Treatment for femoral pseudoaneurysms (Review)

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[Intervention Review]

Treatment for femoral pseudoaneurysms

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ABSTRACT

Background

Femoral pseudoaneurysms may complicate up to 8% of vascular interventional procedures. Small pseudoaneurysms can spontaneously clot, but sometimes definitive treatment is needed. Surgery has traditionally been considered the 'gold standard' treatment, although it is not without risk in patients with severe cardiovascular disease. Less invasive treatment options such as Duplex ultrasound-guided compression and percutaneous thrombin injection are available, however, evidence of their efficacy is limited. This is an update of a Cochrane review first published in 2006.

Objectives

To assess the effects of different treatments for femoral pseudoaneurysms resulting from endovascular procedures, specifically assessing less invasive treatment options such as blind manual or mechanical compression, ultrasound-guided compression, or percutaneous thrombin injection.

Search methods

For this update the Cochrane Peripheral Vascular Diseases Group Trials Search Co-ordinator searched the Specialised Register (last searched October 2013) and CENTRAL (2013, Issue 9).

Selection criteria

Randomised controlled trials (RCTs) comparing two treatments for femoral pseudoaneurysms following vascular interventional procedures were considered for inclusion in the review.

Data collection and analysis

Four studies were included in the analyses comparing: manual compression versus ultrasound-guided compression; ultrasound-guided application of a mechanical device (FemoStop) versus blind application; and ultrasound-guided compression versus percutaneous thrombin injection (two studies). There were no studies with a surgical intervention arm. Data were extracted independently by both authors.

Main results

Compression (manual or FemoStop) was effective in achieving pseudoaneurysm thrombosis although ultrasound-guided application failed to confer any benefit (risk ratio (RR) 0.96; 95% confidence interval (CI) 0.88 to 1.04).

Percutaneous thrombin injection was more effective than a single session of ultrasound-guided compression in achieving primary pseudoaneurysm thrombosis within individual RCTs but merged data failed to show statistical significance (RR 2.81; 95% CI 0.44 to 18.13). There was no statistically significant difference in the length of hospital stay between the two groups and no complications were reported apart from one deep vein thrombosis in the compression group.

Authors' conclusions

The limited evidence base appears to support the use of thrombin injection as an effective treatment for femoral pseudoaneurysm. A pragmatic approach may be to use compression (blind or ultrasound-guided) as first-line treatment, reserving thrombin injection for those in whom the compression procedure fails.

PLAIN LANGUAGE SUMMARY

Treatments for swelling of an artery in the groin following vascular procedures

People with heart disease and diseased leg arteries often undergo investigations and treatments that involve placing a needle into the main artery in the groin (endovascular procedures, for example diagnostic arteriogram, angioplasty, cardiac catheterization). One possible complication is the formation of a large swelling in the artery (a pseudoaneurysm) in the groin. This happens when the hole that the needle makes in the wall of the artery does not seal properly afterwards and blood collects, causing pain, swelling and bruising. Small pseudoaneurysms may clot spontaneously or surgery may be required. Less invasive treatment is now possible to stop the blood flow into the swelling. This involves sedation or analgesia to allow pressure to be placed over the puncture in the artery using a special mechanical device or a probe guided by ultrasound. Another option is injection of a clotting agent (thrombin) through the skin into the swelling.

The review authors searched the medical literature and found four randomised controlled trials. No new studies were included in this update. Application of pressure (compression) with a mechanical device for some 30 minutes caused clotting of the blood in the pseudoaneurysm in three-quarters of people (38 people aged between 40 and 85 years) within 24 hours. It made no difference if the probe was placed blindly or using ultrasound. A further study of 168 people found that compression caused clotting of the pseudoaneurysm in more than 90% of people at 24 hours; again, using ultrasound did not seem to make any difference. Injection of bovine thrombin appeared to be more effective that ultrasound-guided compression (in two studies, including 68 patients in total). There are, however, concerns about allergy to the thrombin and introduction of infectious agents, thought to be responsible for transmission of some degenerative diseases, as well as the possibility of causing a blood clot in the artery. No complications were reported in these studies apart from one deep vein thrombosis in the people treated with compression.

BACKGROUND

Description of the condition

A pseudoaneurysm (false aneurysm) occurs when blood escapes from the lumen of an artery through a defect in one or more layers of the arterial wall and forms a localized pocket of flow either beneath the adventitia (outer wall of the artery) or in the surrounding tissues. They are most commonly found in the groin as a complication of endovascular procedures (for example diagnostic arteriogram, angioplasty, cardiac catheterization); vascular trauma; or following open vascular surgery (for example aortobifemoral bypass, femoro-popliteal bypass). Pseudoaneurysms following previous vascular surgery are often associated with vascular graft infection and require debridement (removal) of infected tissue and often complete or partial graft removal. This review only considers pseudoaneurysms following endovascular procedures (that is

iatrogenic pseudoaneurysms).

Pseudoaneurysms result from poor haemostasis (failure to control blood flow) at the time of the initial treatment, that is inadequate compression of the puncture site after withdrawing the catheter or sheath, or failure to use a closure device. Frequently these patients are anticoagulated (receiving anti-clotting therapy) or have a coagulopathy (clotting disorder) and this may compound the problem. Pseudoaneurysms are reported to occur in 1% of diagnostic arteriograms and up to 8% of therapeutic endovascular interventions (Eternad-Rezai 2003). Symptoms include pain, swelling, and bruising in the groin area and possible rupture of the pseudoaneurysm.

Description of the intervention

The aim of treatment is to cause thrombosis (clotting) of the pseudoaneurysm. Duplex ultrasound is the diagnostic test of choice and demonstrates a high velocity jet through a defect in the arterial wall on colour flow imaging. A proportion of small pseudoaneurysms may spontaneously clot over time and active observation is, therefore, an option. For those pseudoaneurysms that need treatment, surgery has traditionally been considered as the 'gold standard'. This may require simple suture of the defect after evacuation of the haematoma (blood-filled swelling) or a patch angioplasty (surgical repair using a patch).

Ultrasound-guided compression is now increasingly used as a therapeutic tool, to avoid the need for surgery. Compression with the ultrasound probe at the site of communication between the false aneurysm and the native artery abolishes flow through the arterial wall and allows thrombosis of the aneurysm sac to occur. Patients will require effective analgesia or sedation, or both, in order to tolerate the procedure, which involves compression for 10 minutes at a time and repeated for up to 60 minutes. Success rates of 63% to 88% have been reported (Morgan 2003). A mechanical device, such as the FemoStop (Radi Medical Systems, Uppsala, Sweden) may also be used to compress a pseudoaneurysm.

A number of studies have reported successful thrombosis of femoral pseudoaneurysms using Duplex ultrasound-guided percutaneous bovine thrombin injection (Edgerton 2002; Friedman 2002; Kruger 2003; Lonn 2002; Sackett 2000). This can be performed as an outpatient procedure. Thrombin in a concentration of 1000 U/ml is injected slowly into the pseudoaneurysm, with thrombosis frequently occurring within five seconds (Eternad-Rezai 2003). The reported dose needed is between 20 U and 6000 U (Eternad-Rezai 2003; Olsen 2002). A primary success rate of 95% to 98% has been reported (Maleux 2003; Mohler 2001). Thrombin injection can be associated with immediate complications such as thrombosis of the native artery and, rarely, venous thrombosis. Delayed reperfusion of the aneurysm may occur in 6% of cases (Olsen 2002). A potential problem with the use of bovine thrombin may be contamination with prions (protein-related infectious agents, thought to be responsible for transmission of some degenerative diseases). One study has overcome this risk by using autologous thrombin prepared from patients' blood for treatment of pseudoaneurysms (Quarmby 2002).

A recent study described the use of para-aneurysmal saline in the treatment of femoral pseudoaneurysms, that is injection of saline around the communication between the false aneurysm and the native artery, abolishing blood flow (Gehling 2003). Endovascular treatment methods such as coil embolization (using a coil to encourage formation of a blood clot, thus filling the aneurysm) or stent-grafts (a prosthetic tube lying within the artery) have also been used to treat femoral pseudoaneurysms (Morgan 2003).

Why it is important to do this review

This review aims to explore the evidence for the efficacy of these modalities in the treatment of femoral pseudoaneurysms.

OBJECTIVES

To assess the effects of different treatments for femoral pseudoaneurysms resulting from endovascular procedures. The main focus of the review was to look at the evidence for ultrasound-guided compression or percutaneous thrombin injection, or both, and determine whether one of these treatments could replace the traditional gold standard of surgery.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials comparing two or more different treatments for femoral pseudoaneurysms were considered for inclusion in this review.

Types of participants

All patients with femoral pseudoaneurysms following endovascular procedures were considered for inclusion, without any restriction on the size of the pseudoaneurysm. Patients with pseudoaneurysms resulting from previous vascular surgery or following trauma were excluded.

Types of interventions

Surgical treatment of femoral pseudoaneurysms; manual compression; mechanical compression; ultrasound-guided compression; percutaneous thrombin injection; other interventions (e.g. paraaneurysmal saline injection, coil embolization, endovascular stent-graft).

Types of outcome measures

Primary outcome

Complete thrombosis of the pseudoaneurysm (confirmed by Duplex ultrasound or alternative imaging) after one treatment and without significant complications.

Secondary outcomes

Objective clinical measures

1. Pseudoaneurysm recurrence rate
2. Rate of re-intervention for pseudoaneurysm
3. Complication rate, specifically native artery thrombosis and deep vein thrombosis
4. Length of hospital stay
5. 30-day mortality rate

Subjective measures

1. Symptoms, such as pain, swelling and bruising; pain scores if available
2. Quality of life measures, using formal quality of life questionnaires administered either in person or by postal delivery

Search methods for identification of studies

Electronic searches

For this update the Cochrane Peripheral Vascular Diseases Group Trials Search Co-ordinator (TSC) searched the Specialised Register (last searched October 2013) and the Cochrane Central Register of Controlled Trials (CENTRAL) 2013, Issue 9, part of *The Cochrane Library*, (www.thecochranelibrary.com) . See (Appendix 1) for details of the search strategy used to search CENTRAL. 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 which have been searched, as well as the search strategies used are described in the (Specialised Register) section of the Cochrane Peripheral Vascular Diseases Group module in *The Cochrane Library* (www.thecochranelibrary.com).

Searching other resources

The reference lists of articles retrieved by electronic searches were searched for additional citations.

Data collection and analysis

Selection of trials

One review author (Paul Tisi) collated all randomised trials identified from the search strategy for potential inclusion in the review.

Quality of trials

Potentially eligible trials were assessed independently by both authors to determine the relevance of each study.Trials were only accepted if both authors agreed on the inclusion criteria. Any disagreements were resolved through discussion. Trials were scrutinized for allocation concealment, ensuring that a trial participant did not influence the randomisation process. Blinding would not be possible if one treatment arm was surgical as the incision would be obvious to the observer. Trials were scrutinized to ascertain whether follow up was explicitly reported, or implied, in order to avoid attrition bias. The Jadad scale was used to ascertain quality of the trials (Jadad 1996).

Data extraction

Data from the trials were extracted independently by Paul Tisi and Michael Callam using a specifically designed data collection form. This included all data relating to both objective and subjective outcome measures, as defined above, in addition to any other relevant data, such as sample size, inclusion and exclusion criteria, follow up. The figures were then cross-checked for agreement.

Statistical analysis

As only four relevant RCTs were included, assessing different treatment options, statistical techniques for looking at heterogeneity of data, publication bias (funnel plot), and subgroup analysis were not used. Results were expressed as Mantel-Haenszel odds ratios (OR) with 95% confidence intervals (CI) for dichotomous variables. For comparisons with a high frequency of events (for example thrombosis of pseudoaneurysm) outcomes were given as Mantel-Haenszel risk ratios (RR) with 95% CI (using a random-effects model), that is the ratio of incidence rates between two different treatments. Results for continuous variables were expressed as standardised mean differences (SMD).

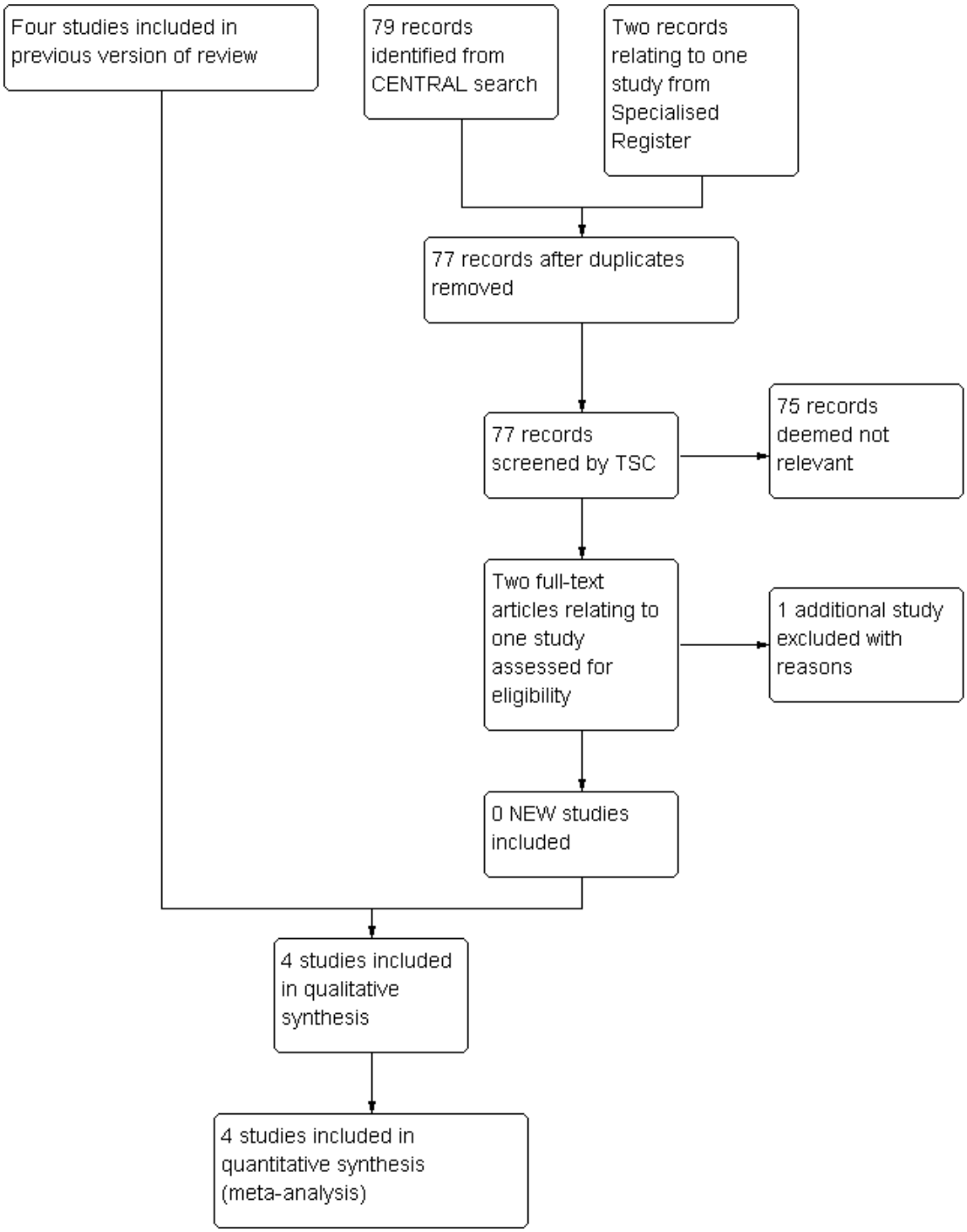
RESULTS

Description of studies

Results of the search

For this 2013 update, no new studies were included and one new study was excluded (Lewandowski 2011). See Figure 1.

Figure 1. Study flow diagram.



Included studies

Four studies were considered for inclusion in the review.

Chatterjee 1999: this study recruited 38 patients with iatrogenic pseudoaneurysms over a two-year period (12 from cardiac catheterisation, 18 following coronary angioplasty, two following electrophysiological studies, and six following percutaneous transluminal angioplasty). The main inclusion criterion was that the pseudoaneurysm was compressible on ultrasound. Patients with local infection, critical limb ischaemia, skin necrosis, and a pseudoaneurysm arising above the level of the inguinal ligament were excluded. In both treatment groups, the pseudoaneurysm was compressed using a FemoStop compression device, which is a pneumatic plastic dome secured around the patient's waist with an adjustable belt. Compression was used for 20 minutes initially, with a further 20 minutes if needed. Patients were randomised into ultrasound-guided application of the FemoStop (n = 19) or blind application over the puncture site (n = 19). The two groups were matched for age, sex, pseudoaneurysm diameter, pseudoaneurysm track diameter (communication between pseudoaneurysm and native artery), use of anticoagulants, and use of antiplatelet drugs. The primary outcome measure was successful thrombosis of the pseudoaneurysm.

Paschalidis 2006: this study recruited patients with pseudoaneurysms following cardiac or peripheral catheterisation over a 28-month period. One hundred and eighty-five patients were diagnosed; 17 were excluded because of imminent pseudoaneurysm rupture, massive haematoma, skin necrosis, infection, and ischaemia; 168 patients were then randomised into manual compression (n = 84) or ultrasound-guided compression (n = 84). Manual compression involved direct pressure over the arterial puncture site until the pulsation in the haematoma or palpable thrill over the artery disappeared (maximum compression time 60 minutes); ultrasound-guided compression was applied using the authors' standard protocol, up to a maximum time of 60 minutes. Patients in both groups had a repeat ultrasound at 24 hours; for failed pseudoaneurysm thrombosis, re-treatment was allowed using the same protocol up to a maximum of three treatments. The two groups were matched for age, sex, pseudoaneurysm size, and use of antithrombotic drugs. The primary outcome measure was successful thrombosis of the pseudoaneurysm within 24 hours.

Lonn 2004: this study recruited 30 patients with iatrogenic pseudoaneurysms over a 22-month period (26 from a coronary artery intervention, four from a peripheral vascular intervention). Consecutive patients with compressible pseudoaneurysms were considered for inclusion in the study. Patients with local skin infection, previous exposure to bovine thrombin, severe allergy, or a pseudoaneurysm neck > 10 mm were excluded. Patients were randomised to ultrasound-guided compression (n = 15) or ultrasound-guided thrombin injection (n = 15). Compression was undertaken using the FemoStopIIPLUS compression device (Radi Medical Systems, Uppsala, Sweden). Compression above diastolic pressure was used initially for 30 minutes, followed by a second 30-minute period if needed. A further 30 minutes of compression was then used at 40 mm Hg followed by two hours at 20 mm Hg. In the thrombin group, a 25-G or 22-G needle attached to a syringe containing 1 ml of bovine thrombin (1000 U/ml) was placed in the pseudoaneurysm cavity under ultrasound control. Injection was stopped once flow ceased in the pseudoaneurysm cavity. The two groups were matched for age, sex, aetiology, use of anticoagulants, and use of antiplatelet drugs. The primary outcome measure was successful thrombosis of the pseudoaneurysm within 24 hours. The secondary outcome measures were thrombosis within 48 hours (allowing for repeat treatments), complication rates, and length of hospital stay.

Liu 2006: this study recruited 38 patients with intervention-induced pseudoaneurysms but did not state whether all pseudoaneurysms were compressible. Exclusion criteria were not stated; neither was the age and sex distribution between the two groups. Patients were randomised to percutaneous thrombin injection (n = 19) or ultrasound-guided compression. The protocols for both treatment arms were not explained in the published abstract. Patients underwent Duplex ultrasound at three days and seven days. The primary outcome measure was successful thrombosis of the pseudoaneurysm at 72 hours. Seconday outcome measures were thrombosis at seven days and change in volume of the haematoma.

Excluded studies

One additional study was excluded for this 2013 update (Lewandowski 2011). Details of the excluded studies can be found within the Characteristics of excluded studies table.

Risk of bias in included studies

Chatterjee 1999 did not state the randomisation method used. Blinding was impossible in this study design and allocation concealment was not used. This study scored one on the Jadad scale (Jadad 1996). Paschalidis 2006 did not state the randomisation method used. Blinding was impossible in this study design and allocation concealment was not used. The Jadad score was two (Jadad 1996). Lonn 2004 randomised patients using sealed envelopes. Blinding was impossible in this study design and allocation concealment was adequate. The Jadad score was three (Jadad 1996). Liu 2006 did not state the randomisation method used. Blinding was impossible in this study design and allocation concealment was not used. The Jadad score was two (Jadad 1996).

Effects of interventions

Four RCTs were included in the review, comparing several different outcomes. Only limited meta-analysis was possible (*see* the 'Methods' section of the review, above).

Ultrasound-guided versus blind compression

Chatterjee 1999: ultrasound-guided application of the FemoStop device achieved thrombosis of the pseudoaneurysm at 12 to 24 hours in 15 patients (79%), compared to 14 patients (74%) with blind application of the FemoStop (RR 1.07; 95% CI 0.75 to 1.53). Ultrasound placement therefore conferred no advantage over blind placement of the FemoStop device. Mean compression time was 28 minutes in the ultrasound-guided group compared to 33 minutes in the blind group; statistical analysis was not possible as no standard deviations were quoted. There were no reported complications.

Paschalidis 2006: ultrasound-guided compression achieved thrombosis of the pseudoaneurysm within 24 hours in 90% of patients compared to 95% of patients with simple manual compression (RR 0.95; 95% CI 0.87 to 1.03). At two days, thrombosis was achieved in 98% of patients in both groups. There was no significant difference in the need for analgesia and sedation between the two groups (OR 0.63; 95% CI 0.24 to 1.63). No patients developed limb ischaemia.

Merged data from these two studies (accepting the limitations of different study designs) showed that ultrasound-guided compression conferred no advantage over blind compression in terms of achieving primary thrombosis of the pseudoaneurysm (RR 0.96; 95% CI 0.88 to 1.04).

Thrombin injection versus ultrasound-guided compression

Lonn 2004: percutaneous thrombin injection achieved thrombosis of the pseudoaneurysm within 24 hours in all 15 patients; compared to two patients (13%) treated with ultrasound-guided compression (RR 6.20; 95% CI 1.98 to 19.43). This significant difference was maintained at 48 hours (allowing for repeat treatments) with thrombosis achieved in all patients treated with thrombin compared to six patients (40%) treated with ultrasound-guided compression (RR 2.38; 95% CI 1.31 to 4.34). There were no reported complications in either group. There was no difference in hospital stay between the two groups (SMD -0.34; 95% CI -1.06 to 0.38).

Liu 2006: percutaneous thrombin injection achieved thrombosis of the pseudoaneurysm at three days in all 19 patients; compared to 13 (68%) of those treated with ultrasound-guided compression (RR 1.44; 95% CI 1.06 to 1.97). At seven days all pseudoaneurysms in both groups were thrombosed. At seven days the mean volume of haematoma had decreased by 9.4 ± 8.6 ml in the thrombin group compared to 8.6 ± 8.7 ml in the ultrasound group (P = 0.78). One patient in the compression group developed a deep vein thrombosis (OR 0.32; 95% CI 0.01 to 8.26).

Merged data for primary thrombosis of the pseudoaneurysm (at < 24 hours Lonn 2004; < 3 days Liu 2006) did not demonstrate that percutaneous thrombin injection was significantly more effective than ultrasound-guided compression (RR 2.81; 95% CI 0.44 to 18.13).

DISCUSSION

The aim of the review was to identify the most efficacious treatment for femoral pseudoaneurysms. However, only four RCTs were identified with a total of 274 patients randomised. There were no RCTs comparing surgery (traditionally considered as the 'gold standard' treatment) with another treatment. Blind compression of the pseudoaneurysm (either using manual pressure or with a FemoStop device) is feasible, with good technical success rates. Ultrasound-guided compression appears to confer no benefit over applying blind compression over the arterial puncture site. Percutaneous thrombin injection appears to be more effective than ultrasound-guided compression in achieving primary thrombosis of a pseudoaneurysm within individual RCTs. However, merged data (using a random-effects model) does not reach statistical significance.

Guidance from the UK National Institute of Health and Clinical Excellence states that 'current evidence on the safety and efficacy of thrombin injections for pseudoaneurysms appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance' (NICE 2004). Neither RCT reported any complications (including arterial thrombosis) from thrombin injection, although these were small sample sizes (a total of 34 patients treated with thrombin). Case studies have suggested that the complication rate from thrombin injection is 0% to 4% (Morgan 2003). Concerns about prion transmission from bovine thrombin still exist. However, a number of reports have used human thrombin in the treatment of pseudoaneurysms, which is available as one of the components of a tissue adhesive (for example Tisseel, Baxter Healthcare) (Morgan 2003).

AUTHORS' CONCLUSIONS

Implications for practice

Overall, results were based on aggregate analyses of relatively small single-center studies and therefore the external validity of the findings is limited. Thrombin appears to be more effective than ultrasound-guided compression for femoral pseudoaneurysms and might be considered as the new 'gold standard'. However, the quality of the randomisation method may limit the internal validity

of these results. There are potentially serious complications with thrombin, although none were reported in the included RCTs. Blind compression appears to be as effective as ultrasound-guided compression.

A pragmatic approach may be to consider compression (with or without ultrasound) as first-line treatment, reserving thrombin injection for those in whom the procedure fails.

Implications for research

A multicentre prospective RCT of thrombin injection versus ultrasound-guided compression may provide further data to support the findings of this review. However, researchers might not approach this from a position of equipoise.

ACKNOWLEDGEMENTS

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Chatterjee 1999

Methods	Study design: parallel-design randomised controlled trial. Method of randomisation: not stated. Blinding: none. Duration of recruitment to study: 24 months. Duration of follow up: 12 to 24 hours.
Participants	Country: Switzerland. Setting: hospital. Number of participants: 38. Age (years): 40 to 85 (matched between the two groups). Sex: 18 men, 20 women (matched between the two groups). Inclusion criteria: iatrogenic femoral pseudoaneurysm confirmed on Duplex scan. Exclusion criteria: local infection; critical limb ischaemia; skin necrosis; pseudoaneurysm track above inguinal ligament Drop-outs: none.
Interventions	(1) Compression with FemoStop device with ultrasound guidance (n=19) (2) Compression with FemoStop device without ultrasound guidance (n=19)
Outcomes	1. Thrombosis of pseudoaneurysm (primary outcome). 2. Compression time (no standard deviation quoted in paper).
Notes	Jadad score: 1.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Liu 2006

Methods	Study design: parallel-design randomised controlled trial. Method of randomisation: not stated. Blinding: none. Duration of recruitment to study: not stated. Duration of follow up: 7 days.
Participants	Country: China. Setting: not stated. Number of participants: 38. Age (years): not stated. Sex: not stated.

Liu 2006 (*Continued*)

	Inclusion criteria: 'intervention-induced' femoral pseudoaneurysms. Exclusion criteria: not stated. Drop-outs: not explicitly stated although results suggest that no drop-outs
Interventions	(1) Thrombin injection (n=19). (2) Ultrasound-guided compression (n=19).
Outcomes	1. Thrombosis of pseudoaneurysm within 3 days (primary outcome). 2. Thrombosis of pseudoaneurysm within 7 days. 3. Compression time (inaccurate as only scanned day 3 and day 7 post-treatment). 4. Complication rate: deep vein thrombosis.
Notes	Jadad score: 2. Study included on basis of English language abstract alone. For outcome two (thrombosis within 7 days) it is unclear whether re-treatment with compression was allowed

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	D - Not used

Lonn 2004

Methods	Study design: parallel-design randomised controlled trial. Method of randomisation: sealed envelopes. Blinding: none. Duration of recruitment to study: 22 months. Duration of follow up: mean 12 months (range 6 to 35 months)
Participants	Country: Sweden. Setting: hospital. Number of participants: 30. Age (years): mean (SD) 67 ± 9 compression group; 66 ± 7 thrombin group. Sex: 22 men, 8 women (matched between the two groups). Inclusion criteria: iatrogenic femoral pseudoaneurysm confirmed on Duplex scan. Exclusion criteria: local skin infection; previous bovine thrombin exposure; severe allergy; pseudoaneurysm neck >10 mm diameter Drop-outs: none.
Interventions	(1) Thrombin injection (n=15). (2) Compression with Femostop device (n=15).
Outcomes	1. Thrombosis of pseudoaneurysm within 24 hours (primary outcome). 2. Thrombosis of pseudoaneurysm within 2 days, allowing retreatment. 3. Length of hospital stay. 4. Complication rate.

Lonn 2004 (*Continued*)

Notes	Jadad score: 3.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Low risk	A - Adequate

Paschalidis 2006

Methods	Study design: parallel-design randomised controlled trial. Method of randomisation: not stated. Blinding: none. Duration of recruitment to study: 28 months. Duration of follow up: up to three days.
Participants	Country: Germany. Setting: hospital. Number of participants: 168. Age (years): not stated (matched between the two groups). Sex: not stated (matched between the two groups). Inclusion criteria: iatrogenic femoral pseudoaneurysm following cardiac or peripheral catheterisation. Exclusion criteria: imminent pseudoaneurysm rupture, massive haematoma, skin necrosis, infection, limb ischaemia Drop-outs: none.
Interventions	(1) Manual compression (n=84). (2) Ultrasound-guided compression (n=84).
Outcomes	1. Thrombosis of pseudoaneurysm within 24 hours (primary outcome) 2. Thrombosis of pseudoaneurysm within two days, allowing retreatment 3. Thrombosis of pseudoaneurysm within three days, allowing retreatment 4. Requirement for analgesia/sedation
Notes	Jadad score: 2.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	D - Not used.

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

Study	Reason for exclusion
Lewandowski 2011	Study compares bolus versus slow injection of thrombin. Neither technique is described in the methods. Does not meet criteria for inclusion in the review
Maca 2003	Not a RCT.

DATA AND ANALYSES

Comparison 1. Ultrasound-guided compression versus blind compression

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Thrombosis of pseudoaneurysm within 24 hours (primary outcome)	2	206	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.88, 1.04]
2 Thrombosis of pseudoaneurysm within 2 days	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Thrombosis of pseudoaneurysm within 3 days	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Requirement for analgesia/sedation	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 2. Thrombin injection versus ultrasound-guided compression

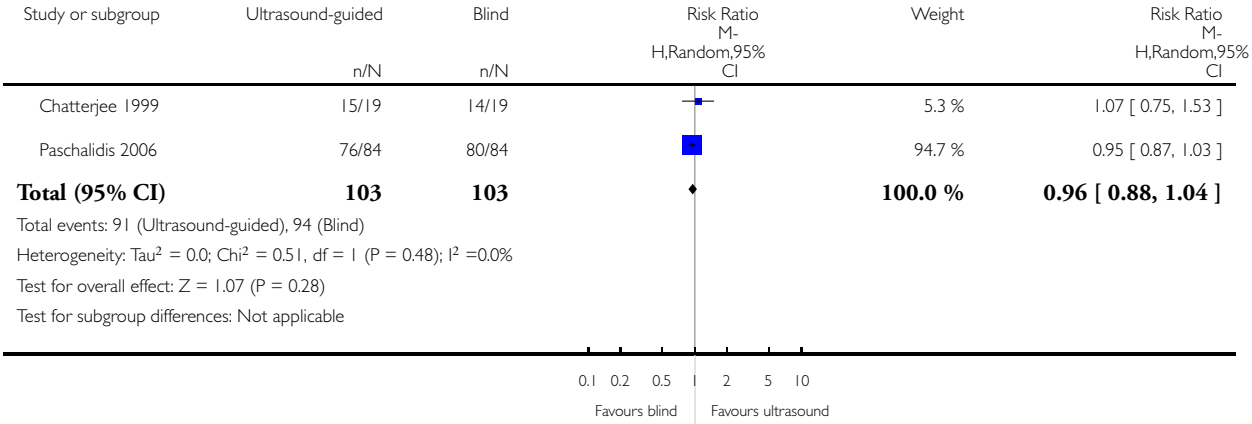
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Thrombosis of pseudoaneurysm within 24 hours (primary outcome)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Thrombosis of pseudoaneurysm within 2 days	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Thrombosis of pseudoaneurysm within 3 days (primary outcome)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Thrombosis of pseudoaneurysm within 7 days	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Primary outcome: thrombosis of pseudoaneurysm	2	68	Risk Ratio (M-H, Random, 95% CI)	2.81 [0.44, 18.13]
6 Complication rate	2	68	Odds Ratio (M-H, Random, 95% CI)	0.32 [0.01, 8.26]
7 Length of hospital stay (days)	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1 Ultrasound-guided compression versus blind compression, Outcome 1 Thrombosis of pseudoaneurysm within 24 hours (primary outcome).

Review: Treatment for femoral pseudoaneurysms

Comparison: 1 Ultrasound-guided compression versus blind compression

Outcome: 1 Thrombosis of pseudoaneurysm within 24 hours (primary outcome)

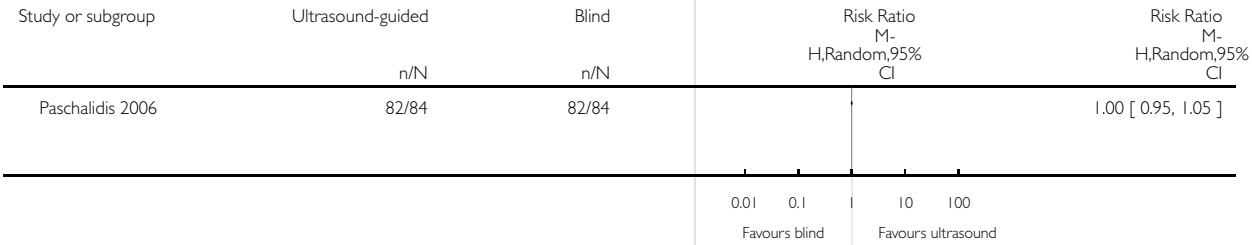


Analysis 1.2. Comparison 1 Ultrasound-guided compression versus blind compression, Outcome 2 Thrombosis of pseudoaneurysm within 2 days.

Review: Treatment for femoral pseudoaneurysms

Comparison: 1 Ultrasound-guided compression versus blind compression

Outcome: 2 Thrombosis of pseudoaneurysm within 2 days

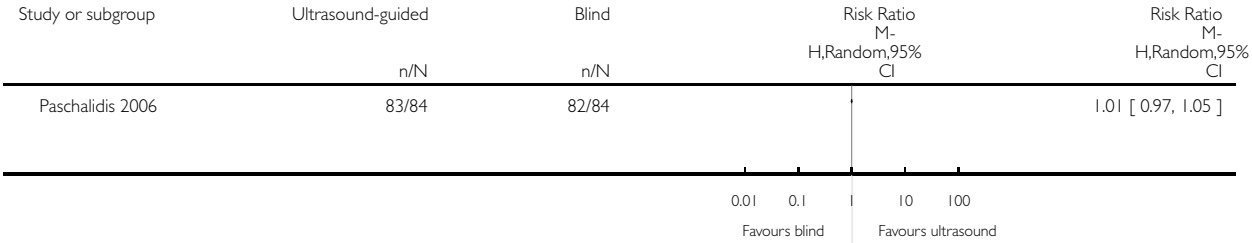


Analysis 1.3. Comparison 1 Ultrasound-guided compression versus blind compression, Outcome 3 Thrombosis of pseudoaneurysm within 3 days.

Review: Treatment for femoral pseudoaneurysms

Comparison: 1 Ultrasound-guided compression versus blind compression

Outcome: 3 Thrombosis of pseudoaneurysm within 3 days

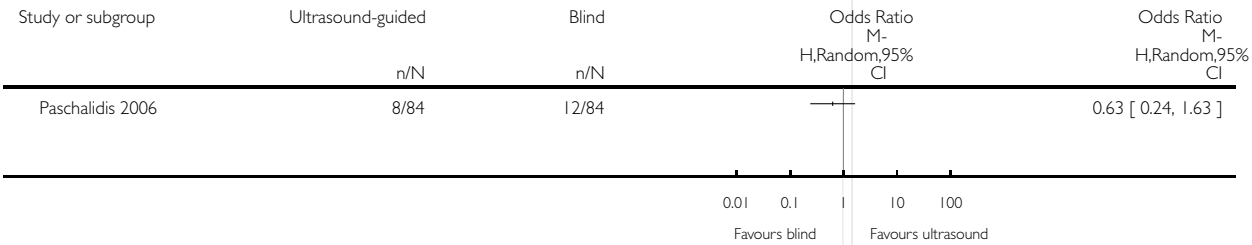


Analysis 1.4. Comparison 1 Ultrasound-guided compression versus blind compression, Outcome 4 Requirement for analgesia/sedation.

Review: Treatment for femoral pseudoaneurysms

Comparison: 1 Ultrasound-guided compression versus blind compression

Outcome: 4 Requirement for analgesia/sedation

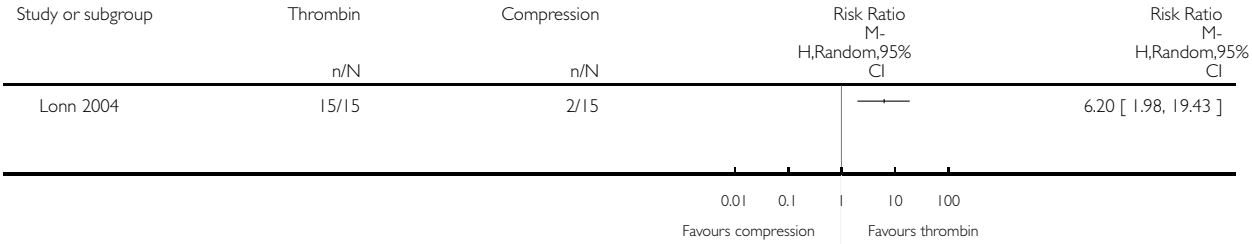


Analysis 2.1. Comparison 2 Thrombin injection versus ultrasound-guided compression, Outcome 1 Thrombosis of pseudoaneurysm within 24 hours (primary outcome).

Review: Treatment for femoral pseudoaneurysms

Comparison: 2 Thrombin injection versus ultrasound-guided compression

Outcome: 1 Thrombosis of pseudoaneurysm within 24 hours (primary outcome)

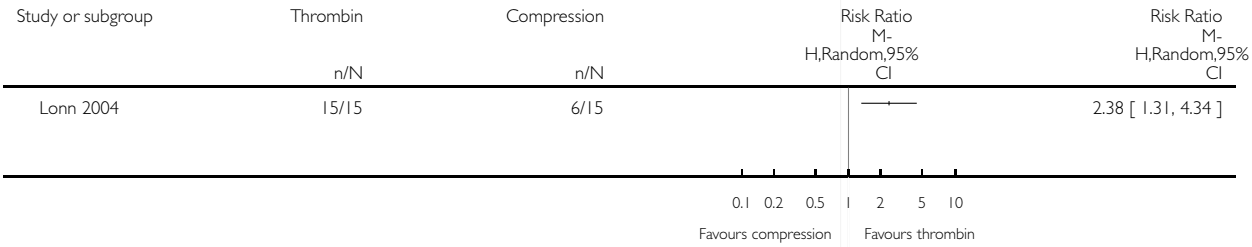


Analysis 2.2. Comparison 2 Thrombin injection versus ultrasound-guided compression, Outcome 2 Thrombosis of pseudoaneurysm within 2 days.

Review: Treatment for femoral pseudoaneurysms

Comparison: 2 Thrombin injection versus ultrasound-guided compression

Outcome: 2 Thrombosis of pseudoaneurysm within 2 days



Analysis 2.3. Comparison 2 Thrombin injection versus ultrasound-guided compression, Outcome 3 Thrombosis of pseudoaneurysm within 3 days (primary outcome).

Review: Treatment for femoral pseudoaneurysms

Comparison: 2 Thrombin injection versus ultrasound-guided compression

Outcome: 3 Thrombosis of pseudoaneurysm within 3 days (primary outcome)

Study or subgroup	Thrombin n/N	Compression n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Liu 2006	19/19	13/19		1.44 [1.06, 1.97]

Analysis 2.4. Comparison 2 Thrombin injection versus ultrasound-guided compression, Outcome 4 Thrombosis of pseudoaneurysm within 7 days.

Review: Treatment for femoral pseudoaneurysms

Comparison: 2 Thrombin injection versus ultrasound-guided compression

Outcome: 4 Thrombosis of pseudoaneurysm within 7 days

Study or subgroup	Thrombin n/N	Compression n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Liu 2006	19/19	19/19		1.00 [0.91, 1.10]

Analysis 2.5. Comparison 2 Thrombin injection versus ultrasound-guided compression, Outcome 5 Primary outcome: thrombosis of pseudoaneurysm.

Review: Treatment for femoral pseudoaneurysms

Comparison: 2 Thrombin injection versus ultrasound-guided compression

Outcome: 5 Primary outcome: thrombosis of pseudoaneurysm

Study or subgroup	Thrombin n/N	Compression n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Liu 2006	19/19	13/19		54.3 %	1.44 [1.06, 1.97]
Lonn 2004	15/15	2/15		45.7 %	6.20 [1.98, 19.43]
Total (95% CI)	**34**	**34**		**100.0 %**	**2.81 [0.44, 18.13]**

Total events: 34 (Thrombin), 15 (Compression)

Heterogeneity: $Tau^2 = 1.64$; $Chi^2 = 9.99$, df = 1 (P = 0.002); $I^2 = 90\%$

Test for overall effect: Z = 1.09 (P = 0.28)

Test for subgroup differences: Not applicable

Analysis 2.6. Comparison 2 Thrombin injection versus ultrasound-guided compression, Outcome 6 Complication rate.

Review: Treatment for femoral pseudoaneurysms

Comparison: 2 Thrombin injection versus ultrasound-guided compression

Outcome: 6 Complication rate

Study or subgroup	Thrombin n/N	Compression n/N	Odds Ratio M-H,Random,95% CI	Odds Ratio M-H,Random,95% CI
Liu 2006	0/19	1/19		0.32 [0.01, 8.26]
Lonn 2004	0/15	0/15		0.0 [0.0, 0.0]
Total (95% CI)	**34**	**34**		**0.32 [0.01, 8.26]**

Total events: 0 (Thrombin), 1 (Compression)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$

Test for overall effect: Z = 0.69 (P = 0.49)

Test for subgroup differences: Not applicable

Analysis 2.7. Comparison 2 Thrombin injection versus ultrasound-guided compression, Outcome 7 Length of hospital stay (days).

Review: Treatment for femoral pseudoaneurysms

Comparison: 2 Thrombin injection versus ultrasound-guided compression

Outcome: 7 Length of hospital stay (days)

Study or subgroup	Thrombin N	Thrombin Mean(SD)	Compression N	Compression Mean(SD)	Std. Mean Difference IV,Random,95% CI	Std. Mean Difference IV,Random,95% CI
Lonn 2004	15	2.8 (1.5)	15	3.5 (2.4)		-0.34 [-1.06, 0.38]

APPENDICES

Appendix 1. CENTRAL search strategy

#1	MeSH descriptor: [Aneurysm, False] explode all trees	26
#2	pseudoaneurysm*:ti,ab,kw (Word variations have been searched)	64
#3	false* near aneurysm*:ti,ab,kw (Word variations have been searched)	45
#4	#1 or #2 or #3 in Trials	79

WHAT'S NEW

Last assessed as up-to-date: 9 October 2013.

Date	Event	Description
12 November 2013	New citation required but conclusions have not changed	New search run. No new studies included. One new study excluded. Minor text changes made. No change to conclusion
12 November 2013	New search has been performed	New search run. No new studies included. One new study excluded

HISTORY

Protocol first published: Issue 4, 2004

Review first published: Issue 1, 2006

Date	Event	Description
17 February 2009	New citation required but conclusions have not changed	The title of this review has been amended.
20 January 2009	New search has been performed	Included two further RCTs. Conclusion modifed to include statement that blind compression as effective as ultrasound-guided compression. Updated reference: NICE (2004)

(*Continued*)

24 July 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Paul Tisi identified trials for inclusion, assessed eligibility and quality of trials, extracted data, and wrote the review.

Michael Callam assessed eligibility and quality of trials, extracted data, and checked the review.

DECLARATIONS OF INTEREST

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 PVD Group editorial base is supported by the Chief Scientist Office.

NOTES

The title of the 2009 update review was changed from "Surgery versus non-surgical treatment for femoral pseudoaneurysms" to "Treatment for femoral pseudoaneurysms" to reflect more accurately the content of the review.

INDEX TERMS

Medical Subject Headings (MeSH)

*Femoral Artery; Aneurysm, False [*therapy]; Hemostatics [therapeutic use]; Pressure; Randomized Controlled Trials as Topic; Thrombin [therapeutic use]; Ultrasonic Therapy [methods]; Ultrasonography, Interventional

MeSH check words

Humans