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Revascularisation of the left subclavian artery for thoracic endovascular aortic repair (Review)

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[Intervention Review]

Revascularisation of the left subclavian artery for thoracic endovascular aortic repair

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ABSTRACT

Background

Controversy exists as to whether revascularisation of the left subclavian artery (LSA) confers improved outcomes in patients undergoing thoracic endovascular aortic repair (TEVAR). Even though preemptive revascularisation of the LSA has theoretical advantages, including a reduced risk of ischaemic damage to vital organs, such as the brain and the spinal cord, it is not without risks. Current practice guidelines recommend routine revascularisation of the LSA in patients undergoing elective TEVAR where achievement of a proximal seal necessitates coverage of the LSA, and in patients who have an anatomy that compromises perfusion to critical organs. However, this recommendation was based on very low-quality evidence.

Objectives

To assess the comparative efficacy of routine LSA revascularisation versus either selective or no revascularisation in patients with descending thoracic aortic disease undergoing TEVAR with coverage of the LSA origin.

Search methods

The Cochrane Vascular Trials Search Co-ordinator (TSC) searched the Specialised Register (June 2015). In addition, the TSC searched the Cochrane Register of Studies (CENTRAL (2015, Issue 5)).Trials databases were also searched (June 2015).

Selection criteria

We had planned to consider all randomised controlled trials (RCTs) that compared routine revascularisation of the LSA with selective or no revascularisation, in patients undergoing TEVAR.

Data collection and analysis

Two review authors independently assessed the title and abstract of articles identified through literature searches. An independent third review author was consulted in the event of disagreement. We had planned for two review authors to independently extract data and assess the risk of bias of identified trials using the criteria recommended in the *Cochrane Handbook for Systematic Reviews of Interventions*.

Main results

We did not identify any RCTs relevant to our review topic. Therefore, no quantitative analysis was conducted.

Authors' conclusions

High quality RCT evidence for or against routine or selective revascularisation of the LSA in TEVAR is not currently available. It is not possible to draw conclusions with regard to the optimal management of LSA coverage in TEVAR, and whether routine revascularisation, which was defined as the intervention of interest in our review, confers beneficial effects, as indicated by reduced mortality, cerebrovascular events, and spinal cord ischaemia. This review highlights the need for continued research to provide RCT evidence and define the role of LSA revascularisation in the context of TEVAR with coverage of the LSA.

PLAIN LANGUAGE SUMMARY

Revascularisation of the left subclavian artery for thoracic endovascular aortic repair

Background

The thoracic aorta is the largest blood vessel in the chest. It originates from the heart and supplies blood to the whole body. It can be affected by several diseases, including an aneurysm, which is an enlargement of a weakened section of the aorta, and dissection, which occurs when a tear in the aortic lining causes blood to flow between the layers of the wall of the aorta, forcing the layers apart. The traditional treatment of these conditions is open surgical repair. Thoracic endovascular aortic repair (TEVAR) has evolved as an alternative treatment for a wide variety of aortic diseases. It is less invasive than open surgery, and involves inserting an artificial graft (a tube composed of fabric) into the thoracic aorta through an artery in the groin (the femoral artery), to help reinforce the aortic wall. A significant proportion of patients with thoracic aortic disease have abnormalities close to, or involving the origin of the left subclavian artery (LSA; one of the branches of the thoracic aorta). In these situations, the aortic stent graft needs to be placed close to the LSA, thereby blocking the blood vessel opening. This can potentially result in reduced blood supply to the brain and spinal cord, causing stroke and spinal cord ischaemia (spinal cord stroke). This review aimed to look at the value of a surgical bypass, which can provide an alternative route for blood supply (revascularisation) to the brain and spinal cord in cases of TEVAR, where the LSA is covered.

Controversy exists as to whether routine revascularisation of the LSA, with a surgical bypass, results in improved outcomes in patients undergoing TEVAR, as measured by a reduced risk of stroke and paraplegia (paralysis of the legs). Even though preemptive LSA revascularisation has theoretical advantages, it is not without risks, including nerve damage, bleeding, and graft infection. The Society for Vascular Surgery Practice Guidelines recommend routine revascularisation of the LSA in non-emergency TEVAR, where the LSA origin is covered. However, this recommendation was based on very low-quality evidence.

We undertook a comprehensive, systematic search of the pertinent literature to identify the best available evidence and had planned to synthesise outcome data from randomised controlled trials (RCTs), in order to assist clinicians and patients to make evidence-based decisions.

Study characteristics and key results

We did not identify any RCTs investigating our study question (evidence current until June 2015). The best available evidence comes from non-randomised comparative studies. There is a need for high quality RCTs providing more robust evidence.

Quality of the evidence

It was not possible to evaluate the quality of evidence in the absence of studies eligible for the review.

BACKGROUND

Description of the condition

Aneurysms and dissection are common pathologies that affect the thoracic aorta, which can lead to potentially catastrophic consequences if left untreated (Bickerstaff 1982; Clouse 2004). Thoracic aortic aneurysm is an enlargement of a weakened area of the upper segment of the aorta above the diaphragm. Aortic dissection occurs when a tear in the aortic lining causes blood to flow between the layers of the wall of the aorta, forcing the layers apart. Conventional treatment consists of open surgical reconstruction of the aorta, which is associated with substantial morbidity and mortality (Trimarchi 2006). In recent years, thoracic endovascular aortic repair (TEVAR) has evolved as a constantly expanding technique for the treatment of a wide variety of thoracic aortic pathologies, including aneurysms and dissection. It involves placing an endograft (covered stent) in the aorta through a remote access site (most commonly, the common femoral artery) under radiographic guidance. In contrast to endovascular abdominal aortic aneurysm repair (EVAR), which has been compared with conventional surgical repair in well-designed randomised controlled trials (RCTs), such as the DREAM trial and the EVAR-1 trial (DREAM; EVAR-1; Paravastu 2014), evidence favouring TEVAR over traditional surgical repair derives from industry-sponsored, non-randomised comparisons to open repair, as well as single-centre series and national or international registries (Buth 2007; Makaroun 2008; Thompson 2007). Nevertheless, TEVAR has been demonstrated to be an attractive alternative method that presents benefits related to the less invasive nature of the procedure, compared with its surgical counterpart (Abraha 2013). Such benefits are reflected in the apparently reduced perioperative morbidity and mortality, and satisfactory early and medium-term results. A systematic review and meta-analysis that included 1109 patients from 17 eligible studies, found TEVAR to be associated with reduced perioperative mortality (odds ratio (OR) 0.36; 95% confidence interval (CI) 0.228 to 0.578) and major neurological injury (OR 0.39; 95% CI 0.25 to 0.62) in patients with thoracic aortic aneurysms (Walsh 2008). This technique has been adopted for the treatment of other aortic pathologies, including dissection, penetrating ulcers, traumatic disruption, and coarctation.

Description of the intervention

A significant proportion of patients with thoracic aortic disease have abnormalities of the thoracic aorta close to or involving the origin of the left subclavian artery (LSA; Freezor 2007). In these situations, the aortic stent graft needs to be placed proximal to the LSA origin, thereby occluding the vessel, in order to obtain a sufficient proximal landing zone for secure fixation and sealing. Even though a collateral arterial network, primarily through the right vertebral artery, the basilar artery, and the circle of Willis, can compensate in several circumstances, revascularisation of the LSA is advocated by several study authors to prevent complications resulting from malperfusion of vital organs, such as the brain and the spinal cord (Weigang 2011).

Left subclavian artery revascularisation is based on conventional techniques used in the setting of chronic occlusive disease of supra-aortic vessels. It consists of either a short bypass (usually using a prosthetic graft) originating from the left common carotid artery or a carotid-subclavian transposition, which carries the advantage of avoiding prosthetic materials, but requires more extensive dissection of the proximal subclavian artery and is contraindicated in patients with patent internal mammary to coronary artery bypass grafts. Both procedures are performed through a short supra-clavicular incision and carry a small risk of cerebrovascular events (stroke or transient ischaemic attack (TIA)), bleeding, and injury to adjacent anatomical structures, primarily the thoracic duct, the phrenic nerve, the vagus nerve, the sympathetic chain, and the brachial plexus. The hybrid procedure can be accomplished by using either a staged approach, in which the revascularisation of the LSA precedes the TEVAR in a separate or the same hospital admission, or as a synchronous procedure during the same anaesthesia.

Revascularisation of the LSA can also be performed with new endovascular methods, including the chimney technique, in-situ fenestration, and branched TEVAR. These techniques are currently in evolution, and literature information and existing evidence regarding their safety, and efficacy in revascularising the LSA in the context of endovascular treatment of thoracic aortic disease, is limited to case reports or small case series (Redlinger 2013; Silveira 2013; Xue 2015).

How the intervention might work

The LSA provides blood supply to upper limb circulation, posterior cerebral circulation, and spinal circulation through the vertebral artery, and coronary circulation in patients with left internal mammary artery bypass graft. Despite the significant contribution of blood flow to these arterial beds, coverage of the LSA is often well tolerated. However, neurological adverse events, including stroke and paraplegia, are well-recognised complications, and are of critical concern in patients undergoing TEVAR (Scali 2014).

Revascularisation of the LSA is particularly relevant when collateral arterial pathways to the brain and spinal cord are compromised. Furthermore, certain anatomic situations mandate LSA revascularisation, including the presence of a patent internal mammary artery to coronary artery bypass graft; absent, diminutive or occluded right vertebral artery; and a functioning arterio-venous shunt in the left arm. The Society for Vascular Surgery Practice Guidelines also strongly recommend revascularisation of the LSA in patients in whom TEVAR is anticipated to compromise collateral circulation to the brain and spinal cord, such as planned long-segment (at least 20 cm) coverage of the descending thoracic aorta, previous infra-renal aortic repair, or hypogastric artery occlusion (Matsumura 2009).

Why it is important to do this review

Controversy exists as to whether revascularisation of the LSA confers improved outcomes in patients undergoing TEVAR, as indicated by reduced incidence of stroke and paraplegia. Even though preemptive LSA revascularisation has well-described potential advantages, it is not without risks, including nerve damage, bleeding, and graft infection. Moreover, a number of authors have reported intentional coverage of the LSA in TEVAR not to be associated with significant morbidity, and it seems that a number of patients do not get the anticipated benefits of LSA revascularisation and are subjected to unnecessary surgical stress (Maldonado 2013; Wojciechowski 2014). In 2009, the Society for Vascular Surgery published clinical practice guidelines for the management of the LSA with TEVAR, which were based on very low levels of evidence (Matsumura 2009). In the presence of persisting

controversy, we undertook a comprehensive systematic search of the pertinent literature to identify the best available evidence and synthesise outcome data from RCTs, in order to assist clinicians and patients to make evidence-based decisions.

OBJECTIVES

To assess the comparative efficacy of routine LSA revascularisation versus either selective or no revascularisation in patients with descending thoracic aortic disease undergoing TEVAR with coverage of the LSA origin.

METHODS

Criteria for considering studies for this review

Types of studies

We considered all RCTs comparing routine revascularisation of the LSA with selective or no revascularisation in patients undergoing TEVAR.

Types of participants

Patients diagnosed with non-traumatic or traumatic disease of the thoracic aorta undergoing TEVAR with coverage of the LSA. Aortic pathologies included true aneurysm, pseudoaneurysm, dissection with or without aortic dilatation, aortic ulcer, or traumatic aortic disruption. Patients with both symptomatic and asymptomatic disease, and treated in an elective, urgent, or emergency setting were eligible.The ostium of the LSA needed to be covered by the aortic endograft either because it was involved in the disease process (e.g. aortic aneurysm) or in order to achieve an adequate proximal landing zone for aneurysm sealing and secure fixation of the endograft.

Types of interventions

We had planned to compare outcomes of patients undergoing TEVAR with routine revascularisation of the LSV with those of patients undergoing TEVAR with selective revascularisation or without preceded revascularisation of the LSA.

Revascularisation of the LSA consists of either a carotid-subclavian bypass or subclavian-carotid transposition. Bypass procedures can be performed with any autogenous (e.g. vein) or any prosthetic material (e.g. Dacron or polytetrafluoroethylene). The surgical revascularisation of the LSA and the TEVAR can be performed either synchronously, as parts of the same operating procedure, or on separate occasions, with the revascularisation of the LSA being followed by TEVAR after a period of time. We also considered endovascular techniques for LSA revascularisation in TEVAR, such as the chimney technique, in-situ fenestration, and branched TEVAR.

Types of outcome measures

Primary outcomes

- Peri-operative mortality.
- Cerebrovascular events (stroke or TIA) related to the anterior or vertebro-basilar circulation.
- Spinal cord ischaemia (defined as temporary or permanent decrease or loss of lower limb neurological function).

Secondary outcomes

- Upper extremity ischaemia (defined as reduced blood supply in the arm producing ischaemic signs and symptoms at rest or with exertion, usually requiring revascularisation to relieve the symptoms).
- Myocardial infarction (both fatal and non-fatal).
- Endoleak.
- LSA revascularisation-related complications (thoracic duct injury, nerve or brachial plexus injury, haematoma requiring drainage, graft infection).

Search methods for identification of studies

Electronic searches

The Cochrane Vascular Trials Search Co-ordinator (TSC) searched the Specialised Register (June 2015). In addition, the TSC searched the Cochrane Register of Studies (CRS) http://www.metaxis.com/CRSWeb/Index.asp (CENTRAL (2015, Issue 5)). See Appendix 1 for details of the search strategy used to search the CRS. The Specialised Register is maintained by the TSC and is constructed from weekly electronic searches of MEDLINE, EMBASE, CINAHL, AMED, and through handsearching relevant journals. The full list of the databases, journals and conference proceedings that have been searched, as well as the search strategies used, are described in the Specialised Register section of the Cochrane Vascular module in the*Cochrane Library* (www.cochranelibrary.com).

The TSC also searched the following trial databases in June 2015 for details of ongoing and unpublished studies, using the terms 'left and subclavian':

- World Health Organization International Clinical Trials Registry http://apps.who.int/trialsearch/
- ClinicalTrials.gov http://clinicaltrials.gov/
- ISRCTN Register http://www.isrctn.com/

Searching other resources

We screened the bibliographies of relevant articles. Furthermore, we searched the following journals for additional potentially eligible trials: the Journal of Vascular Surgery (Volume 23, January 1996, Issue 1 to Volume 62, November 2015, Issue 5), the European Journal of Vascular and Endovascular Surgery (Volume 11, January 1996, Issue 1 to Volume 50; November 2015, Issue 5) and the Journal of Endovascular Therapy (Volume 3, February 1996, Issue 1 to Volume 22; October 2015, Issue 5).

Data collection and analysis

Selection of studies

Two review authors (GAA and SAA) independently assessed all studies identified from the described literature search and selected those eligible for inclusion in this review. We had planned to send selected trials to a third author (FT), who would assess and confirm their suitability for inclusion and act as an adjudicator in the event of disagreement. We developed a flow diagram of the study selection process.

Data extraction and management

We had planned to develop a data extraction sheet, based on proformas designed by Cochrane Vascular for intervention

reviews, pilot-test it in three randomly selected included studies, and adjust it accordingly. Two review authors (GAA and SAA) would have independently extracted data . We had planned to resolve disagreements by discussion between the two authors, and a third author (FT) would check discrepancies in the collected information. We had planned to contact the principal investigators of selected trials to obtain missing or additional data, if required. We had planned to collect baseline demographic and clinical characteristics of the trial populations, procedure-related information, and technical details (e.g. type of bypass graft and modes of spinal cord protection), and outcome data as outlined above. We had planned to extract data from the text of the article, tables, or graphs.

We had planned to organise the outcome measures into a two by two table to permit calculation of effect sizes for routine LSA revascularisation in comparison with selective or no revascularisation with regard to each dichotomous outcome.

Assessment of risk of bias in included studies

We had planned to apply the Cochrane tool for the assessment of the risk of bias of the selected trials (Higgins 2011a). Briefly, this tool evaluates six main domains: random sequence generation and allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other sources of bias. For each individual domain, we would have classified studies into low, unclear, or high risk of bias. Two review authors (GAA, SAA) would have independently assessed the risk of bias . A third author (FT) would have acted as an adjudicator if disagreements existed.

Measures of treatment effect

We had planned to calculate dichotomous outcome measures, such as the incidence of spinal cord ischaemia, using OR and 95% CI to reflect the uncertainty of the point estimate of effects. For continuous variables, we would have computed the mean difference (MD) or standardised mean difference (SMD) and corresponding 95% CI.

Unit of analysis issues

The unit of analysis would have been the individual patient. Considering the trial design and defined outcome parameters, we did not anticipate that the selected trials would have a mixture of units of analysis.

Dealing with missing data

We had planned to contact original investigators to request any missing data. We had planned to undertake sensitivity analyses and comment on the potential impact of missing data on the review findings, if missing data remained a concern. We had planned to perform intention-to-treat analysis, extracting the number of patients originally allocated to each treatment group, where possible.

Assessment of heterogeneity

We had planned to assess inter-study heterogeneity visually using forest plots. Furthermore, we had planned to examine heterogeneity with the combination of Cochrane's χ^2 test and the I^2 statistic (Higgins 2011b). We would have used a P value of 0.05 as a cut-off value to determine statistical significance for heterogeneity. Moreover, we had planned to consider I^2 values less than 50% as indicative of low heterogeneity, I^2 values between 50% and 75% as indicative of moderate heterogeneity, and I^2 values greater than 75% as indicative of significant heterogeneity.

Assessment of reporting biases

To prevent reporting and publication biases, we had planned to attempt to obtain data from unpublished trials and include them in the meta-analysis. If sufficient studies in any single meta-analysis had been available (more than 10 studies), we had planned to construct a funnel plot (Sterne 2011). We had planned to assess publication bias visually, by evaluating the symmetry of such funnel plots, and formally using the Egger's regression intercept (Sterne 2011).

Data synthesis

We had planned to enter data into RevMan software (RevMan 2014). We had planned to use the inverse-variance fixed-effect method to calculate the pooled treatment effect for dichotomous and continuous outcome data. If significant heterogeneity among the studies had been identified (defined as Cochrane's χ^2 test P value less than 0.05 and I^2 value greater than 75%), we had planned to apply the random-effects model of DerSimonian and Laird (Deeks 2011). We had intended to create a forest plot for each treatment effect, as per Cochrane Vascular guidelines.

Subgroup analysis and investigation of heterogeneity

If available data had permitted, we would have performed subgroup analyses by:

- the type of LSA revascularisation;
- the aortic pathology;
- the extent of aortic disease;
- elective, urgent, or emergency procedure;
- synchronous or asynchronous procedure (LSA revascularisation and aortic stenting performed on separate occasions); and
- gender.

Sensitivity analysis

We had aimed to undertake sensitivity analyses to assess the contribution of risk of bias in several domains (as described in the section Assessment of risk of bias in included studies), risk of missing outcome data, and unpublished studies.

Summary of findings table

We had planned to construct a 'Summary of findings' table to present the main findings of the review. Patients undergoing TEVAR would have constituted the studied population. We had planned to make comparisons between routine and selective or no revascularisation of the LSA. We had intended to use weighted mean numbers of events in the control group of the included studies to calculate assumed control intervention risks. We would have presented typical risks for participants receiving the control interventions (selective or no revascularisation of the LSA) in the form of a number of people experiencing the event per 1000 people. We had planned to assess the quality of the body of evidence using the system of quality grading produced by the Grades

of Recommendation, Assessment, Development and Evaluation Working Group (Grade 2004). We had intended to include the main outcomes listed in the Types of outcome measures section, which were considered essential for decision-making, in the 'Summary of findings' table.

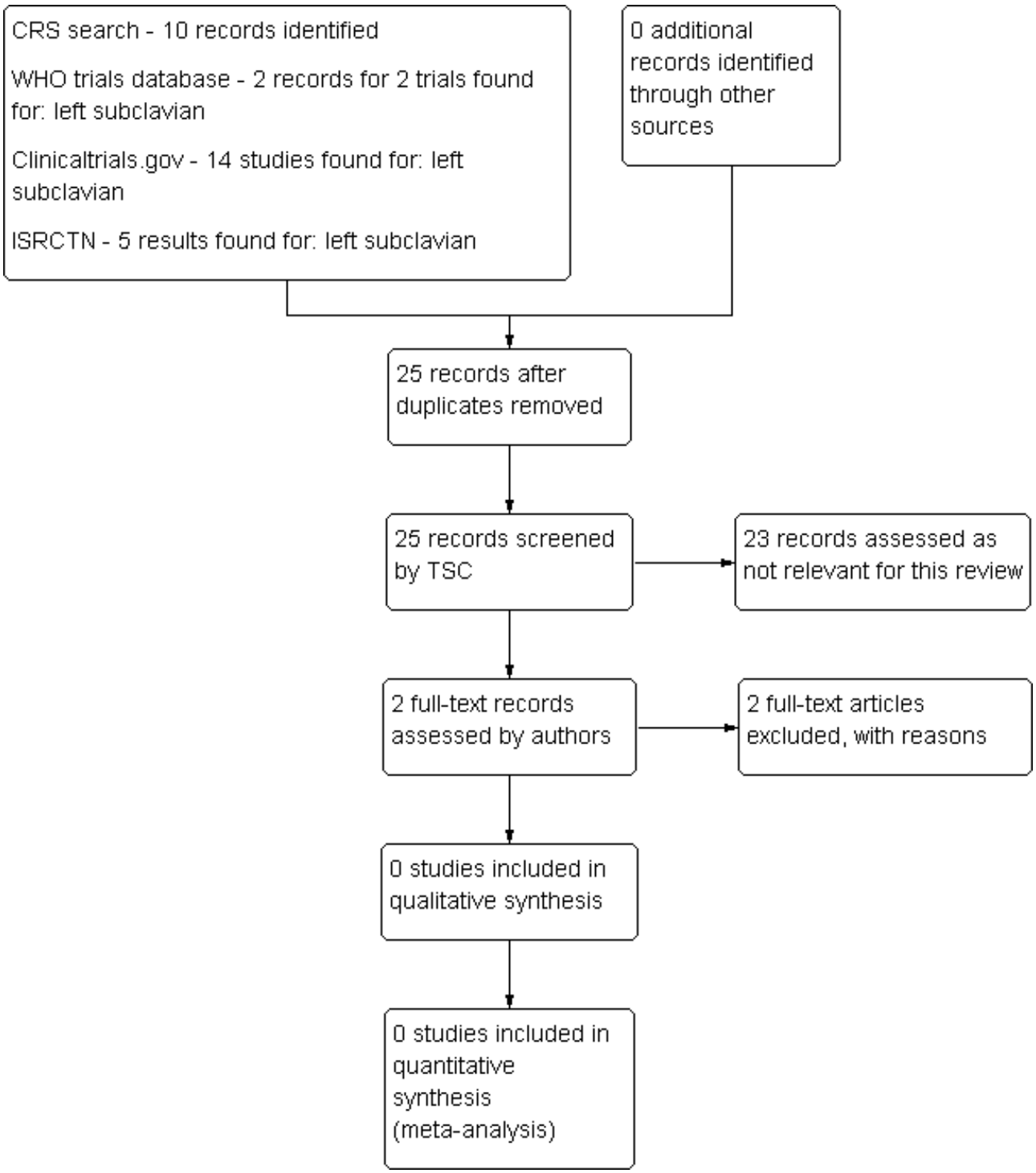
RESULTS

Description of studies

Results of the search

See Figure 1. Electronic searches identified no RCTs relevant to our review topic.

Figure 1. Study flow diagram.



Included studies

No studies were identified that fulfilled our inclusion criteria.

Excluded studies

Two studies were excluded (McBride 2015; Wojciechowski 2014). The reasons for exclusion are outlined in the Characteristics of excluded studies table. Both are non-randomised observational studies investigating outcomes in patients undergoing TEVAR with and without coverage of the LSA. The McBride 2015 study included patients treated for traumatic aortic injury, whereas the Wojciechowski 2014 study reported on patients undergoing TEVAR for aortic pathologies including aneurysm, dissection, pseudoaneurysm, and transection.

Risk of bias in included studies

No studies were identified for inclusion in this review, therefore no risk of bias assessment could be undertaken.

Effects of interventions

No published or unpublished RCTs were identified that investigated the effects of routine LSA revascularisation versus selective or no LSA revascularisation.

DISCUSSION

Summary of main results

This review documents the absence of evidence from RCTs that assessed the efficacy of routine LSA revascularisation versus either selective or no revascularisation in TEVAR with coverage of the LSA origin. It is not possible to draw conclusions with regard to the optimal management of LSA coverage in such cases, and whether routine revascularisation, which was defined as the intervention of interest in our review, confers beneficial effects, as indicated by reduced mortality, cerebrovascular events, or spinal cord ischaemia. Our searches failed to identify ongoing clinical trials.

Overall completeness and applicability of evidence

There is currently no evidence from RCTs that assessed the efficacy of routine LSA revascularisation versus either selective or no revascularisation in TEVAR with coverage of the LSA origin.

The Society for Vascular Surgery selected an expert committee and applied the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) method to develop practice guidelines for the management of LSA coverage in TEVAR (Matsumura 2009). The document highlighted the absence of and requirement for RCTs to guide clinical practice. Based on very low-quality evidence, the guideline suggested routine revascularisation in patients who needed elective TEVAR, where achievement of a proximal seal necessitates coverage of the LSA. Matsumura 2009 also recommended that routine LSA revascularisation be performed in selected patients who have an anatomy that compromises perfusion to critical organs. Furthermore, in patients who need urgent TEVAR for life-threatening acute aortic syndromes, where achievement of a proximal seal necessitates coverage of the LSA, Matsumura 2009 suggested that revascularisation be individualized and address expectantly on the basis of anatomy, urgency, and availability of surgical expertise.

Quality of the evidence

It was not possible to assess the quality of the evidence in the absence of RCTs eligible for the review.

Potential biases in the review process

There were no RCTs fulfilling our inclusion criteria for this review. The Cochrane Vascular TSC performed a comprehensive search of the literature, which was conducted in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). Furthermore, we performed searches of the following journals in vascular and endovascular surgery to identify relevant trials: the Journal of Vascular Surgery, the European Journal of Vascular and Endovascular Surgery, and the Journal of Endovascular Therapy. Any disagreements regarding study selection were resolved by discussion.

Agreements and disagreements with other studies or reviews

There is no published systematic review and meta-analysis investigating comparative outcomes in patients who had their LSA covered to achieve proximal seal in TEVAR with or without revascularisation of the LSA.

Weigang 2011 reviewed various management strategies to treat patients requiring LSA coverage in TEVAR. They classified 23 studies based on three basic treatment concepts for LSA revascularisation: prophylactic, conditional prophylactic, and no prophylactic LSA revascularisation, and recommended prophylactic LSA revascularisation in all elective cases. However, this was a narrative review and no statistical analysis was undertaken to support the conclusions. Furthermore, Weigang 2011 included heterogeneous case-series and cohort studies, which did not directly compare outcomes with and without LSA revascularisation. Cooper 2009 conducted a meta-analysis of 13 studies investigating outcomes of revascularisation of the LSA prior to TEVAR in cases where the origin of the LSA had to be compromised to achieve a proximal landing zone and seal. They concluded that revascularisation of the LSA offered no protection against cerebrovascular events, but may reduce the incidence of spinal cord ischaemia. However, the comparative control group comprised of patients undergoing TEVAR without LSA coverage. Therefore, no direct comparison between LSA coverage with or without revascularisation was made which, undoubtedly, affected the robustness of Cooper 2009's conclusions.

The Society for Vascular Surgery produced a practice guideline which recommends preoperative LSA revascularisation in patients undergoing elective TEVAR with LSA coverage (Matsumura 2009). This guideline was based on the findings of a systematic review of the literature and meta-analysis conducted by Rizvi 2009, who synthesized the available evidence related to complications associated with LSA coverage in TEVAR. This was a comprehensive analysis of the best available evidence up to 2009, when the practice guideline document was published. The pertinent evidence at the time was identified to be of low or very low quality. The analysis compared outcomes in TEVAR with and without coverage of the LSA, and revealed an increased risk of ischaemic and neurological complications in cases where the LSA

was covered. Specifically, coverage of the LSA was found to be associated with a significantly increased risk of arm ischaemia (OR 47.7; 95% CI 9.9 to 229.3; I^2 = 72%) and vertebrobasilar ischaemia (OR 10.8; 95% CI 3.17 to 36.7; I^2 = 0%), and a non-significant increase in the risk of spinal cord ischaemia (OR 2.69; 95% CI 0.75 to 9.68; I^2 = 40%) and anterior circulation stroke (OR 2.58; 95% CI 0.82 to 8.09; I^2 = 64%). However, Rizvi 2009 did not provide comparative outcomes of LSA revascularisation versus no LSA revascularisation in cases where the TEVAR necessitated coverage of the LSA origin.

We conducted a comprehensive literature search to identify studies comparing outcomes of TEVAR with landing of the aortic endograft proximal to the LSA with and without revascularisation of the LSA. Electronic searches included MEDLINE, EMBASE, CINAHL, and AMED. Thesaurus headings, search operators, and limits were adapted in each of the above databases. We also handsearched bibliographic lists of relevant articles and reviews for further potentially eligible studies. We identified five retrospective observational studies (Lee 2011; Maldonado 2013; Patterson 2014; Zamor 2015; Contrella 2015) reporting on a total of 1161 patients, of whom 444 patients underwent revascularisation of the LSA and the remaining 717 patients had the LSA covered and not revascularised. We conducted a meta-analysis of their reported outcomes. Our analysis demonstrated that revascularisation of the LSA was associated with a similar risk of stroke (OR 0.70; 95% CI 0.43 to 1.14), spinal cord ischaemia (OR 0.56; 95% CI 0.28 to 1.10), and mortality (OR 0.87; 95% CI 0.55 to 1.39) compared with no LSA revascularisation. Insufficient data were provided in relation to secondary outcome parameters, including upper limb ischaemia, myocardial infarction, endoleak, and LSA revascularisation-related complications. Furthermore, the method of spinal cord protection is a confounding factor, but, again, insufficient information was available to perform further analyses and investigate its impact on outcomes. This analysis was limited by the fact that it was based on a small number of retrospective cohort studies that were inevitably subject to selection bias. Furthermore, inconsistency among the authors existed with regard to the defined criteria for revascularisation of the LSA, which reflects varying attitudes among individual groups and is a significant confounding factor.

AUTHORS' CONCLUSIONS

Implications for practice

The current evidence base is insufficient to suggest routine or selective LSA revascularisation in cases of TEVAR with coverage of the LSA origin. No relevant randomised clinical trials were identified, and therefore, we were unable to draw conclusions with regard to implications for clinical practice.

Numerous observational studies have investigated outcomes in TEVAR with and without coverage of the LSA. Systematic reviews and meta-analyses suggest that preemptive revascularisation of the LSA may offer protection against ischaemic damage of vital organs, reducing the risk of spinal cord and vertebrobasilar ischaemia (Cooper 2009; Matsumura 2009). Current practice guidelines, based on very low-quality evidence, recommend routine revascularisation of the LSA in elective cases of TEVAR where achievement of a proximal seal necessitates coverage of the LSA, and in patients who have an anatomy that compromises perfusion to critical organs (Matsumura 2009). Our search failed to identify evidence coming from RCTs to support these recommendations. Five observational studies have investigated comparative outcomes of TEVAR in which the LSA was covered by the thoracic aortic endograft with and without revascularisation of the LSA. Meta-analysis of these studies revealed similar outcomes in patients with and without LSA revascularisation, as indicated by the risk of stroke, spinal cord ischaemia, and mortality in the two groups.

Implications for research

This review highlights the need for continued research to define the role of LSA revascularisation in the context of TEVAR with coverage of the LSA. High quality RCTs are required to provide robust evidence on the role of routine or selective LSA revascularisation in such cases. In addition to neurological complications and mortality, other outcomes, such as upper limb ischaemia, endoleak, LSA revascularisation-related complications, and the impact on quality of life and use of resources, need to be evaluated in future research. Furthermore, the efficacy of subclavian artery revascularisation is not yet proven, therefore future studies need to determine the physiological effect of this intervention, i.e. functional measurements of blood flow in the circle of Willis.

ACKNOWLEDGEMENTS

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CHARACTERISTICS OF STUDIES

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

Study	Reason for exclusion
McBride 2015	Non-randomised study evaluating effects of intentional LSA coverage in TEVAR on symptoms and return-to-normal activity in patients with traumatic aortic injury compared with a similarly treated group whose LSA was not covered
Wojciechowski 2014	Retrospective, non-randomised, single-arm study evaluating outcomes of TEVAR with coverage of the LSA

LSA: left subclavian artery
TEVAR: thoracic endovascular aortic repair

APPENDICES

Appendix 1. CRS search strategy

#1	MESH DESCRIPTOR Aortic Aneurysm EXPLODE ALL TREES	518
#2	pseudoaneurysm*	84
#3	aort* near3 (aneur* or balloon* or dilat* or bulg*):TI,AB,KY	898
#4	aort* near3 (dissect* or disrup* or ulcer* or trauma*)	124
#5	thora* near3 (aneur* or balloon* or dilat* or bulg*):TI,AB,KY	81
#6	thora* near3 (dissect* or disrup* or ulcer* or trauma*)	87
#7	AAA :TI,AB,KY	296
#8	TAAA :TI,AB,KY	9
#9	MESH DESCRIPTOR Aorta EXPLODE ALL TREES WITH QUALIFIERS IN,SU	297
#10	TEVAR:TI,AB,KY	20
#11	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	1393
#12	MESH DESCRIPTOR Subclavian Artery EXPLODE ALL TREES	16
#13	*subclavian:TI,AB,KY	320
#14	#12 OR #13	320
#15	#11 AND #14	10

HISTORY

Protocol first published: Issue 6, 2015
Review first published: Issue 4, 2016

Date	Event	Description
11 June 2015	Amended	Conflict of interest statement amended by author FT

CONTRIBUTIONS OF AUTHORS

George A Antoniou (GAA) served as contact author. GAA designed the protocol with Stavros A Antoniou (SAA) and Francesco Torella (FT). GAA and SAA assessed studies for inclusion in the review. GAA, Shahin Hajibandeh (Shahin H) and Shahab Hajibandeh (Shahab H) wrote the review. Shahin H and Shahab H performed literature searches to identify observational studies comparing outcomes of LSA coverage in TEVAR with and without LSA revascularisation, and conducted a meta-analysis of the identified studies. All authors critically reviewed and revised the article. GAA has the overall responsibility of this work.

DECLARATIONS OF INTEREST

Shahin H: None known
Shahab H: None known
GAA: None known
SAA: I have received funds from the European Association for Endoscopic Surgery (EAES) for travel and accommodation expenses associated with the duties of the Journal and Publication Committee Members of the EAES, and for travel, accommodation and congress participation expenses for the 21st International Congress of the EAES. I have also received funds from the European Hernia Society for travel and accommodation expenses associated with the development of the Guidelines on the Closure of Abdominal Wall Incisions, and presentation of part of the Guidelines on the Closure of Abdominal Wall Incisions at the 36th International Congress of the European Hernia Society.
FT: I have received proctorship fees, research and educational grants from Endologix.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We had planned to conduct a comprehensive analysis of the outcomes defined in the review protocol. However, no eligible trials were identified.

We have revised the title of the review to reflect the study question more accurately.

INDEX TERMS

Medical Subject Headings (MeSH)

*Endovascular Procedures; Aorta, Thoracic [*surgery]; Subclavian Artery [*surgery]

MeSH check words

Humans