title that they were not relevant. All titles of the relevant studies meeting the criteria to be included were screened for abstracts. If the abstract screen was found not of relevance to visceral arterial reconstruction, it was excluded. When a title or abstract screen was inconclusive to include or reject, full text was examined. Two review authors (GG and RD) independently assessed the studies for inclusion and resolved differences between their assessments by discussion and in consultation with a third review author (PD). In the case of duplicate publications and companion papers of a primary study, all available data was obtained for complete information. When multiple reports of the same

study existed, the studies were linked together. A decision on which study should be included was based on the inclusion criteria. Fig.1 (PRISMA flow diagram) illustrates the selection process of studies included in the review where k represents the number of records.

[Insert Figure1 here]

Data extraction and management

The data extraction form was constructed based on the review objectives. Two review authors (GG, RD) independently extracted data from included publications on to an Excel spreadsheet. Items under which data was extracted included – authors, institution, country, period of study, type of study, methods of patients selection, inclusion, exclusion, age (average, mean and range), gender, number patients, statistical analysis, aetiology, co-morbidities, type of interventions, number of vessels reconstructed, graft type, follow up period, morbidity and mortality, patency rates, graft related complications, conflict of interest and ethical approval. Efforts were taken to minimise bias by extracting data independently using a piloted data extraction tool.

Assessment of methodological quality of included studies

All studies included were case series and we used Joanna Briggs Institute (JBI) critical appraisal checklist for case series [7]. The tool consists of 10 items and we have excluded studies that did not indicate a consecutive and complete inclusion of participants. Hence, six studies were included for the final analysis.

Data analysis

Data was extracted for all the outcomes, and pooled proportion was estimated using the random effect model wherever appropriate. We reported pooled proportions with 95% confidence intervals (CI), heterogeneity index (Q), degrees of freedom (df) and I^2 statistic.

We used '*metaprop*' command for meta-analysis and confidence intervals were computed using score method [8]. Proportions are presented in a forest plot; however, all the results are displayed in percentages for ease of understanding. All the outcomes except mortality were analysed with the denominator being number of reconstructed vessels.

Results

1. Study characteristics

We identified 9399 records from the database search and 38 records from additional sources. Among these 9437 records, 9259 were excluded after title and abstract screening. Full text of the remaining 178 articles were screened and only six were found to fulfill the eligibility criteria. (Fig 1). Six studies [9-15] which met the inclusion criteria and quality assessment had a total of 218 patients and 281 vessels re-vascularized (Table 1). Two studies had data about AVG, three studies had data about SG and one study had both AVG and SG data. Four studies were retrospective case series [9,11-13], one was a prospective case series [14] and the other was unspecified case series [10]. The period of study ranged from 1970 to 2019. All patients had some form of radiological imaging as a workup towards the diagnosis. The number of patients in the 6 studies in this review ranged from 12 to 75 (Mean = 36). Four studies included chronic mesenteric ischaemia[10,12-14] and two included patients with renovascular hypertension secondary to renal artery stenosis [9,11]. Age ranged from 22 to 72 years. There were 54 males and 89 females in 5 studies. There was no mention of the gender in the Dean et al series [9]. Four studies originated from the USA [9-12], one from Slovenia [13] and one from Italy [14]. There was no specific mention of ethnicity in any of the studies. Follow-up period was available in all 6 studies ranging from 1 to 119 months (four studies mentioned a mean follow-up of 27 months to 71 months) [10,12-14].

Studies reporting outcomes for vein graft

There were three studies, two mesenteric artery[10,11] and one renal artery[9] revascularisation in which vein grafts were used (117 patients, 132 vessels revascularised). Pooled primary patency rate at one year (n= 132) in the 3 studies, was 87% (95% CI = 71%, 97%) (Fig 2). Overall graft thrombosis rate (Fig 3) in the three studies (n= 132) was 6% (95% CI = 0%, 16%) (Fig 3). Dean et al[9] reported vein graft dilatation in 20.5% (17 to 47% dilatation in 8/39 bypass grafts 2 to 6 years after bypass and true aneurysmal dilatation of 87% -106% in two bypass grafts at 3 and 6 years in a subgroup of 29 patients. None of these dilatations or aneurysms progressed on further surveillance and did not need any intervention. Pooled Stenosis rate at one-year was 11% (95% CI 1%, 28%) (Fig 4). There were no deaths reported in the first 30 days after surgery in the Stanton et al[10] and Straffon et al[11] series and 3.2% in the Dean et al[9] series amounting to a pooled 30-day mortality of 1% (95% CI 0%, 4%). Stanton et al[10] and Straffon et al[11] continued this trend at one year, having no mortalities. Stanton et al[10] reported a mortality of 25% (2/8) at 5 years, all due to myocardial infarction (Table 2). There was no data on infection and pseudoaneurysm in any of the studies.

Table 1. Characteristics of included studies

Sl No .	Authors	Period of study	Type of study	Total no. of patients	Age (Mean)	Diagnosis	Type of graft	No. of vessels revascularised
1	Dean RH et al 1974 ⁹	1962 - 1973	Retrospective case series	75	No mean (13-67)	Renovascular hypertension	AVG	89
2	Stanton PE et al 1986 ¹⁰	1976-1985	Non specified Case series	12	64.75	Chronic intestinal ischaemia	AVG and SG	9 and 4 *

3	Straffon R et al 1970 ¹¹	1965-1969	Retrospective case series	33	22 - 55	Renovascular hypertension	AVG	34
4	Jimenez JG et al 2002 ¹²	1987-2001	Retrospective case series	47	62	Chronic mesenteric ischaemia	SG	94
5	Flis V et al 2015 ¹³	1999 - 2009	Retrospective case series	27	72	Chronic mesenteric ischaemia	SG	27
6	Illuminati G et al 2017 ¹⁴	1999-2016	Prospective case series	24	61	Chronic mesenteric ischaemia	SG	24

[insert Figure 2.]

[insert Figure 3.]

[insert Figure 4.]

Table 2 Mortality with vein grafts in VAR

Sl No.	Outcomes	Total number of studies	Total number of patients	Pooled Percentage (95% CI)	Q	df	I ²
1	30-day mortality with vein grafts	3	117	1 % (0%, 4%)	1.12	2	0%
2	One-year mortality with vein grafts	2	42	0% (0%, 3%)	-	1	-
3	Five year mortality with vein grafts	1	8	25%	-	-	-

Studies reporting outcomes of synthetic grafts

Four studies [10,12-14] reported individual outcomes for synthetic grafts (106 patients, 147 vessels revascularised) with a pooled primary patency at one year (Fig 5) of 100% (95% CI 99%, 100%). Pooled primary 5-year patency rate was 88% (95% CI 69%, 100%) (Fig 6). Jimenez et al [12] reported 100% secondary patency in 7 out of 47 patients followed up at 5 years. Flis et al [13] and Illuminati et al [14] reported to have had no graft infection in their series. Overall pooled percentage of graft thrombosis and stenosis at one year was 0%. Of the four studies, Jimenez et al [12] ^{had} one graft thrombosis at 20 months and two graft stenosis at 46 and 49 months. Illuminati et al [14] reported graft thrombosis/occlusion in 2/24 patients at 22- and 52-months post revascularisation. Jimenez et al [12] reported a 0% incidence of true aneurysms in their series of 94 grafts. Overall pooled 30-day and one-year mortality was 1% (95% CI 0%, 6%) and 7% (95% CI 0%, 20%) respectively (Table 3) . The Five-year mortality was 39% (95% CI (11%, 72%). There was no mention of graft dilatation or pseudoaneurysms in any of the four studies and so their occurrence or non-occurrence was not clear from the data.

[insert Figure 5.]

[insert Figure 6.]

Table 3 Mortality in synthetic grafts in VAR

Sl No.	Outcomes	Total number of studies	Total number of patients	Pooled Percentage (95% CI)	Q	df	I ²
1	30-day mortality for synthetic grafts	4	102	1% (0%, 6%)	4.53	3	33.72

2	One-year mortality for synthetic grafts	4	102	7% (0%, 20%)	8.21	3	63.45
3	Five year mortality for synthetic graft	4	61	39% (11%, 72%)	24.14	3	87.57

Discussion

In studies that had separate data for synthetic vein and grafts, primary patency at one year seemed to be better with synthetic grafts compared to vein grafts, 100% vs 87%. The Stanton et al [10] series was the only one which compared vein (n=9) and synthetic grafts (n=4), with a 100% patency at one year in both groups. Being a small case series, these results should be interpreted accordingly. Graft thrombosis and anastomotic stenosis were higher with vein grafts compared to synthetic grafts (6% vs 0% and 11% vs 0%, respectively). One would expect better outcomes with vein grafts if the outcomes reported with peripheral bypass procedures were to be compared. The lower patency rates with vein graft is noticeable within the first year of the procedure, suggesting a mechanical cause for the failing graft. The mesenteric bypass being a short bypass involving medium sized arteries, may not be comparable to the lower limb bypass procedures, possibly accounting for the better outcome with synthetic graft in the former. The stability offered by the synthetic graft placed in the abdomen compared to vein grafts, the latter being subject to acute angulation with changing positions of the abdominal viscera may be another factor for the better outcomes with synthetic grafts. Experimental studies have also suggested better outcomes of vein grafts when they are externally supported by either a stent or a tightly woven sheath of synthetic graft by preventing intermittent dilatation, lengthening of the graft, angulation, and helical distortion [15] and prevent the development of intimal hyperplasia [16]. In renal artery revascularisation, the right sided bypasses had a tendency for late mid-graft stenosis in the

vein grafts, which is attributed to the retrocaval routing of the graft⁹. There may be a case for anterior routing of the vein grafts to prevent this occurrence.

In the studies that included vein grafts [9-11] the 30-day mortality was 1% (Table 2) in a total of 125 patients. One-year mortality was reported only in two studies [10,11] and was 0%. In the synthetic grafts group, 30-day and one-year mortality rate was 1% and 7%, respectively (Table 3). 5-year mortality reported by two authors in the vein graft group [10,11] (n=41) and 4 in the synthetic graft group [10,12-14] (n=61) was 1% and 39% respectively. The mortality data should have included a uniform method of reporting cause of death as well as predictive pre-operative morbidity and morbidity scores for correlation. Visceral artery disease specific mortality was not extractable from any of the studies. There has been a high dropout rate from follow up, which makes the interpretation erroneous.

The other complications, namely, graft infection, graft dilatation and aneurysmal dilatation were not reported in most studies. It is likely that these complications did not happen, but, it is difficult to assume that it is the case as they have not been explicitly documented and hence not further analysed. Flis [13] specifically mentioned that they did not have any graft infection in their synthetic graft series. Graft dilatation which is a concern with many experts in the field when vein graft is used was reported by Feng et al [17] (not included in this review) with an incidence of 5.13% (mild dilatation noted in 2 bypass grafts at two and three years) and by Dean et al [9] with an incidence of 20.5% (17 to 47% dilatation noted at 2 to 6 years after bypass in 8 out of 39 grafts). Most of these were not true aneurysmal dilatations. Even when there was true aneurysmal dilatation of 87-106%, in the two patients in the Dean et al [9] series, no intervention was deemed necessary as none of them progressed any further at later surveillance. However, with modern day surveillance and availability of

endovascular treatment options, stenting the aneurysmal grafts would be an option. Although paediatric patients were not included in this review, it is highly likely that vein graft dilatation may be an issue in this group of patients in the long run. With the current availability of imaging facilities, a focused follow up of these patients would give us useful information. There was a report of a nine-year-old boy who had an external iliac vein as a conduit for SMA bypass and ilio-hypogastric artery for renal artery bypass [18] in whom the hypogastric artery conduit underwent a 100% dilatation, and the saphenous vein graft underwent a 300% dilatation within three years.

Conclusions:

Our analysis of the available data points towards better patency rates with synthetic grafts compared to vein grafts but more robust studies in terms of study design, data collection and analysis and long term follow up are required to emphatically state this conclusion. Mortality seemed to be higher in the synthetic grafts, but in the absence of prognostic and morbidity indices, we would not draw firm conclusions. Graft dilatation does occur with vein grafts. However, it seems from this review that intervention is not required as the dilatation does not progress indefinitely. With the present day imaging techniques and the ease of their availability, monitoring their progress is rather easy. In addition, interventional options are now advanced, and these dilated grafts can be easily treated with endovascular stents. Reporting standards for these studies needs to be standardised for homogenous data and a better understanding of the outcomes.

How this review will affect clinical practice

With limited information available in the present literature, we cannot recommend on the type of graft to be used. However, it looks like the synthetic graft has better patency compared to vein grafts. We would continue to select the type of graft depending on the clinical condition of the patient, mainly the presence or absence of bowel necrosis. Graft dilatation is an issue that needs to be considered when vein graft is used in these patients. It is probably more common in the paediatric population where the graft has to remain in-situ for longer periods and is subject to the growth of the child with changing haemodynamics.

Limitations and strengths of the review

The reporting standards of the outcomes included was haphazard as we could not extract data for vein and synthetic grafts separately in many studies and hence were either excluded or the data limited to what was available. Studies with combined aortic aneurysm repair and mesenteric revascularisation were excluded as the mortality with aneurysm would have skewed the outcomes. Some authors mentioned outcomes in their discussion and some in the results and some others only in their tables or abstracts. When studies had both vein grafts and synthetic grafts in their series, we had to manually separate out the data where possible. There was a high rate of drop out of patients in the follow up, making long term results unreliable. We recommend uniform reporting of outcomes for these procedures in future publications. We have suggested a reporting protocol in the supplementary file 2, which could be considered to create uniformity in reporting.

Future research recommendations

Focused prospective studies comparing synthetic and autologous vein grafts with clearly separable and standardised outcome reporting at fixed intervals would shed more light on the concerns related to this topic. Paediatric patients undergoing visceral arterial reconstruction

would be an interesting cohort to follow up for graft dilatation and long-term outcomes specifically related to growth.

Recommendations for future practice and policy

We have compiled a reporting protocol related to visceral artery reconstruction which is appended as Supplementary file 2.

Fig 1: PRISMA flow diagram

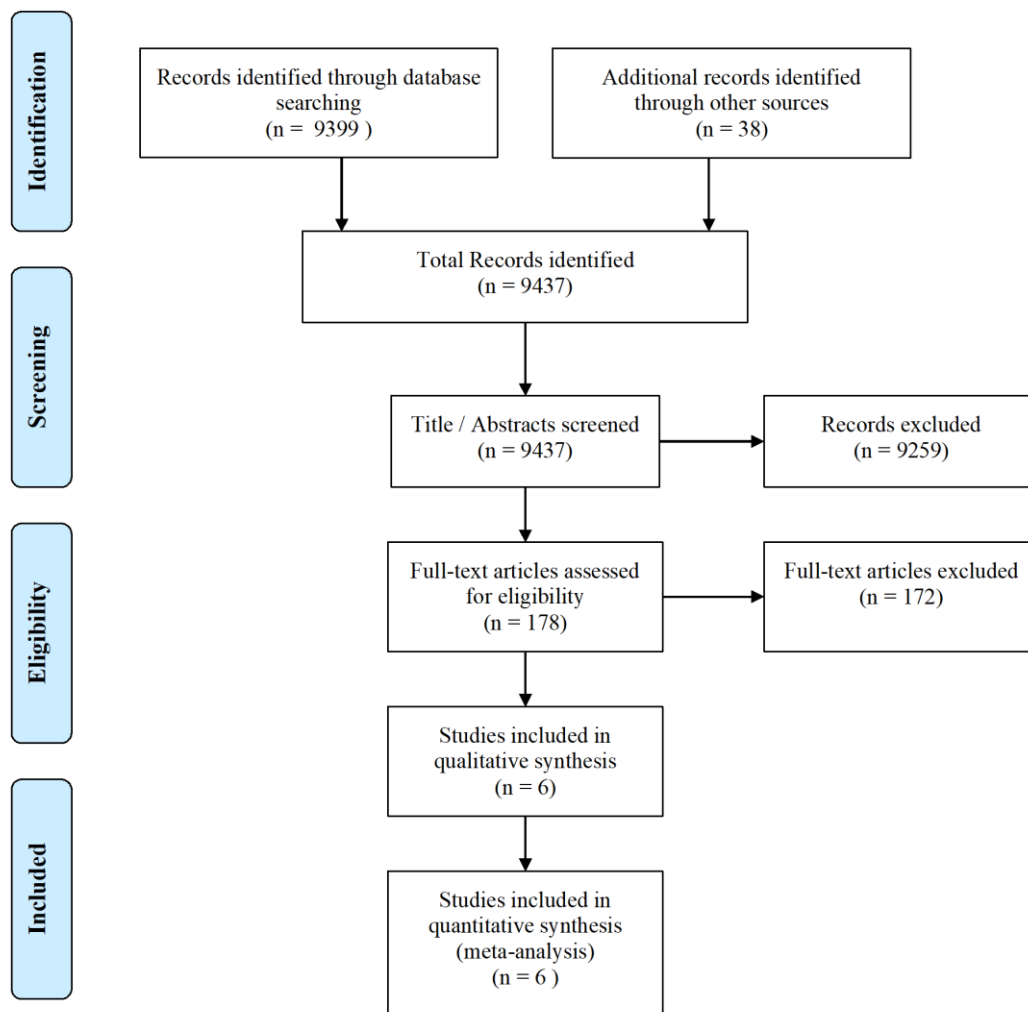


Fig 2: One-year primary patency with AVG

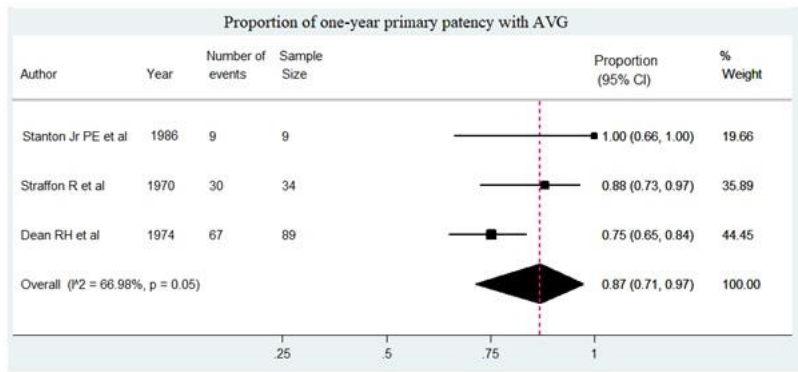


Fig 3: Graft thrombosis rate with AVG

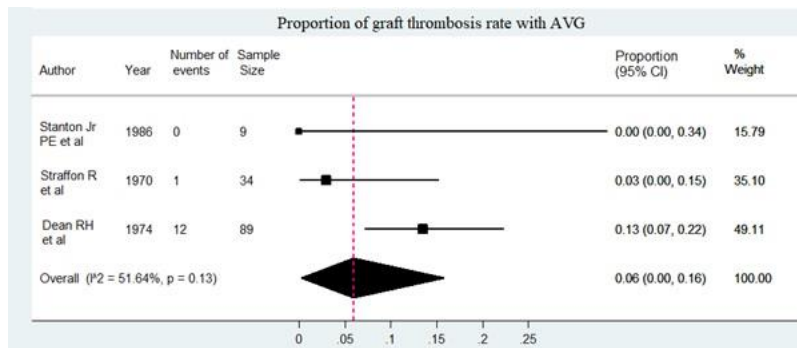


Fig 4. Graft stenosis rate with vein grafts

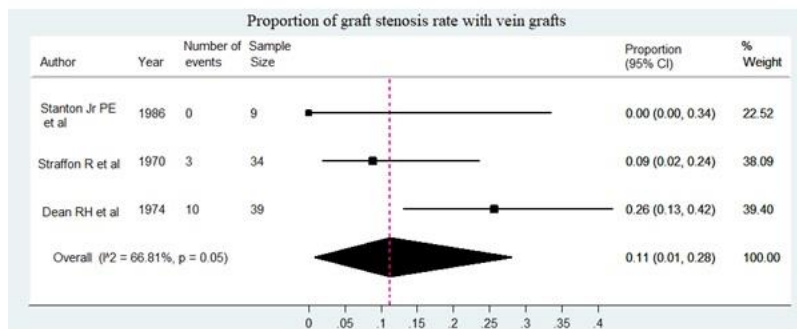


Fig 5: Pooled primary patency rate at One-year

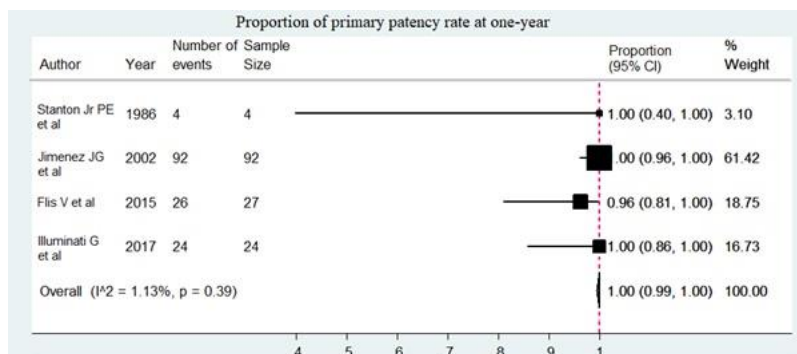


Fig 6: Pooled primary 5-year patency with synthetic grafts

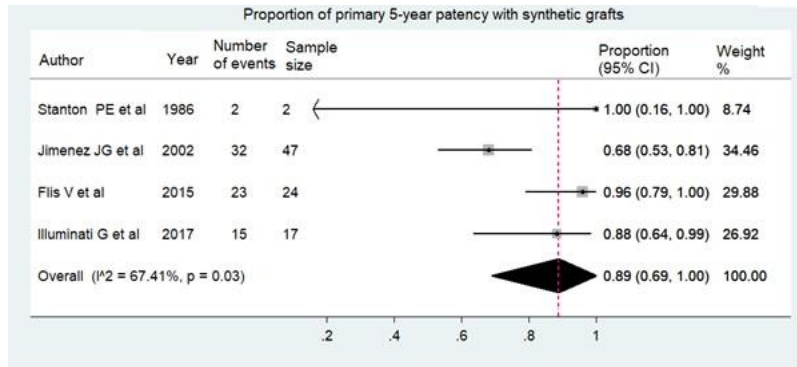


Figure Legends

Fig 1: PRISMA flow diagram

Fig 2: One-year primary patency with AVG

Fig 3: Graft thrombosis rate with AVG

Fig 4. Graft stenosis rate with vein grafts

Fig 5: Pooled primary patency rate at One-year

Fig 6: Pooled primary 5-year patency with synthetic grafts

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Conflicts of interest

Authors declare that that there is no conflict of interest.

Ethics Approval

Not applicable as this is a review article.

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