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Abstract

Introduction Peripheral vascular disease is a major cause of death and disability. The extent to which volume influences outcome of lower limb (LL) vascular surgery remains unclear. This review evaluated the relationship between hospital/surgeon volume and outcome in LL surgery. Methodology Electronic databases; Medline, Embase, the Cochrane Library Databases, Science Citation Index, and CINAHL, proceedings from conferences, citations, and references of included studies were searched. Studies from Europe, of adults undergoing LL vascular surgery reporting outcomes by hospital or surgeon volume were included. Quality of studies was assessed using a modified ACROBAT-NRSI(Robins1) tool. Association between hospital/surgeon volume and outcome were summarised using tables. Results Nine studies from different European countries, comprising 67,445 patients who had undergone diverse LL surgeries were included. Increase in hospital/surgeon volume was associated with a decrease in amputations. The evidence on association between hospital/surgeon volume and mortality was contradictory, but mortality and amputations may co-vary by hospital volume. There were an insufficient number of studies reporting on hospitals/surgeons repeated surgeries but their results suggest an association between high volume hospitals/ surgeons and high volume of repeated revascularisations. The associations between hospital/surgical volume on adverse events and length of hospitalisation were inconclusive. Conclusion This review found an association between high volume hospitals/surgeons and fewer amputations. This finding has implications on re-organisation of vascular surgery services, however due to the small number and poor quality of some of the included studies, decisions on reorganisation of LL vascular surgery services should be supplemented by results from clinical audits. There is need for standardisation of definition of volume stratification of outcomes by patient's clinical conditions.

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Title page

The relationship between hospital or surgeon volume and outcomes in lower limb vascular surgery in the United Kingdom and Europe

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Introduction

Peripheral vascular disease is a major cause of death and disability. The extent to which volume influences outcome of lower limb (LL) vascular surgery remains unclear. This review evaluated the relationship between hospital/surgeon volume and outcome in LL surgery.

Methodology

Electronic databases; Medline, Embase, the Cochrane Library Databases, Science Citation Index, and CINAHL, proceedings from conferences, citations, and references of included studies were searched. Studies from Europe, of adults undergoing LL vascular surgery reporting outcomes by hospital or surgeon volume were included. Quality of studies was assessed using a modified ACROBAT-NRSI(Robins1) tool. Association between hospital/surgeon volume and outcome were summarised using tables.

Results

Nine studies from different European countries, comprising 67,445 patients who had undergone diverse LL surgeries were included. Increase in hospital/surgeon volume was associated with a decrease in amputations. The evidence on association between hospital/surgeon volume and mortality was contradictory, but mortality and amputations may co-vary by hospital volume. There were an insufficient number of studies reporting on hospitals/surgeons repeated surgeries but their results suggest an association between high volume hospitals/surgeons and high volume of repeated revascularisations. The associations between hospital/surgical volume on adverse events and length of hospitalisation were inconclusive.

Conclusion

This review found an association between high volume hospitals/surgeons and fewer amputations. This finding has implications on re-organisation of vascular surgery services, however due to the small number and poor quality of some of the included studies, decisions on reorganisation of LL vascular surgery services should be supplemented by results from clinical audits. There is need for standardisation of definition of volume stratification of outcomes by patient's clinical conditions.

Key words: Peripheral vascular disease; Critical leg ischaemia; Claudication; Hospital or surgeon volume; Amputation; Mortality.

1. Introduction

Health care service commissioning groups in the United Kingdom (UK), Europe, and globally are faced with the complex challenge of organizing the health delivery service so as to minimise cost, maximise cost-effectiveness, local access, service quality, effectiveness in achieving better clinical outcomes, and improving patients quality of life. A 2008 study by Holt et al[1] reported that higher-volume hospitals/surgeons achieve better outcomes for high-risk procedures, and suggested the reconfiguration of health care services based on the volume model.

Some researchers; Awopetu et al[2], Killeen et al[3], Gandjour et al[4], and Shackley et al[5] have reviewed the association between hospital/surgeon volume and outcome in lower limb vascular surgery. However, of the four reviews[2-5], only one[2] drew firm conclusions; reporting that high volume hospitals (HVH) had significantly lower mortality compared with low volume hospitals (LVH). The other three[3-5], found inconclusive or ambiguous results, due to the small number of identified studies, and the heterogeneity in their findings.

1.1. Rationale for conducting the review

Among previous reviews on the association between volume in LL surgery and outcome, Shackley et al.,[3] focused mainly on abdominal aortic aneurism (AAA) and carotid endarterectomy; including only four studies considering LL surgery which found contradictory results and authors failing to reach conclusions due to the small number of studies. The other reviews[2-4], included studies mostly conducted in the United States of America (USA), making the outcomes more relevant to USA context. The significance of hospital/surgeon volume in lower limb (LL) vascular surgery, in influencing outcomes, in UK and Europe, has therefore not been clearly elucidated. There is need for an up-to-date evidence relevant to European settings, to aid in the planning and delivery of healthcare in a manner which will maximise local access, viability, and service quality, in the UK and Europe, hence the importance of this review.

1.2. Objectives of the review

This study aimed to investigate:

1. The relationship between the volume of LL vascular surgery undertaken by individual surgeons and risk of mortality, amputation, repeat surgery, length of hospitalisation, and adverse events (AEs).
2. The relationship between the volume of LL vascular surgery undertaken in individual hospitals and risk of mortality, amputation, repeat surgery, length of hospitalisation, and AEs.

2. Methodology

2.1. Search strategy

The review followed the PRISMA guideline and a protocol as registered on PROSPERO (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014014850). Comprehensive literature searches were conducted on Medline and Medline in Process, Embase, the Cochrane Library Databases, Science Citation Index, and CINAHL. Proceedings from five key conferences held between 2010 and 2015, and citations and references of included studies were also searched. Literature searching involved two phases; an initial strategy based on a 2000 systematic review by Michaels et al[6], was adapted and run in MEDLINE and other electronic databases as detailed in Appendix 1. A second search extended the initial strategy using the keywords and index terms focussing on surgical procedures and patient outcomes. Further relevant terms for these concepts were generated by consulting with the clinicians in the project team. Details of data sources and the search strategies are provided in Appendix 1.

2.2. Inclusion and exclusion criteria

The research question was focused using the PICOS criteria. Study selection was based on pre-specified criteria summarised in Table 1.

2.3. Study selection and quality assessment

Titles and abstracts of all records were screened by EG and PP. Full text papers were retrieved for studies that appeared to meet inclusion criteria. When needed, a third reviewer (EP or ME) was consulted to resolve disagreements. Data was extracted using a pre-piloted Excel form. Abstracted data included study characteristics (e.g. year and place of publication, study design, and characteristics of participants), and relevant outcomes reported according to specified strata of hospital or surgeon volume. Study quality was assessed using a modified version of A Cochrane Risk Of Bias Assessment Tool: for Non-Randomized Studies of Interventions (ACROBAT-NRSI; now known as Robins1)[7] tool. Details of the tool and the domains used in the assessment are provided in Appendix 2. A second reviewer double-checked data from all included studies (EG/PP). Disagreements were resolved by discussion with a third reviewer (EP/ME).

2.4. Data analysis

Due to the heterogeneity in the types of procedures carried out in included studies (endarterectomy, bypass, stents, or angioplasty), and case-mix (gangrene, ischaemia or claudication), a meta-analysis could not be conducted; therefore a narrative synthesis was undertaken. Odds ratios and other raw data of outcomes by hospital or surgeon volume were summarised using tables.

3. Results

The search from all sources identified 16,719 records. After removing duplicates, the abstracts and titles of 14,486 were screened for eligibility. Twenty seven (27) full articles seemed to meet the inclusion criteria, and were retrieved and read in full. Nine studies[8-16] met the inclusion criteria and were included (Figure 1). A list of studies excluded at full text level and reasons for exclusion is given in Appendix 3.

3.1. Characteristics of included studies

3.1.1. Study design and location: All studies were from Europe, of which three[8,9,13] were from the United Kingdom, one[12] from UK and the Ireland, two[10,14] from Sweden, two[11,16] from Finland, and one[15] from Denmark. Studies included in this review were mainly observational studies that utilised clinical/administrative data (Table 2); two studies[9,13] retrospectively analysed data on vascular procedures extracted from the Hospital Episodes Statistic (HES) database (for 2002 to 2006; and 2007 to 2011), the other seven studies[8,10-12,14-16] analysed retrospectively collected data from different vascular projects. Together the nine studies recruited 67,445 patients, with 439 as the lowest number and 31,821 as the highest, and varied in duration from 3 months to 20 years. Only one of the nine studies[11] reported both hospital and surgeon specific volume outcomes. Five studies[8-10,13,15] reported outcomes by hospital volume only, whereas three[12,14,16] reported surgeon volume only. There was heterogeneity with regard to the definition of surgeon and hospital volume by studies. Six studies[9,11-14,16] classified volume as quantiles, whereas three[8,10,15] used continuous volume. The designation of a low-volume hospital ranged from 2 to <20 procedures, and a high-volume institution from >20 to >67. Low volume surgeons were defined as those performing 10 up to 20 surgeries annually, and high-volume surgeons as those performing >10 to >50 surgeries per year (Table 2).

3.1.2. Case and procedure mix: Patients who had LL surgeries in the included studies had a mean age range of 62 to 74.5 years (median 66 to 71 years), and mostly male; percentage male range 46% to 70% (Table 2). The types of procedures and indications for surgery greatly differed by studies; Moxey et al[9] analysed data for femoropopliteal and femorodistal bypasses in patients with intermitted claudication or gangrene, whereas Troeg et al[14] investigated outcomes after femoropopliteal grafting in patients with chronic leg ischaemia or claudication. The procedures in Kantonen et al[11] included endarterectomies, patch-angioplasties, and percutaneous transluminal angioplasties (PTA). Other procedures included infrainguinal reconstructions in patients with critical leg ischaemia[10,12], elective and non-elective stenting of the iliac artery[13], and unspecified vascular surgeries in patients with critical leg ischaemia[8] (Table 2).

3.1.3. Assessment of bias: Study quality was assessed using a modified version of the ACROBAT-NRSI (Robins1)[7]. All the studies were considered to have high risk of selection bias (Figure 2).

Studies that had used quantiles to define hospital/surgeon volume[9,11-14] were considered to have high risk of volume measurement bias. Four studies[8-10,14], did not report details of number of patients not included in the final analysis, and were therefore classified as having unclear risk of attrition. Studies that had prospectively recorded outcomes[11,12,14-16] were considered to have low risk of bias of outcome measurement, especially for mortality; however those which had used healthcare administrative databases[8,9,13], were classified as having high risk of outcome measurement bias. Five studies[9,11,14-16] adjusted for, or compared prevalence of various confounders at baseline[12], and were deemed to have low risk of confounding, whereas the others, either did not adjust for confounders, or adjusted for only age and sex, and were thought to be highly to moderately confounded. Most of the studies[8,9,11-16], did not mention whether analyses conducted were based on a prior published protocol, and were therefore classified as having unclear risk of reporting bias.

3.2. Volume and post-operative amputations

3.3.1. Hospital volume and amputations: Three studies[9-11] investigated this outcome and all found an association between volume and amputation (Table 3). Specifically, Moxey et al[9], reported that at 1 year, high volume hospitals had lower secondary major amputations, in patients who had femoropoliteal bypass surgery (OR: 0.955, 95% CI: 0.928–0.983 p=0.002), and femorodistal bypass (OR: 0.658 (0.517–0.838, p= < 0.001). Kantonen et al[11] reported a similar outcome 30 days post-operation (OR: 1.49, 95% CI: 1.0 - 2.25, p = 0.05), whereas Elfstorm et al[10] found significant association at both 30 days and 1 year post-operation (OR: 5.01, 95% CI: 2.24 – 3.41, p = 0.01, and OR: 2.05, 95% CI: 1.24 – 3.42, p = 0.01 respectively).

3.3.2. Surgeon volume and amputations: Three studies[11,12,16] reported the association between surgeon volume and post-operative amputations 30 days post-surgery and all found a correlation between surgeon volume and secondary amputations. Kantonen et al[11] and Biancari et al[16], who adjusted for most of the confounders, found that experienced surgeons performed fewer post-operative amputations (OR: 1.89, 95% CI: 1.15 - 2.80, p = 0.01 and OR: 0.40, 95% CI: 0.18–0.91, p

= 0.03 respectively). Further, the VSGBI[12] study, which did not adjust for confounders, reported a similar outcome (OR: 0.41, 95% CI: 0.24 – 0.69, p = 0.0006) (see Table 3). The indication for surgery in all the three studies[11,12,16] was critical leg ischaemia.

3.3. Volume and mortality

3.2.1. Hospital volume and mortality: Five studies[9-11,13,15], reported data on hospital volume and mortality (Table 4). Four of these[9-11,15], adjusted for most confounders, whereas one[13], adjusted only for age and sex.

The evidence on this outcome was contradictory, with two of the five studies reporting an association; Moxey et al[9] found an association between increase in hospital volume and a decrease in mortality during index admission (OR: 0.960, 95% CI: 0.929–0.992, p = 0.014), but not at 1 year (OR: 0.987, 95% CI: 0.966–1.007, p = 0.197), in femoropopliteal bypass but not in femorodistal procedures (Table 4). Elfstorm et al[10], reported an association between an increase in hospital volume and decrease in mortality at 1 year (OR: 1.66, 95% CI: 1.06 - 2.60). Over half of the patients in Moxey et al[9] (55% femoropopliteal/54% femorodistal) had surgery due to intermittent claudication whereas all patients in Elfstorm et al[10] were operated on because of chronic critical limb ischaemia. The definition of volume ranged from 11.2 to 110.7 patients per annum in Moxey et al[9] and 85 to 115 patients per annum in Elfstorm et al[10]; these might confound the outcome. The insignificant finding in femorodistal bypass surgeries suggests poor outcome in lower extremity vascular disease.

The other three studies, Kantonen et al[11], Bredahl et al[15] and Goode et al[13], found no association between hospital volume and 30 day mortality post-operative (Table 4). The indications for surgery in[11,15] were chronic critical limb ischaemia or intermittent claudication, but Goode et al[13] did not report the conditions that necessitated surgery. The definition of volume also differed among these studies; Kantonen et al[11] using a cut-off of 20, Goode et al[13] a range of 1 to 111 in elective and 613 for non-elective, while Bredahl et al[15] used continuous annual number of cases; these might confound the outcome. The result could also be obscured by patient-mix.

3.2.2. Surgeon volume and mortality: Three studies[11,12,16], reported data on surgeon volume and mortality (Table 3). Of these two Kantonen et al[11], and Biancari et al[16], adjusted for most of the confounders, whereas VSGBI[12], did not adjust for confounders. All found no association between surgeon volume and in-hospital or 30 days mortality (Table 4). Patients in all the three studies[11,12,16] presented with critical leg ischaemia, but the definition of volume quantiles differed; Kantonen et al[11] and the Vascular Society of Great Britain and Ireland (VSGBI)[12] used a cut-off of 10, whereas Biancari et al[16] used 40 and this might have affected outcome. In all the three studies[11,12,16], outcome was within 30 days post-surgery. It is possible that the outcomes could be different if they were measured 1 year post surgery.

3.4. Volume and number of re-operations

3.4.1. Hospital volume and volume of re-operations: Only one study Moxey et al[9] reported association between hospital volume and number of repeated surgery in patients with intermitted claudication and other conditions. They found that high volume hospitals conducted more revisional bypass procedures at 1 year (OR: 1.031, 95%, CI: 1.005–1.057, p=0.018), but not during index admission (OR: 1.017, 95% CI: 0.965–1.070, p=0.532). No such association was observed in femorodistal surgeries, suggesting poor outcome in lower extremity bypasses (Table 5).

3.4.2. Surgeon experience and volume of revascularisations: Two studies, the VSGBI[12] and Biancari et al[16] investigated the association between surgeon volume and rates of revascularisation or limb salvage. The VSGBI[12] found that surgeons with a lower annual experience tended to undertake fewer revascularisations (60.6% vs. 74.9%; $\chi2$= 8.9, p = 0.003), and that low volume/experienced surgeons had a lower mean limb salvage rate than high volume/experienced surgeons (65.4 vs. 81.3, $\chi2$= 12.8, p = 0.0003). In addition, Biancari et al[16] also reported a similar finding (Table 5).

The small number and poor quality of the included studies, included in the above two analyses, makes it difficult to draw any firm conclusions on association between volume and repeated surgery.

3.5. Volume and any adverse events

Surgical operations for peripheral vascular disease are associated with a number of adverse events including systemic or wound infection/patency, bleeding/haemorrhage, lesions and gangrene, cardiac and pulmonary comorbidities, renal failure, or prolonged hospitalisations which might result in bed sores (pressure ulcers)[17,18]. In this review, four of the included studies investigated the impact of hospital[9,13,15] and surgeon volume[14], respectively, on occurrence of any adverse events (Table 6), while three studies reported the impact of hospital[8,13] and surgeon volume[16] on length of hospitalisation (LOS)-(Table 7).

3.5.1. Hospital volume and AEs: Evidence from three studies[9,13,15] that reported this outcome was inconclusive; Moxey et al[9] found that an increase in volume was associated with a decrease in AEs during index admission in femoropopliteal bypass surgeries (OR: 0.968; 95% CI, 0.940–0.998; p=0.034), but not in femorodistal surgeries (ORs not reported). A similar finding was reported by Bredahl et al[15]. On the contrary, Goode et al[13], who adjusted only for age and sex, found no association between hospital volume and AEs occurring during admission (OR: 1.0, 95%CI: 1.0 – 1.0) for both elective and non-elective surgery (Table 6). The conflicting outcomes here may be either due to differences in patient-mix, volume quantiles used, or locality of vascular insufficiency.

3.5.2. Surgeon volume and AEs: Only Troeg et al[14] analysed the association between surgeon volume and AEs. They found no association between volume and any AEs (Table 6). It is difficult to draw any conclusions on the association between surgeon volume and AEs as only one study had data on this outcome.

3.6. Volume and length of hospitalisation (LOS)

3.6.1. Hospital volume and LOS: Two studies[8,13] analysed the association between hospital volume and LOS and reported contradicting results. Goode et al[13] found no association between hospital volume and LOS, regression coefficient -0.010, 95% CI: -0.045 – 0.26 for elective, and -0.310, 95% CI: -0.642 – 0.022 for non-elective iliac artery operations. However Berridge et al[8] found clearly marked difference in LOS between high and low volume hospitals among patients who had major amputations (Table 7). The association between hospital volume and LOS cannot therefore be determined.

3.6.2. Surgeon volume and LOS: Only one study Biancari et al[16] reported on surgeon volume and LOS, and found no association (Table 7). Since only one study reported on this outcome, it is difficult to ascertain the significance of surgeon volume on LOS.

4. Discussion and conclusion

This review found an association between an increase in hospital[9-11] or surgeon[11,16] volume and decrease in post-operation amputations. There may be an association between high volume hospitals/surgeons and number of repeated surgeries, but we did not find enough studies to enable us draw firm conclusions on this outcome. The direction of association between hospital volume and risk of mortality is inconclusive; whilst some studies found that high volume hospitals had lower mortality rates[9,10], others[11,13,15] found no such association. However, the evidence suggests that mortality and amputations may co-vary by hospital volume. Also, the association between volume and length of hospitalisation and AEs was inconclusive. Our finding on association between volume and amputations agrees with previous studies[2,6,19,20], and that about hospital volume and mortality is similar to reviews by Awopetu et al[2], Gandjour et al[4], Killeen et al[3], and Shackley et al[5]; who also found inconclusive or ambiguous results on association between volume and mortality.

The heterogeneity in findings could be confounded by the diverse case-mix (including, among others; chronic/critical leg ischaemia, or chronic/intermittent claudication[21], and different types of procedures (endarterectomies, angioplasties, elective or non-elective stenting, infrainguinal reconstructions, femoropopleteal or femorodistal bypasses) in LL vascular surgery. The type of procedure a patient receives largely depends on the severity of their illness[22,23]. Some studies have reported that patients with chronic leg ischaemia are more likely to undergo amputations[22,23]. In some of the studies, indication for surgery and type of procedure were adjusted for, and were found to be independent significant predictors of amputation and mortality[10,11,15], apart from hospital volume. Given that the type of procedure a patient receives is dependent on the patients clinical presentation[22,23], the possibility that differences in the findings in the studies included in this review, were confounded by differences in case-mix between hospitals and differences in types of procedures patients received, should be borne in mind when interpreting our results. Unfortunately, studies included in this review did not provide outcome data (on the relationship between hospital/surgeon volumes) stratified by indication for surgery and therefore we could not carry out a stratified analysis on the effect of volume on this variable. Also, the conclusions, in the included studies, relate to a range of different surgical and endovascular procedures and to earlier and more recent publications, but none of the papers looked specifically at how the balance between endovascular and open procedures varied over time and whether this was related to hospital or clinician volume. Thus the changing mix of procedures, particularly if the uptake of new procedures is related to hospital volume, may be a confounding factor, but, since the papers, did not provide data on patient outcomes, stratified by the type of procedure, we could not conduct a stratified analysis on this variable.

Included studies used different sources of data. The majority of the studies were observational using administrative databases and as such lack clinical detail. For studies that used historical data such as the HES database, where major diagnosis codes were used to identify LL surgery, there may be variability in coding by different hospitals, or different departments, even prospectively collected data, sometimes do not capture all the available cases[10], and variables of all confounding factors, and this may have introduced selection bias. Also, studies included in this review were drawn form a number of different countries, which might have different regional health systems and referrals within those regions, and this might have further introduced selection bias. Therefore the existence of selection bias, and confounding due to inability to control for all important confounders, in the included studies, should be borne in mind. However, the strengths of this study include that a comprehensive literature search, focusing on studies conducted in the UK and Europe, and a rigorous systematic review of the identified studies, were conducted.

The definition of mortality varied from in-hospital mortality[12,13], to 30-days[9-11] and 1-year[9,10] post-operatives. However, no consistency was observed between the mortality proxy measure used and outcome. Thus the two studies that analysed in-hospital mortality[12,13] found no association between volume and mortality, whereas the three that employed 30-day mortality[9-11] found conflicting results. The difference in findings in[9-11] could as well be due to case-mix. Some authors have argued that the aim of vascular surgery is to improve long term quality of life of the patient, and 30-day follow-up would only give an indication of the technical validity of the procedure; suggesting that a 1-year follow-up may give the true benefit of the surgery[24]. However, in this review, there was a contradiction; Elfstorm et al.,[10] found a significant variation in mortality by hospital volume at 1 year, whereas Moxey et al[9] found no association. More research is needed to determine the best mortality time points in LL vascular surgery.

The quantification of hospital or surgeon volume has not been standardised. Six studies[9,11-14,16] classified volume as quantiles, whereas three[8,10,15] used continuous volume. The justification for choosing the different volume cut-off points has varied from study to study. Kantonen et al[11] chose the cut-off point of 10 cases per surgeon and 20 cases per hospital based on the VSGBI[12] report which suggested that surgeons who conducted >10 operations per year had better results. In summarising the results of the SWEDVASC study, Bergqvist et al[24] suggested that confidence intervals are likely to be wide unless there are at least 50 operations, and urged that comparisons of surgeon/hospital volume <50 should not be conducted. In this review, the findings among the six studies that used volume quantiles[9,11-14,16], and the three[8,10,15] that employed continuous volume, varied. As the significance of the various volume quantiles has not been clearly demonstrated, we recommend continuous volume be used as a standard volume measure in future volume research.

We could have constructed funnel plots to investigate the existence of publication bias in this review. However, for each outcome, we only had three to four studies reporting that outcome. Such a funnel plot would therefore not give any meaningful result. But only studies published in the English language were included in this review, and this may have introduced publication bias. Also five[10-12,14,16] of the nine included studies in the final analysis are 18 years old or more. Therefore, the possibility of publication bias should therefore be borne in mind when interpreting our results. However, this review was systematic and was based on rigorous methods of literature search, and we hope that this might have eliminated most of this bias.

5. Conclusion

This review found an association between high volume hospitals/surgeons and fewer post-operative amputations. There might also be an association between high hospital/surgeon volume and more repeated surgeries. The association between hospital/surgeon volume and mortality is still unclear, but mortality and number of post-operative amputations may co-vary by hospital volume. An association between high hospital and surgeon volume and less number of post-operative amputations has implications on re-organisation of vascular surgery services. However due to the small number and poor quality of some of the included studies, decisions on reorganisation of lower limb vascular surgery services should be supported by clinical audits, where outcomes in vascular surgery are stratified by indications for surgery and types of procedures; prospective mandatory clinical audits on this subject, commissioned and funded through national registries and quality improvement programmes, could aid in generating more evidence. There is need for the standardisation of reporting and definition of volumes in vascular research.

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Title page

The relationship between hospital or surgeon volume and outcomes in lower limb vascular surgery in the United Kingdom and Europe

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Abstract

Introduction

Peripheral vascular disease is a major cause of death and disability. The extent to which volume influences outcome of lower limb (LL) vascular surgery remains unclear. This review evaluated the relationship between hospital/surgeon volume and outcome in LL surgery.

Methodology

Electronic databases; Medline, Embase, the Cochrane Library Databases, Science Citation Index, and CINAHL, proceedings from conferences, citations, and references of included studies were searched. Studies from Europe, of adults undergoing LL vascular surgery reporting outcomes by hospital or surgeon volume were included. Quality of studies was assessed using a modified ACROBAT-NRSI(Robins1) tool. Association between hospital/surgeon volume and outcome were summarised using tables.

Results

Nine studies from different European countries, comprising 67,445 patients who had undergone diverse LL surgeries were included. Increase in hospital/surgeon volume was associated with a decrease in amputations. The evidence on an association between hospital/surgeon volume and mortality was contradictory, but mortality and amputations may co-vary by hospital volume. There were an insufficient number of studies reporting on the other variables to draw firm conclusions; but their results suggest high volume hospitals may undertake more repeated surgeries/revascularisations and limb salvage. The impact of hospital/surgical volume on adverse events and length of hospitalisation could not be determined.

Conclusion

High volume hospitals/surgeons may undertake fewer amputations and mortality and amputations may co-vary. The finding that hospital and surgeon volume affected the number of secondary

amputations has implications on re-organisation of vascular surgery services. However due to the small number and poor quality of some of the included studies, decisions on reorganisation of LL vascular surgery services should be supplemented by results from clinical audits. There is need for standardisation of definition of volume stratification of outcomes by patient's clinical conditions.

Key words: Peripheral vascular disease; Critical leg ischaemia; Claudication; Hospital or surgeon volume; Amputation; Mortality.

1. Introduction

Health care service commissioning groups in the United Kingdom (UK), Europe, and globally are faced with the complex challenge of organizing the health delivery service so as to minimise cost, maximise cost-effectiveness, local access, service quality, effectiveness in achieving better clinical outcomes, and improving patients quality of life. A 2008 study by Holt et al[1] reported that higher-volume hospitals/surgeons achieve better outcomes for high-risk procedures, and suggested the reconfiguration of health care services based on the volume model.

Some researchers; Awopetu et al[2], Killeen et al[3], Gandjour et al[4], and Shackley et al[5] have reviewed the association between hospital/surgeon volume and outcome in lower limb vascular surgery. However, of the four reviews[2-5], only one[2] drew firm conclusions; reporting that high volume hospitals (HVH) had significantly lower mortality compared with low volume hospitals (LVH). The other three[3-5], found inconclusive or ambiguous results, due to the small number of identified studies, and the heterogeneity in their findings.

1.1. Rationale for conducting the review

Among previous reviews on the association between volume in LL surgery and outcome, Shackley et al.,[3] focused mainly on abdominal aortic aneurism (AAA) and carotid endarterectomy; including only four studies considering LL surgery which found contradictory results and authors failing to reach conclusions due to the small number of studies. The other reviews[2-4], included studies mostly conducted in the United States of America (USA), making the outcomes more relevant to USA context. The significance of hospital/surgeon volume in lower limb (LL) vascular surgery, in influencing outcomes, in UK and Europe, has therefore not been clearly elucidated. There is need for an up-to-date evidence relevant to European settings, to aid in the planning and delivery of healthcare in a manner which will maximise local access, viability, and service quality, in the UK and Europe, hence the importance of this review.

1.2. Objectives of the review

This study aimed to investigate:

1. The relationship between the volume of LL vascular surgery undertaken by individual surgeons and risk of mortality, amputation, repeat surgery, length of hospitalisation, and other adverse events (AEs).
2. The relationship between the volume of LL vascular surgery undertaken in individual hospitals and risk of mortality, amputation, repeat surgery, length of hospitalisation, and other AEs.

2. Methodology

2.1. Search strategy

The review was undertaken according to the PRISMA guideline and followed a registered protocol on PROSPERO (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014014850). Comprehensive literature searches were conducted on Medline and Medline in Process, Embase, the Cochrane Library Databases, Science Citation Index, and CINAHL. Proceedings from five key conferences held between 2010 and 2015, and citations and references of included studies were also searched. Literature searching involved two phases; an initial strategy based on a 2000 systematic review by Michaels et al[6], was adapted and run in MEDLINE and other electronic databases as detailed in Appendix 1. A second search iteration extended the initial strategy using the keywords and index terms focussing on surgical procedures and patient outcomes. Further relevant terms for these concepts were generated by consulting with the clinicians in the project team. Details of data sources and the search strategies are provided in Appendix 1.

2.2. Inclusion and exclusion criteria

The research question was focused using the PICOS criteria. Study selection was based on pre-specified criteria summarised in Table 1.

2.3. Study selection and quality assessment

Titles and abstracts of all records were screened by PP and EG. Full text papers were retrieved for studies that appeared to meet inclusion criteria. When needed, a third reviewer (EP or ME) was consulted to resolve disagreements. Data was extracted using a pre-piloted Excel form. Abstracted data included study characteristics (e.g. year and place of publication, study design, and characteristics of participants), and relevant outcomes reported according to specified strata of hospital or surgeon volume. Study quality was assessed using a modified version of A Cochrane Risk Of Bias Assessment Tool: for Non-Randomized Studies of Interventions (ACROBAT-NRSI)[7] (Robins1) tool. Details of the tool and the domains used in the assessment are provided in Appendix 2. A second reviewer double-checked data from all included studies (PP/EG). Disagreements were resolved by discussion with a third reviewer (EP/ME).

2.4. Data analysis

Due to the heterogeneity in the types of procedures carried out in included studies (endarterectomy, bypass, stents, or angioplasty), and case-mix (gangrene, ischaemia or claudication), a meta-analysis could not be conducted; therefore a narrative synthesis was undertaken. Odds ratios and other raw data of outcomes by hospital or surgeon volume were summarised using tables.

3. Results

The search from all sources identified 16,719 records. After removing duplicates, the abstracts and titles of 14,486 were screened for eligibility. Twenty seven (27) full articles seemed to meet the inclusion criteria, and were retrieved and read in full. Nine studies[8-16] met the inclusion criteria and were included (Figure 1). A list of studies excluded at full text level and reasons for exclusion is given in Appendix 3.

3.1. Characteristics of included studies

3.1.1. Study design: Studies included in this review were mainly observational studies that utilised clinical/administrative data (Table 2); two studies[9,13] retrospectively analysed data on vascular procedures extracted from the Hospital Episodes Statistic (HES) database (for 2002 to 2006; and 2007 to 2011), the other seven studies[8,10-12,14-16] analysed retrospectively collected data from different vascular projects. All studies were from Europe, of which three[8,9,13] were from the United Kingdom, one[12] from UK and the Ireland, two[10,14] from Sweden, two[11,16] from Finland, and one[15] from Denmark. Together the nine studies recruited 67,445 patients, with 439 as the lowest number and 31,821 as the highest, and varied in duration from 3 months to 20 years. Only one of the nine studies[11] reported both hospital and surgeon specific volume outcomes. Five studies[8-10,13,15] reported outcomes by hospital volume only, whereas three[12,14,16] reported surgeon volume only. There was heterogeneity with regard to the definition of surgeon and hospital volume by studies. Six studies[9,11-14,16] classified volume as quantiles, whereas three[8,10,15] used continuous volume. The designation of a low-volume hospital ranged from 2 to <20 procedures, and a high-volume institution from >20 to >67. On the other hand, low volume surgeons were defined as those performing 10 up to 20 surgeries annually, and high-volume surgeons as those performing >10 to >50 surgeries per year (Table 2).

3.1.2. Case and procedure mix: Patients who had LL surgeries in the included studies had a mean age range of 62 to 74.5 years (median 66 to 71 years), and mostly male; percentage male range 46% to 70% (Table 2). The types of procedures and indications for surgery greatly differed by studies; Moxey et al[9] analysed data for femoropopliteal and femorodistal bypasses in patients with intermitted claudication or gangrene, whereas Troeg et al[14] investigated outcomes after femoropopliteal grafting in patients with chronic leg ischaemia or claudication. The procedures in Kantonen et al[11] included endarterectomies, patch-angioplasties, and percutaneous transluminal angioplasties (PTA). Other procedures included infrainguinal reconstructions in patients with critical leg ischaemia[10,12], elective and non-elective stenting of the iliac artery[13], and unspecified vascular surgeries in patients with critical leg ischaemia[8] (Table 2).

3.1.3. Assessment of bias: Study quality was assessed using a modified version of the ACROBAT-NRSI (Robins1)[7]. All the studies were considered to have high risk of selection bias (Figure 2).

Studies that had used quantiles to define hospital/surgeon volume[9,11-14] were considered to have high risk of volume measurement bias. Four studies[8-10,14], did not report details of number of patients not included in the final analysis, and were therefore classified as having unclear risk of attrition. Studies that had prospectively recorded outcomes[11,12,14-16] were considered to have low risk of bias of outcome measurement, especially for mortality; however those which had used healthcare administrative databases[8,9,13], were classified as having high risk of outcome measurement bias. Five studies[9,11,14-16] adjusted for, or compared prevalence of various confounders at baseline[12], and were deemed to have low risk of confounding, whereas the others, either did not adjust for confounders, or adjusted for only age and sex, and were thought to be highly to moderately confounded. Most of the studies[8,9,11-16], did not mention whether analyses conducted were based on a prior published protocol, and were therefore classified as having unclear risk of reporting bias.

3.2. Volume and mortality

3.2.1. Hospital volume and mortality: Five studies[9-11,13,15], reported data on hospital volume and mortality (Table 3). Four of these[9-11,15], adjusted for most confounders, whereas one[13], adjusted only for age and sex.

The evidence on this outcome was contradictory, with two of the five studies reporting an association; Moxey et al[9] found an association between increase in hospital volume and a decrease in mortality during index admission (OR: 0.960, 95% CI: 0.929–0.992, p = 0.014), but not at 1 year (OR: 0.987, 95% CI: 0.966–1.007, p = 0.197), in femoropopliteal bypass but not in femorodistal procedures (Table 3). Similarly, Elfstorm et al[10], reported an association between an increase in hospital volume and decrease in mortality at 1 year (OR: 1.66, 95% CI: 1.06 - 2.60). Over half of the patients in Moxey et al[9] (55% femoropopliteal/54% femorodistal) had surgery due to intermittent claudication whereas all patients in Elfstorm et al[10] were operated on because of chronic critical limb ischaemia. The definition of volume ranged from 11.2 to 110.7 patients per annum in Moxey et al[9] and 85 to 115 patients per annum in Elfstorm et al[10]; these might confound the outcome. The insignificant finding in femorodistal bypass surgeries suggests poor outcome in lower extremity vascular disease.

On the other hand the other three studies, Kantonen et al[11], Bredahl et al[15] and Goode et al[13], found no association between hospital volume and 30 day mortality post-operative (Table 3). The indications for surgery in[11,15] were chronic critical limb ischaemia or intermittent claudication, but Goode et al[13] did not report the conditions that necessitated surgery. The definition of volume also differed among these studies; Kantonen et al[11] using a cut-off of 20, Goode et al[13] a range of 1 to 111 in elective and 613 for non-elective, while Bredahl et al[15] used continuous annual number of cases; these might confound the outcome. The result could also be obscured by patient-mix.

3.2.2. Surgeon volume and mortality: Three studies[11,12,16], reported data on surgeon volume and mortality (Table 3). Of these two Kantonen et al[11], and Biancari et al[16], adjusted for most of the confounders, whereas VSGBI[12], did not adjust for confounders. All found no association between surgeon volume and in-hospital or 30 days mortality (Table 3). Patients in all the three studies[11,12,16] presented with critical leg ischaemia, but the definition of volume quantiles differed; Kantonen et al[11] and the Vascular Society of Great Britain and Ireland (VSGBI)[12] used a cut-off of 10, whereas Biancari et al[16] used 40 and this might have affected outcome. In all the three studies[11,12,16], outcome was within 30 days post-surgery. It is possible that the outcomes could be different if they were measured 1 year post surgery.

3.3. Volume and post-operative amputations

3.3.1. Hospital volume and amputations: Three studies[9-11] investigated this outcome and all found an association between volume and amputation (Table 4). Specifically, Moxey et al[9], reported that at 1 year, high volume hospitals had lower secondary major amputations, in patients who had femoropoliteal bypass surgery (OR: 0.955, 95% CI: 0.928–0.983 p=0.002), and femorodistal bypass (OR: 0.658 (0.517–0.838, p= < 0.001). Kantonen et al[11] reported a similar outcome 30 days post-operation (OR: 1.49, 95% CI: 1.0 - 2.25, p = 0.05), whereas Elfstorm et al[10] found significant association at both 30 days and 1 year post-operation (OR: 5.01, 95% CI: 2.24 – 3.41, p = 0.01, and OR: 2.05, 95% CI: 1.24 – 3.42, p = 0.01 respectively).

3.3.2. Surgeon volume and amputations: Three studies[11,12,16] reported the association between surgeon volume and post-operative amputations 30 days post-surgery and all found a correlation between surgeon volume and secondary amputations. Kantonen et al[11] and Biancari et al[16], who adjusted for most of the confounders, found that experienced surgeons performed fewer post-operative amputations (OR: 1.89, 95% CI: 1.15 - 2.80, p = 0.01 and OR: 0.40, 95% CI: 0.18–0.91, p = 0.03 respectively). Similarly, the VSGBI[12] study, which did not adjust for confounders, reported a similar outcome (OR: 0.41, 95% CI: 0.24 – 0.69, p = 0.0006) (see Table 4). The indication for surgery in all the three studies[11,12,16] was critical leg ischaemia.

3.4. Volume and re-operation, revascularisations, or limb salvage

3.4.1. Hospital volume and re-operation: Only one study Moxey et al[9] reported association between hospital volume and repeated surgery in patients with intermitted claudication and other conditions. They found that high volume hospitals conducted more revisional bypass procedures at 1 year (OR: 1.031, 95%, CI: 1.005–1.057, p=0.018), but not during index admission (OR: 1.017, 95% CI: 0.965–1.070, p=0.532). No such association was observed in femorodistal surgeries, suggesting poor outcome in lower extremity bypasses (Table 5).

3.4.2. Surgeon experience and volume of revascularisations and limb salvage: Two studies, the VSGBI[12] and Biancari et al[16] investigated the association between surgeon volume and rates of revascularisation or limb salvage. The VSGBI[12] found that surgeons with a lower annual experience tended to undertake fewer revascularisations (60.6% vs. 74.9%; $\chi 2= 8.9$, $p = 0.003$), and that low volume/experienced surgeons had a lower mean limb salvage rate than high volume/experienced surgeons (65.4 vs. 81.3, $\chi 2= 12.8$, $p = 0.0003$). In addition, Biancari et al[16] also reported a similar finding (Table 5). The small number and poor quality of the included studies, makes it difficult to draw any firm conclusions.

3.5. Volume and any adverse events

Surgical operations for peripheral vascular disease are associated with a number of adverse events including systemic or wound infection/patency, bleeding/haemorrhage, lesions and gangrene, cardiac and pulmonary comorbidities, renal failure, or prolonged hospitalisations which might result in bed sores (pressure ulcers)[17,18]. In this review, four of the included studies investigated the impact of hospital[9,13,15] and surgeon volume[14], respectively, on occurrence of any adverse events (Table 6), while three studies reported the impact of hospital[8,13] and surgeon volume[16] on length of hospitalisation (LOS)-(Table 7).

3.5.1. Hospital volume and AEs: Evidence from three studies[9,13,15] that reported this outcome was inconclusive; Moxey et al[9] found that an increase in volume was associated with a decrease in AEs during index admission in femoropopliteal bypass surgeries (OR: 0.968; 95% CI, 0.940–0.998; p=0.034), but not in femorodistal surgeries (ORs not reported). A similar finding was reported by Bredahl et al[15]. On the contrary, Goode et al[13], who adjusted only for age and sex, found no association between hospital volume and AEs occurring during admission (OR: 1.0, 95%CI: 1.0 – 1.0) for both elective and non-elective surgery (Table 6). The conflicting outcomes here may be either due to differences in patient-mix, volume quantiles used, or locality of vascular insufficiency.

3.5.2. Surgeon volume and AEs: Only Troeg et al[14] analysed the association between surgeon volume and AEs. They found no association between volume and any AEs (Table 6). It is difficult to draw any conclusions on the association between surgeon volume and AEs as only one study had data on this outcome.

3.6. Volume and length of hospitalisation (LOS)

3.6.1. Hospital volume and LOS: Two studies[8,13] analysed the association between hospital volume and LOS and reported contradicting results. Goode et al[13] found no association between hospital volume and LOS, regression coefficient -0.010, 95% CI: -0.045 – 0.26 for elective, and -0.310, 95% CI: -0.642 – 0.022 for non-elective iliac artery operations. However Berridge et al[8] found clearly marked difference in LOS between high and low volume hospitals among patients who had major amputations (Table 7). The association between hospital volume and LOS cannot therefore be determined.

Surgeon volume and LOS: Only one study Biancari et al[16] reported on surgeon volume and LOS, and found no association (Table 7). Since only one study reported on this outcome, it is difficult to ascertain the significance of surgeon volume on LOS.

4. Discussion and conclusion

This review found an association between an increase in hospital[9-11] or surgeon[11,16] volume and decrease in post-operation amputations. The direction of association between hospital volume and risk of mortality is inconclusive; whilst some studies found that high volume hospitals had lower mortality rates[9,10], others[11,13,15] found no such association. The results suggest that high volume hospitals may undertake more revascularisations, limb salvage, and repeated surgeries, but the association between volume and length of hospitalisation and AEs could not be determined. Our finding on association between volume and amputations agrees with previous studies[2,6,19,20]. Whereas that about hospital volume and mortality is similar to reviews by Awopetu et al[2], Gandjour et al[4], Killeen et al[3], and Shackley et al[5] who also found inclusive or ambiguous results on association between volume and mortality.

The heterogeneity in findings could be confounded by the diverse case-mix (including, among others; chronic/critical leg ischaemia, or chronic/intermittent claudication[21], and different types of procedures (endarterectomies, angioplasties, elective or non-elective stenting, infrainguinal reconstructions, femoropopleteal or femorodistal bypasses) in LL vascular surgery. The type of procedure a patient receives largely depends on the severity of their illness[22,23]. Some studies have reported that patients with chronic leg ischaemia are more likely to undergo amputations[22,23]. Unfortunately, studies included in this review did not provide outcome data (on the relationship between hospital/surgeon volumes) stratified by indication for surgery or type of procedure conducted, and therefore we could not carry out a stratified analysis on the effect of volume by these variables. However, in some of the studies, indication for surgery and type of procedure were adjusted for, and were found to be independent significant predictors of amputation and mortality[10,11,15], apart from hospital volume. Given that the type of procedure a patient receives is dependent on the patients clinical presentation[22,23], the possibility that differences in the findings in the studies included in this review, were confounded by differences in case-mix between hospitals and differences in types of procedures patients received, should be borne in mind when interpreting our results.

Included studies used different sources of data. The majority of the studies were observational using administrative databases and as such lack clinical detail. For studies that used historical data such as the HES database, where major diagnosis codes were used to identify LL surgery, there may be variability in coding by different hospitals, or different departments, even prospectively collected data, sometimes do not capture all the available cases[10], and variables of all confounding factors, and this may have introduced selection bias. Also, studies included in this review were drawn form a number of different countries, which might have different regional health systems and referrals within those regions, and this might have further introduced selection bias. Therefore the existence of selection bias, and confounding due to inability to control for all important confounders, in the included studies, should be borne in mind. However, the strengths of this study include that a comprehensive literature search, focusing on studies conducted in the UK and Europe, and a rigorous systematic review of the identified studies, were conducted.

The definition of mortality varied from in-hospital mortality[12,13], to 30-days[9-11] and 1-year[9,10] post-operative. However, no consistency was observed between the mortality proxy measure used and outcome. Thus the two studies that analysed in-hospital mortality[12,13] found no association between volume and mortality, whereas the three that employed 30-day mortality[9-11] found conflicting results. The difference in findings in[9-11] could as well be due to case-mix. Some authors have argued that the aim of vascular surgery is to improve long term quality of life of the patient, and 30-day follow-up would only give an indication of the technical validity of the procedure. Suggesting that a 1-year follow-up may give the true benefit of the surgery[24]. However, in this review, there was a contradiction; Elfstorm et al.,[10] found a significant variation in mortality by hospital volume at 1 year, whereas Moxey et al[9] found no association. More research is needed to determine the best mortality time points in LL vascular surgery.

The quantification of hospital or surgeon volume has not been standardised. Six studies[9,11-14,16] classified volume as quantiles, whereas three[8,10,15] used continuous volume. The justification for choosing the different volume cut-off points has varied from study to study. Kantonen et al[11] chose the cut-off point of 10 cases per surgeon and 20 cases per hospital based on the VSGBI[12] report which suggested that surgeons who conducted >10 operations per year had better results. In summarising the results of the SWEDVASC study, Bergqvist et al[24] suggested that confidence intervals are likely to be wide unless there are at least 50 operations, and urged that comparisons of surgeon/hospital volume <50 should not be conducted. In this review, the findings among the six studies that used volume quantiles[9,11-14,16], and the three[8,10,15] that employed continuous volume, varied. As the significance of the various volume quantiles has not been clearly demonstrated, we recommend continuous volume be used as a standard volume measure in future volume research.

We could have constructed funnel plots to investigate the existence of publication bias in this review. However, for each outcome, we only had three to four studies reporting that outcome. Such a funnel plot would therefore not give any meaningful result. But only studies published in the English language were included in this review, and this may have introduced publication bias. Also five[10-12,14,16] of the nine included studies in the final analysis are 18 years old or more. Therefore, the possibility of publication bias should therefore be borne in mind when interpreting our results. However, this review was systematic and was based on rigorous methods of literature search, and we hope that this might have eliminated most of the bias.

5. Conclusion

The evidence from this review suggests that high volume hospitals/surgeons may undertake fewer post-operative amputations. They might also undertake more revascularisations, and repeated surgeries. The relationship between hospital/surgeon volume and mortality is still unclear, but mortality and amputations may co-vary by hospital volume. The finding that hospital and surgeon volume affected the number of secondary amputations has implications on re-organisation of vascular surgery services. However due to the small number and poor quality of some of the included studies, decisions on reorganisation of lower limb vascular surgery services should be supported by clinical audits. Prospective mandatory clinical audits on this subject, commissioned and funded through national registries, and quality improvement programmes funded using standard definitions, could aid in generating more evidence. There is need for the standardisation of reporting and definition of volumes in vascular research.

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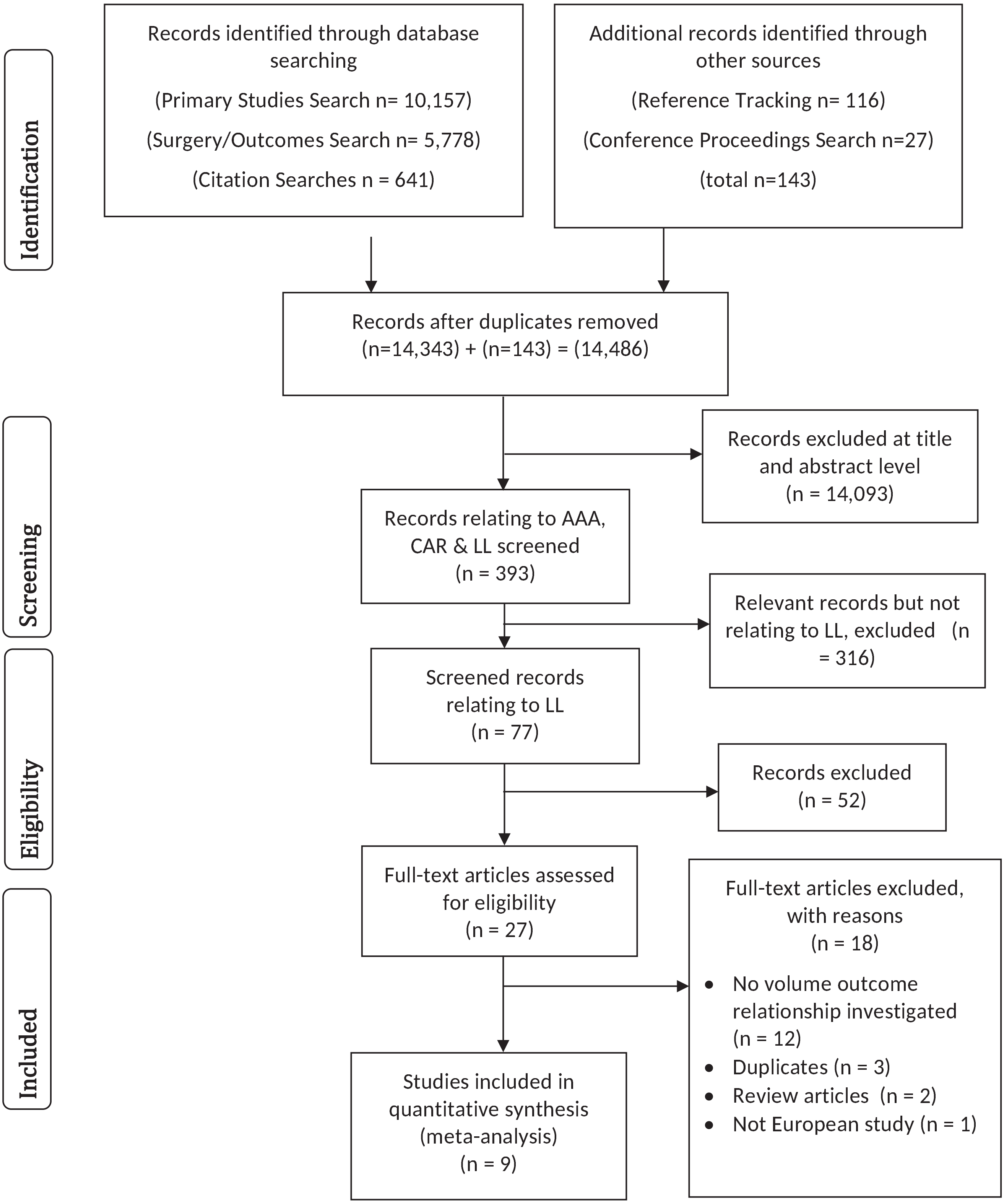

Figure 1: PRISMA diagram of search results and study selection

Notes: The search strategy combined terms for surgeries for three vascular conditions; abdominal aortic aneurysm repair (AAA), carotid endarterectomy (CER) or stenting (CAS), and lower limb vascular surgeries (LL). Three hundred and ninety three (393) abstracts and titles were screened to tag the studies whether they related to AAA, CAR, or LL and whether they were conducted in Europe or not. Among the 77 studies tagged as relating to LL, 25 were deemed relevant and full texts downloaded and assessed for eligibility for inclusion into the LL review.

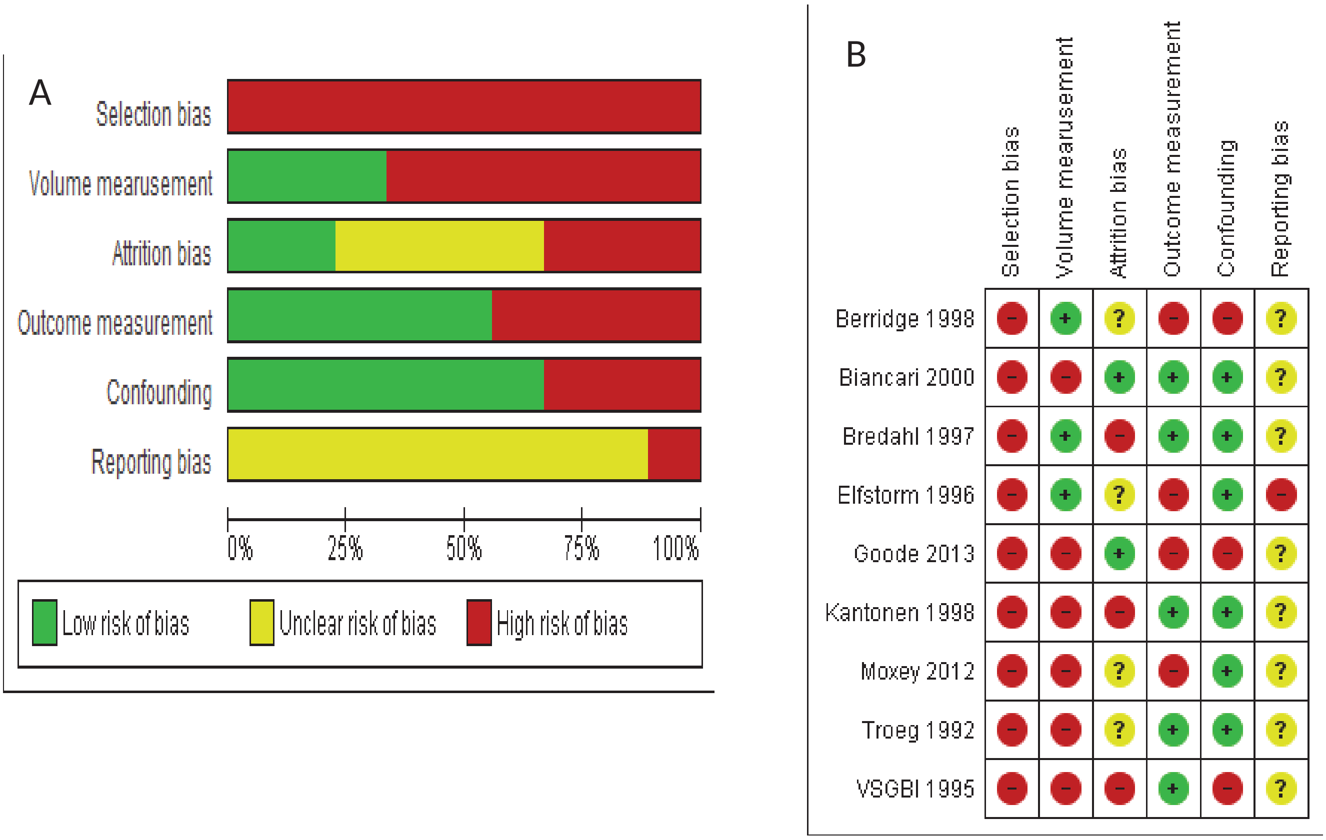

Figure 2: Risk of bias assessment of the included studies, A) summary for all the studies, B) bias by category in the 9 studies. **Notes:** Studies that had used quantiles to define hospital/surgeon volume were considered to have high risk of volume measurement bias, as the accuracy of the applied volume quantiles to correctly predict outcome cannot be ascertained. Studies that had prospectively recorded outcomes were considered to have low risk of bias of outcome measurement especially for mortality, however the measurement of other outcomes, other than mortality could still be biased. Those which had used healthcare administrative database were classified as having high risk of outcome measurement bias, because of the possibility that inter-hospital variation in codes for a similar condition and coding errors might have introduced bias.

Table 1: Inclusion and exclusion criteria

PICOS	Inclusion criteria	Exclusion criteria
Population	Studies recruiting adults (aged 18 years and over) undergoing elective or emergency peripheral vascular surgery	Studies in patients <18 years old, undefined/ mixed groups of vascular patients or mixed vascular and non-vascular populations, where data cannot be extracted separately for the population of interest.
Intervention	Patients who had undergone invasive procedures intended to maintain and repair blood vessels external to the heart and brain such as endarterectomies, bypasses, angioplasties	Patients who had undergone procedures to blood vessels of the heart or brain, such as coronary artery bypass grafting or repairs to subarachnoid haemorrhages; thoracic-aortic aneurysm repairs; renal or visceral artery procedures; interventions that are intended primarily as an aid to diagnosis; vascular surgical procedures related to acute traumatic injury
Comparator	Low vs. high volume hospitals or surgeons	Did not report outcomes by hospital/surgeon volume
Outcome	Mortality, amputation after surgery, repeated surgery, re-admission, length of hospital stay, any adverse events	Any other outcomes other than these risk factors to surgery
Study design	Prospective or retrospective designs with a contemporaneous comparison between low and high volume hospitals or surgeons.	Reviews, case reports, studies where allocation to group on the basis of outcome – (e.g. case-control studies)

Table 2: Characteristics of included studies

	Berridge et al[8]	Elfstrom et al[10]	Goode et al[13]	Kantonen et al[11]	Moxey et al[9]	Troeg et al[14]	VSGBI[12]	Bredahl et al[15]	Biancari et al[16]
Study design and country	Retrospective analysis of data from the CHKS database, UK	Retrospective analysis of the SWEDVASC database, Sweden	Retrospective analysis of data from HES database, UK	Retrospective analysis of data from the Finnvasc database, Finland	Retrospective analysis of data from HES database, UK	Retrospective analysis of data from the SWEDVASC database, Sweden	Clinical audit, prospective survey, UK and Ireland	Retrospective analysis of data from the Danish Vascular Registry database, Denmark	Observational study of outcomes of vascular procedures , Finland
Study duration	1995 (8 months; April-Dec)	1988-1990 (1 yr)	2007-2011 (4 yrs)	1991-1994 (3 yrs)	2002-2006 (1 yr)	1987-1989 (2 yrs)	1993 (3 months)	1993-2012 (20 yrs)	1991-1997 (6 yrs)
Sample size & (No of hospitals/ surgeons)	2,780 (3 hospitals)	809 (6 hospitals)	23,308 (262 hospitals)	2,296 (25 hospitals) No of surgeons not reported	31,821; FP (27,660, 160 hospitals), FD (4161, 140 hospitals)	809 (23 hospitals) No of surgeons not reported	590 (57 surgeons)	3767 (No of hospitals not reported)	439 (single centre study)
Definition of volume	HA, HB, HC, number of revascularisations and amputations performed by each hospital (continuous)	H1 (85) H2 (83) H3 (117) H4 (189) H5 (175), H6 (115) number of surgeries performed by each hospital (continuous)	Q1 (1-17) Q2 (18-27) Q3 (28-41) Q4 (42-66) Q5 (67-111) the total number of procedures conducted at the hospital over the 4 year period	H <20 vs >20 S <10 vs >10 operations by each hospital or surgeon/ year	FP, Q1 (11.2) Q2 (40.4) Q3, 50.0) Q4 (70.4) Q5 (110.7) FD, Q1 (2) Q2 (6.9) Q3 (10.0) Q4 (13.4) Q5 (19.0) median number of procedures performed by each hospital/ year	S1 (<20), S2 (20-50), S3 (>50), number of surgeries performed by each surgeon over the 2 years	S1 (0-10) S2 (11-20) S3 (21-30) S4 (>30) number of infrainguinal reconstructions performed by each surgeon annually	Continuous annual hospital case load	>40 during the entire study period (6 years) = experienced surgeon

Table 2: Characteristics of included studies, continued

	Berridge et al[8]	Elfstrom et al[10]	Goode et al[13]	Kantonen et al[11]	Moxey et al[9]	Troeg et al[14]	VSGBI[12]	Bredahl et al[15]	Biancari et al[16]
Mean/Median age/ years (SD/range)	Not reported	74.5	Elective median 66 (59 - 74), non-elective median 61.6 (62 - 78)	70.5	FP (69), FD (71)	Intermittent claudication median 66 (55-86), critical ischaemia 73 (61-96)	Not reported	62 (SD, 9)	71.8 (range, 24-96)
Sex (Males)%	Not reported	54% (410/764)	67.2% (13,456/20,027)	58% (10,21/1761)	FP (68%), FD (70%)	Intermittent claudication (65.5), critical ischaemia (50.0)	60.0% (406/679)	46% (1734/3767)	51.9% (223/430)
Indications for surgery & procedures carried out	Vascular/venous surgeries in patients with critical leg ischaemia	Infrainguinal operations in patients with ulcer or gangrene, rest pain, claudication and other conditions	Elective/non-elective iliac artery angioplasty and stenting, (conditions not stated)	Endarterectomies and angioplasties in patients with chronic critical leg ischaemia	Femoropopliteal and femorodistal bypass in patients with intermitted claudication or gangrene)	Vascular surgeries in patients with chronic leg ischaemia or claudication	Infrainguinal reconstructions in patients with critical leg ischaemia	Aortobifemoral (ABF) or an aortobiiliac (ABI) bypass for chronic critical limb ischemia or intermittent claudication	Revascularization procedures (infrapopliteal bypass grafts) to the infrapopliteal arteries in patients with critical leg ischemia.
Adjustment for confounders	Unadjusted	Adjusted for most confounders; only odds ratios for hospital 1 vs. 6 reported	Age and sex	Adjusted for most confounders	Adjusted for most confounders	Adjusted for most confounders	Unadjusted but confounders equally distributed	Adjusted for most confounders	Adjusted for most confounders

Notes: HA-hospital volume A, HB – volume B, and HC volume C, S-surgeon volume, Q1-quantile 1-Q2, quantile 2 etc, FP-Femoropopliteal bypass procedures, FD-femorodistal bypass procedures, HES-hospital episodes data, FINVASC-National vascular registry in Finland, SWEDVASC-Swedish National Registry for Vascular Surgery, CHKS-National Comparative Database (UK).

Table 3: Hospital and surgeon volume in lower limb vascular surgery and mortality

Study	Definition of volume	Indication for surgery	Time of event					
			30 days post-surgery			1 year post-surgery		
			OR	95% CI	p	OR	95% CI	p
A. Hospital volume and mortality								
Adjusted for most confounders								
Moxey 2012[9]G7	q1(<11.2), q2(40.4), q3(50.0), q4(70.4), q5(110.7)	Intermittent claudication 55.0%, gangrene 24%, others not stated	0.96	0.93–0.99	0.014*	0.99	0.97–1.0	0.197
FD	q1(2), q2(6.9), q3(10.0), q4(13.4), q5(19)	Intermittent claudication 54.2%, gangrene 24%, others operation not stated		No association			No association	
Elfstorm 1996[10]	q1(<85), q2(83), q3(117), q4(189), q5(175), q6(115)	Ulcer/gangrene (38%), rest pain 36%, Claudication (11%), other (14%)	1.82	0.83 - 4.00	-	1.66	1.06 - 2.60	0.05*
Kantonen 1998[11]	<20 vs. >20	Chronic critical leg ischaemia		No association		-	-	-
Bredahl 1997[15]	Continuous annual number of cases	Chronic critical limb ischaemia or intermittent claudication		No association		-	-	-
-								
Adjusted for only Age and Sex								
Goode 2013[13] EL	q1(1-17), q2(18-27), q3(28-41), q4(42-66) , q5(67-111)	Conditions that necessitated operation not stated	1	1.00 – 1.00	-	-	-	-
Non-EL	q1(1-113), q2(114-163), q3(164-202), q4(202-349) , q5(350-613)		1	1.00 – 1.00	-	-	-	-
B. Surgeon volume and mortality								
Adjusted for most confounders								
Kantonen 1998[11]	<10 vs. >10	Chronic critical leg ischaemia		No association		-	-	-
Biancari 2000[16]	<40 vs >40 during the entire study period (6 years)	Critical leg ischaemia		No association		-	-	-
Unadjusted								
VSGBI 1995[12]	q1(0-10), q2(11-20), q3(21-30) , q4(>30)	Critical leg ischaemia	1.1	0.58-2.07	0.76	-	-	-

Notes: FP-femoropopliteal, FD-femorodistal, EL- elective iliac artery angioplasty, Non-EL-non-elective iliac artery angioplasty, VSGBI – The vascular society of Great Britain and Ireland. No association means the authors reported in text that they found no association between volume and outcome but no odds ratios were provided. A dash (-) means data for that statistic was not provided. Volumes were defined as average annual number of procedures conducted by each hospital or surgeon. Bredahl 1997[15] did not provide the exact number of procedures conducted by each hospital. .* means the statistic was significant at $\alpha = 0.05$.

Table 4: Hospital/surgeon volume in lower limb surgery and post-operative amputations

Study	Definition of volume	Indication for surgery	Time of event					
			30 days post-surgery			1 yr post-surgery		
			OR	95% CI	p	OR	95% CI	p
A) Hospital volume and amputations								
Adjusted for most confounders								
Moxey 2012[9]b6	q1(<11.2), q2(40.4), q3(50.0), q4(70.4), q5(110.7)	Intermittent claudication 55.0%, gangrene 24%, others not stated	0.96	0.92–1.00	0.06	0.96	0.93–0.98	0.002*
FD	q1(2), q2(6.9), q3(10.0), q4(13.4), q5(19)	Intermittent claudication 54.2%, gangrene 24%, others not stated		No association		0.66	0.52–0.84	< 0.001*
Elfstorm 1996[10]	q1(<85), q2(83), q3(117), q4(189), q5(175), q6(115)	Ulcer/gangrene (38%), rest pain 36%, Claudication (11%), other (14%)	5.01	2.24 – 3.41	0.01*	2.05	1.24 – 3.42	0.01*
Kantonen 1998[11]	<20 vs. >20	Chronic critical leg ischaemia	1.49	1.00 - 2.25	0.05*	-	-	-
B) Surgeon volume and amputations								
Adjusted for most confounders								
Kantonen 1998[11]	<10 vs. >10	Chronic critical leg ischaemia	1.89	1.15 - 2.80	0.01*	-	-	-
Biancari 2000[16]	<40 vs >40 during the entire study period (6 years)	Critical leg ischaemia	0.40	0.18–0.91	0.03*	-	-	-
Unadjusted								
VSGBA 1995[12]	q1(0-10), q2(11-20), q3(21-30) , q4(>30)	Critical leg ischaemia	0.41	0.24-0.69	0.0006*	-	-	-

Notes: FP-femoropopliteal, FD-femorodistal, VSGBI – The vascular society of Great Britain and Ireland. No association means the authors reported in text that they found no association between volume and outcome but no odds ratios were provided. A dash (-) means data for that statistic was not provided. Volumes were defined as average annual number of procedures conducted by each hospital or surgeon.* means the statistic was significant at α = 0.05.

Table 5: Hospital volume and repeated surgery/ Surgeon experience and limb salvage rate in lower limb vascular surgery

Study	Definition of volume	Indication for surgery	Time to event					
			30 days post-surgery			1 yr post-surgery		
			OR	95% CI	p	OR	95% CI	p
A) Hospital volume and repeated surgery								
Adjusted for most confounders								
Moxey 2012[9]	q1(<11.2), q2(40.4), q3(50.0), q4(70.4), q5(110.7)	Intermittent claudication 55%, gangrene 24%, others not stated	1.02	0.97–1.07	0.532	1.03	1.01-1.06	0.018*
FD	q1(2), q2(6.9), q3(10.0), q4(13.4), q5(19)	Intermittent claudication 54.2%, gangrene 24%, others not stated	No association			No association		
B) Surgeon experience and limb salvage rate								
Unadjusted								
Biancari 2000[16]	<40 vs >40 during the entire study period (6 years)	Critical leg ischaemia	2.36	1.36-4.11	0.002*	-	-	-
VSGBI[12]	q1(0-10), q2(11-20), q3(21-30) , q4(>30)	Critical leg ischaemia	2.93	1.69-5.09	<0,0001*	-	-	-

Notes: FP-femoropopliteal, FD-femorodistal, VSGBI – The vascular society of Great Britain and Ireland No association means the authors reported in text that they found no association between volume and outcome but no odds ratios were provided. A dash (-) means data for that statistic was not provided. Volumes were defined as average annual number of procedures conducted by each hospital or surgeon.* means the statistic was significant at $\alpha = 0.05$.

Table 6: Hospital/surgeon volume and adverse events in lower limb vascular surgery

Study	Definition of volume	Indication for surgery	Time of event					
			30 days post-surgery			1 year post-surgery		
			OR	95% CI	p	OR	95% CI	p
A) Hospital volume and adverse events								
Adjusted for most confounders								
Moxey 2012[9]**pm**	q1(<11.2), q2(40.4), q3(50.0), q4(70.4), q5(110.7)	Intermittent claudication 55.0%, gangrene 24%, others not stated	0.97	0.94–0.10	0.034*	0.99	0.97–1.00	0.132
FD	q1(2), q2(6.9), q3(10.0), q4(13.4), q5(19)	Intermittent claudication 54.2%, gangrene 24%, others not stated	No association			No association		
Adjusted for age and sex								
Goode 2013[13] EL	q1(1-17), q2(18-27), q3(28-41), q4(42-66) , q5(67-111)	Conditions that necessitated operation not stated	1	1.0 – 1.0	-	-	-	-
Non-EL	q1(1-17), q2(18-27), q3(28-41), q4(42-66) , q5(67-111)	Conditions that necessitated operation not stated	1	1.0 – 1.0	-	-	-	-
Bredahl 1997[15]	Continuous annual number of cases	Chronic critical limb ischaemia or intermittent claudication	Increase in volume was associated with fewer adverse events*			-	-	-
B) Surgeon volume and adverse events								
Unadjusted								
Troeg 1992[14]	S1 (<20), S2 (20-50), S3 (>50)	Chronic critical limb ischaemia	2.1	0.45-3.75	0.15	-	-	-

Notes: FP-femoropopliteal, FD-femorodistal. EL- elective iliac artery angioplasty, Non-EL-non-elective iliac artery angioplasty. No association means the authors reported in text that they found no association between volume and outcome but no odds ratios were provided. A dash (-) means data for that statistic was not provided. Volumes were defined as average annual number of procedures conducted by each hospital or surgeon.* means the statistic was significant at α = 0.05.

Table 7: Hospital and surgeon volume of vascular surgery and length of hospitalisation

Study		Definition of volume	Indication for surgery	Procedure	Low volume	High volume	Conclusion
A) Hospital volume and length of hospitalisation							
Adjusted for age and sex							
Goode 2013	EL	q1(1-17), q2(18-27), q3(28-41), q4(42-66) , q5(67-111)	Conditions that necessitated operation not stated	Iliac artery Angioplasty	1.9 days	1.8 days	No association
	Non-EL	q1(1-113), q2(114-163), q3(164-202), q4(202-349) , q5(350-613)	Conditions that necessitated operation not stated	Iliac artery Angioplasty	12.5 days	10.5 days	No association
Unadjusted							
Berridge		Continuous annual number of cases	Critical leg ischaemia	Major amputations	32.4 days	18.3 days	Marked difference
B) Surgeon volume and length of hospitalisation							
Adjusted for most confounders							
Biancari		<40 vs >40 during the entire study period (6 year	Critical leg ischaemia	Femoropopliteal bypass	-	-	No association

Notes: EL- elective iliac artery angioplasty, Non-EL-non-elective iliac artery angioplasty. Volumes were defined as average annual number of procedures conducted by each hospital or surgeon.

Appendix 1: Search strategy

Data Sources

Data Sources Scoping Search

Medline and Medline in Process via Ovid
Embase via Ovid
The Cochrane library of systematic reviews via Wiley
Database of Abstracts of Effects (DARE) via Wiley

Data Sources Primary Studies Search

Medline and Medline in Process via Ovid
Embase via Ovid
The Cochrane library (all databases) via Wiley
Science Citation Index/ Book Citation Index - Science and Conference Proceedings Citation Index - Science via Thomson Reuters
CINAHL via EBSCO

Data Sources Surgery/Outcomes Search

As for primary studies search

Data Sources Conference Proceedings Search

The websites for the following conferences were scanned for outputs (posters or oral presentations) with any relevance to the topics of volume of vascular surgery and patient outcomes:

UK Vascular Society.
http://www.vascularsociety.org.uk

European Vascular Society
http://www.esvs.org

BSIR (British Society of Interventional Radiology)
http://www.bsir.org,

ISVS (International Society for Vascular Surgery)
(http://www.isvs.com)

SVS (Society for Vascular Surgery)
http://www.vascularweb.org/educationandmeetings/2015vam/Pages/home.aspx.

Data Sources Citation Search

Science Citation Index (Web of Science) via Thomson Reuters

Scopus via Elsevier (where results not found in WoS)

Search Strategies

Scoping Search

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

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1 exp Vascular Surgical Procedures/ut [Utilization] (1806)

2 vascular surg$.mp. (33992)

3 exp Endarterectomy/ut (176)

4 Peripheral Arterial Disease/ (2447)

5 exp Peripheral Vascular Diseases/ (45653)

6 Intermittent Claudication/ (7157)

7 Amputation/ (16658)

8 (Peripheral arterial disease$ or peripheral vascular disease$).mp. (23163)

9 intermittent claudication.mp. (8577)

10 (Aortic aneurysm or triple A or true aneurysm).mp. (43979)

11 Aortic Aneurysm/ (18847)

12 Aortic Aneurysm, Abdominal/ (14281)

13 (carotid disease or carotid angioplasty or carotid surgery).mp. (3114)

14 exp Carotid Artery Diseases/ (38964)

15 exp Carotid arteries/ (51386)

16 (transient isch?emic attack or TIA or stroke).mp. (196320)

17 exp Stroke/ (91854)

18 Cerebrovascular Disorders/ (44229)

19 exp Brain Ischemia/ (85599)

20 (venous insufficiency or varicose vein$ or venous leg ulcer$).mp. (20286)

21 exp Venous Insufficiency/ (6093)

22 exp Varicose Veins/ (15810)

23 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 (485513)

24 (surgeon volume or case volume or hospital Volume or workload).mp. (30063)

25 (surgery and (volume or outcome)).ti. (6182)

26 (surgery adj5 (volume or outcome)).ab. (13415)

27 exp Physician's Practice Patterns/ (43633)

28 exp Health services misuse/ (7557)

29 exp Utilization review/ (10730)

30 (surgery adj3 (utilisation or utilization)).ti,ab. (252)

31 24 or 25 or 26 or 27 or 28 or 29 or 30 (106459)

32 23 and 31 (4107)
33 Meta-Analysis as Topic/ (14509)
34 meta analy$.tw. (71100)
35 metaanaly$.tw. (1422)
36 Meta-Analysis/ (53861)
37 (systematic adj (review$1 or overview$1)).tw. (60909)
38 exp Review Literature as Topic/ (8068)
39 or/33-38 (136655)
40 cochrane.ab. (34565)
41 embase.ab. (33513)
42 (psychlit or psyclit).ab. (932)
43 (psychinfo or psycinfo).ab. (14233)
44 (cinahl or cinhal).ab. (11624)
45 science citation index.ab. (2193)
46 bids.ab. (388)
47 cancerlit.ab. (606)
48 or/40-47 (59856)
49 reference list$.ab. (10939)
50 bibliograph$.ab. (12608)
51 hand-search$.ab. (4356)
52 relevant journals.ab. (799)
53 manual search$.ab. (2606)
54 or/49-53 (27997)
55 selection criteria.ab. (21640)
56 data extraction.ab. (11276)
57 55 or 56 (31152)
58 Review/ (1969448)
59 57 and 58 (20616)
60 Comment/ (620891)
61 Letter/ (877156)
62 Editorial/ (373781)
63 animal/ (5531985)
64 human/ (14013133)
65 63 not (63 and 64) (3985649)
66 or/60-62,65 (5328963)
67 39 or 48 or 54 or 59 (171961)
68 67 not 66 (161249)

69 32 and 68 (100)

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Primary Studies Search

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

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1 exp Vascular Surgical Procedures/ut [Utilization] (1816)

2 vascular surg$.mp. (34473)

3 exp Endarterectomy/ (13415)

4 Peripheral Arterial Disease/ (2520)

5 exp Peripheral Vascular Diseases/ (45855)

6 Intermittent Claudication/ (7171)

7 Amputation/ (16863)

8 (Peripheral arterial disease$ or peripheral vascular disease$).mp. (23380)

9 intermittent claudication.mp. (8603)

10 (Aortic aneurysm or triple A or true aneurysm).mp. (44255)

11 Aortic Aneurysm/ (18915)

12 Aortic Aneurysm, Abdominal/ (14335)

13 (carotid disease or carotid angioplasty or carotid endarterectomy or carotid surgery).mp. (10408)

14 exp Carotid Artery Diseases/ (39195)

15 carotid stenosis/ (12586)

16 (venous insufficiency or varicose vein$ or venous leg ulcer$).mp. (20408)

17 exp Venous Insufficiency/ (6132)

18 exp Varicose Veins/ (15867)

19 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 13 or 14 or 15 or 16 or 17 or 18 (170939)

20 (surgeon volume or case volume or hospital Volume or workload).mp. (30386)

21 ((surgery or surgeon$ or surgical$) and (volume or outcome)).ti. (10958)

22 ((surgery or surgeon$ or surgical$) adj5 (volume or outcome)).ab. (29362)

23 exp Physician's Practice Patterns/ (44152)

24 exp Health services misuse/ (7624)

25 exp Utilization review/ (10888)

26 (surgery adj3 (utilisation or utilization)).ti,ab. (261)

27 20 or 21 or 22 or 23 or 24 or 25 or 26 (125387)

28 19 and 27 (2535)

29 10 or 11 or 12 (44255)

30 27 and 29 (763)

31 limit 30 to yr="2004 -Current" (487)

32 28 or 31 (2796)

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Surgery/Outcomes Search

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

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1 (Profundaplasty or carotid endarterectomy or amputation or aortic aneurysm repair or aorto-bifemoral bypass or femoro-popliteal bypass or femoro-distal bypass or endovascular aneurysm repair or EVAR or (carotid adj2 stent$) or CAS or angioplasty or balloon dilation or revascularisation or ((vascular or endovascular) adj2 (procedure or repair)) or (carotid adj2 (operation$ or surgery or procedure$)) or ((lower limb or arterial) adj2 (operation$ or surgery or procedure$)) or (arterial adj2 (operation$ or surgery or procedure$ or bypass or repair))).ti,ab. (101073)

2 exp *Vascular Surgical Procedures/ (140406)

3 1 or 2 (204334)

4 (re-admission or readmission or re admission or re-do or redo or re do or re-operation or reoperation or re operation or limb salvage or wound heal$ or length of stay).ti,ab. (104217)

5 (((post-operative or post-operative or postoperative) adj2 complication$) or mortality rate or hospital mortality or adverse outcome$ or survival rate or treatment outcome or stroke rate or fatal outcome or case fatality rate or outcome or outcome assessment or process assessment or complication or surgical mortality monitoring or ((clinical or surgical) adj2 performance) or ((amputation or morbidity or infection) adj2 rate)).ti,ab. (978814)

6 *postoperative complications/ or *hospital mortality/ or *survival rate/ or *treatment outcome/ (129746)

7 4 or 5 or 6 (1142018)

8 3 and 7 (52014)

9 (practice pattern$ or caseload or volume or clinical competence or surgical speciality).ti,ab. (426993)

10 *Physician's Practice Patterns/ or *Specialities, Surgical/ (25900)

11 9 or 10 (450589)

12 8 and 11 (1945)

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Appendix 2: Quality assessment tool (Modified ACROBAT-NRSI)

Bias category	Judgement
Bias due to selection	
Was selection of study participants appropriate? (e.g. consecutive patients or a random sample)	yes (low risk), no (high risk, or unclear risk)
Was eligibility criteria administered uniformly across all participants and centres? (use of ICD codes or similar)	yes (low risk), no (high risk, or unclear risk)
Are baseline characteristics provided and are participant characteristics across volume groupings similar at baseline?	yes (low risk), no (high risk)
Bias due to volume measurement	
Was volume presented as continuous data measurement categorised or categorical (quartiles, quintiles etc.)	quantiles yes (high risk), continuous (low risk)
Bias due to Attrition	
Were there complete data for all participants at the end of the study? Were all study participants or cases (e.g. number of procedures) accounted for (or included) in the final analysis of results?	yes (low risk), no (high risk, or unclear risk)
Bias due to outcome measurement	
Is the measurement of outcome objective and administered uniformly throughout the course of the study (between centres and over time)?	yes (low risk), no (high risk)
Were methods of outcome measurements pre-specified and described?	yes (low risk), no (unclear risk)
Bias due to adjustment for confounding	
Was there any adjustment for confounding, no = high risk of bias, yes for any adjustment - then consider extent of adjustment and source of data used in adjustment to reach conclusion on overall risk of bias	adjusted for most confounders (low risk), adjusted for some confounders e.g. age and sex (medium risk), no adjustment (high risk)
Bias due to reporting	
Was the study pre-registered with accessible protocol?	yes (low risk), no (high risk, or unclear)
Is the reported effect estimate unlikely to be selected, on the basis of the results, from multiple analyses of the volume-outcome relationship?	yes (low risk), no (high risk)

Notes: Studies that had used quantiles to define hospital/surgeon volume were considered to have high risk of volume measurement bias, as the accuracy of the applied volume quantiles to correctly predict outcome cannot be ascertained. Studies that had prospectively recorded outcomes were considered to have low risk of bias of outcome measurement especially for mortality, however the measurement of other outcomes, other than mortality could still be biased. Those which had used healthcare administrative database were classified as having high risk of outcome measurement bias, because of the possibility that inter-hospital variation in codes for a similar condition and coding errors might have introduced bias.

Appendix 3: List of studies excluded at full text and reason for exclusion

	Study reference	Study title	Reasons for exclusion
1	Bergqvist et al[25]	Auditing surgical outcome. 10 Years with the Swedish Vascular Registry; Swedvasc	No volume outcome relationship investigated
2	Biancari et al[26]	Predictive factors for adverse outcome of pedal bypasses	No volume outcome relationship investigated
3	Goode et al[27]	Does case volume affect outcome for elective and emergency iliac intervention?	Conference abstract same data as in Goode et al[5]
4	Holdsworth[28]	District Hospital Management and Outcome of Critical Lower Limb Ischaemia: Comparison with National Figures	No volume outcome relationship investigated
5	Huntington et al[29]	Lower limb occlusive arterial disease in the North of England: Workload and development of management guidelines	No volume outcome relationship investigated
6	Lepanatalo[30]	Should Vascular Surgery be Centralised or Decentralised? A Nordic Point of View	Review article
7	Luther and Lepantalo[31]	Infrainguinal reconstructions: Influence of surgical experience on outcome	No volume outcome relationship investigated
8	Mao et al[32]	Outcomes and Characteristics of Patients Undergoing Percutaneous Angioplasty Followed by Below-Knee or Above-Knee Amputation for Peripheral Artery Disease	Not European study
9	Michaels et al[33]	Relation between rates of leg amputation and distal arterial reconstructive surgery. Oxford Regional Vascular Audit Group.	No volume outcome relationship investigated
10	Michaels et al[34]	Cost and outcome implications of the organisation of vascular services	Review article
11	Moxey et al[35]	Establishing a volume-outcome relationship in lower limb bypass surgery using multi-level logistic regression modelling	Conference abstract, full text Moxey et al[1]
12	Moxey et al[36]	Trends and outcomes after surgical lower limb revascularization in England	No volume outcome relationship investigated, same data as Moxey et al[1]
13	O'Shaughnessy et al[37]	Surgery in the treatment of varicose veins	No volume outcome relationship investigated
14	Prytherch et al[38]	A model for national outcome audit in vascular surgery	No volume outcome relationship investigated
15	Troeng et al[39]	Incidence and causes of adverse outcomes of operation for chronic ischaemia of the leg	Same data as in Troeng et al[14]
16	VSGBI[40]	The national vascular database report 2009	No volume outcome relationship investigated
17	VSGBI[41]	UK audit of vascular surgical services and carotid endarterectomy	No volume outcome relationship investigated
18	WVS study group[42]	Variations of Rates of Vascular Surgical Procedures for Chronic Critical Limb Ischaemia and Lower Limb Amputation Rates in Western Swedish Counties	No volume outcome relationship investigated

Reference list for studies excluded at full text level

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