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Controlled hypotension versus normotensive resuscitation strategy for people with ruptured abdominal aortic aneurysm (Review)

Moreno DH, Cacione DG, Baptista-Silva JCC

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[Intervention Review]

Controlled hypotension versus normotensive resuscitation strategy for people with ruptured abdominal aortic aneurysm

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ABSTRACT

Background

An abdominal aortic aneurysm (AAA) is the pathological enlargement of the aorta and can develop in both men and women. Progressive aneurysm enlargement can lead to rupture. The rupture of an AAA is frequently fatal and accounts for the death from haemorrhagic shock of at least 45 people per 100,000 population. The outcome of people with ruptured AAA varies among countries and healthcare systems, with mortality ranging from 53% to 90%. Definitive treatment for ruptured AAA includes open surgery or endovascular repair. The management of haemorrhagic shock is crucial for the person's outcome and aims to restore organ perfusion and systolic blood pressure above 100 mmHg through immediate and aggressive fluid replacement. This rapid fluid replacement is known as the normotensive resuscitation strategy. However, evidence suggests that infusing large volumes of cold fluid causes dilutional and hypothermic coagulopathy. The association of these factors may exacerbate bleeding, resulting in a 'lethal triad' of hypothermia, acidaemia, and coagulopathy. An alternative to the normotensive resuscitation strategy is the controlled (permissive) hypotension resuscitation strategy, with a target systolic blood pressure of 50 mmHg to 100 mmHg. The principle of controlled or hypotensive resuscitation has been used in some management protocols for endovascular repair of ruptured AAA. It may be beneficial in preventing blood loss by avoiding the clot disruption caused by the rapid increase in systolic blood pressure; avoiding dilution of clotting factors, platelets and fibrinogen; and by avoiding the temperature decrease that inhibits enzyme activity involved in platelet and clotting factor function. This is an update of a review first published in 2016.

Objectives

To compare the effects of controlled (permissive) hypotension resuscitation and normotensive resuscitation strategies for people with ruptured AAA.

Search methods

The Cochrane Vascular Information Specialist searched the Specialised Register (August 2017), the Cochrane Register of Studies (CENTRAL (2017, Issue 7)) and EMBASE (August 2017). The Cochrane Vascular Information Specialist also searched clinical trials databases (August 2017) for details of ongoing or unpublished studies.

Selection criteria

We sought all published and unpublished randomised controlled trial (RCTs) that compared controlled hypotension and normotensive resuscitation strategies for the management of shock in patients with ruptured abdominal aortic aneurysms.

Data collection and analysis

Two review authors independently assessed identified studies for potential inclusion in the review. We used standard methodological procedures in accordance with the *Cochrane Handbook for Systematic Review of Interventions*.

Main results

We identified no RCTs that met the inclusion criteria.

Authors' conclusions

We found no RCTs that compared controlled hypotension and normotensive resuscitation strategies in the management of haemorrhagic shock in patients with ruptured abdominal aortic aneurysm that assessed mortality, presence of coagulopathy, intensive care unit length of stay, and the presence of myocardial infarct and renal failure. High quality studies that evaluate the best strategy for managing haemorrhagic shock in ruptured abdominal aortic aneurysms are required.

PLAIN LANGUAGE SUMMARY

Controlled hypotension versus normotensive resuscitation strategy for people with ruptured abdominal aortic aneurysm

Background

An abdominal aortic aneurysm (AAA) is a swelling (aneurysm) of the aorta, the main blood vessel that leads away from the heart and through the abdomen to the rest of the body. It can develop in both men and women. A growing aneurysm can burst (rupture), which leads to massive blood loss and shock. It is frequently fatal and accounts for the death of at least 45 people per 100,000 population.

One option to fix a ruptured AAA is to open the abdomen and place a tube graft in the aorta (open repair); the second approach is to place a stent graft inside the aorta through the large artery in the thigh (femoral artery; endovascular repair).

This review focused on the initial management of bleeding and low blood pressure caused by the ruptured aneurysms, also known as haemorrhagic shock. Patients are generally given intravenous (giving medicines or fluids through a needle or tube inserted into a vein) saline solutions in the emergency room or surgery centre to restore circulatory volume.

Rapid fluid replacement immediately restores normal blood pressure. It is known as the normotensive resuscitation strategy and can lead to an increase in bleeding because the clot can be removed and coagulation factors in the blood can be diluted. An alternative approach is the controlled (permissive) hypotension resuscitation strategy. This strategy consists of fluid replacement, the use of drugs, or both, to keep systolic blood pressure between 50 mmHg and 100 mmHg, until the aneurysms can be repaired with open surgery or endovascular repair. This strategy might work because it does not introduce a large volume of cool saline solution and consequently avoids the outcomes listed above.

Study characteristics and key results

We searched for evidence that directly compared strategies to manage haemorrhagic shock and to restore normal blood pressure initially, and during surgery, in patients with ruptured AAA. Our searches up to August 2017, did not identify any randomised controlled trials (clinical studies where people are randomly put into one of two or more treatment groups; one of which is the control group) meeting our criteria. Studies are needed to help emergency physicians, vascular surgeons, and anaesthesiologists choose the best option for treating haemorrhagic shock caused by ruptured abdominal aortic aneurysms.

Quality of the evidence

We found no randomised controlled trials that met our criteria.

BACKGROUND

Description of the condition

An abdominal aortic aneurysm (AAA) is the pathological enlargement of the aorta and can develop in both men and women (Badger 2017). Prevalence rates vary according to age, gender, and geographical location (Moll 2011). According to randomised trials to assess the benefits of screening and large epidemiological screening studies, it is most commonly seen in men over the age of 65 years, with total prevalence varying from 4% to 8.9% (Moll 2011). The NHS Abdominal Aortic Aneurysm Screening Programme reported a prevalence of 1.5% during 2011 and 2012 of the men invited for screening, a lower detection rate than expected (NHS 2013). Important risk factors for developing AAA are age, male gender, and smoking. Progressive aneurysm enlargement can lead to rupture, and the most important risk factors associated with this complication, across several studies, include large aneurysm diameter, female gender, smoking, hypertension, and AAA expansion rate (Brown 1999; Hatakeyama 2001; Moll 2011; Powell 2008). The rupture of an AAA is frequently fatal, and accounts for death from haemorrhagic shock of at least 45 people per 100,000 population (Anjum 2012). The outcome of people with ruptured AAA (rAAA) varies among countries, with different results reported for different healthcare systems;death ranges from 53% to 90% (Karthikesalingan 2014). Technical aspects, organisational factors, and hospital-related factors all play an important role in patient care (Karthikesalingan 2014).

Description of the intervention

Definitive treatment for rAAA includes open surgery or endovascular repair (Badger 2017; Toomtong 2010). The management of haemorrhagic shock in the pre- and intra-operative period is crucial for the person's outcome, and aims to restore organ perfusion and systolic blood pressure above 100 mmHg by immediate and aggressive fluid replacement. This rapid intravenous fluid replacement (usually by crystalloid infusion, possibly by blood or volume expanders) is known as the normotensive resuscitation strategy (ATLS 2004; Roberts 2005). However, evidence suggests that infusing large volumes of cold fluid causes dilutional coagulopathy (loss or dilution of coagulation factors when blood is replaced with fluids that do not contain coagulation factors) and hypothermic coagulopathy (inhibition of enzyme activity involved in platelet and clotting factor function caused by low temperatures). The association of these factors may exacerbate bleeding, as the increased blood flow, increased perfusion, and decreased blood viscosity may result in clot disruption from vessel walls (Moll 2011; Roberts 2001), resulting in a 'lethal triad' of hypothermia, acidaemia, and coagulopathy (Morrison 2011; Roberts 2005). An alternative to the normotensive resuscitation strategy is the controlled (permissive) hypotension resuscitation strategy. This strategy has the target systolic blood pressure of 50 mmHg to 100 mmHg. The principle of controlled or hypotensive resuscitation has been used in some management protocols for endovascular repair of rAAA (Mehta 2006; Park 2013).

How the intervention might work

In the management of people with rAAA, controlled hypotension resuscitation aims to replace sufficient fluid to maintain the blood pressure between 50 mmHg and 100 mmHg during the pre-operative and intra-operative period. The controlled hypotension strategy avoids large volumes of crystalloid replacement. It may help to prevent blood loss by avoiding: the clot disruption caused by a rapid increase in systolic blood pressure; the dilution of clotting factors, platelets, and fibrinogen; and the temperature decrease that inhibits enzyme activity involved in platelet and clotting factor function. The principle of controlled hypotension is widely adopted for people with trauma and has been applied for people with rAAA with great success (Park 2013).

Why it is important to do this review

In 1991, Crawford showed a survival benefit with the adoption of a controlled hypotension strategy with a target systolic blood pressure of 50 mmHg to 70 mmHg in people with rAAA (Crawford 1991). There is evidence that a controlled hypotension strategy reduces blood requirements and severe coagulopathy in people with trauma (Morrison 2011). However, one trial reported that the 30-day mortality was higher among people with rAAA with recorded systolic blood pressure less than 70 mmHg compared with people with systolic blood pressure above 70 mmHg in the pre-operative stage (IMPROVE 2013). People with rAAA are usually elderly and more likely to have coronary and renal atherosclerotic disease, and unlike younger people with trauma, are at greater risk of myocardial infarction and renal insufficiency if submitted to low systolic blood pressure levels.

The European Society for Vascular Surgery, in their 2011 guidelines on the management of abdominal aortic aneurysms, recommended the hypotensive resuscitation strategy in case of abdominal aortic aneurysm rupture, suggesting the systolic blood pressure should range between 50 mmHg and 100 mmHg depending on the patient's condition at admission. The European Society for Vascular Surgery established this strategy as level 4, recommendation C (case series and poor quality cohort and case control studies) evidence, according to the levels of evidence from the Oxford Centre For Evidence-Based Medicine (Moll 2011). In 2018, the Society for Vascular Surgery published practice guidelines on the care of patients with an abdominal aortic aneurysm. These practice guidelines recommend restricting aggressive volume infusion and implementing the permissive hypotension strategy with the target systolic blood pressure between 70 mmHg and 90 mmHg to limit excessive haemorrhage, for patients with rAAA. The level of recommendation was described as strong with the quality of the evidence graded as moderate (Chaikof 2018). According to GRADE this can be interpreted as the benefits of the intervention outweighs its risks or, alternatively, the risks outweigh its benefits, but that further research is likely to have an important impact on the estimate of effect (GRADE 2004).

In this review we wish to assess the available evidence of a possible benefit of the controlled hypotension resuscitation strategy among people with rAAA and to identify the systolic blood pressure range that might be established to treat people with rAAA in the initial management stage. This is an update of a review first published in 2016.

OBJECTIVES

To compare the effects of controlled (permissive) hypotension resuscitation and normotensive resuscitation strategies for people with ruptured AAA.

METHODS

Criteria for considering studies for this review

Types of studies

We had planned to include randomised controlled trials (RCTs) that compared a controlled hypotensive resuscitation strategy with a normotensive resuscitation strategy in the treatment of people with rAAA. We excluded non-randomised case series and data from trials that had inferential data on the use of permissive hypotension in the treatment of people with rAAA.

Types of participants

We had planned to include all participants in whom a rAAA has been diagnosed by ultrasonography, computerised tomography, angiography, or magnetic resonance angiography. There had to have been evidence of rupture on imaging, or objective acute symptoms of rupture of the aneurysm (abdominal or back pain in a person with an aneurysm).

Types of interventions

Intervention: controlled hypotension or hypotensive resuscitation strategy, which included all types of intravenous fluid replacement or use of vasoactive drugs in pre- and intra-operative stages with the target to achieve systolic blood pressure between 50 mmHg and 100 mmHg in pre- and intra-operative stages.

Comparison: normotensive resuscitation strategy, which included all types of intravenous fluid replacement or use of vasoactive drugs with the target to achieve systolic blood pressure higher than 100 mmHg in pre- and intra-operative stages.

Types of outcome measures

Primary outcomes

- 30-day mortality (short term, due to haemorrhagic shock, myocardial infarction, or renal insufficiency).
- Presence of coagulopathy (defined as International Normalised Ratio (INR) greater than 1 to 3).
- Blood transfusion (measured by units or volume).

Secondary outcomes

- Intermediate mortality (30 days to one year).
- Long-term mortality (longer than one year).
- Total days of intensive care unit stay.
- Myocardial infarction.
- Renal failure.

Search methods for identification of studies

We had placed no restrictions on language or publication status.

Electronic searches

For this update the Cochrane Vascular Information Specialist (CIS) searched the Specialised Register (14 August 2017), the Cochrane Register of Studies (CRS, http://crso.cochrane.org/) (CENTRAL (2017, Issue 7)) and EMBASE (8 August 2017).

In addition, the CIS searched the following trial databases (8 August 2017) for details of ongoing and unpublished studies:

- ICTRP search portal (apps.who.int/trialsearch/);
- ClinicalTrials.gov (clinicaltrials.gov/).

See Appendix 1 for details of the search strategies.

Searching other resources

We searched guidelines from the following societies from 2000 to 2015:

- The European Society for Vascular Surgery;
- The Society for Vascular Surgery;
- The College of Emergency Medicine;
- The Royal College of Radiologists.

We had planned to supplement the above searches by checking the references of included trials for further relevant studies. We had also planned to contact the authors of included trials to request any unpublished data.

Data collection and analysis

Selection of studies

Two review authors (DHM, DGC) independently evaluated the trials to determine if they were appropriate to include. We resolved disagreements by discussion within the review team.

Data extraction and management

We had intended that two review authors (DHM and DGC) would independently extract the data. We had planned to resolve disagreements by discussion within the review team.

Assessment of risk of bias in included studies

We had intended that three review authors (DHM, DGC, and JBS) would independently assess the risk of bias using Cochrane's 'Risk of bias' tool, described in Section 8.5 of the *Cochrane Handbook for Systematic Reviews of interventions* (Higgins 2011). We had planned to resolve disagreements by discussion within the review team.

Measures of treatment effect

We had planned to use risk ratio (RR) for dichotomous data and mean difference (MD) or standardised mean difference (SMD) for continuous data with 95% confidence intervals (CI).

Unit of analysis issues

We had intended that the individual participant would be the unit of analysis.

Dealing with missing data

We had intended to analyse only the available data and had planned to contact the trial authors to request missing data. We had planned to use intention-to-treat analysis.

Assessment of heterogeneity

We had intended to assess heterogeneity using the I^2 statistic. We had planned to use these ranges to guide our interpretation of the I^2 statistic: 0% to 30% indicated low heterogeneity, 30% to 60% indicated moderate heterogeneity, 60% to 90% indicated substantial heterogeneity, and 90% to 100% indicated considerable heterogeneity.

Assessment of reporting biases

We had intended to assess the presence of publication bias and other reporting bias using funnel plots if sufficient studies (more than 10) had been included in the meta-analysis (Higgins 2011).

Data synthesis

We had planned to synthesise the data using Review Manager 5 software (RevMan 2014). We had planned to use the fixed-effect model to synthesise the data if there had been low to moderate levels of heterogeneity. If there had been substantial heterogeneity, we had planned to use a random-effects model. Had there been considerable heterogeneity, we had planned to not undertake a meta-analysis, but to describe the data in the text.

Subgroup analysis and investigation of heterogeneity

If sufficient data had been available, we had planned to perform subgroup analyses for the following:

- Participant characteristics: age, gender, presence of cardiopathy, renal dysfunction;
- Systolic blood pressure in pre-operative stage: 50 mmHg to 70 mmHg and 70 mmHg to 100 mmHg;
- Intervention: type of treatment - open surgery or endovascular surgery.

Sensitivity analysis

We had planned to exclude studies with a high risk of bias from meta-analysis to compare the overall treatment effect with and without them.

Summary of findings

We had planned to prepare a 'Summary of findings' table to provide the key information of the review. If trials are included in future updates, the 'Summary of findings' table will include information about population at risk, interventions, and comparisons. The table will contain a list of outcomes, the measure of burden of these outcomes, absolute and relative magnitude of effect, numbers of participants and studies addressing these outcomes, overall quality of the body of evidence for each outcome, using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach, and any relevant comments. We intend to base this table on methods described in Chapter 11 and Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions,* and justify any departures from the standard methods (GRADE 2004; Higgins 2011). The Types of outcome measures section describes the review's main outcomes to be included in this table.

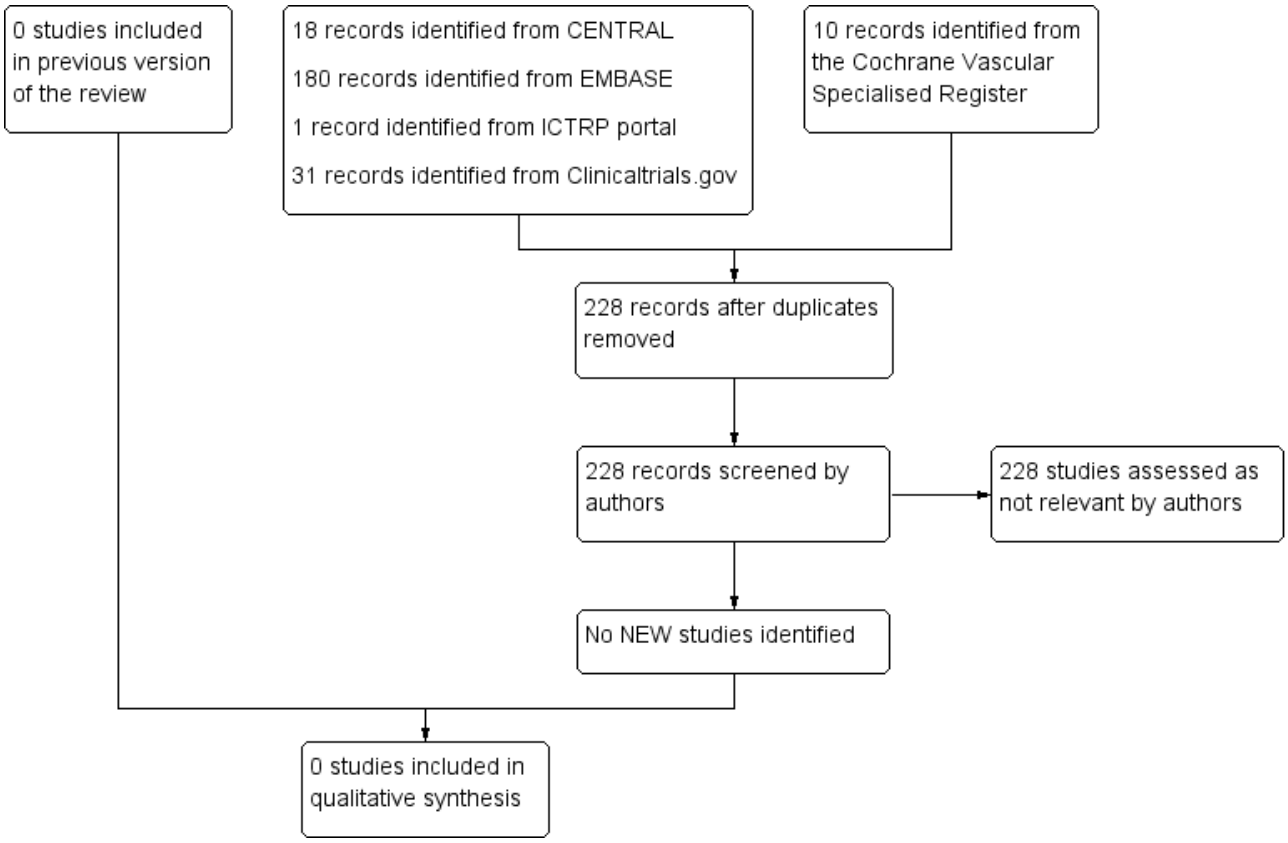
RESULTS

Description of studies

Results of the search

See Figure 1

Figure 1. Study flow diagram.



For this update we found no new RCTs that met the inclusion criteria for this review.

From the titles and abstracts of the identified records, we classified all 228 studies identified for this update as not relevant because they were either not randomised controlled trials, or they did not compare the specific types of interventions that we had planned to assess.

Included studies

We found no studies that met the inclusion criteria.

Excluded studies

We excluded no studies from this review.

Risk of bias in included studies

It was not possible to assess methodological quality, as we found no studies that met the inclusion criteria.

Effects of interventions

We identified no RCTs that compared controlled hypotension and normotensive resuscitation strategy for people with ruptured abdominal aortic aneurysm.

DISCUSSION

The concept of controlled hypotension in the management of haemorrhagic shock has its basis in clinical trials of trauma patients and animal model studies. The concept of permissive or controlled hypotension is extrapolated for haemorrhagic shock caused by ruptured abdominal aortic aneurysms by emergency physicians, vascular and endovascular surgeons, and anaesthesiologists, but there are no high-quality studies in this group of patients. There is widespread use of permissive hypotension strategy as a basic principle in the management of ruptured aneurysms, but the European Aortic Aneurysm Management practice guidelines list it as a Level 4, Recomendation C (case series, poor quality cohort and case control studies; Moll 2011).

Summary of main results

We found no RCTs comparing controlled hypotension versus normotensive resuscitation strategies in patients with ruptured abdominal aortic aneurysms.

Overall completeness and applicability of evidence

We found no RCTs that evaluated the management of haemorrhagic shock with controlled hypotension versus normotensive resuscitation strategies in patients with ruptured abdominal aortic aneurysms. For this update we identified 228 studies, which we classified as not relevant because they were either not randomised controlled trials or they did not compare the specific types of interventions that we had planned to assess. We acknowledge that designing and conducting an appropriate study for this topic is difficult, considering the logistics and detailed monitoring that is required for patients in the emergency room, during transport, and in the operating theatre. Controlled hypotension is widely used by vascular and endovascular surgeons, although there is no evidence based on randomised controlled trials to support its use. This fact reinforces the importance of this review, and serves as an incentive for further investigation.

Quality of the evidence

We found no RCTs that were eligible for this review.

Potential biases in the review process

We identified no RCTs that were eligible for this review. The Cochrane Vascular Information Specialist performed a comprehensive search of the literature and we selected studies according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Agreements and disagreements with other studies or reviews

In a systematic review published in 2014, which included several experimental studies of trauma in animals, randomised trials of trauma in humans and a prospective study on the treatment of ruptured aneurysms in humans, Hamilton 2014 concluded that the use of controlled hypotension in ruptured aortic aneurysms is safe; in hospital systems, when diagnostic and logistics considerations are optimised, permissive hypotension and delayed volume resuscitation have apparent benefit, but the ideal target blood pressure is not yet confirmed in elderly vascular patients. Hamilton 2014 referred to Crawford's conclusion of an editorial published in 1991: "Crawford felt that no significant attempt should be made for blood volume resuscitation until the time of operation. Systolic blood pressure should be maintained at 50 mmHg to 70 mmHg with small volumes of whole blood or crystalloid until the aorta is clamped" (Hamilton 2014). Crawford based this conclusion on the analysis of a case series, in which aggressive fluid replacement was used in the pre-hospital resuscitation phase.

Van der Vliet 2007 published on the first series of patients who received a controlled hypotension resuscitation strategy, which included the use of pharmacological agents, and had a target systolic blood pressure of 50 mmHg to 100 mmHg. They concluded that controlled hypotension in association with endovascular treatment was feasible in their tertiary referral centre.

Observations from the IMPROVE trial (EVAR versus open repair for ruptured aortic aneurysms) on the haemodynamic status of patients with ruptured abdominal aortic aneurysms, showed a 30-day mortality rate of 51% among patients with a systolic blood pressure lower than 70 mmHg and 34.1% in patients with a recorded systolic blood pressure above 70 mmHg; systolic blood pressure was directly related to the outcome in a linear fashion. These findings suggest that maintaining systolic blood pressure at less than 70 mmHg could be harmful to elderly patients, who often experience atherosclerotic comorbidities, such as coronariopathy, renal disorders, and atherosclerosis (IMPROVE 2013).

AUTHORS' CONCLUSIONS

Implications for practice

The application of the controlled hypotension resuscitation strategy in patients with ruptured abdominal aortic aneurysms is founded on basic principles and evidence from trauma studies and animal models. Its use is currently accepted and is included in protocols of management of ruptured abdominal aortic aneurysms. However, we found no RCTs that compared controlled hypotension versus normotensive resuscitation strategies in patients with ruptured abdominal aortic aneurysms.

Implications for research

High-quality RCTs that compare controlled hypotensive resuscitation with normotensive resuscitation strategies in people with ruptured abdominal aortic aneurysms are needed.

However, designing and conducting an appropriate study for this topic is difficult. Possible study designs could: (a) assess shock management strategies in patients with ruptured abdominal aortic aneurysms who are scheduled for endovascular treatment or open surgery and randomise patients to receive either controlled hypotension or normotensive resuscitation, and (b) assess shock management strategies as part of RCTs designed to compare endovascular versus open repair for ruptured abdominal aortic aneurysms.

In addition to the selected outcomes from this review, there are other important outcomes that should be included in primary studies investigating shock management in ruptured abdominal aortic aneurysms, such as lower limb ischaemia, bowel ischaemia, stroke respiratory failure, and quality of life. Platelets and fibrinogen doses could be assessed as an indicator of coagulopathy. A cost analysis should also be considered as an outcome in future studies.

ACKNOWLEDGEMENTS

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APPENDICES

Appendix 1. Search strategies

Source	Search strategy	Hits retrieved
1. VASCULAR REGISTER IN CRSW	AAA* AND INREGISTER	10
2. CENTRAL	#1 MESH DESCRIPTOR Aortic Aneurysm EXPLODE ALL TREES	18
	#2 MESH DESCRIPTOR Aneurysm, Ruptured EXPLODE ALL TREES	
	#3 ((aneurysm* near4 (abdom* or thoracoabdom* or thoraco-abdom* or aort*))):TI,AB,KY	
	#4 ((aort* near3 (ballon* or dilat* or bulg*))):TI,AB,KY	
	#5 AAA*:TI,AB,KY	
	#6 MESH DESCRIPTOR Aorta, Abdominal EXPLODE ALL TREES	
	#7 #1 OR #2 OR #3 OR #4 OR #5 OR #6	
	#8 MESH DESCRIPTOR Fluid Therapy EXPLODE ALL TREES	
	#9 MESH DESCRIPTOR Infusions, Intravenous EXPLODE ALL TREES	
	#10 MESH DESCRIPTOR Lactic Acid EXPLODE ALL TREES	
	#11 MESH DESCRIPTOR Glucose EXPLODE ALL TREES 15305	
	#12 MESH DESCRIPTOR Saline Solution, Hypertonic EXPLODE ALL TREES	
	#13 MESH DESCRIPTOR Mannitol EXPLODE ALL TREES	
	#14 MESH DESCRIPTOR Albumins EXPLODE ALL TREES	
	#15 MESH DESCRIPTOR Dextrans EXPLODE ALL TREES	
	#16 MESH DESCRIPTOR Isotonic Solutions EXPLODE ALL TREES	
	#17 MESH DESCRIPTOR Plasma Substitutes EXPLODE ALL TREES	
	#18 MESH DESCRIPTOR Osmotic Pressure EXPLODE ALL TREES	

References to other published versions of this review

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Moreno DH, Cacione DG, Baptista-Silva JCC. Controlled hypotension versus normotensive resuscitation strategy for people with ruptured abdominal aortic aneurysm. *Cochrane Database of Systematic Reviews* 2015, Issue 4. [DOI: 10.1002/14651858.CD011664]

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(Continued)

#19 MESH DESCRIPTOR Hemodilution EXPLODE ALL TREES

#20 MESH DESCRIPTOR Hemoglobins EXPLODE ALL TREES

#21 MESH DESCRIPTOR Blood Pressure EXPLODE ALL TREES

#22 MESH DESCRIPTOR Shock, Hemorrhagic EXPLODE ALL TREES

#23 MESH DESCRIPTOR Resuscitation EXPLODE ALL TREES

#24 MESH DESCRIPTOR Hypotension EXPLODE ALL TREES

#25 MESH DESCRIPTOR Hydroxyethyl Starch Derivatives EXPLODE ALL TREES

#26 starch:TI,AB,KY

#27 hydroxyethyl*:TI,AB,KY

#28 ((haemoglobin or hemoglobin)):TI,AB,KY 22443

#29 fluid:TI,AB,KY 17013

#30 ((saline or NaCl)):TI,AB,KY 21476

#31 dextran:TI,AB,KY

#32 ringer:TI,AB,KY

#33 lactate:TI,AB,KY

#34 glucose:TI,AB,KY

#35 gelatin:TI,AB,KY

#36 ((HES 130*)):TI,AB,KY

#37 voluven:TI,AB,KY

#38 albumin:TI,AB,KY

#39 mannitol:TI,AB,KY

#40 HBOC-201:TI,AB,KY

#41 ((crystalloid or colloid)):TI,AB,KY

#42 isovol*:TI,AB,KY

#43 normovol*:TI,AB,KY

#44 electrolyte:TI,AB,KY

#45 hypertonic:TI,AB,KY

#46 ((osmotic pressure)):TI,AB,KY

#47 ((volume loading)):TI,AB,KY

#48 ((volume expansion)):TI,AB,KY

#49 ((volume substitution)):TI,AB,KY

#50 ((haemodilution or hemodilution)):TI,AB,KY

#51 resuscitation:TI,AB,KY

#52 hypotens*:TI,AB,KY

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	#53 normotensive :TI,AB,KY #54 ((organ perfusion)):TI,AB,KY #55 ((systolic blood pressure)):TI,AB,KY #56 #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 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 #57 #7 AND #56 #58 (2016 OR 2017):YR #59 #57 AND #58	
3. Clinicaltrials.gov	Condition/disease: abdominal aortic aneurysm	31
4. ICTRP Search Portal	abdominal aortic aneurysm OR Aneurysm, Ruptured OR Ruptured Aneurysm AND hypotens* OR resuscitat* OR Infus* OR fluid* OR normotens*	1
5. EMBASE (via Ovid)	1 exp aorta aneurysm/ 2 exp aneurysm rupture/ 3 (aneurysm* adj4 (abdom* or thoracoabdom* or thoraco-abdom* or aort*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word] 4 (aort* adj3 (ballon* or dilat* or bulg*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word] 5 AAA*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word] 6 exp abdominal aorta/ 7 1 or 2 or 3 or 4 or 5 or 6 8 exp fluid therapy/ 9 exp intravenous drug administration/ 10 exp lactic acid/ 11 exp glucose/ 12 *sodium chloride/ 13 exp mannitol/ 14 exp albuminoid/ 15 exp dextran/ 16 exp isotonic solution/ 17 exp plasma substitute/ 18 exp osmotic pressure/	180

(Continued)

19 exp hemodilution/

20 exp hemoglobin/

21 exp blood pressure/

22 exp hemorrhagic shock/

23 exp fluid resuscitation/

24 exp hypotension/

25 exp hetastarch derivative/

26 exp starch/

27 (haemoglobin or hemoglobin).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

28 fluid.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

29 (saline or NaCl).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

30 dextran.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

31 ringer.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

32 lactate.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

33 glucose.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

34 gelatin.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

35 HES 130*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

36 voluven.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

37 albumin.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

38 mannitol.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

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39 HBOC-201.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

40 (crystalloid or colloid).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

41 isovol*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

42 normovol*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

43 electrolyte.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

44 hypertonic.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

45 osmotic pressure.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

46 "volume loading".mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

47 "volume expansion".mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

48 "volume substitution".mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

49 (haemodilution or hemodilution).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

50 resuscitation.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

51 hypotens*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

52 normotensive.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

53 "organ perfusion".mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

54 "systolic blood pressure".mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

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	55 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 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 56 7 and 55 57 randomized controlled trial/ 58 exp controlled clinical trial/ 59 random*.ab. 60 placebo.ab. 61 trial.ab. 62 groups.ab. 63 57 or 58 or 59 or 60 or 61 or 62 64 2017*.em. 65 56 and 63 and 64
TOTAL before de-duplication	240
TOTAL after de-duplication	228

WHAT'S NEW

Date	Event	Description
23 May 2018	New citation required but conclusions have not changed	Searches rerun, no new studies identified, Minor edits made. Conclusions not changed.
23 May 2018	New search has been performed	Searches rerun, no new studies identified.

CONTRIBUTIONS OF AUTHORS

Study selection: DHM and DGC.
Data extraction: DHM and DGC, with discussion by all three authors DHM, DGC and JBS.
Assessment of risk of bias of studies: DHM, DGC and JBS.
Guarantor of the review: DHM.

DECLARATIONS OF INTEREST

DHM: none known.
DGC: none known.
JBS: none known.

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.

INDEX TERMS

Medical Subject Headings (MeSH)

*Blood Pressure; *Hypotension, Controlled; Aortic Aneurysm, Abdominal [*complications]; Aortic Rupture [*complications]; Resuscitation [*methods]; Shock, Hemorrhagic [etiology] [*therapy]; Systole

MeSH check words

Humans