Cochrane Library

Cochrane Database of Systematic Reviews

Hybrid repair versus conventional open repair for aortic arch dissection (Protocol)

Kavanagh EP, Jordan F, Hynes N, Elhelali A, Devane D, Veerasingam D, Sultan S

Kavanagh EP, Jordan F, Hynes N, Elhelali A, Devane D, Veerasingam D, Sultan S.
Hybrid repair versus conventional open repair for aortic arch dissection.
Cochrane Database of Systematic Reviews 2018, Issue 1. Art. No.: CD012920.
DOI: 10.1002/14651858.CD012920.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Protocol]

Hybrid repair versus conventional open repair for aortic arch dissection

Edel P Kavanagh[1], Fionnuala Jordan[2], Niamh Hynes[1], Ala Elhelali[3], Declan Devane[2], Dave Veerasingam[4], Sherif Sultan[5]

[1]Department of Vascular and Endovascular Surgery, The Galway Clinic, Galway, Ireland. [2]School of Nursing and Midwifery, National University of Ireland Galway, Galway, Ireland. [3]Mechanical and Industrial Engineering, Galway-Mayo Institute of Technology, Galway, Ireland. [4]Cardiothoracic Surgery, Galway University Hospital, Galway, Ireland. [5]Vascular Surgery, Galway University Hospital, Galway, Ireland

Contact address: Edel P Kavanagh, Department of Vascular and Endovascular Surgery, The Galway Clinic, Suite 24, Doughiska, Galway, Ireland. edelpkavanagh@gmail.com.

Editorial group: Cochrane Vascular Group.
Publication status and date: New, published in Issue 1, 2018.

Citation: Kavanagh EP, Jordan F, Hynes N, Elhelali A, Devane D, Veerasingam D, Sultan S. Hybrid repair versus conventional open repair for aortic arch dissection. *Cochrane Database of Systematic Reviews* 2018, Issue 1. Art. No.: CD012920. DOI: 10.1002/14651858.CD012920.

ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To assess the effectiveness and safety of a hybrid technique of treatment over conventional open repair in the management of aortic arch dissection.

BACKGROUND

See Appendix 1 for Glossary of terms

Description of the condition

The aorta is the main artery in the body. It originates in the heart and supplies blood to all parts of the body. The aorta consists of three layers: the intima, which is the innermost layer; the media, which is the middle layer; and the adventitia, which is the outermost layer. A dissection of the aorta is a separation or tear of the intima from the media. This tear allows blood to flow not only through the original aortic flow channel (known as the true lumen), but also through a second channel between the intima and media (known as the false lumen). A dissection can then propagate along the artery, secondary to the blood flowing into the space. Aortic dissection is a life-threatening condition which can be rapidly fatal. It occurs more frequently in men, and uncontrolled blood pressure (hypertension) is a leading risk factor (Nienaber 2004). Predominate risk factors for genetic or familial aortic dissection are connective tissue disorders such as Loeys-Dietz syndrome, Marfan syndrome, and Ehlers-Danlos syndrome (Murphy-Ryan 2010).

According to the reporting standards for thoracic endovascular aortic repair, the aorta is divided into 12 treatment zones, zone 0 to zone 11. Aortic arch dissection occurs between zone 0 and zone 4 (Fillinger 2010). Zone 0 refers to an area between the aortic sinus and the brachiocephalic artery origin; zone 1 is distal to the brachiocephalic artery but proximal to the left common carotid artery origin; zone 2 is distal to the left common carotid artery but proximal to the subclavian artery; zone 3 is within 2 cm of the left subclavian artery without covering it; and zone 4 refers to an area 2

cm or more distal to the left subclavian artery and ends within the proximal half of the descending thoracic aorta (Fillinger 2010). There are two classification systems for aortic dissection:

- the Stanford classification, which categorises dissection into Type A and Type B (Daily 1970; DeBakey 1966). Type A occurs in the ascending aorta or aortic arch, or both, with possible involvement of the descending aorta. Type B occurs in the descending aorta, beyond the left subclavian artery; and
- the DeBakey classification, which categorises dissection into Type I, Type II, and Type III. Type I involves the ascending and descending aorta (Stanford Type A and B), Type II involves the ascending aorta only (Stanford Type A), and Type III involves the descending aorta only, beginning after the left subclavian artery (Stanford Type B) (Daily 1970; DeBakey 1966).

Aortic dissection is also classified based on the age of the dissection (chronicity), as the mortality rates vary with chronicity (Wong 2008). These classifications are, from the onset of symptoms: less than 24 hours (hyper-acute); less than 2 weeks (acute); 2 to 6 weeks (sub-acute); and more than 6 weeks (chronic). As the dissection progresses in chronicity, the separated arterial layers that divide the true and false lumen (the intraluminal septum) increase in rigidity and reduce in elasticity and mobility, causing the septum to become stiff.

Description of the intervention

Aortic dissection that affects the ascending aorta, aortic arch and the descending aorta is a challenging pathology for physicians. Patients with this type of aortic disease pose a surgical challenge and this is an area of continuing development and innovation (Cochennec 2013; Kurimoto 2015; Lu 2013). Treatment of aortic dissection can be via open repair, endovascular repair, or a hybrid repair (Antoniou 2010; Cao 2012; Cochennec 2013; Murphy 2012; O'Callaghan 2014). There is debate on the optimum surgical approach for aortic arch dissection. Patients with ascending aortic dissection have poor rates of survival and to date, open surgical repair (OSR) is regarded as the standard treatment for aortic arch dissection (DeBakey 1966; Suzuki 2003).

Open surgical repair

Current treatment for complex aortic arch dissection involves removal of the ascending portion of the aorta, replacement and open distal anastomosis (connection) with a surgical graft, known as a hemi-arch replacement. This is carried out under artificially induced circulatory arrest (a method of slowing the blood flow) with varying degrees of hypothermia (cooling of core body temperature), and a selection of cerebral protection techniques, including antegrade or retrograde cerebral perfusion, or deep hypothermia alone. Potential complications of open surgical repair include stroke, cardiac arrhythmia (irregular heartbeat), coagulopathy (failure to clot blood), and hypokalaemia (lower than normal level of potassium in the blood) (Groysman 2011). This type of repair is high risk and carries a mortality risk of 21.6%, due to the utilisation of circulatory arrest and cerebral perfusion techniques (Patel 2011).

Complete debranching of the aortic arch consists of revascularisation (restoring blood to the vessel) of at least the brachiocephalic artery and the left common carotid artery via a prosthetic bypass from the ascending aorta. After induction of pharmacologic hypotension (inducing state of low blood pressure to reduce blood loss), the ascending aorta is clamped tangentially and the proximal end of a prosthetic graft sutured in an end-to-side anastomosis. The left subclavian artery is revascularised through the sternotomy (division of the chest bone) or through an incision above the clavicle (collar bone). Aortic arch branch vessels can be bypassed via a singular, bifurcated (two branches) or trifurcated (three branches) tube graft. Alternatively, cervical debranching can be performed through cervicotomies (incision in the neck) and consists of retro-oesophageal right common carotid-to-left common carotid artery bypass using a Dacron graft. According to surgeon's preference, the left subclavian artery can be ligated (tied up) or revascularised via a transposition into the left common carotid artery or a carotid artery bypass.

Hybrid repair

Hybrid techniques use a combination of endovascular approaches (intervention through the arteries using wires to carry grafts) and open surgical approaches to treat arch pathologies. These methods are designed to be less invasive than conventional, open techniques. The aorta is treated with a surgical graft in combination with the less invasive approach of endovascular implantation of an aortic stent endograft. Purely endovascular implantation of an endograft in the aorta is made via peripheral arterial access sites such as the femoral arteries, with no invasive surgical intervention. However, techniques for total endovascular repair, although promising, are still in their infancy (Nordon 2012), and reports estimate that in anatomical terms only 30% to 50% of patients with Standford Type A aortic dissection are suitable for total endovascular repair with current technologies (Moon 2011; Sobocinski 2011).

Hybrid repair involves surgical arch debranching of the supra-aortic vessels, thereby creating a proximal landing zone of adequate length, followed by endovascular stent graft insertion in the surgically constructed landing zone within the aortic arch. Specialist thoracic arch-debranching grafts such as the 'frozen or stented elephant trunk' have been developed for the purpose of a single-stage hybrid repair. Elephant trunk is a vascular technique used to repair patients with extensive disease in their aorta. It consists of two stages, 1) open surgery to replace a portion of the ascending aorta, leaving a section of graft hanging within the descending aorta, 2)

this graft section can then be used to place an endovascular stent (known as stented elephant trunk technique). This technique can also be carried out as a single stage (known as frozen elephant trunk technique).

During hybrid repair the endovascular intervention can be carried out in isolation or concurrently with the surgical intervention. In patients with extensive disease of the thoracic arch and descending aorta, a single-stage approach under circulatory arrest is more favourable (Moulakakis 2013).

Hybrid approaches are classified into three types according to the extent of the aortic arch lesion and presence of the proximal and distal landing zones (Moulakakis 2013):

- Type I: the debranching procedure consists of brachiocephalic bypass and endovascular repair of the aortic arch. This approach is reserved for patients with isolated disease exhibiting an adequate proximal landing zone in the ascending aorta and a distal landing zone in the descending thoracic aorta (Stanford Type A/DeBakey Type II);
- Type II: an open ascending aorta reconstruction that creates an appropriate proximal landing zone, supra-aortic vessel revascularisation, and endoluminal dissection coverage. This approach is designed for patients with ascending aortic lesions with a limited extension into the distal arch (Stanford Type A/DeBakey Type I); and
- Type III: an elephant trunk procedure with a complete endovascular repair of the thoracoabdominal aorta. This technique is reserved for patients with extensive aortic lesions that involve the ascending, transverse arch, and descending thoracic aorta (Stanford Type A/DeBakey Type I).

How the intervention might work

Although to date trial results using hybrid repair techniques for aortic arch dissection are promising, opinion is divided on its efficaciousness among the wider vascular surgery community (Kurimoto 2015). The aim of both hybrid repair and OSR is to stop further dissection progression in the aortic artery by covering the dissection entry points and also by promoting false lumen thrombosis; OSR is regarded as the standard for aortic arch dissection. Intervention for aortic arch dissection via a hybrid approach would reduce the incidence of highly invasive surgery when compared to OSR, while duration of cardiopulmonary bypass, hypothermic circulatory arrest and antegrade/retrograde cerebral perfusion can be reduced. Cardiopulmonary bypass is a technique that temporarily takes over the function of the heart and lungs during surgery, maintaining the circulation of blood and oxygen in the body. Hypothermic circulatory arrest temporarily suspends blood flow under very cold body temperatures. Antegrade cerebral perfusion involves sewing a small graft to the axillary/brachiocephalic artery or left common carotid artery. The graft is connected to a heart-lung machine, and allows blood to flow through the brain during complex surgery of the aorta. Retrograde cerebral perfusion requires cannulation of the vena cava with perfusion pressures not exceeding 25 mmHg. Antegrade perfusion permits blood flow through the arterial system, allowing for varying temperature control. Retrograde perfusion permits blood flow through the venous system. The high associated risks using these methods including mortality (death) (6.6% to 9.9%), stroke (2.7% to 6.6%), paraplegia (18%), cardiac arrhythmia (irregular heartbeat), venous congestion and cerebral oedema would therefore be reduced or negated (Estrera 2003; Kamiya 2007; Okita 2001).

Why it is important to do this review

To date, no Cochrane review has assessed the effectiveness of hybrid repair compared to the standard OSR. There is an agreement that intervention is necessary for aortic arch dissection, however complex open aortic arch repair still carries a high degree of health risks and death due to the use of cardiopulmonary bypass, hypothermic circulatory arrest, and antegrade or retrograde cerebral perfusion during the procedure (Lu 2013; Murphy 2012; Rampoldi 2007; Vohra 2012). Deciding if a patient will undergo a hybrid versus open repair depends on surgical skill and physician preference, the overall quality of the supra-aortic vessels (the brachiocephalic artery, the left common carotid artery, and subclavian artery) and the ability to clamp them, and whether cerebral perfusion can be maintained adequately.

We are undertaking this review as there is a critical need within the cardiovascular community for a synthesis of high quality evidence to inform decisions on optimal management of aortic arch dissection. Our systematic review will focus on aortic arch dissection treatments (specifically of Stanford Type A, i.e. DeBakey Type I and Type II) using hybrid and open repair. Examining hybrid interventions treating aortic arch dissection will allow us to determine the effectiveness and safety of this technique over standard open repair.

OBJECTIVES

To assess the effectiveness and safety of a hybrid technique of treatment over conventional open repair in the management of aortic arch dissection.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs) and controlled clinical trials (CCTs) assessing the effects of hybrid repair techniques compared to open surgical repair (OSR) of aortic arch dissection.

Types of participants

We will include all participants with a diagnosis of aortic arch dissection. This will include classifications of dissection according to Stanford Type A (DeBakey Type I and Type II). Diagnosis will be made by relevant diagnostic modalities, i.e. computed tomography (CT) or Magnetic Resonance Imaging (MRI), or both. There will be no limitation on participant gender, age, ethnicity, treatment setting (e.g. elective versus emergency repair), or dissection chronicity (acute or chronic). Patients that required a concomitant aortic valve repair will be excluded.

Types of interventions

We will include the following comparisons:

- Type I hybrid repair versus OSR;
- Type II hybrid repair versus OSR; and
- Type III hybrid repair versus OSR.

Types of outcome measures

Outcomes will be guided and defined by the International Aortic Arch Surgery Study Group (Yan 2014; see also Table 1 for more details).

Primary outcomes

- Dissection-related mortality and all-cause mortality at 30 days and 12 months (Grade V)
- Neurological deficit (defined by global, focal and spinal events, Grade I to IV)
- Cardiac injury (defined by myocardial ischaemia, low cardiac output syndrome, arrhythmia, pericardial effusion, Grade I to IV)
- Respiratory compromise (defined by parenchymal and pleural complications, Grade I to IV)
- Renal ischaemia (defined by RIFLE classification Bellomo 2004, Grade I to IV)

Secondary outcomes

- False lumen thrombosis (defined by partial or complete thrombosis)
- Mesenteric ischaemia (defined by gut complications, Grade I to IV)

Search methods for identification of studies

We will apply no restrictions according to language.

Electronic searches

The Cochrane Vascular Information Specialist (CIS) will search the following databases for relevant trials.

- The Cochrane Vascular Specialised Register.
- The Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Register of Studies Online.

See Appendix 2 for details of the search strategy which will be used to search CENTRAL.

The Cochrane Vascular Specialised Register is maintained by the CIS and is constructed from weekly electronic searches of MEDLINE Ovid, EMBASE Ovid, CINAHL, AMED, and through handsearching relevant journals. The full list of the databases, journals and conference proceedings which 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).

In addition, the CIS will search the following trial registries for details of ongoing and unpublished studies.

- ClinicalTrials.gov (www.clinicaltrials.gov).
- World Health Organization International Clinical Trials Registry Platform (www.who.int/trialsearch).

For the purpose of this review, we will also include studies published as abstracts only if we can extract sufficient information. In cases where insufficient data are published, we will first contact the trial authors to access required information. If data remain insufficient after contacting the trial authors, we will exclude the study from our review.

Searching other resources

We will search the reference lists of all included studies.

Data collection and analysis

Selection of studies

Two review authors (EPK and AE) will independently assess the titles and abstracts of each identified study. Both review authors (EPK and AE) will assess full texts of all studies categorised as included or unclear at title/abstract screening. If the review authors disagree on the inclusion or exclusion of a study, the reasons will be discussed. If there is no agreement between the two review authors, then we will discuss with a third reviewer (NH). Reasons for exclusions will be recorded in the 'Characteristics of excluded studies' table. We will describe the selection process in an adapted PRISMA flow chart (Liberati 2009).

Data extraction and management

Full-text reports of the studies selected will be obtained and two review authors (EPK and AE) will independently extract data using an adapted data extraction form provided by Cochrane Vascular. If there is disagreement between the two review authors, issues will be resolved by discussion with a third review author (NH). For studies with duplicate or multiple publications (or both), we will collate all available data, presenting this as one study dataset.
We will aim to describe the studies according to the following:

- trial design;
- diagnosis of aortic arch dissection;
- demographic characteristics of participants;
- type of intervention (hybrid and open repair); and
- frequency of primary and secondary outcomes.

Assessment of risk of bias in included studies

Two review authors (EPK and AE) will independently assess the potential risks of bias in all included RCTs and CCTs using the Cochrane 'Risk of bias' tool (Higgins 2011). Each domain will be judged as low risk, high risk, or unclear risk of bias and we will provide a statement to support each judgment. If there is disagreement between the two review authors, these will be resolved by discussion, and if necessary, discussion with a third review author (NH).
We will assess the risk of bias in the following domains:

- selection bias (random sequence generation and allocation concealment);
- performance bias (blinding of participants and personnel);
- detection bias (blinding of outcome assessors);
- attrition bias (incomplete outcome data);
- reporting bias (selective outcome reporting); and
- other sources of bias.

Measures of treatment effect

Dichotomous data

We will express the results for dichotomous outcomes as risk ratios (RRs) with 95% confidence intervals (CIs), to reflect uncertainty of the point estimate of effects.

Continuous data

We will express the results for continuous scales of measurement as mean differences (MDs), standard deviation (SD) and associated 95% CIs. Where there is a difference in scales for the same outcome, we will use the standardised mean difference with 95% CIs to combine the outcomes.

Time-to-event data

Survival analysis will be used to present time-to-event data expressed as hazard ratios (HRs) with 95% CIs. Methods used to analyse time-to-event outcomes will be guided by those described by Parmar 1998 and Tierney 2007, and as detailed in Chapter 7, section 7.7.6. of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Unit of analysis issues

We will consider the unit of analysis within each trial to be each participant.

Dealing with missing data

In studies that have incomplete data, we will contact the study authors to seek additional data. For all outcomes, we will carry out analyses, as far as possible, on an intention-to-treat basis (i.e. based on the initial treatment assignment and not on the treatment eventually received).

Assessment of heterogeneity

We will evaluate clinical heterogeneity based on participant data, the intervention and outcomes of each study. We will assess the degree of heterogeneity by visual inspection of forest plots and by examining the Chi^2 test for heterogeneity. We will use the I^2 statistic, Tau^2 statistic and Chi^2 test to determine statistical heterogeneity among studies, according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).
We will regard statistical heterogeneity as substantial if an I^2 is greater than 50% and either the Tau^2 is greater than zero, or there is a low P value (less than 0.10) in the Chi^2 test for heterogeneity. If we identify substantial heterogeneity, we will explore possible reasons using subgroup analyses.

Assessment of reporting biases

We will address publication bias and other reporting biases (such as multiple publication bias) using funnel plots, as per Cochrane Vascular guidelines, if there are 10 or more included studies (Higgins 2011).

Data synthesis

We will enter the collected data into Review Manager software (RevMan 2014). We will use fixed-effect meta-analysis for synthesising data where it is reasonable to assume that trials are estimating the same underlying treatment effect. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity is detected, we will use random-effects meta-analysis to produce

an overall summary where the average treatment effect is clinically meaningful. If we identify clinical, methodological or statistical heterogeneity across included trials sufficient to cause concerns as to the appropriateness of pooling results, we will not report pooled results from the meta-analysis but will instead use a narrative approach to data synthesis. We will create a forest plot for each treatment effect, as per Cochrane Vascular guidelines (Higgins 2011).

Subgroup analysis and investigation of heterogeneity

If considerable heterogeneity is identified within the included studies, we will carry out subgroup analyses to investigate possible reasons for this heterogeneity. In addition, we will also perform the following subgroup analyses, which will be guided by DISSECT, a mnemonic-based approach to the categorisation of aortic dissection (Dake 2013).

- Duration of disease (i.e. acute dissection (less than 14 days) versus chronic dissection (14 days or more))
- Intimal tear location (i.e. ascending aorta versus aortic arch)
- Segmental extent of the disease (i.e. DeBakey Type I versus DeBakey Type II)
- Size of the dissected aorta (i.e. maximum diameter less than 5.5 cm versus 5.5 cm or more (Pape 2007))
- Presence or absence of complication
- Thrombosis of aortic false lumen
- Presence or absence of connective tissue disorder
- Gender (Nienaber 2004)
- Age (i.e. less than 70 years versus 70 years or older (Trimarchi 2010)

Sensitivity analysis

We will perform sensitivity analyses on the following:

- High-quality trials, defined as studies with a low risk of bias for sequence generation and allocation concealment; and
- RCTs compared with CCTs.

Summary of findings

We will prepare a 'Summary of findings' table according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We intend to use GRADE profiler software to create the tables (GRADEproGDT 2015). For each comparator, we will include all primary and secondary outcomes as described in the Types of outcome measures section. We have included an example table in this protocol (Table 2). Using the GRADE approach, we will assess the quality of the body of evidence for each outcome as high, moderate, low or very low, based on the criteria of risk of bias, inconsistency, indirectness, imprecision and publication bias (Atkins 2004; GRADE Working Group 2014, Guyatt 2008a, Guyatt 2008b; Schünemann 2006).

ACKNOWLEDGEMENTS

We are very grateful to Cochrane Vascular for their support and guidance in the preparation of this protocol.

REFERENCES

Additional references

Antoniou 2010
Antoniou GA, El Sakka K, Hamady M, Wolfe JH. Hybrid treatment of complex aortic arch disease with supra-aortic debranching and endovascular stent graft repair. *European Journal of Vascular and Endovascular Surgery* 2010;**39**(6): 683–90.

Atkins 2004
Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. *British Medical Journal* 2004;**328** (7454):1490–4.

Bellomo 2004
Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute Dialysis Quality Initiative Workgroup. Acute renal failure: definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Critical Care* 2004;**8**(4): R204–12.

Cao 2012
Cao P, De Rango P, Czerny M, Evangelista A, Fattori R, Nienaber C, et al. Systematic review of clinical outcomes in hybrid procedures for aortic arch dissections and other arch diseases. *The Journal of Thoracic and Cardiovascular Surgery* 2012;**144**(6):1286–300.

Cochennec 2013
Cochennec F, Tresson P, Cross J, Desgranges P, Allaire E, Becquemin JP. Hybrid repair of aortic arch dissections. *Journal of Vascular Surgery* 2013;**57**(6):1560–7.

Daily 1970
Daily PO, Trueblood HW, Stinson EB, Wuerflein RD, Shumway NE. Management of acute aortic dissections. *The Annals of Thoracic Surgery* 1970;**10**(3):237-47.

Dake 2013
Dake MD, Thompson M, van Sambeek M, Vermassen F, Morales JP, DEFINE Investigators. DISSECT: a new mnemonic-based approach to the categorization of aortic dissection. *European Journal of Vascular and Endovascular Surgery* 2013;**46**(2)):175–90.

DeBakey 1966
DeBakey ME, Beall AC Jr, Cooley DA, Crawford ES, Morris GC Jr, Garrett HE, et al. Dissecting aneurysms of the aorta. *The Surgical Clinics of North America* 1966;**46**(4): 1045–55.

Estrera 2003
Estrera AL, Garami Z, Miller CC 3rd, Sheinbaum R, Huynh TT, Porat EE, et al. Determination of cerebral blood flow dynamics during retrograde cerebral perfusion using power M-mode transcranial Doppler. *Annals of Thoracic Surgery* 2003;**76**(3):704-10.

Fillinger 2010
Fillinger MF, Greenberg RK, McKinsey JF, Chaikof EL. Society for Vascular Surgery Ad Hoc Committee on TEVAR Reporting Standards. Reporting standards for thoracic endovascular aortic repair (TEVAR). *Journal of Vascular Surgery* 2010;**52**(4):1022–33.

GRADE Working Group 2014
GRADE Working Group. Grading quality of evidence and strength of recommendations. *British Medical Journal* 2004; **328**(19):1490–4.

GRADEproGDT 2015 [Computer program]
McMaster University (developed by Evidence Prime, Inc.). GRADEpro GDT. Version accessed 4 January 2018. Hamilton (ON): McMaster University (developed by Evidence Prime, Inc.), 2015.

Groysman 2011
Groysman LI, Emanuel BA, Kim-Tenser MA, Sung GY, Mack WJ. Therapeutic hypothermia in acute ischemic stroke. *Neurosurgical Focus* 2011;**30**(6):E17.

Guyatt 2008a
Guyatt GH, Oxman AD, Kunz R, Vist GE, Falck-Ytter Y, Schünemann HJ. What is 'quality of evidence' and why is it important to clinicians?. *British Medical Journal* 2008;**336** (7651):995–8.

Guyatt 2008b
Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *British Medical Journal* 2008;**336**(7650):924–6.

Higgins 2011
Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.handbook.cochrane.org.

Kamiya 2007
Kamiya H, Hagl C, Kropivnitskaya I, Böthig D, Kallenbach K, Khaladj N, et al. The safety of moderate hypothermic lower body circulatory arrest with selective cerebral perfusion: a propensity score analysis. *The Journal of Thoracic and Cardiovascular Surgery* 2007;**133**(2):501–9.

Kurimoto 2015
Kurimoto Y, Maruyama R, Ujihira K, Nishioka N, Hasegawa K, Iba Y, et al. Thoracic Endovascular Aortic Repair for Challenging Aortic Arch Diseases Using Fenestrated Stent Grafts From Zone 0. *The Annals of Thoracic Surgery* 2015;**100**(1):24–33.

Liberati 2009
Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Medicine* 2009;**6**(7):e1000100.

Lu 2013
Lu Q, Feng J, Zhou J, Zhao Z, Bao J, Feng R, et al. Endovascular repair of ascending aortic dissection: a novel treatment option for patients judged unfit for direct surgical repair. *Journal of the American College of Cardiology* 2013;**61** (18):1917–24.

Moon 2011
Moon MC, Greenberg RK, Morales JP, Martin Z, Lu Q, Dowdall JF, et al. Computed tomography-based anatomic characterization of proximal aortic dissection with consideration for endovascular candidacy. *Journal of Vascular Surgery* 2011;**53**(4):942–9.

Moulakakis 2013
Moulakakis KG, Mylonas SN, Markatis F, Kotsis T, Kakisis J, Liapis CD. A systematic review and meta-analysis of hybrid aortic arch replacement. *Annals of Cardiothoracic Surgery* 2013;**2**(3):247–60.

Murphy 2012
Murphy EH, Stanley GA, Ilves M, Knowles M, Dimaio JM, Jessen ME, et al. Thoracic endovascular repair (TEVAR) in the management of aortic arch pathology. *Annals of Vascular Surgery* 2012;**26**(1):55–66.

Murphy-Ryan 2010
Murphy-Ryan M, Psychogios A, Lindor NM. Hereditary disorders of connective tissue: a guide to the emerging differential diagnosis. *Genetics in Medicine* 2010;**12**(6): 344–54.

Nienaber 2004
Nienaber CA, Fattori R, Mehta RH, Richartz BM, Evangelista A, Petzsch M, et al. Gender-related differences in acute aortic dissection. *Circulation* 2004;**109**(24): 3014–21.

Nordon 2012
Nordon IM, Hinchliffe RJ, Morgan R, Loftus IM, Jahangiri M, Thompson MM. Progress in endovascular management of type A dissection. *European Journal of Vascular and Endovascular Surgery* 2012;**44**(4):406–10.

O'Callaghan 2014
O'Callaghan A, Mastracci TM, Greenberg RK, Eagleton MJ, Bena J, Kuramochi Y. Outcomes for supra-aortic branch vessel stenting in the treatment of thoracic aortic disease. *Journal of Vascular Surgery* 2014;**60**(4):914–20.

Okita 2001
Okita Y, Minatoya K, Tagusari O, Ando M, Nagatsuka K, Kitamura S. Prospective comparative study of brain protection in total aortic arch replacement: deep hypothermic circulatory arrest with retrograde cerebral

perfusion or selective antegrade cerebral perfusion. *The Annals of Thoracic Surgery* 2001;**72**(1):72–9.

Pape 2007
Pape LA, Tsai TT, Isselbacher EM, Oh JK, O'Gara PT, Evangelista A, et al. Aortic diameter≥ 5.5 cm is not a good predictor of Type A aortic dissection observations from the International Registry of Acute Aortic Dissection (IRAD). *Circulation* 2007;**116**(10):1120–7.

Parmar 1998
Parmar MK, Torri V, Stewart L. Extracting summary statistics to perform meta-analyses of the published literature for survival endpoints. *Statistics in Medicine* 1998;**17**(24): 2815–34.

Patel 2011
Patel HJ, Nguyen C, Diener AC, Passow MC, Salata D, Deeb GM. Open arch reconstruction in the endovascular era: analysis of 721 patients over 17 years. *The Journal of Thoracic and Cardiovascular Surgery* 2011;**141**(6):1417–23.

Rampoldi 2007
Rampoldi V, Trimarchi S, Eagle KA, Nienaber CA, Oh JK, Bossone E, et al. Simple risk models to predict surgical mortality in acute type A aortic dissection: the International Registry of Acute Aortic Dissection score. *The Annals of Thoracic Surgery* 2007;**83**(1):55–61.

RevMan 2014 [Computer program]
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2013.

Schünemann 2006
Schünemann HJ, Jaeschke R, Cook DJ, Bria WF, El-Solh AA, Ernst A, et al. An official ATS statement: grading the quality of evidence and strength of recommendations in ATS guidelines and recommendations. *American Journal of Respiratory and Critical Care Medicine* 2006;**174**(5):605–14.

Sobocinski 2011
Sobocinski J, O'Brien N, Maurel B, Bartoli M, Goueffic Y, Sassard T, et al. Endovascular approaches to acute aortic type A dissection: a CT-based feasibility study. *European Journal of Vascular and Endovascular Surgery* 2011;**42**(4): 442–7.

Suzuki 2003
Suzuki T, Mehta RH, Ince H, Nagai R, Sakomura Y, Weber F, et al. Clinical profiles and outcomes of acute type B aortic dissection in the current era: lessons from the International Registry of Aortic Dissection (IRAD). *Circulation* 2003;**108** (10 Suppl 1):II312–7.

Tierney 2007
Tierney JF, Stewart LA, Ghersi D, Burdett S, Sydes MR. Practical methods for incorporating summary time-to-event data into meta-analysis. *Trials* 2007;**8**(1):1–16.

Trimarchi 2010
Trimarchi S, Eagle KA, Nienaber CA, Rampoldi V, Jonker FH, De Vincentiis C, et al. Role of age in acute type A aortic dissection outcome: report from the International Registry of Acute Aortic Dissection (IRAD). *The Journal of Thoracic and Cardiovascular Surgery* 2010;**140**(4)):784–9.

Vohra 2012
Vohra HA, Modi A, Barlow CW, Ohri SK, Livesey SA, Tsang GM. Repair of acute type A aortic dissection: results in 100 patients. *Asian Cardiovascular and Thoracic Annals* 2012;**20**(2):160–7.

Wong 2008
Wong DR, Lemaire SA, Coselli JS. Managing dissections of the thoracic aorta. *The American Surgeon* 2008;**74**(5): 364–80.

Yan 2014
Yan TD, Tian DH, LeMaire SA, Hughes GC, Chen EP, Misfeld M, et al. Standardizing clinical end points in aortic arch surgery: a consensus statement from the International Aortic Arch Surgery Study Group. *Circulation* 2014;**129** (15):1610–6.

* *Indicates the major publication for the study*

ADDITIONAL TABLES

Table 1. Definition of outcome measures (Yan 2014)

Types of outcome measures	Defined by	Including
Primary outcomes		
Mortality	Dissection related and all cause	(Grade V) All deaths at 30 days and 12 months

Table 1. Definition of outcome measures (Yan 2014) (*Continued*)

Neurological deficit	Global events	(Grade I - IV) Postoperative agitation, delirium, obtundation, or myoclonic movements, without localised cerebral neurological signs
	Focal events	(Grade I - IV) Lateralising sensory or motor deficit or focal seizure activity
	Spinal neurological events	(Grade I - IV) Paraplegia, paraparesis
Cardiac injury	Myocardial ischaemia	(Grade I - IV)
	Low cardiac output syndrome	(Grade I - IV)
	Arrhythmia	(Grade I - IV)
	Pericardial effusion	(Grade I - IV)
Respiratory compromise	Parenchymal complications	(Grade I - IV) Atelectasis, pneumonia, pulmonary oedema, and acute respiratory distress syndrome
	Pleural complications	(Grade I - IV) Pneumothorax, pleural effusion
Renal ischaemia	Modified RIFLE classification (Bellomo 2004): Risk (I), Injury (II), Failure (III), Loss/End-Stage Kidney Dysfunction (IV)	(Grade I - IV) Serum creatinine increase, glomerular filtration rate (GFR) decrease, anuria, haemodialysis
Secondary outcomes		
False lumen thrombosis	Partial or complete thrombosis	-
Mesenteric ischaemia	Gut complications	(Grade I - IV) Ileus or gastric paresis, gut ischaemia manifested as metabolic acidosis or increased lactate

Grades as defined by Yan 2014:
Grade I: any deviation from the normal postoperative course but self-limiting or requiring simple therapeutic regimens (including antiemetics, antipyretics, analgesics, electrolytes, and physiotherapy);
Grade II: complications requiring pharmacological treatment for resolution;
Grade III: complications requiring surgical, endoscopic, or radiological intervention but not requiring regional or general anaesthesia or requiring interdisciplinary intervention;
Grade IV: complications requiring surgical, endoscopic, or radiological intervention under regional or general anaesthesia, or requiring new intensive care unit (ICU) admission or ongoing ICU management for > 7 days or hospitalisation for > 30 days, or causing secondary organ failure;

Table 1. Definition of outcome measures (Yan 2014) (*Continued*)

Grade V: death caused by a complication.

Table 2. Summary of findings

Summary of findings for the main comparison: Hybrid repair versus conventional open repair for aortic arch dissection						
Patient or population: patients with a diagnosis of aortic arch dissection **Settings:** hospital **Intervention:** hybrid repair **Comparison:** open repair						
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**Number of Participants (studies)**	**Quality of the evidence (GRADE)**	**Comments**
	Assumed risk	**Corresponding risk**				
	Open repair	**Hybrid repair**				
Mortality, Follow up: median N (months)	**Study population**		**HR** **N** (N to N)	N (N)	⊕◯◯◯ **very low** ⊕⊕◯◯ **low** ⊕⊕⊕◯ **moderate** ⊕⊕⊕⊕ **high**	
	N per 1000	**N per 1000** (N to N)				
Neurological deficit, Follow up: median N (months)	**Study population**		**RR** **N** (N to N)	N (N)	⊕◯◯◯ **very low** ⊕⊕◯◯ **low** ⊕⊕⊕◯ **moderate** ⊕⊕⊕⊕ **high**	
	N per 1000	**N per 1000** (N to N)				
Cardiac injury, Follow up: median N (months)	**Study population**		**RR** **N** (N to N)	N (N)	⊕◯◯◯ **very low** ⊕⊕◯◯ **low** ⊕⊕⊕◯ **moderate** ⊕⊕⊕⊕ **high**	

Table 2. Summary of findings (*Continued*)

	N per 1000	**N per 1000** (N to N)				
Respiratory compromise, Follow up: median N (months)	**Study population**		**RR** **N** (N to N)	N (N)	⊕◯◯◯ **very low** ⊕⊕◯◯ **low** ⊕⊕⊕◯ **moderate** ⊕⊕⊕⊕ **high**	
	N per 1000	**N per 1000** (N to N)				
Renal ischaemia, Follow up: median N (months)	**Study population**		**RR** **N** (N to N)	N (N)	⊕◯◯◯ **very low** ⊕⊕◯◯ **low** ⊕⊕⊕◯ **moderate** ⊕⊕⊕⊕ **high**	
	N per 1000	**N per 1000** (N to N)				
False lumen thrombosis, Follow up: median N (months)	**Study population**		**RR** **N** (N to N)	N (N)	⊕◯◯◯ **very low** ⊕⊕◯◯ **low** ⊕⊕⊕◯ **moderate** ⊕⊕⊕⊕ **high**	
	N per 1000	**N per 1000** (N to N)				
Mesenteric ischaemia, Follow up: median N (months)	**Study population**		**RR** **N** (N to N)	N (N)	⊕◯◯◯ **very low** ⊕⊕◯◯ **low** ⊕⊕⊕◯ **moderate** ⊕⊕⊕⊕ **high**	
	N per 1000	**N per 1000** (N to N)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **N:** number; **HR:** Hazard ratio; **RR:** Risk Ratio

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

Table 2. Summary of findings (*Continued*)

change the estimate.
Very low quality: We are very uncertain about the estimate.

APPENDICES

Appendix 1. Glossary of terms

A
Anastomosis is a connection made surgically between adjacent blood vessels.
Antegrade cerebral perfusion (ACP) is a method of supplying blood to the brain during surgery, while the function of the heart and lungs is temporarily stopped.
Aortic dissection is a separation or tear of the intima layer from the media layer of the aorta.
B
Bifurcated refers to a division in an object in to two objects, e.g. one part into two parts.
C
Cardiac arrhythmia is an irregular heart beat.
Cardiopulmonary bypass is a technique that temporarily takes over the function of the heart and lungs during surgery, maintaining the circulation of blood and oxygen in the body.
Cervical is an anatomical term used for an section of the spine in the neck (cervical spine).
Circulatory arrest is an artificially induced method of slowing the blood flow around the body during surgical interventions.
Clavicle is an anatomical term for the collar bone.
Coagulopathy is a failure in the blood to clot, leading to excessive bleeding.
Distal refers to a point that is farthest away from the centre of the body.
E
Elephant trunk is a vascular technique used to repair patients with extensive disease in their aorta. It consists of two stages, 1) open surgery to replace a portion of the ascending aorta, while leaving a section of graft hanging within the descending aorta. 2) This graft section can then be used to place an endovascular stent (known as stented elephant trunk technique). This technique can also be carried out as a single-stage (known as frozen elephant trunk technique).
Endovascular repair involves intervention through the arteries using wires to carry grafts to the area of interest to be repaired.
H
Hypokalaemia is related to the status of potasium in the blood, specifically when the level is lower than normal.
Hypothermia refers to cooling of core body temperature.
Hypothermic circulatory arrest temporarily suspends blood flow under very cold body temperatures.
L
Landing zone refers to the zone of landing for a graft in the aorta.
Lesion is a region in an organ or tissue which has suffered damage through injury or disease, for example a wound, ulcer, abscess, or tumour.
M
Mortality is also known as death.
O
Open surgical repair (OSR) involves surgical intervention through a large incision made through the skin, revealing the inner organs to be repaired. It also involves induced circulatory arrest or hypothermia, and methods of brain protection.
P
Peripheral arterial access is the point of access to the blood in an artery, specifically in the limbs of the body, e.g. the arms or the legs.

Pharmacologic hypotension refers to a method of inducing a state of low blood pressure using a drug(s) during surgery, in order to reduce the amount of blood lost.
Proximal refers to a point that is closest to the centre of the body.
R
Retrograde Cerebral Perfusion (RCP) is a method of supplying blood to the brain during surgery, while the function of the heart and lungs is temporarily stopped. The blood receives oxygen outside the body, and is washed of toxins, and blood clots, and is cannulated back into the body through a vein.
Revascularisation is a process of restoring blood to a vessel or organ following a state of deprivation.
S
Stroke occurs when the blood flow to the brain is obstructed, resulting in cellular death.
T
Transposition is a term used when a vessel is transferred onto another vessel.
Trifurcated refers to division in an object in to three objects, e.g. one part into three parts.

Appendix 2. CENTRAL search strategy

#1	MESH DESCRIPTOR Aneurysm, Dissecting
#2	MESH DESCRIPTOR Aorta WITH QUALIFIERS SU
#3	(aortic arch):TI,AB,KY
#4	((aort* near4 dissect*)):TI,AB,KY
#5	((aort* near4 tear*)):TI,AB,KY
#6	((aort* near4 trauma*)):TI,AB,KY
#7	(deBakey):TI,AB,KY
#8	(de Bakey):TI,AB,KY
#9	Stanford:TI,AB,KY
#10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9
#11	hybrid:TI,AB,KY
#12	debranch*:TI,AB,KY
#13	supraaortic:TI,AB,KY
#14	rerouting:TI,AB,KY
#15	MESH DESCRIPTOR Endovascular Procedures EXPLODE ALL TREES
#16	MESH DESCRIPTOR Stents EXPLODE ALL TREES

(*Continued*)

#17	MESH DESCRIPTOR Blood Vessel Prosthesis EXPLODE ALL TREES
#18	MESH DESCRIPTOR Blood Vessel Prosthesis Implantation EXPLODE ALL TREES
#19	endovasc*:TI,AB,KY
#20	endostent*:TI,AB,KY
#21	endoluminal:TI,AB,KY
#22	endoprosthe*:TI,AB,KY
#23	(graft or endograft*):TI,AB,KY
#24	percutaneous*:TI,AB,KY
#25	stent*:TI,AB,KY
#26	TEVAR:TI,AB,KY
#27	branched:TI,AB,KY
#28	fenestrated:TI,AB,KY
#29	(elephant trunk):TI,AB,KY
#30	(landing zone):TI,AB,KY
#31	#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30
#32	#10 AND #31

CONTRIBUTIONS OF AUTHORS

EPK: designing and drafting protocol, acquiring trial reports, trial selection, data extraction, data analysis, data interpretation, review drafting, future review updates, and guarantor of the review

FJ: designing and revising protocol, and data interpretation

NH: designing and revising protocol, trial selection, and data interpretation

AE: designing and revising protocol, acquiring trial reports, trial selection, and data extraction

DD: designing and revising protocol, and data interpretation

DV: revising protocol, and review drafting

SS: revising protocol, and review drafting

DECLARATIONS OF INTEREST

EPK: none known

FJ: none known

NH: has received payment as a member of the Peripheral Advisory Board and for consultation on Regulatory Documents from Lake Region Medical, for medical device design at Boston Scientific (Enterprise Ireland Bioinnovate Fellow). Her institution has received payment for lectures and presentations from Gore Medical. She has no competing interests, relationships, conditions or circumstances which will conflict with this review.

AE: none known

DD: none known

DV: none known

SS: has received payment for training physicians on endovascular aortic repair from Gore Medical and is the Prinicpal Invesigator in the INSIGHT post Market Surveillance trial of the INCRAFT© abdominal aortic endograft (Cordis/Cardinal health). He has no conflict of interest which will effect this review.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Chief Scientist Office, Scottish Government Health Directorates, The Scottish Government, UK.

The Cochrane Vascular editorial base is supported by the Chief Scientist Office.

NOTES

Parts of the methods section of this protocol are based on a standard template established by Cochrane Vascular.