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Vascular closure devices for femoral arterial puncture site haemostasis (Review)

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[Intervention Review]

Vascular closure devices for femoral arterial puncture site haemostasis

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ABSTRACT

Background

Vascular closure devices (VCDs) are widely used to achieve haemostasis after procedures requiring percutaneous common femoral artery (CFA) puncture. There is no consensus regarding the benefits of VCDs, including potential reduction in procedure time, length of hospital stay or time to patient ambulation. No robust evidence exists that VCDs reduce the incidence of puncture site complications compared with haemostasis achieved through extrinsic (manual or mechanical) compression.

Objectives

To determine the efficacy and safety of VCDs versus traditional methods of extrinsic compression in achieving haemostasis after retrograde and antegrade percutaneous arterial puncture of the CFA.

Search methods

The Cochrane Vascular Trials Search Co-ordinator searched the Specialised Register (April 2015) and the Cochrane Central Register of Controlled Trials (CENTRAL) (2015, Issue 3). Clinical trials databases were searched for details of ongoing or unpublished studies. References of articles retrieved by electronic searches were searched for additional citations.

Selection criteria

We included randomised and quasi-randomised controlled trials in which people undergoing a diagnostic or interventional procedure via percutaneous CFA puncture were randomised to one type of VCD versus extrinsic compression or another type of VCD.

Data collection and analysis

Two authors independently extracted data and assessed the methodological quality of trials. We resolved disagreements by discussion with the third author. We performed meta-analyses when heterogeneity (I^2) was < 90%. The primary efficacy outcomes were time to haemostasis and time to mobilisation (mean difference (MD) and 95% confidence interval (CI)). The primary safety outcome was a major adverse event (mortality and vascular injury requiring repair) (odds ratio (OR) and 95% CI). Secondary outcomes included adverse events.

Main results

We included 52 studies (19,192 participants) in the review. We found studies comparing VCDs with extrinsic compression (sheath size ≤ 9 Fr), different VCDs with each other after endovascular (EVAR) and percutaneous EVAR procedures and VCDs with surgical closure after open exposure of the artery (sheath size ≥ 10 Fr). For primary outcomes, we assigned the quality of evidence according to GRADE (Grades of

Recommendation, Assessment, Development and Evaluation) criteria as low because of serious imprecision and for secondary outcomes as moderate for precision, consistency and directness.

For time to haemostasis, studies comparing collagen-based VCDs and extrinsic compression were too heterogenous to be combined. However, both metal clip-based (MD -14.81 minutes, 95% CI -16.98 to -12.63 minutes; five studies; 1665 participants) and suture-based VCDs (MD -14.58 minutes, 95% CI -16.85 to -12.32 minutes; seven studies; 1664 participants) were associated with reduced time to haemostasis when compared with extrinsic compression.

For time to mobilisation, studies comparing collagen-, metal clip- and suture-based devices with extrinsic compression were too heterogeneous to be combined. No deaths were reported in the studies comparing collagen-based, metal clip-based or suture-based VCDs with extrinsic compression. For vascular injury requiring repair, meta-analyses demonstrated that neither collagen (OR 2.81, 95% CI 0.47 to 16.79; six studies; 5731 participants) nor metal clip-based VCDs (OR 0.49, 95% CI 0.03 to 7.95; three studies; 783 participants) were more effective than extrinsic compression. No cases of vascular injury required repair in the study testing suture-based VCD with extrinsic compression.

Investigators reported no differences in the incidence of infection between collagen-based (OR 2.14, 95% CI 0.88 to 5.22; nine studies; 7616 participants) or suture-based VCDs (OR 1.66, 95% CI 0.22 to 12.71; three studies; 750 participants) and extrinsic compression. No cases of infection were observed in studies testing suture-based VCD versus extrinsic compression. The incidence of groin haematoma was lower with collagen-based VCDs than with extrinsic compression (OR 0.46, 95% CI 0.40 to 0.54; 25 studies; 10,247 participants), but no difference was evident when metal clip-based (OR 0.79, 95% CI 0.46 to 1.34; four studies; 1523 participants) or suture-based VCDs (OR 0.65, 95% CI 0.41 to 1.02; six studies; 1350 participants) were compared with extrinsic compression. The incidence of pseudoaneurysm was lower with collagen-based devices than with extrinsic compression (OR 0.74, 95% CI 0.55 to 0.99; 21 studies; 9342 participants), but no difference was noted when metal clip-based (OR 0.76, 95% CI 0.20 to 2.89; six studies; 1966 participants) or suture-based VCDs (OR 0.79, 95% CI 0.25 to 2.53; six studies; 1527 participants) were compared with extrinsic compression. For other adverse events, researchers reported no differences between collagen-based, clip-based or suture-based VCDs and extrinsic compression.

Limited data were obtained when VCDs were compared with each other. Results of one study showed that metal clip-based VCDs were associated with shorter time to haemostasis (MD -2.24 minutes, 95% CI -2.54 to -1.94 minutes; 469 participants) and shorter time to mobilisation (MD -0.30 hours, 95% CI -0.59 to -0.01 hours; 469 participants) than suture-based devices. Few studies measured (major) adverse events, and those that did found no cases or no differences between VCDs.

Percutaneous EVAR procedures revealed no differences in time to haemostasis (MD -3.20 minutes, 95% CI -10.23 to 3.83 minutes; one study; 101 participants), time to mobilisation (MD 1.00 hours, 95% CI -2.20 to 4.20 hours; one study; 101 participants) or major adverse events between PerClose and ProGlide. When compared with sutures after open exposure, VCD was associated with shorter time to haemostasis (MD -11.58 minutes, 95% CI -18.85 to -4.31 minutes; one study; 151 participants) but no difference in time to mobilisation (MD -2.50 hours, 95% CI -7.21 to 2.21 hours; one study; 151 participants) or incidence of major adverse events.

Authors' conclusions

For time to haemostasis, studies comparing collagen-based VCDs and extrinsic compression were too heterogeneous to be combined. However, both metal clip-based and suture-based VCDs were associated with reduced time to haemostasis when compared with extrinsic compression. For time to mobilisation, studies comparing VCDs with extrinsic compression were too heterogeneous to be combined. No difference was demonstrated in the incidence of vascular injury or mortality when VCDs were compared with extrinsic compression. No difference was demonstrated in the efficacy or safety of VCDs with different mechanisms of action. Further work is necessary to evaluate the efficacy of devices currently in use and to compare these with one other and extrinsic compression with respect to clearly defined outcome measures.

PLAIN LANGUAGE SUMMARY

Effectiveness and safety of devices designed to close femoral artery puncture sites

Background

Endovascular procedures require access to the inside of an artery. A small hole is made in the artery at the groin, and a catheter is guided along to the site of interest. Once the procedure is complete, the hole in the artery must be closed and the bleeding stopped (haemostasis). Traditionally, the main method of closing the artery is compression, during which up to 30 minutes of manual pressure or mechanical clamps is applied directly to the patient's groin. This manual pressure can be painful and requires up to eight hours of bedrest. The process of closing the artery can lead to complications such as damage to the artery and bleeding, ranging from minor to life-threatening. Pressure applied to the artery also affects the nearby vein and may cause blood clots (deep vein thrombosis). Vascular closure devices (VCDs) are designed to close the hole and stop bleeding. VCDs were developed in the 1990s in an attempt to reduce the time to stop bleeding, to enable earlier walking after a procedure and to improve patient comfort. Four main types of VCDs are based on the material used: collagen plugs, suture-based, disc-based and metal clips. No consensus has been reached on the effectiveness of VCDs in reducing procedure time, length of stay or time to mobilisation, and it is unknown whether they confer a cost benefit when compared with compression.

Study characteristics

This review measures the effectiveness and safety of these VCDs compared with one other and with manual or mechanical compression. After searching for relevant studies, we found 52 studies with a combined total of 19,192 participants (current until April 2015). Studies compared different VCDs with manual or mechanical compression and/or with one other. The main measures of effectiveness were time to haemostasis and time to mobilisation. The main safety outcomes included adverse events such as bleeding, arterial damage, infection and development of clots in the adjacent vein.

Key results

This review showed that for time to haemostasis and time to mobilisation, the studies were too different to be combined in a statistical analysis when VCDs are compared with compression. For safety outcomes, no robust evidence shows that VCDs reduce the number of serious puncture site complications, when compared with manual or mechanical compression. Furthermore, this review showed no difference in effectiveness or safety for one type of VCD versus another, but few studies made these comparisons. Further good quality studies are required before firm conclusions can be drawn.

Quality of the evidence

For time to haemostasis and time to mobilisation, the studies were too different to be combined and therefore were judged to provide low-quality evidence. The quality of the evidence for the other outcomes was judged as moderate for precision, consistency and directness.

BACKGROUND

Description of the condition

Percutaneous puncture of the common femoral artery is performed to enable sheath access to the arterial system for diagnostic catheter angiography and arterial intervention. Percutaneous arterial access carries risks of damage to the artery and adjacent vein, including haematoma and pseudoaneurysm formation and arterial dissection (Koreny 2004). If the adjacent vein is damaged at the time of the puncture, arteriovenous fistula formation is also possible (Merriweather 2012).

On completion of the procedure, haemostasis can be achieved by external compression of the artery against the underlying bone, either manually or with a mechanical compression device. After haemostasis has been achieved in this way, the patient is required to rest in bed, normally for four to six hours (Schwartz 2010). Successful and persistent haemostasis reduces the incidence of arterial bleeding and decreases the incidence of haematoma and pseudoaneurysm formation. Deep vein thrombosis has been reported after prolonged extrinsic compression of the adjacent artery (Zahn 1997).

Description of the intervention

Percutaneously deployed vascular closure devices (VCDs) are adjuncts to haemostasis that are deployed at the time of sheath removal. VCDs are suitable for use in many patients to provide instant haemostasis, obviating the need for extrinsic compression and prolonged bedrest. Over the past two decades, VCD use has been widely accepted by practitioners of endovascular medicine.

VCDs fall into four main categories: clip-based (e.g. StarClose; Abbott), suture-based (e.g. PerClose, ProStar; both Abbott), disc-based (e.g. Cardiva Catalyst II; Cardiva Medical) and plug-based (e.g. AngioSeal; St Jude Medical; ExoSeal; Cordis), in which the plugs are predominantly collagen in composition, except for ExoSeal, which is Polyglycolic Acidsee (Table 1). Indications for VCD use are device-specific and depend on patient characteristics, calibre and quality of the arterial wall and arteriotomy size. Most devices are licenced to close 6 to 8 Fr puncture sites in non-diseased arteries for patients without significant obesity. Recently, so-called "pre-closure" devices have become available (e.g. ProStar XL;, Abbott) that can close larger arteriotomies and can be used in large-calibre arterial interventions such as percutaneous endovascular aortic aneurysm repair (EVAR) or transcatheter aortic valve implantation (TAVI). Device selection should be consistent with instructions for use. Operator and unit preference and device cost also play a significant role in device selection.

Why it is important to do this review

VCDs are thought to reduce time to haemostasis, but no consensus indicates whether they affect the incidence of complications at the arteriotomy site compared with haemostasis achieved through extrinsic compression (Smilowitz 2012). Furthermore, introduction of a delivery system and a foreign body into a patient could further damage the artery, and little is known about potentially increased incidence of complications arising directly from closure device use. This review compares the benefits and complications of different types of VCD with one other and with extrinsic compression.

OBJECTIVES

To determine the efficacy and safety of VCDs versus traditional methods of extrinsic compression in achieving haemostasis after retrograde and antegrade percutaneous arterial puncture of the common femoral artery (CFA).

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomised and quasi-randomised controlled clinical trials comparing vascular closure devices (VCDs) against manual compression (MC) or mechanical compression devices (MCDs), or both, for achieving common femoral artery (CFA) puncture site haemostasis. The review also encompasses comparisons between different vascular closure devices.

Types of participants

All studies involving people of both genders undergoing a diagnostic or interventional procedure in which vascular access was achieved through percutaneous puncture of the common femoral artery.

Types of interventions

- Haemostasis after diagnostic or interventional endovascular procedures (sheath size ≤ 9 Fr).
  - Vascular closure device (VCD) versus manual compression (MC) or mechanical compression device (MCD), or both.
  - One type of VCD versus another.
- Haemostasis after percutaneous EVAR (sheath size ≥ 10 Fr).
  - One type of VCD versus another.
- Haemostasis after EVAR with open exposure of CFA (sheath size ≥ 10 Fr).
  - One type of VCD versus another.
  - Surgical suture-based closure versus VCD.

Types of outcome measures

Primary outcomes

Primary end point: efficacy

- Time to haemostasis: Haemostasis is defined as no or minimal subcutaneous bleeding and absence of expanding or developing haematoma.
- Time to mobilisation: This was defined as the time between sheath removal and when the participant was able to mobilise without recurrence of bleeding.
- Major adverse event (occurring at any time).
  - Mortality.
  - Vascular injury requiring vascular repair by surgical or non-surgical techniques.

Secondary outcomes

- Adverse events (occurring up to 30 days after arterial closure).
  - Infection.
  - Groin haematoma.
  - Retroperitoneal haemorrhage.
  - Pseudoaneurysm.

- Arterial dissection.
- Arteriovenous fistula.
- Embolisation resulting in loss of distal pulse.
- Deep vein thrombosis.
- Limb ischaemia.
- Femoral artery thrombosis.

- Technical failure of VCDs.
- Time spent in angiography suite.
- Length of hospital stay.
- Participant satisfaction.
- Costs of VCD and extrinsic compression.

Search methods for identification of studies

Electronic searches

The Cochrane Vascular Trials Search Co-ordinator (TSC) searched the Specialised Register (April 2015). In addition, the TSC searched the Cochrane Register of Studies (CRS) at http://www.metaxis.com/CRSWeb/Index.asp (the Cochrane Central Register of Controlled Trials (CENTRAL) (2015, Issue 3)). See Appendix 1 for details of the search strategy used to search the CRS. The Specialised Register is maintained by the TSC and is constructed from weekly electronic searches of MEDLINE, EMBASE, CINAHL, AMED, and through handsearching relevant journals. The full list of the databases, journals and conference proceedings 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).

The TSC searched the following trial databases in April 2015 for details of ongoing and unpublished studies using the terms 'vascular' and 'closure'.

- World Health Organization International Clinical Trials Registry (http://apps.who.int/trialsearch/).
- ClinicalTrials.gov (http://clinicaltrials.gov/).
- International Standard Randomized Controlled Trial Number (ISRCTN) register (http://www.isrctn.com/).

Searching other resources

We searched citations within identified studies and contacted authors of identified studies to ask about unpublished studies. We applied no restrictions on language.

Data collection and analysis

All randomised and quasi-randomised trials that compared the safety and efficacy of vascular closure devices with manual compression or mechanical compression methods, or both, were eligible for inclusion.

Selection of studies

Two review authors (LR and AA) independently assessed studies identified for inclusion in the review using the criteria stated above. They resolved disagreements by discussion or by consultation with a third review author (FC).

Data extraction and management

Two review authors (LR and AA) independently extracted data from the included studies using a standard data extraction form created for the review. Disagreements between the two review authors were resolved by discussion or by consultation with a third review author (FC).

Assessment of risk of bias in included studies

Two review authors (LR and AA) assessed the risk of bias for each study as described in the *Cochrane Handbook for Systematic Reviews of Interventions* 5.1.0 (Higgins 2011) for each of the following domains.

- Randomisation sequence generation.
- Allocation concealment.
- Blinding (of participants, personnel and outcome assessors).
- Completeness of data.
- Selective outcome reporting.
- Other sources of bias.

The review authors evaluated each criterion as 'Low risk' of bias or 'High risk' of bias according to Higgins 2011. If these criteria were not discussed in the publication, the review authors assessed risk of bias as 'Unclear'. Disagreements between the two review authors were resolved by discussion or by consultation with a third review author (FC).

Measures of treatment effect

When dealing with dichotomous outcome measures, we calculated a pooled estimate of the treatment effect for each outcome across trials using the odds ratio (OR) (the odds of an outcome among treatment-allocated participants to the corresponding odds of the same outcome among participants in the control group) and estimated the 95% confidence interval (CI). For continuous outcomes, we recorded either the mean change from baseline for each group or mean post-intervention values and standard deviation (SD) for each group. When appropriate, we calculated a pooled estimate of the treatment effect by calculating the mean difference (MD) and the SD.

Unit of analysis issues

The unit of analysis was the individual participant. We did not include cross-over trials in the review because only a single treatment was designated to each group. In the case of cluster-randomised trials, when the unit of randomisation was not the same as the unit of analysis, we performed appropriate adjustment for clustering, as outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Dealing with missing data

The review authors requested missing data from the original investigators, if appropriate. When these could not be obtained, an intention-to-treat (ITT) analysis was carried out. For the ITT analysis, we used data on the number of participants with each outcome event by allocated treatment group, irrespective of compliance and whether or not the participant was later thought to be ineligible or otherwise excluded from treatment or follow-up.

Assessment of heterogeneity

If a meta-analysis was possible, we assessed statistical heterogeneity by using the I^2 statistic to quantify inconsistencies among included studies. A guide to interpretation of the I^2 statistic is provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) as follows: 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity; 75% to 100% represents considerable heterogeneity. For the purposes of this review, 90% was the cutoff point for considerable heterogeneity. If considerable heterogeneity was observed ($I^2 \geq 90\%$), the data were not pooled into a meta-analysis. If heterogeneity was observed, we planned to conduct a subgroup analysis to explore possible causes.

Assessment of reporting biases

We investigated publication bias by using funnel plots if we were able to include a sufficient number of studies (≥ 10), as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011; Sterne 2001). If we detected asymmetry, we explored causes other than publication bias. Asymmetrical funnel plots can indicate outcome reporting bias (ORB) or heterogeneity. If we suspected ORB, we contacted trialists. Outcome reporting bias can be assessed by comparing the Methods section of a published trial with the Results section when the original protocol is not available.

Data synthesis

We used a fixed-effect model in our analysis (Higgins 2011). If we detected heterogeneity ($I^2 > 75\%$), we reassessed the significance of the treatment effect by using and reporting a random-effects model.

Subgroup analysis and investigation of heterogeneity

The original protocol stipulated that the following analyses should be performed.

- VCD for the conventional interventional vascular procedure using introducer sheaths up to 9 Fr versus VCD requiring larger introducer sheaths (e.g. for EVAR).
- Comparison between antegrade and retrograde punctures.

However, data from the included studies did not permit these subgroup analyses.

In the presence of heterogeneity, we used a random-effects model. To investigate heterogeneity further, we performed analyses comparing type of procedure (diagnostic or interventional) and brand of VCD when possible.

Sensitivity analysis

We planned to perform a sensitivity analysis to assess the impact of trials with high risk of bias on the overall outcome of pooling of data. However, most studies were classified as having low or unclear risk of bias; therefore, this was not possible.

Quality of evidence

We graded the quality of the evidence according to the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) principles described in Higgins 2011 and GRADE 2004.

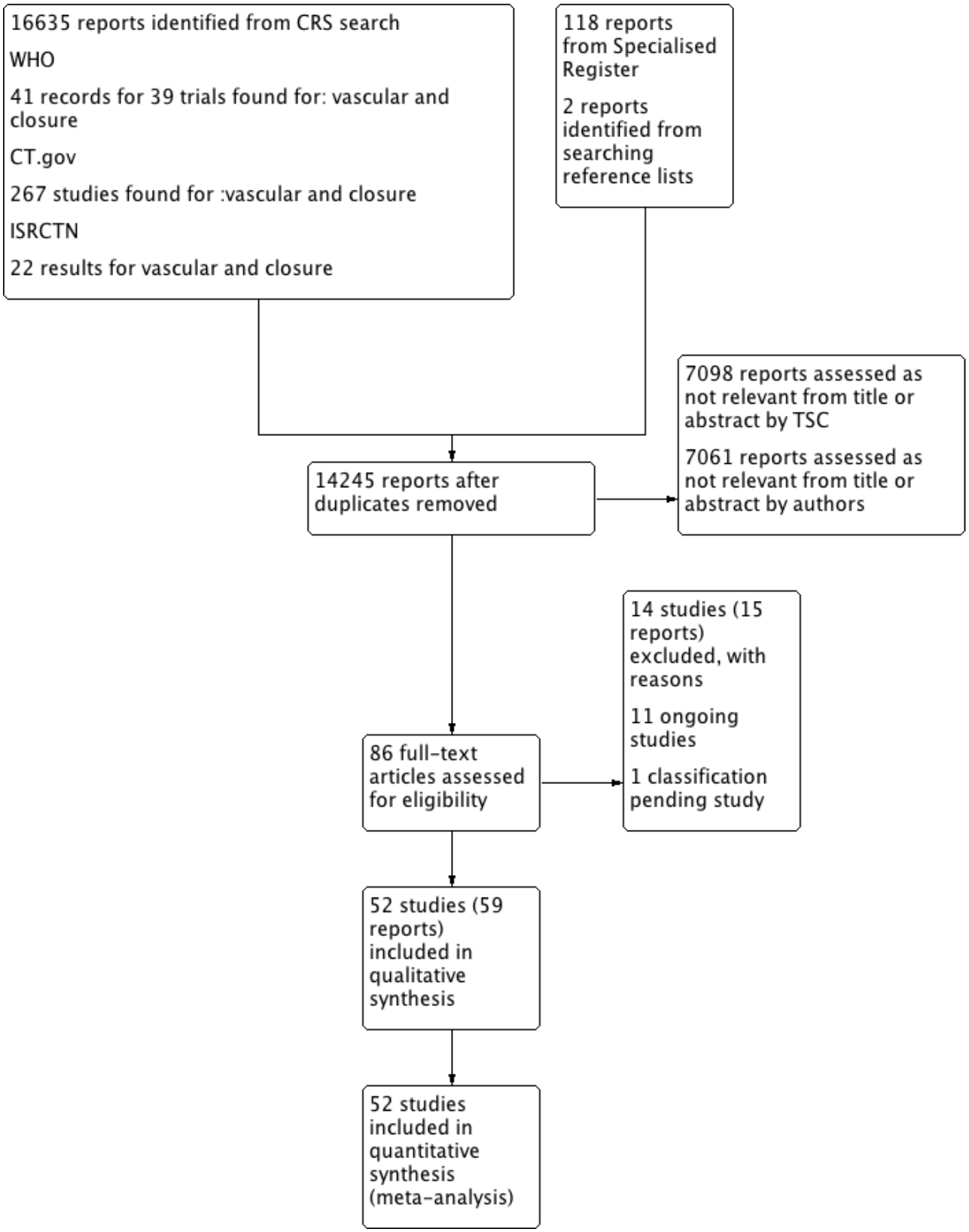
RESULTS

Description of studies

Results of the search

See Figure 1.

Figure 1. Study flow diagram.



Included studies

See Characteristics of included studies.

We included in the review 52 studies involving a total of 19,192 participants (Amin 2000; Amine 1999; Ansel 2006; Behan 2007;

Brachmann 1998; Camenzind 1994; Carere 2000; Castañeda 2003; Chen 2013; Deuling 2008; Diaz 2001; Doneaux 2001; Fargen 2011; Gerckens 1998; Gwechenberger 1997; Hattab 2012; Hermanides 2010; Hermiller 2005; Hermiller 2006; Holm 2014; Jensen 2008; Juergens 2004; Kalsch 2008; Kussmaul 1995; Legrand 2005; Machnik 2012; Magosaki 1999; Martin 2008; Michalis 2002; Nelson 2014; Noguchi 2000; Park 2005; Perlowski 2011; Rastan 2008; Reddy 2004; Rickli 2002; Sanborn 1993; Schräder 1992; Schulz-Schüpke 2014; SEAL Trial Study Team; Seidelin 1997; Shammas 2002; Silber 1998; Sun 2009; Tron 2003; Upponi 2007; Veasey 2008; von Hoch 1995; Ward 1998; Wetter 2000; Wong 2009; Yadav 2003).

In all, 51 studies assessed the effectiveness of VCDs after diagnostic or interventional endovascular procedures (sheath size ≤ 9 Fr). One study compared the effectiveness of VCDs in people undergoing percutaneous EVAR and in those with open exposure of the common femoral artery (both sheath size ≥ 10 Fr) (Nelson 2014).

Eleven studies looked at the effectiveness of VCDs after diagnostic catheterisation procedures (Amine 1999; Behan 2007; Fargen 2011; Hermiller 2005; Holm 2014; Jensen 2008; Reddy 2004; Schulz-Schüpke 2014; Seidelin 1997; Veasey 2008; Ward 1998), and 15 studies assessed interventional procedures (Amin 2000; Camenzind 1994; Chen 2013; Doneaux 2001; Hattab 2012; Hermiller 2006; Juergens 2004; Legrand 2005; Machnik 2012; Martin 2008; Rickli 2002; Silber 1998; Tron 2003; von Hoch 1995; Wetter 2000). Twenty-four studies looked at both diagnostic and interventional procedures (Ansel 2006; Brachmann 1998; Carere 2000; Castañeda 2003; Deuling 2008; Diaz 2001; Gerckens 1998; Gwechenberger 1997; Kalsch 2008; Kussmaul 1995; Magosaki 1999; Michalis 2002; Noguchi 2000; Park 2005; Perlowski 2011; Rastan 2008; Sanborn 1993; Schräder 1992; SEAL Trial Study Team; Shammas 2002; Sun 2009; Upponi 2007; Wong 2009; Yadav 2003). One study (Nelson 2014) measured the effectiveness of two VCDs after percutaneous EVAR; the same study also compared devices with surgical suture-based closure versus VCDs after EVAR with open exposure of the CFA.

Collagen-based VCD versus manual or mechanical compression

Thirty studies measured the effectiveness of a collagen-based vascular closing device versus manual or mechanical compression (Amin 2000; Behan 2007; Brachmann 1998; Camenzind 1994; Castañeda 2003; Deuling 2008; Diaz 2001; Doneaux 2001; Gwechenberger 1997; Hermanides 2010; Holm 2014; Jensen 2008; Juergens 2004; Kussmaul 1995; Legrand 2005; Machnik 2012; Magosaki 1999; Martin 2008; Reddy 2004; Sanborn 1993; Schräder 1992; Schulz-Schüpke 2014; SEAL Trial Study Team; Seidelin 1997; Silber 1998; Upponi 2007; von Hoch 1995; Ward 1998; Wong 2009; Yadav 2003). Seventeen trials studied the AngioSeal device (Amin 2000; Behan 2007; Deuling 2008; Diaz 2001; Doneaux 2001; Hermanides 2010; Jensen 2008; Juergens 2004; Kussmaul 1995; Legrand 2005; Machnik 2012; Magosaki 1999; Martin 2008; Reddy 2004; Seidelin 1997; Upponi 2007; Ward 1998) - seven in diagnostic procedures (Behan 2007; Deuling 2008; Doneaux 2001; Jensen 2008; Reddy 2004; Seidelin 1997; Ward 1998), six in interventional procedures (Amin 2000; Hermanides 2010; Juergens 2004; Legrand 2005; Machnik 2012; Martin 2008) and four (Diaz 2001; Kussmaul 1995; Magosaki 1999; Upponi 2007) in both diagnostic and interventional procedures. Seven studies tested the VasoSeal device (Brachmann 1998; Camenzind 1994; Gwechenberger 1997; Sanborn 1993; Schräder 1992; Silber 1998; von Hoch 1995) - three (Camenzind 1994; Silber 1998; von Hoch 1995) in interventional procedures and four (Brachmann 1998; Gwechenberger 1997; Sanborn 1993; Schräder 1992) in both diagnostic and interventional procedures. One study (SEAL Trial Study Team) tested the Duett device, which is a liquid collagen and thrombin device, two studied QuickSeal (Castañeda 2003; Yadav 2003), two studied FemoSeal (Holm 2014; Schulz-Schüpke 2014) and two studied ExoSeal (Schulz-Schüpke 2014; Wong 2009), a device that uses a polyglycolic acid plug. Schulz-Schüpke 2014 tested ExoSeal in interventional procedures, and Wong 2009 tested ExoSeal in both diagnostic and interventional procedures.

Metal clip-based VCD versus manual or mechanical compression

Six studies measured the effectiveness of a metal clip-based device versus manual compression (Ansel 2006; Deuling 2008; Hermiller 2005; Hermiller 2006; Perlowski 2011; Sun 2009). Four studied the StarClose device (Deuling 2008; Hermiller 2005; Hermiller 2006; Perlowski 2011) - one (Hermiller 2005) in diagnostic procedures, one (Hermiller 2006) in interventional procedures and two (Deuling 2008; Perlowski 2011) in both diagnostic and interventional procedures. Sun 2009 was a three-armed trial that compared StarClose, PerClose and manual compression in participants undergoing both diagnostic and interventional procedures. Finally, one study measured the effectiveness of the Angiolink EVS closure device (Ansel 2006) with both diagnostic and interventional procedures.

Suture-based VCD versus manual or mechanical compression

Ten studies (Amine 1999; Carere 2000; Gerckens 1998; Jensen 2008; Martin 2008; Noguchi 2000; Rickli 2002; Sun 2009; Tron 2003; Wetter 2000) measured the effectiveness of a suture-based device versus manual compression. Seven studies (Amine 1999; Jensen 2008; Martin 2008; Rickli 2002; Sun 2009; Tron 2003; Wetter 2000) looked at PerClose - two (Amine 1999; Jensen 2008) in diagnostic participants, four (Martin 2008; Rickli 2002; Tron 2003; Wetter 2000) in interventional participants and one (Sun 2009) in both types of procedures. Three studies (Carere 2000; Gerckens 1998; Noguchi 2000) tested ProStar in participants undergoing diagnostic and interventional procedures.

Collagen-based VCD versus metal clip-based VCD: AngioSeal versus StarClose

Three studies compared AngioSeal versus StarClose (Deuling 2008; Rastan 2008; Veasey 2008). Veasey 2008 tested the device after diagnostic procedures, and Deuling 2008 and Rastan 2008 looked at both diagnostic and interventional procedures.

Collagen-based VCD versus suture-based VCD

Five studies (Hattab 2012; Jensen 2008; Kalsch 2008; Martin 2008; Park 2005) compared a collagen-based VCD with a suture-based VCD. Three studies (Jensen 2008; Kalsch 2008; Martin 2008) compared AngioSeal with PerClose - one (Jensen 2008) in diagnostic participants, one (Martin 2008) in interventional participants and one (Kalsch 2008) in both diagnostic and interventional participants. One study (Park 2005) compared AngioSeal with Closure S in diagnostic and interventional participants, and Hattab 2012 compared ExoSeal with ProGlide in participants undergoing intervention. Park 2005 included participants with several femoral artery punctures. Outcomes are based on the number of punctures rather than on the number of individual participants. After personal communication with the

study author, it was decided that although this study was relevant and met the inclusion criteria, data would not be included in the analyses, as they were not comparable with data based on individuals from the other included studies.

Metal clip-based VCD versus suture-based VCD: StarClose versus PerClose

One study (Sun 2009) compared the metal clip-based StarClose with the suture-based PerClose in participants undergoing diagnostic and interventional procedures.

Disc-based VCD versus suture-based VCD: Boomerang versus PerClose

One study (Chen 2013) compared a disc-based device (Boomerang) with a suture-based device (PerClose) in 60 participants undergoing coronary intervention.

Collagen-based VCD versus collagen-based VCD: AngioSeal versus VasoSeal

Two studies (Michalis 2002; Shammas 2002) compared the collagen-based devices AngioSeal and VasoSeal in both diagnostic and interventional procedures.

Collagen-based VCD versus collagen-based VCD: AngioSeal versus Mynx

One study (Fargen 2011) measured vascular injury requiring repair, infection, groin haematoma and patient satisfaction in diagnostic participants treated with the AngioSeal or another collagen device, Mynx.

Collagen-based VCD versus collagen-based VCD: AngioSeal versus Duett

Michalis 2002 was a three-armed trial that tested the collagen devices AngioSeal and Duett in participants undergoing diagnostic and interventional procedures.

Collagen-based VCD versus collagen-based VCD: VasoSeal versus Duett

Michalis 2002 also tested the VasoSeal and Duett collagen devices.

Collagen-based VCD versus collagen-based VCD: FemoSeal versus ExoSeal

One study (Schulz-Schüpke 2014) compared the collagen devices FemoSeal and ExoSeal in participants undergoing diagnostic procedures.

PerClose ProGlide versus ProStar XL after percutaneous EVAR (sheath size ≥ 10 Fr)

One study (Nelson 2014) compared PerClose ProGlide with ProStar XL in participants undergoing percutaneous EVAR.

PerClose ProGlide and ProStar XL versus suture-based closure after EVAR with open exposure of CFA (sheath size ≥ 10 Fr)

Nelson 2014 also compared the PerClose ProGlide and ProStar XL devices with surgical suture-based closure in participants undergoing open femoral exposure of the CFA.

Excluded studies

See Characteristics of excluded studies.

We excluded 14 studies (Baim 2000; Beyer-Enke 1996; Chalmers 2007; Chevalier 2000; Jean-Baptiste 2008; Kurşaklioğlu 2008; Larzon 2015; Leinbudgut 2013; Lupi 2012; Neudecker 2003; Ratnam 2007; Slaughter 1995; Smilowitz 2012; Starnes 2003). Seven were not randomised controlled trials (Jean-Baptiste 2008; Kurşaklioğlu 2008; Lupi 2012; Ratnam 2007; Neudecker 2003; Ratnam 2007; Smilowitz 2012), two (Baim 2000; Starnes 2003) used 7 to 10 Fr sheath sizes and did not present data by sheath size and one (Chalmers 2007) used EVICEL and another (Larzon 2015) used the fascia suture technique (neither of which are VCDs); another study (Chevalier 2000) measured adverse events included in this review but did not present data, one (Leinbudgut 2013) randomised people by the drug they received to prevent bleeding rather than by VCD and another study (Beyer-Enke 1996) was not clear on whether access for the procedure was attained through the femoral artery. For studies on which we had queries regarding data (Baim 2000; Beyer-Enke 1996; Chevalier 2000; Starnes 2003), we wrote to the study authors but received no response and therefore had to exclude these studies from the review.

Risk of bias in included studies

See Figure 2 and Figure 3.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

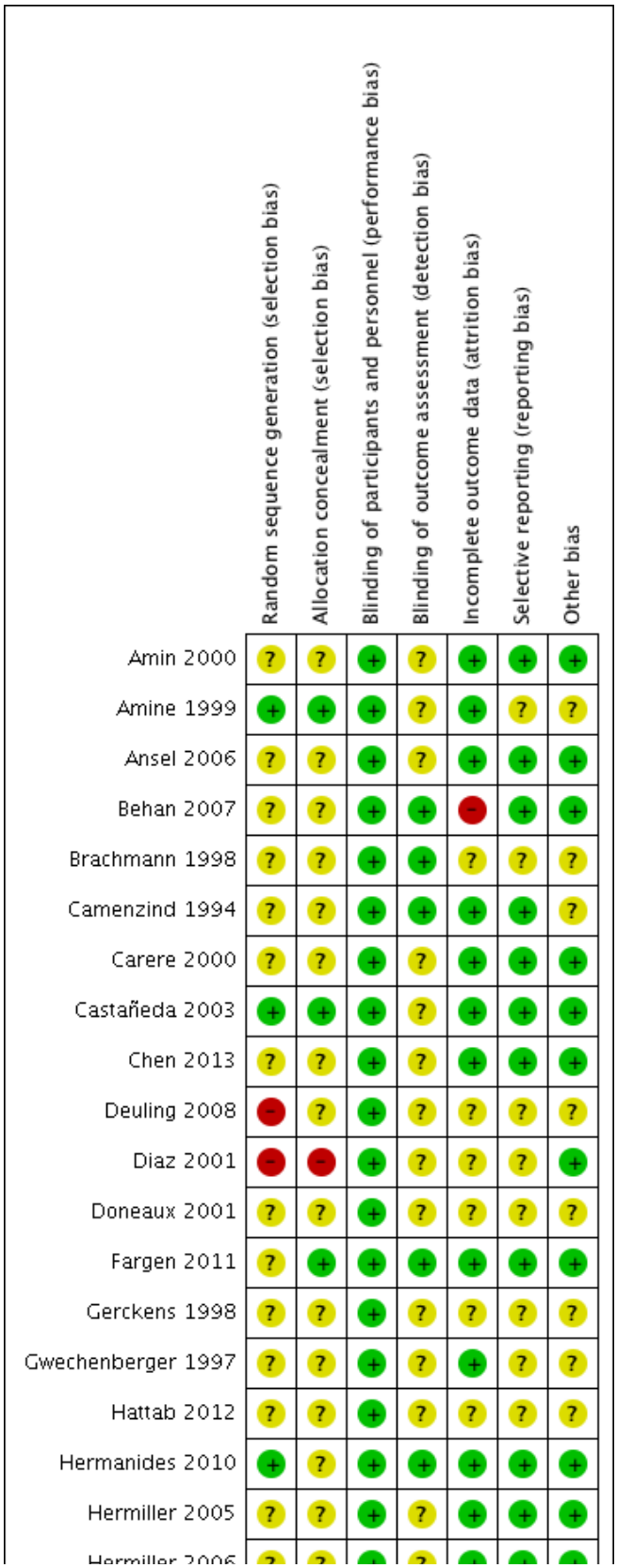


Figure 2. (Continued)

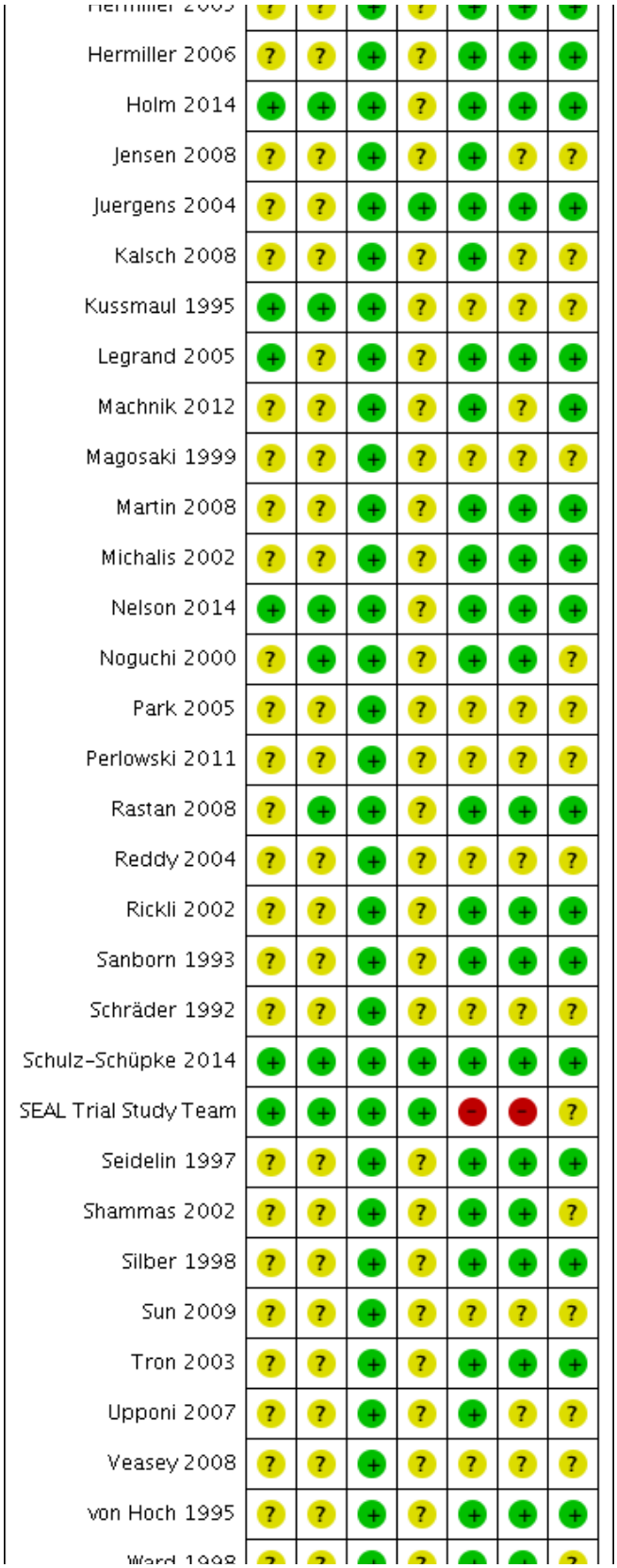


Figure 2. (Continued)

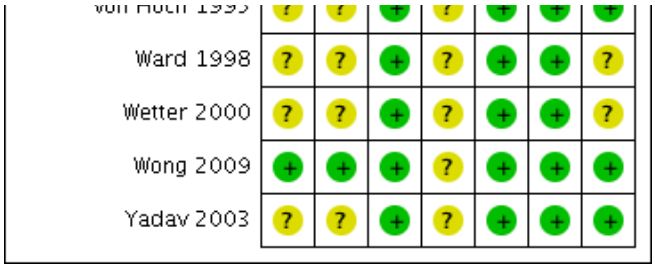
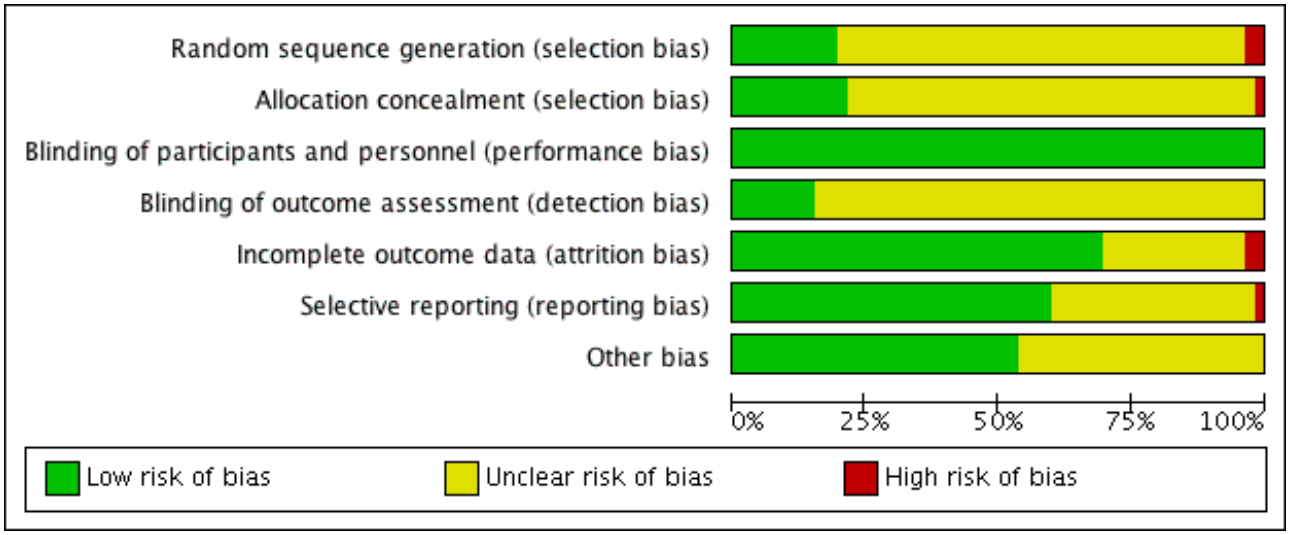


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

Random sequence generation: Of the 52 studies included in this review, 10 were deemed to be at low risk of bias (Amine 1999; Castañeda 2003; Hermanides 2010; Holm 2014; Kussmaul 1995; Legrand 2005; Nelson 2014; Schulz-Schüpke 2014; SEAL Trial Study Team; Wong 2009). Three studies (Legrand 2005; Schulz-Schüpke 2014; Wong 2009) reported that randomisation was computer-assisted, and another seven studies (Amine 1999; Castañeda 2003; Hermanides 2010; Holm 2014; Kussmaul 1995; Nelson 2014; SEAL Trial Study Team) reported using a block design to generate the random sequence. Two studies were judged to be at high risk of bias, as participants were assigned to treatment not randomly but rather on order of presentation (Deuling 2008) or by odd and even numbers (Diaz 2001). The remaining 40 studies did not provide enough information about the randomisation process to permit judgement on the risk of bias.

Allocation concealment: One study was deemed to be at high risk of bias as allocation was based on alternation (Diaz 2001). Eleven studies were at low risk of bias, as they reported using sealed envelopes (Amine 1999; Castañeda 2003; Fargen 2011; Kussmaul 1995; Nelson 2014; Noguchi 2000; Rastan 2008; SEAL Trial Study Team; Wong 2009) or a computer-based system (Holm 2014; Schulz-Schüpke 2014) to conceal allocation of treatment. The remaining 40 did not provide enough information about allocation concealment to permit judgement on the risk of selection bias.

Blinding

Blinding of study participants and personnel was not possible. However, we determined that outcomes of the review were not likely to be influenced by lack of blinding and therefore judged all studies to be at low risk of performance bias.

Blinding of outcome assessors was possible, and eight studies (Behan 2007; Brachmann 1998; Camenzind 1994; Fargen 2011; Hermanides 2010; Juergens 2004; Schulz-Schüpke 2014; SEAL Trial Study Team) were judged to be at low risk of detection bias as study authors reported that outcome assessors were blinded to treatment assignment. No study was found to be at high risk of detection bias. In the remaining 44 studies included in this review, risk of detection bias was deemed to be unclear because reporting of blinding of outcome assessors was inadequate.

Incomplete outcome data

Thirty-six of the 52 included studies were judged to be at low risk of attrition bias (Amin 2000; Amine 1999; Ansel 2006; Camenzind 1994; Carere 2000; Castañeda 2003; Chen 2013; Fargen 2011; Gwechenberger 1997; Hermanides 2010; Hermiller 2005; Hermiller 2006; Holm 2014; Jensen 2008; Juergens 2004; Kalsch 2008; Legrand 2005; Machnik 2012; Martin 2008; Michalis 2002; Nelson 2014; Noguchi 2000; Rastan 2008; Rickli 2002; Sanborn 1993; Schulz-Schüpke 2014; Seidelin 1997; Shammas 2002; Silber 1998; Tron 2003; Upponi 2007; von Hoch 1995; Ward 1998; Wetter 2000;

Wong 2009; Yadav 2003). Two studies were judged to be at high risk of attrition bias: SEAL Trial Study Team reported that only 227 of 392 participants treated with the Duett device completed the seven-day and 30-day quality of life study and did not explain the reason for this large loss to follow-up and Behan 2007 reported that only 72% of AngioSeal and 71% of manual compression participants completed follow-up at one week. The remaining 14 studies did not provide enough information about incomplete outcome data to permit judgement on the risk of attrition bias.

Selective reporting

One study (SEAL Trial Study Team) was judged to be at high risk of reporting bias, as study authors reported quality of life results at seven days and 30 days post procedure, but quality of life was not a clearly specified outcome of the study. Thirty-one studies adequately reported data on all pre-specified outcomes and therefore were judged to be at low risk of reporting bias (Amin 2000; Ansel 2006; Behan 2007; Camenzind 1994; Carere 2000; Castañeda 2003; Chen 2013; Fargen 2011; Hermanides 2010; Hermiller 2005; Hermiller 2006; Holm 2014; Juergens 2004; Legrand 2005; Martin 2008; Michalis 2002; Nelson 2014; Noguchi 2000; Rastan 2008; Rickli 2002; Sanborn 1993; Schulz-Schüpke 2014; Seidelin 1997; Shammas 2002; Silber 1998; Tron 2003; von Hoch 1995; Ward 1998; Wetter 2000; Wong 2009; Yadav 2003). The remaining 20 studies did not provide enough information to permit judgement on low or high risk of reporting bias; therefore, the risk was deemed unclear.

Other potential sources of bias

Twenty-eight studies appeared to be free from other sources of bias (Amin 2000; Ansel 2006; Behan 2007; Carere 2000; Castañeda 2003; Chen 2013; Diaz 2001; Fargen 2011; Hermanides 2010; Hermiller 2005; Hermiller 2006; Holm 2014; Juergens 2004; Legrand 2005; Machnik 2012; Martin 2008; Michalis 2002; Nelson 2014; Rastan 2008; Rickli 2002; Sanborn 1993; Schulz-Schüpke 2014; Seidelin 1997; Silber 1998; Tron 2003; von Hoch 1995; Wong 2009; Yadav 2003). No study was deemed to be at high risk of bias. The remaining 24 studies included in the review did not provide enough information; therefore, risk of bias was unclear.

Effects of interventions

Haemostasis after diagnostic or interventional endovascular procedures (sheath size ≤ 9 Fr)

Collagen-based VCD versus manual or mechanical compression

Thirty studies measured the effectiveness of a collagen-based vascular closing device versus manual or mechanical compression (Amin 2000; Behan 2007; Brachmann 1998; Camenzind 1994; Castañeda 2003; Deuling 2008; Diaz 2001; Doneaux 2001; Gwechenberger 1997; Hermanides 2010; Holm 2014; Jensen 2008; Juergens 2004; Kussmaul 1995; Legrand 2005; Machnik 2012; Magosaki 1999; Martin 2008; Reddy 2004; Sanborn 1993; Schräder 1992; Schulz-Schüpke 2014; SEAL Trial Study Team; Seidelin 1997; Silber 1998; Upponi 2007; von Hoch 1995; Ward 1998; Wong 2009; Yadav 2003).

Time to haemostasis

Nineteen studies that compared a collagen-based VCD with manual compression measured time to haemostasis (Brachmann 1998; Castañeda 2003; Diaz 2001; Doneaux 2001; Gwechenberger 1997; Holm 2014; Juergens 2004; Kussmaul 1995; Magosaki 1999; Martin 2008; Reddy 2004; Sanborn 1993; Schulz-Schüpke 2014; SEAL Trial Study Team; Seidelin 1997; Silber 1998; Ward 1998; Wong 2009; Yadav 2003). Data from 12 studies were entered into a meta-analysis (Brachmann 1998; Castañeda 2003; Diaz 2001; Gwechenberger 1997; Juergens 2004; Kussmaul 1995; Magosaki 1999; Reddy 2004; Sanborn 1993; Seidelin 1997; Silber 1998; Wong 2009). Seven studies were not included in the meta-analysis: Four studies (Doneaux 2001; Martin 2008; Ward 1998; Yadav 2003) did not report standard deviations for mean time to haemostasis, and three studies (Holm 2014; Schulz-Schüpke 2014; SEAL Trial Study Team) presented time to haemostasis as a median and as an interquartile range.

When the 12 studies were combined in a meta-analysis, considerable heterogeneity was evident (I^2 = 98%) (Analysis 1.1). Subgroup analyses by type of procedure, brand of VCD and quality of the included studies revealed no differences between groups. Individually, 11 of the 12 studies showed that the collagen-based VCD was associated with significantly shorter time to haemostasis when compared with manual compression (Brachmann 1998; Castañeda 2003; Diaz 2001; Gwechenberger 1997; Juergens 2004; Kussmaul 1995; Magosaki 1999; Sanborn 1993; Seidelin 1997; Silber 1998; Wong 2009). Only one study showed no significant improvement between the collagen-based VCD and manual compression (Reddy 2004). Juergens 2004 reported a significantly longer time to haemostasis for both VCD and manual compression participants than was reported in other included studies. We contacted the study author, who did not reply to clarify whether results reported in the paper were correct. Exclusion of this study from the meta-analysis had little impact on heterogeneity.

Time to mobilisation

Thirteen studies were included in a meta-analysis (Behan 2007; Brachmann 1998; Castañeda 2003; Diaz 2001; Holm 2014; Juergens 2004; Legrand 2005; Machnik 2012; Magosaki 1999; Sanborn 1993; Schräder 1992; Seidelin 1997; Wong 2009). Doneaux 2001; Martin 2008; SEAL Trial Study Team; Ward 1998; and Yadav 2003 reported time to ambulation but did not provide standard deviations; the SEAL Trial Study Team reported time to ambulation as median and as interquartile range. We contacted the authors of these studies but did not obtain requested data.

Meta-analysis of the 13 studies indicated heterogeneity (I^2 = 100%) (Analysis 1.2). Subgroup analyses by type of procedure, brand of VCD and quality of included studies showed no differences between groups. All 13 studies individually showed that the collagen-based VCD was associated with significantly shorter time to mobilisation than was seen with manual compression (Behan 2007; Brachmann 1998; Castañeda 2003; Diaz 2001; Holm 2014; Juergens 2004; Legrand 2005; Machnik 2012; Magosaki 1999; Sanborn 1993; Schräder 1992; Seidelin 1997; Wong 2009).

Major adverse events

Mortality

Only one study (Castañeda 2003) presented data on mortality and reported no deaths in 141 participants (Analysis 1.3).

Vascular injury requiring vascular repair by surgical or non-surgical techniques

Five studies (Sanborn 1993; Schulz-Schüpke 2014; Seidelin 1997; Ward 1998; Yadav 2003) reported on this outcome (Analysis 1.3).

Of 3727 participants treated with a collagen-based VCD, five (0.1%) had vascular injury requiring repair compared with none of 2004 manual compression participants (OR 2.81, 95% CI 0.47 to 16.79; P value = 0.26).

Adverse events

Infection

Nine studies (Behan 2007; Castañeda 2003; Deuling 2008; Holm 2014; Sanborn 1993; Schulz-Schüpke 2014; SEAL Trial Study Team; Seidelin 1997; von Hoch 1995) recorded puncture site infection (Analysis 1.4). Of 4674 participants treated with a VCD, 15 (0.3%) experienced infection compared with six of 2942 (0.2%) participants treated with manual compression (OR 2.14, 95% CI 0.88 to 5.22; P value = 0.09). However, five of the nine included studies (Behan 2007; Castañeda 2003; Deuling 2008; Schulz-Schüpke 2014; SEAL Trial Study Team) found no cases of infection, and another study (Seidelin 1997) included only 50 people.

Groin haematoma

A total of 25 studies (Amin 2000; Camenzind 1994; Castañeda 2003; Deuling 2008; Diaz 2001; Doneaux 2001; Gwechenberger 1997; Hermanides 2010; Holm 2014; Jensen 2008; Juergens 2004; Kussmaul 1995; Legrand 2005; Machnik 2012; Magosaki 1999; Reddy 2004; Sanborn 1993; Schräder 1992; Schulz-Schüpke 2014; Seidelin 1997; Silber 1998; Upponi 2007; Ward 1998; Wong 2009; Yadav 2003) measured groin haematoma (Analysis 1.5). Haematoma occurred in 327 of 6019 (5.4%) participants treated with a collagen-based VCD compared with 456 of 4228 (10.8%) participants treated with manual compression, leading to an OR of 0.46 (95% CI 0.40 to 0.54; P value < 0.00001).

Retroperitoneal haemorrhage

Three studies (Behan 2007; Martin 2008; Wong 2009), based on a total of 744 participants, found retroperitoneal haemorrhage in three of 444 (0.7%) VCD participants and one of 300 (0.3%) manual compression participants (OR 1.5, 95% CI 0.22 to 11.42; P value = 0.65) (Analysis 1.6).

Pseudoaneurysm

Twenty-one studies (Amin 2000; Behan 2007; Camenzind 1994; Deuling 2008; Doneaux 2001; Gwechenberger 1997; Holm 2014; Juergens 2004; Legrand 2005; Machnik 2012; Magosaki 1999; Martin 2008; Reddy 2004; Sanborn 1993; Schulz-Schüpke 2014; SEAL Trial Study Team; Silber 1998; Upponi 2007; von Hoch 1995; Ward 1998; Yadav 2003) reported pseudoaneurysm as an outcome (Analysis 1.7). Meta-analysis showed that pseudoaneurysm occurred in 92 of 5573 (1.6%) VCD participants and in 83 of 3769 (2.2%) manual compression participants, leading to an OR of 0.74 (95% CI 0.55 to 0.99; P value = 0.04).

Arterial dissection

None of the included studies measured arterial dissection as an outcome.

Arteriovenous fistula

Meta-analysis of eight studies (Gwechenberger 1997; Hermanides 2010; Machnik 2012; Martin 2008; Schulz-Schüpke 2014; SEAL Trial Study Team; Upponi 2007; von Hoch 1995) showed that arteriovenous fistula occurred in 14 of 3868 (0.4%) VCD participants and in nine of 2285 (0.4%) manual compression participants (OR 0.98, 95% CI 0.43 to 2.21; P value = 0.96) (Analysis 1.8).

Embolisation resulting in loss of distal pulse

None of the included studies measured this as an outcome.

Deep vein thrombosis

Among three studies (Camenzind 1994; Sanborn 1993; Seidelin 1997), deep vein thrombosis (DVT) occurred in four of 332 (1.2%) VCD participants and in one of 297 (0.3%) manual compression participants, leading to an OR of 2.41 (95% CI 0.46 to 12.50; P value = 0.30) (Analysis 1.9).

Limb ischaemia

Three studies (Behan 2007; Machnik 2012; Schulz-Schüpke 2014) measured limb ischaemia as an outcome (Analysis 1.10). No cases occurred in the 3242 VCD participants nor in the 1728 participants treated with manual compression.

Femoral artery thrombosis

One study (Upponi 2007) measured femoral artery thrombosis but found no cases in VCD nor manual compression participants (Analysis 1.11).

Technical failure of VCDs

In 24 studies (Amin 2000; Behan 2007; Castañeda 2003; Deuling 2008; Doneaux 2001; Gwechenberger 1997; Jensen 2008; Juergens 2004; Kussmaul 1995; Legrand 2005; Machnik 2012; Magosaki 1999; Martin 2008; Reddy 2004; Sanborn 1993; Schräder 1992; SEAL Trial Study Team; Seidelin 1997; Silber 1998; Upponi 2007; von Hoch 1995; Ward 1998; Wong 2009; Yadav 2003) with a combined total of 3033 participants treated with a collagen-based VCD, 118 unsuccessful device deployments led to a technical failure rate of 3.9%.

Time spent in angiography suite

None of the included studies reported on this outcome.

Length of hospital stay

Eight studies (Castañeda 2003; Juergens 2004; Machnik 2012; Magosaki 1999; Silber 1998; Ward 1998; Wong 2009; Yadav 2003) measured length of hospital stay. However, Ward 1998 and Yadav 2003 did not report standard deviations for the mean stay and therefore could not be included in the meta-analysis. Meta-analysis of the six studies based on a random-effects model showed considerable heterogeneity (I^2 = 90%) (Analysis 1.12). Subgroup analyses that excluded two studies (Magosaki 1999; Silber 1998) with significantly longer hospital stay than the other studies showed no differences between groups.

Patient satisfaction

Six studies (Amin 2000; Holm 2014; Juergens 2004; Legrand 2005; Martin 2008; Schräder 1992) reported on patient satisfaction. However, these studies used different measurement tools and scales; therefore, the results could not be meta-analysed. Five studies reported that collagen-based devices were associated with less pain and bedrest than were seen with manual compression (Amin 2000; Juergens 2004; Legrand 2005; Martin 2008; Schräder 1992). However, in one study (Holm 2014), participants in the VCD group reported greater pain and discomfort during the

closure procedure when compared with participants in the manual compression group.

Cost of VCD and extrinsic compression

None of the included studies compared the cost of VCD versus manual compression.

Metal clip-based VCD versus manual or mechanical compression

Six studies measured the effectiveness of a metal clip-based device versus manual compression (Ansel 2006; Deuling 2008; Hermiller 2005; Hermiller 2006; Perlowski 2011; Sun 2009).

Time to haemostasis

Five studies (Ansel 2006; Hermiller 2005; Hermiller 2006; Perlowski 2011; Sun 2009) measured time to haemostasis, four using StarClose (Hermiller 2005; Hermiller 2006; Perlowski 2011; Sun 2009) and one using Angiolink (Ansel 2006). Ansel 2006 presented results according to type of procedure and therefore provided data on both diagnostic and interventional participants. Meta-analysis using a random-effects model indicated that the metal clip-based VCD was associated with statistically significantly less time to haemostasis than manual compression (MD -14.81 minutes, 95% CI -16.98 to -12.63; participants = 1665; I^2 = 84%; P value < 0.00001) (Analysis 2.1).

Time to mobilisation

Three studies (Ansel 2006; Hermiller 2005; Sun 2009) including a total of 1303 participants measured time to haemostasis with Angiolink (Ansel 2006) or StarClose (Hermiller 2005; Sun 2009). Ansel 2006 presented results according to type of procedure, including data on both diagnostic and interventional participants. Meta-analysis using a random-effects model indicated substantial heterogeneity (I^2 = 100%), and subgroup analysis performed by type of procedure and brand of VCD showed no differences between groups (Analysis 2.2). Individually, all three studies (Ansel 2006; Hermiller 2005; Sun 2009) showed that the metal clip-based VCD was associated with significantly reduced time to mobilisation when compared with manual compression.

Major adverse event

Three studies (Hermiller 2005; Hermiller 2006; Perlowski 2011) with a combined total of 564 participants reported no deaths in either treatment group (Analysis 2.3). Three studies (Deuling 2008; Hermiller 2005; Hermiller 2006) with a combined total of 783 participants reported no differences in the incidence of vascular injury requiring repair (OR 0.49, 95% CI 0.03 to 7.95; P value = 0.62).

Adverse events

Infection

No cases of infection were reported in the 470 VCD and 313 manual compression participants among three studies reporting on infection (Deuling 2008; Hermiller 2005; Hermiller 2006) (Analysis 2.4).

Groin haematoma

Four studies (Deuling 2008; Hermiller 2005; Hermiller 2006; Sun 2009) determined that the incidence of groin haematoma was 30 of 939 (3.2%) and 28 of 584 (4.8%) VCD and manual compression participants, respectively (OR 0.79, 95% CI 0.46 to 1.34; P value = 0.38) (Analysis 2.5).

Retroperitoneal haemorrhage

None of the studies comparing metal clip-based VCDs with manual compression measured retroperitoneal haemorrhage as an outcome.

Pseudoaneurysm

Pseudoaneurysm was reported in six of the included studies (Ansel 2006; Deuling 2008; Hermiller 2005; Hermiller 2006; Perlowski 2011; Sun 2009) (Analysis 2.6). The combined incidence was four of 1221 (0.3%) metal clip-based VCD participants compared with three of 745 (0.4%) manual compression participants (OR 0.76, 95% CI 0.20 to 2.89; P value = 0.69).

Arterial dissection

None of the studies comparing metal clip-based VCDs with manual compression measured arterial dissection as an outcome.

Arteriovenous fistula

No cases of arteriovenous fistula were reported in 564 participants in three studies (Hermiller 2005; Hermiller 2006; Perlowski 2011) (Analysis 2.7).

Embolisation resulting in loss of distal pulse

None of the studies comparing metal clip-based VCDs with manual compression measured embolisation with loss of distal pulse as an outcome.

Deep vein thrombosis

No cases of DVT were reported among 483 participants in two studies (Hermiller 2005; Hermiller 2006) (Analysis 2.8).

Limb ischaemia

None of the 320 VCD participants nor 163 manual compression participants in two studies developed limb ischaemia (Hermiller 2005; Hermiller 2006) (Analysis 2.9).

Femoral artery thrombosis

None of the studies comparing metal clip-based VCDs with manual compression measured femoral artery thrombosis as an outcome.

Technical failure of VCDs

In six studies (Ansel 2006; Deuling 2008; Hermiller 2005; Hermiller 2006; Perlowski 2011; Sun 2009) on a combined total of 1039 participants treated with a metal clip-based VCD, 71 unsuccessful device deployments occurred, leading to a technical failure rate of 6.8%.

Time spent in angiography suite

Time spent in the angiography suite was not measured in any of the studies comparing metal clip VCDs and manual compression.

Length of hospital stay

Length of hospital stay was not measured in any of the studies comparing metal clip VCDs and manual compression.

Patient satisfaction

One study (Hermiller 2006) measured pain on a scale of 0 to 10 and found StarClose to be non-inferior to manual compression. A pain scale of 0 to 3 was reported by 87.3% of StarClose versus 93.3% of

manual compression participants. Pain scales of 8 to 10 were seen in 2.2% of StarCose and 3.3% of compression participants.

Cost of VCD and extrinsic compression

No studies considered the costs of the different treatments.

Suture-based VCD versus manual or mechanical compression

Ten studies (Amine 1999; Carere 2000; Gerckens 1998; Jensen 2008; Martin 2008; Noguchi 2000; Rickli 2002; Sun 2009; Tron 2003; Wetter 2000) measured the effectiveness of a suture-based device versus manual compression.

Time to haemostasis

Eight studies (Amine 1999; Gerckens 1998; Martin 2008; Noguchi 2000; Rickli 2002; Sun 2009; Tron 2003; Wetter 2000) measured time to haemostasis. However, Martin 2008 did not report standard deviations and therefore was not included in the meta-analysis. Pooled analysis of the seven studies using a random-effects model showed that suture-based VCDs were associated with a statistically significant reduction in time to haemostasis when compared with manual compression (MD -14.58 minutes; 95% CI -16.85 to -12.32; participants = 1664; I^2 = 86%; P value < 0.0001) (Analysis 3.1).

Time to mobilisation

Eight studies (Amine 1999; Carere 2000; Gerckens 1998; Martin 2008; Noguchi 2000; Rickli 2002; Sun 2009; Wetter 2000) measured time to mobilisation. Martin 2008 did not report standard deviations and therefore was not included in the meta-analysis. Pooled analysis of the seven studies (Amine 1999; Carere 2000; Gerckens 1998; Noguchi 2000; Rickli 2002; Sun 2009; Wetter 2000) showed significant heterogeneity (I^2 = 98%), and subgroup analysis performed by type of procedure and by brand of VCD showed no differences between groups (Analysis 3.2). Individually, all seven studies (Amine 1999; Carere 2000; Gerckens 1998; Noguchi 2000; Rickli 2002; Sun 2009; Wetter 2000) showed that the suture-based VCD was associated with significantly reduced time to mobilisation when compared with manual compression.

Major adverse event

Only one study (Noguchi 2000) measured mortality and vascular injury requiring repair but reported no cases in either treatment group (Analysis 3.3).

Adverse events

Infection

Three studies (Amine 1999; Gerckens 1998; Noguchi 2000) with 750 participants reported the incidence of infection, describing two cases of infection in the VCD groups compared with one in the manual compression groups (OR 1.66, 95% CI 0.22 to 12.71; P value = 0.63) (Analysis 3.4).

Groin haematoma

Six studies (Amine 1999; Carere 2000; Gerckens 1998; Jensen 2008; Noguchi 2000; Sun 2009) including a total of 1350 participants measured the incidence of groin haematoma and found an incidence of 5.4% (34/633) among suture-based VCD participants compared with 7.2% (52/717) among manual compression participants (OR 0.65, 95% CI 0.41 to 1.02; P value = 0.06) (Analysis 3.5).

Retroperitoneal haemorrhage

One study measured the incidence of retroperitoneal haemorrhage in 63 suture-based VCD (0/63) and 67 manual compression participants (1/67), reporting no association (OR 0.35, 95% CI 0.01 to 8.73) (Analysis 3.6).

Pseudoaneurysm

Six studies (Gerckens 1998; Martin 2008; Noguchi 2000; Rickli 2002; Sun 2009; Wetter 2000) measured this outcome. Pseudoaneurysm occurred in five of 720 (0.7%) suture-based VCD and seven of 807 (0.9%) manual compression participants, leading to an OR of 0.79 (95% CI 0.25 to 2.53; P value = 0.70) (Analysis 3.7).

Arterial dissection

Arterial dissection was not a reported outcome in any of the studies comparing suture-based VCDs with manual compression.

Arteriovenous fistula

Four studies (Amine 1999; Gerckens 1998; Martin 2008; Noguchi 2000) reported on the incidence of arteriovenous fistula. Of the 441 VCD participants, none had an arteriovenous fistula, and one of the 439 (0.2%) manual compression participants experienced this outcome (OR 0.33, 95% CI 0.01 to 8.02; P value = 0.49) (Analysis 3.8).

Embolisation resulting in loss of distal pulse

One study (Noguchi 2000) measured distal embolisation but reported no cases in the VCD or manual compression group (Analysis 3.9).

Deep vein thrombosis

Deep vein thrombosis was not an outcome in any of the studies examining suture-based VCDs and manual compression.

Limb ischaemia

Limb ischaemia was measured in two studies (Gerckens 1998; Martin 2008); the combined incidence was one of 361 (0.3%) VCD and one of 359 (0.3%) manual compression participants, respectively (OR 1.02, 95% CI 0.14 to 7.22; P value = 0.98) (Analysis 3.10).

Femoral artery thrombosis

None of the studies comparing suture-based VCDs with manual compression measured the incidence of femoral artery thrombosis.

Technical failure of VCDs

In 10 studies (Amine 1999; Carere 2000; Gerckens 1998; Jensen 2008; Martin 2008; Noguchi 2000; Rickli 2002; Sun 2009; Tron 2003; Wetter 2000) with a combined total of 843 participants who received a suture-based VCD, 56 unsuccessful device deployments were reported, leading to a technical failure rate of 6.7%.

Time spent in angiography suite

This was not a reported outcome in any of the included studies.

Length of hospital stay

Three studies (Carere 2000; Noguchi 2000; Tron 2003) based on a total of 327 participants reported length of hospital stay. Meta-analysis of the three studies using a random-effects model showed that the suture-based VCD was associated with shorter hospital stay

when compared with manual compression (MD -11.66 hours, 95% CI -20.46 to -2.85; I^2 = 85%; P value = 0.009) (Analysis 3.11).

Patient satisfaction

One study (Martin 2008) measured patient satisfaction in a questionnaire designed to address issues of discomfort and inconvenience at hospital discharge. On a 1 to 4 scale, mean groin discomfort was rated at 1.7 with the PerClose device compared with 2.0 among manual compression participants. Mean scores for the inconvenience of bedrest were 1.8 and 2.0 among VCD and manual compression participants, respectively. Discomfort at the time of sheath removal was 1.6 in both study arms.

Noguchi 2000 measured whether participants would be willing to undergo another procedure with the ProStar device if a repeat intervention was needed. Of 30 participants, 24 (80%) stated that ProStar would be their preferred choice.

Another study (Carere 2000) measured participant perception of the sheath removal procedure by questionnaire 24 hours after the procedure. Participants treated with the ProStar-Plus device reported a more acceptable duration of bedrest when compared with those undergoing manual compression. Although discomfort during the procedure was similar between ProStar-Plus and manual compression groups, discomfort after the procedure was greater among ProStar-Plus participants. Overall, the 42 participants treated with ProStar reported that the procedure was very acceptable compared with 24 participants undergoing haemostasis by manual compression.

Participant comfort was reported on a visual analogue scale (VAS) (0 best to 10 worst) by Rickli 2002. Mean pain at sheath removal was 1.7 (SD 2.2) in PerClose and 2.9 (SD 2.7) in manual compression groups, with back pain reported as 2.8 (SD 2.7) and 4.5 (SD 2.9) and groin pain during follow-up as 3.0 (SD 2.0) and 2.0 (SD 2.2), respectively.

Cost of VCD and extrinsic compression

Carere 2000 reported a total per-patient cost (incremental savings) of $460.21 in the ProStar-Plus group compared with $759.16 in the manual compression group but did not provide standard deviations for these means.

Noguchi 2000 reported that the hospital cost was $300 less in the ProStar group than in the manual compression group ($1310 (SD 248) vs $1613 (SD 460)).

Rickli 2002 measured treatment costs and reported that post-percutaneous coronary intervention (PCI) costs were reduced in the PerClose group (€469 (SD 145) vs €539 (SD 57)) compared with the manual compression group. Additional costs of the PerClose device (€225) were exceeded by savings of ward costs due to earlier discharge (PerClose €178 (SD 132) vs manual compression €481 (SD 55)). PerClose was also associated with less cardiologist time (13.8 (SD 5.4) minutes vs 32.9 (SD 13.9) minutes) and less nursing time (6.9 (SD 3.5) vs 11.5 (SD 7.0) minutes).

Collagen-based VCD versus metal clip-based VCD: AngioSeal versus StarClose

Three studies compared AngioSeal versus StarClose (Deuling 2008; Rastan 2008; Veasey 2008).

Time to haemostasis

None of the studies comparing a collagen-based VCD with a metal clip-based VCD measured time to haemostasis.

Time to mobilisation

Time to mobilisation was not a reported outcome in any of the studies comparing collagen-based and metal clip-based VCDs.

Major adverse event

One study measured mortality and reported no deaths (Rastan 2008). Two studies (Deuling 2008; Rastan 2008) measured vascular injury requiring repair and found no differences between the two treatment groups (OR 0.33, 95% CI 0.01 to 8.22; P value = 0.50) (Analysis 4.1).

Adverse events

Infection

No cases of infection occurred in two studies reporting this outcome (Deuling 2008; Veasey 2008) among a combined total of 701 participants (Analysis 4.2).

Groin haematoma

Two studies (Deuling 2008; Rastan 2008) compared AngioSeal and StarClose devices among a combined total of 871 participants. Meta-analysis using a random-effects model showed no differences in the incidence of groin haematoma between the two devices (OR 0.84, 95% CI 0.43 to 1.65; P value = 0.61). The incidence was 3.9% (17/435) and 4.6% (20/436) among collagen-based and metal clip-based VCD participants, respectively (Analysis 4.3).

Retroperitoneal haemorrhage

Only one study (Veasey 2008) measured the incidence of retroperitoneal haemorrhage and reported no cases in the collagen VCD (n = 208) nor metal clip VCD (n = 193) arms (Analysis 4.4).

Pseudoaneurysm

Pseudoaneurysm was measured in three studies (Deuling 2008; Rastan 2008; Veasey 2008). The incidence was four of 643 (0.6%) among collagen-based VCD and eight of 629 (1.3%) among metal clip-based VCD participants (OR 0.50, 95% CI 0.15 to 1.66; P value = 0.26) (Analysis 4.5).

Arterial dissection

Arterial dissection was not reported in any of the included studies.

Arteriovenous fistula

Only one study (Rastan 2008) measured arteriovenous fistula. Rastan 2008 reported one case in 285 collagen-based VCD participants but no cases in 286 metal clip-based VCD participants (OR 3.02, 95% CI 0.12 to 74.47) (Analysis 4.6).

Embolisation resulting in loss of distal pulse

This was not measured in any of the included studies.

Deep vein thrombosis

Deep vein thrombosis was not reported in any of the studies comparing collagen-based and clip-based VCDs.

Limb ischaemia

One study (Veasey 2008) measured limb ischaemia but reported no cases in either treatment group (Analysis 4.7).

Femoral artery thrombosis

Femoral artery thrombosis was not reported in any of the studies comparing collagen-based with clip-based VCDs.

Technical failure of VCDs

Three studies (Deuling 2008; Rastan 2008; Veasey 2008) reported the technical failure of AngioSeal versus StarClose devices. The device failed in 22 of 643 (3.4%) AngioSeal participants compared with 53 of 629 (8.4%) StarClose participants, suggesting that the collagen-based device has a significantly lower failure rate than the StarClose device (OR 0.38, 95% CI 0.23 to 0.64; P value = 0.0003) (Analysis 4.8).

Time spent in angiography suite

Time spent in the angiography suite was not a reported outcome in any of the included studies.

Length of hospital stay

Length of hospital stay was not measured in any of the studies comparing collagen-based and metal clip-based VCDs.

Patient satisfaction

No study compared patient satisfaction with collagen-based versus metal clip-based VCDs.

Cost of VCD and extrinsic compression

Cost of the device was not reported in any of the included studies.

Collagen-based VCD versus suture-based VCD

Five studies (Hattab 2012; Jensen 2008; Kalsch 2008; Martin 2008; Park 2005) compared a collagen-based VCD with a suture-based VCD.

Time to haemostasis

Martin 2008 measured time to haemostasis among participants treated with AngioSeal and PerClose ProGlide. Although investigators reported the mean time to haemostasis, they did not provide standard deviations for the mean; therefore, it was not possible to perform statistical analysis on mean differences. We attempted to obtain these data, but study authors did not respond to our request. Martin 2008 did report that AngioSeal was associated with significantly reduced time to haemostasis compared with PerClose (P value < 0.01).

Time to mobilisation

Martin 2008 also reported mean time to mobilisation but did not present standard deviations; therefore, statistical tests on the mean difference could not be performed. However, study authors reported that AngioSeal was associated with reduced time to mobilisation when compared with the PerClose device (P value < 0.01).

Major adverse event

None of the five studies measured death or vascular injury requiring repair (Hattab 2012; Jensen 2008; Kalsch 2008; Martin 2008; Park 2005).

Adverse events

Infection

Kalsch 2008 measured the incidence of infection in 212 AngioSeal and 154 PerClose participants, reporting no cases of infection in either treatment group (Analysis 5.1).

Groin haematoma

Three studies (Hattab 2012; Jensen 2008; Kalsch 2008) measured the incidence of groin haematoma in a combined total of 510 participants. . Haematoma occurred in 34 of 284 (12.0%) AngioSeal participants compared with 22 of 226 (9.7%) ExoSeal participants, resulting in an OR of 1.26 (95% CI 0.71 to 2.22; P value = 0.43); therefore, neither AngioSeal nor ExoSeal was superior in the prevention of haematoma (Analysis 5.2).

Retroperitoneal haemorrhage

Martin 2008 reported one case of retroperitoneal haemorrhage in 70 AngioSeal participants but no cases in 63 PerClose ProGlide participants (OR 2.74, 95% CI 0.11 to 68.51; P value = 0.54) (Analysis 5.3).

Pseudoaneurysm

Martin 2008 reported no cases of pseudoaneurysm in 70 AngioSeal participants but one case in 63 PerClose ProGlide participants (OR 0.30, 95% CI 0.01 to 7.39; P value = 0.46) (Analysis 5.4).

Arterial dissection

This outcome was not measured in any of the studies included in this review.

Arteriovenous fistula

No cases of arteriovenous fistula were reported among participants treated with AngioSeal (n = 70) nor PerClose ProGlide (n = 63) in the study by Martin 2008 (Analysis 5.5).

Embolisation resulting in loss of distal pulse

Embolisation was not reported as an outcome in any study.

Deep vein thrombosis

Deep vein thrombosis was not measured in any of the studies comparing collagen-based and suture-based VCDs.

Limb ischaemia

None of the studies comparing collagen-based and suture-based VCDs reported limb ischaemia.

Femoral artery thrombosis

Femoral artery thrombosis was not a reported outcome in any study.

Technical failure of VCDs

Three studies (Hattab 2012; Jensen 2008; Kalsch 2008) compared the technical failure of a collagen-based VCD versus a suture-based VCD. Two studies (Jensen 2008; Kalsch 2008) compared AngioSeal

with PerClose, and Hattab 2012 compared ExoSeal with ProGlide. Meta-analyses showed no differences in the technical failure of VCDs (OR 0.24, 95% CI 0.08 to 0.69; I^2 = 74%; P value = 0.008) (Analysis 5.6).

Time spent in angiography suite

Time spent in the angiography suite was not an outcome in any of the included studies.

Length of hospital stay

Length of hospital stay was not measured in any studies comparing collagen-based and suture-based VCDs.

Patient satisfaction

No study compared patient satisfaction with collagen-based versus suture-based VCDs.

Cost of VCD and extrinsic compression

Cost of treatment was not measured in any of the studies comparing collagen-based and suture-based VCDs.

Metal clip-based VCD versus suture-based VCD: StarClose versus PerClose

One study (Sun 2009) compared the metal clip-based StarClose with the suture-based PerClose.

Time to haemostasis

One study (Sun 2009) on 469 participants tested a metal clip-based VCD (StarClose) against a suture-based VCD (PerClose). Data on time to haemostasis were presented separately by type of procedure. For the purposes of the review, the mean and standard deviations for this outcome were combined according to the formula given in Table 7.7.a in Chapter 7 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). This study found that StarClose was associated with shorter time to haemostasis than PerClose (MD -2.24 minutes, 95% CI -2.54 to -1.94; P value < 0.00001) (Analysis 6.1).

Time to mobilisation

Sun 2009 also presented data on time to mobilisation separately according to the type of procedure. As above, the mean and standard deviations for this outcome were combined according to the formula given in Table 7.7.a in Chapter 7 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). This study found that the StarClose device was associated with a reduction in the mean time to mobilisation (MD -0.30 hours, 95% CI -0.59 to -0.01; P value = 0.05) (Analysis 6.2).

Major adverse event

Sun 2009 did not report mortality nor vascular injury requiring repair.

Adverse events

Infection

Sun 2009 did not report infection.

Groin haematoma

Sun 2009 measured the incidence of haematoma at 0.3% (1/286) in StarClose participants and 1.6% (3/183) in PerClose participants, leading to an OR of 0.21 (95% CI 0.02 to 2.04; P value = 0.18) (Analysis 6.3).

Retroperitoneal haemorrhage

Sun 2009 did not report retroperitoneal haemorrhage.

Pseudoaneurysm

In the Sun 2009 study, pseudoaneurysm did not occur in any of the StarClose participants, and one case was reported among the 183 (0.5%) PerClose participants (OR 0.21, 95% CI 0.01 to 5.24; P value = 0.34) (Analysis 6.4).

Arterial dissection

This outcome was not measured in the Sun 2009 study.

Arteriovenous fistula

Sun 2009 did not report arteriovenous fistula.

Embolisation resulting in loss of distal pulse

Embolisation was not reported as an outcome in the Sun 2009 study.

Deep vein thrombosis

Sun 2009 did not report deep vein thrombosis.

Limb ischaemia

Sun 2009 did not report limb ischaemia.

Femoral artery thrombosis

Sun 2009 did not report femoral artery thrombosis.

Technical failure of VCDs

In the Sun 2009 study, the StarClose device demonstrated fewer incidences of technical failure compared with the PerClose device (OR 0.34, 95% CI 0.12 to 0.92; P value = 0.03) (Analysis 6.5)..

Time spent in angiography suite

Time spent in the angiography suite was not reported as an outcome in the Sun 2009 study.

Length of hospital stay

Sun 2009 did not measure length of hospital stay.

Patient satisfaction

Sun 2009 did not measure patient satisfaction.

Cost of VCD and extrinsic compression

Cost of treatment was not measured in the Sun 2009 study.

Disc-based VCD versus suture-based VCD: Boomerang versus PerClose

Chen 2013 compared a disc-based device (Boomerang) with a suture-based device (PerClose).

Time to haemostasis

Chen 2013 measured time to haemostasis in participants treated with the Boomerang and PerClose devices. The Boomerang device was associated with significantly longer time to haemostasis than

the PerClose device (MD 32.05 minutes, 95% CI 29.09 to 35.01; P value < 0.00001) (Analysis 7.1).

Time to mobilisation

Chen 2013 also reported mean time to mobilisation but found no difference between the two devices (MD -0.04 hours, 95% CI -0.14 to 0.06 hours; P value = 0.41) (Analysis 7.2).

Major adverse event

Chen 2013 did not report mortality nor vascular injury requiring repair.

Adverse events

Infection

Chen 2013 did not report infection.

Groin haematoma

Chen 2013 found no difference in the incidence of groin haematoma between the Boomerang and PerClose devices (OR 10.36, 95% CI 0.53 to 201.45; P value = 0.12) (Analysis 7.3).

Retroperitoneal haemorrhage

Chen 2013 did not report retroperitoneal haemorrhage.

Pseudoaneurysm

Chen 2013 did not report pseudoaneurysm.

Arterial dissection

This outcome was not measured in the Chen 2013 study.

Arteriovenous fistula

Chen 2013 did not report arteriovenous fistula.

Embolisation resulting in loss of distal pulse

Embolisation was not reported as an outcome in the Chen 2013 study.

Deep vein thrombosis

Chen 2013 did not report deep vein thrombosis.

Limb ischaemia

Chen 2013 did not report limb ischaemia.

Femoral artery thrombosis

Chen 2013 did not report femoral artery thrombosis.

Technical failure of VCDs

Chen 2013 found no difference in the rate of technical failure between the Boomerang and PerClose devices (OR 2.07, 95% CI 0.18 to 24.15; P value = 0.56) (Analysis 7.4).

Time spent in angiography suite

Time spent in the angiography suite was not reported as an outcome in the Chen 2013 study.

Length of hospital stay

Chen 2013 did not measure length of hospital stay.

Patient satisfaction

Chen 2013 measured pain on a scale of 0 to 10, with 0 representing no pain and 10 representing the worst possible pain. Results indicated that participants treated with the Boomerang device reported significantly lower pain levels (mean 1.10, SD 1.71) compared with participants treated with PerClose (mean 6.40, SD 2.92).

Cost of VCD and extrinsic compression

Cost of treatment was not measured in the Chen 2013 study.

Collagen-based VCD versus collagen-based VCD: AngioSeal versus VasoSeal

Two studies (Michalis 2002; Shammas 2002) compared the collagen-based devices AngioSeal and VasoSeal.

Time to haemostasis

Both studies (Michalis 2002; Shammas 2002) presented time to haemostasis separately for diagnostic and interventional procedures. When these studies were combined in a meta-analysis, considerable heterogeneity was evident (I^2 = 90%). When AngioSeal was compared with VasoSeal, VasoSeal was associated with shorter time to haemostasis for interventional procedures (MD 8.63, 95% CI 1.46 to 15.80; P value = 0.02; I^2 = 86%) but not for diagnostic procedures (MD 6.68, 95% CI -2.31 to 15.67; P value = 0.15; I^2 = 96%) (Analysis 8.1).

Time to mobilisation

Both studies (Michalis 2002; Shammas 2002) compared the time to mobilisation between AngioSeal and VasoSeal devices. AngioSeal was not associated with a difference in time to mobilisation compared with VasoSeal, for both diagnostic (MD 0.01 hours, 95% CI -1.04 to 1.06; P value = 0.98; I^2 = 90%) and interventional procedures (MD 0.45, 95% CI -1.91 to 2.82; P value = 0.71; I^2 = 74%) (Analysis 8.2).

Major adverse event

Shammas 2002 found no cases of mortality nor vascular injury requiring repair (Analysis 8.3). Michalis 2002 did not measure mortality nor vascular injury requiring repair.

Adverse events

Infection

Shammas 2002 reported no cases of infection (Analysis 8.4). Michalis 2002 did not measure infection.

Groin haematoma

Both studies measured groin haematoma between collagen-based devices (Michalis 2002; Shammas 2002). Shammas 2002 found no haematoma, but the incidence of haematoma in Michalis 2002led to an OR of 0.49 (95% CI 0.16 to 1.47; P = 0.20) (Analysis 8.5).

Retroperitoneal haemorrhage

Both studies (Michalis 2002; Shammas 2002) measured retroperitoneal haemorrhage as an outcome. They reported no cases in 367 AngioSeal-treated participants and only one case in 353 VasoSeal-treated participants, leading to an OR of 0.36 (95% CI 0.01 to 9.09; P value = 0.54) (Analysis 8.6).

Pseudoaneurysm

Shammas 2002 reported just one case of pseudoaneurysm (OR 0.31, 95% CI 0.01 to 7.71; P value = 0.47) (Analysis 8.7). Michalis 2002 did not measure pseudoaneurysm.

Arterial dissection

Arterial dissection was not reported in the Michalis 2002 and Shammas 2002 studies.

Arteriovenous fistula

Shammas 2002 reported no cases of arteriovenous fistula (Analysis 8.8). Michalis 2002 did not measure arteriovenous fistula.

Embolisation resulting in loss of distal pulse

The studies by Michalis 2002 and Shammas 2002 did not report on embolisation resulting in loss of distal pulse.

Deep vein thrombosis

Deep vein thrombosis was not an outcome of the Michalis 2002 and Shammas 2002 studies.

Limb ischaemia

Limb ischaemia was not an outcome of the Michalis 2002 and Shammas 2002 studies.

Femoral artery thrombosis

Femoral artery thrombosis was not an outcome of the Michalis 2002 and Shammas 2002 studies.

Technical failure of VCDs

Michalis 2002 showed that the device failed in 19 of 290 AngioSeal participants compared with 26 of 280 VasoSeal participants, leading to an OR of 0.68 (95% CI 0.37 to 1.26; P value = 0.22) (Analysis 8.9). Shammas 2002 did not report on the technical failure of the VCD.

Time spent in angiography suite

Neither Michalis 2002 nor Shammas 2002 reported on time spent in the angiography suite.

Length of hospital stay

Length of hospital stay was not an outcome of the Michalis 2002 and Shammas 2002 studies.

Patient satisfaction

Patient satisfaction was not an outcome of the Michalis 2002 and Shammas 2002 studies.

Cost of VCD and extrinsic compression

Device cost was not assessed in the two included studies (Michalis 2002; Shammas 2002).

Collagen-based VCD versus collagen-based VCD: AngioSeal versus Mynx

One study compared AngioSeal versus Mynx (Fargen 2011).

Time to haemostasis

Fargen 2011 did not measure time to haemostasis as an outcome.

Time to mobilisation

Fargen 2011 did not measure time to mobilisation as an outcome.

Major adverse event

Fargen 2011 did not measure mortality and found no cases of vascular injury requiring repair (Analysis 9.1).

Adverse events

Infection

Fargen 2011 found no cases of infection (Analysis 9.2).

Groin haematoma

Fargen 2011 found no cases of groin haematoma (Analysis 9.3).

Retroperitoneal haemorrhage

Retroperitoneal haemorrhage was not reported as an outcome of the Fargen 2011 study.

Pseudoaneurysm

Pseudoaneurysm was not reported as an outcome of the Fargen 2011 study.

Arterial dissection

Arterial dissection was not reported as an outcome of the Fargen 2011 study.

Arteriovenous fistula

Arteriovenous fistula was not reported as an outcome of the Fargen 2011 study.

Embolisation resulting in loss of distal pulse

Fargen 2011 did not report on embolisation resulting in loss of distal pulse.

Deep vein thrombosis

Deep vein thrombosis was not reported as an outcome of the Fargen 2011 study.

Limb ischaemia

Limb ischaemia was not reported as an outcome of the Fargen 2011 study.

Femoral artery thrombosis

Femoral artery thrombosis was not reported as an outcome of the Fargen 2011 study.

Technical failure of VCDs

Fargen 2011 did not report technical failure of the VCDs.

Time spent in angiography suite

Fargen 2011 did not report on time spent in the angiography suite.

Length of hospital stay

Length of hospital stay was not reported as an outcome of the Fargen 2011 study.

Patient satisfaction

Fargen 2011 measured pain at closure and pain increase from baseline to closure, reporting that 88% of AngioSeal participants reported closure as the most painful part compared with 34% of Mynx participants.

Cost of VCD and extrinsic compression

Device cost was not assessed in the Fargen 2011 study.

Collagen-based VCD versus collagen-based VCD: AngioSeal versus Duett

Michalis 2002 compared AngioSeal with Duett.

Time to haemostasis

Data regarding time to haemostasis were presented separately for diagnostic and interventional procedures. The Duett device was associated with shorter time to haemostasis when compared with AngioSeal in both diagnostic (MD 10.60 minutes, 95% CI 9.74 to 11.46) and interventional procedures (MD 12.00 minutes, 95% CI 9.57 to 14.43) (Analysis 10.1).

Time to mobilisation

Michalis 2002 showed that AngioSeal was associated with shorter time to mobilisation when compared with the Duett device in diagnostic procedures (MD -0.40 hours, 95% CI -0.51 to -0.29). However, no difference was noted when AngioSeal was compared with the Duett device in interventional procedures (MD -0.32 hours, 95% CI -0.71 to 0.07) (Analysis 10.2).

Major adverse event

Michalis 2002 did not measure mortality nor vascular injury requiring repair.

Adverse events

Infection

Michalis 2002 did not measure infection as an outcome.

Groin haematoma

Michalis 2002 reported the incidence of haematoma as 1.7% (5/290) in AngioSeal participants compared with 1.8% (5/281) in Duett participants (OR 0.97, 95% CI 0.28 to 3.38; P value = 0.97) (Analysis 10.3).

Retroperitoneal haemorrhage

Michalis 2002 measured retroperitoneal haemorrhage as an outcome, reporting no cases in AngioSeal nor Duett participants (Analysis 10.4).

Pseudoaneurysm

Michalis 2002 did not measure pseudoaneurysm as an outcome.

Arterial dissection

Arterial dissection was not reported as an outcome in the Michalis 2002 study.

Arteriovenous fistula

Michalis 2002 did not measure arteriovenous fistula as an outcome.

Embolisation resulting in loss of distal pulse

Michalis 2002 did not report on embolisation resulting in loss of distal pulse.

Deep vein thrombosis

Deep vein thrombosis was not reported as an outcome of the Michalis 2002 study.

Limb ischaemia

Limb ischaemia was not reported as an outcome of the Michalis 2002 study.

Femoral artery thrombosis

Femoral artery thrombosis was not reported as an outcome of the Michalis 2002 study.

Technical failure of VCDs

Michalis 2002 showed that the device failed in 19 of 290 AngioSeal participants compared with 32 of 281 Duett participants, leading to an OR of 0.54 (95% CI 0.30 to 0.99; P value = 0.04) (Analysis 10.5).

Time spent in angiography suite

Michalis 2002 did not report on time spent in the angiography suite.

Length of hospital stay

Length of hospital stay was not reported as an outcome of the Michalis 2002 study.

Patient satisfaction

Patient satisfaction was not reported as an outcome of the Michalis 2002 study.

Costs of VCD and extrinsic compression

Device cost was not assessed in the included study (Michalis 2002).

Collagen-based VCD versus collagen-based VCD: VasoSeal versus Duett

One study compared VasoSeal and Duett (Michalis 2002).

Time to haemostasis

Michalis 2002 presented data regarding time to haemostasis separately for diagnostic and interventional procedures. No difference was found when VasoSeal was compared with the Duett device in diagnostic (MD -0.50 minutes, 95% CI -1.11 to 0.11) nor interventional (MD -1.00 minutes, 95% CI -3.15 to 1.15) procedures (Analysis 11.1).

Time to mobilisation

Michalis 2002 showed that when VasoSeal was compared with the Duett device, no differences in time to mobilisation were noted for diagnostic (MD 0.08 hours, 95% CI 0.05 to 0.21) nor interventional procedures (MD 0.16 hours, 95% CI -0.17 to 0.49) (Analysis 11.2).

Major adverse event

Michalis 2002 did not measure mortality nor vascular injury requiring repair.

Adverse events

Infection

Michalis 2002 did not measure infection as an outcome.

Groin haematoma

Michalis 2002 found no difference in the incidence of haematoma when the VasoSeal was compared with the Duett device (OR 2.00, 95% CI 0.67 to 5.95; P value = 0.21) (Analysis 11.3).

Retroperitoneal haemorrhage

Michalis 2002 reported only one case of retroperitoneal haemorrhage in 280 VasoSeal participants and no cases in Duett participants (OR 2.77, 95% CI 0.11 to 69.59; P value = 0.54) (Analysis 11.4).

Pseudoaneurysm

Michalis 2002 did not measure pseudoaneurysm as an outcome.

Arterial dissection

Arterial dissection was not reported in the Michalis 2002 study.

Arteriovenous fistula

Michalis 2002 did not measure arteriovenous fistula as an outcome.

Embolisation resulting in loss of distal pulse

Michalis 2002 did not report on embolisation resulting in loss of distal pulse.

Deep vein thrombosis

Deep vein thrombosis was not reported as an outcome of the Michalis 2002 study.

Limb ischaemia

Limb ischaemia was not reported as an outcome of the Michalis 2002 study.

Femoral artery thrombosis

Femoral artery thrombosis was not reported as an outcome of the Michalis 2002 study.

Technical failure of VCDs

Michalis 2002 showed that the Duett device failed in 32 of 281 participants, leading to an OR of 0.80 (95% CI 0.46 to 1.30; P value = 0.42) when compared with 26/280 failures with the VasoSeal device (Analysis 11.5).

Time spent in angiography suite

Michalis 2002 did not report on time spent in the angiography suite.

Length of hospital stay

Length of hospital stay was not reported as an outcome of the Michalis 2002 study.

Patient satisfaction

Patient satisfaction was not reported as an outcome of the Michalis 2002 study.

Cost of VCD and extrinsic compression

Device cost was not assessed in the Michalis 2002 study.

Collagen-based VCD versus collagen-based VCD: FemoSeal versus ExoSeal

One study compared FemoSeal and ExoSeal (Schulz-Schüpke 2014).

Time to haemostasis

Schulz-Schüpke 2014 presented time to haemostasis as a median and as an interquartile range. Time to haemostasis was 0.5 minute (IQR 0.5 minute to 1 minute) in the group treated with FemoSeal and 2 minutes (IQR 1 minute to 2 minutes) in the group treated with ExoSeal.

Time to mobilisation

Schulz-Schüpke 2014 did not measure time to mobilisation.

Major adverse event

Schulz-Schüpke 2014 did not report on mortality and reported no cases of vascular injury requiring repair in either group (Analysis 12.1).

Adverse events

Infection

Schulz-Schüpke 2014 found no cases of infection in the group treated with ExoSeal and only one case in the group treated with FemoSeal (OR 3.00, 95% CI 0.12 to 73.60; P value = 0.50) (Analysis 12.2).

Groin haematoma

Schulz-Schüpke 2014 measured the incidence of groin haematoma as 4.3% (65/1509) and 5.3% (80/1506) in the two groups, respectively (OR 0.80, 95% CI 0.57 to 1.12; P value = 0.20) (Analysis 12.3).

Retroperitoneal haemorrhage

Schulz-Schüpke 2014 did not report on retroperitoneal haemorrhage.

Pseudoaneurysm

Schulz-Schüpke 2014 reported that the incidence of pseudoaneurysm was 1.5% (22/1509) in FemoSeal and 2.1% (31/1506) in ExoSeal participants (OR 0.70, 95% CI 0.41 to 1.22; P value = 0.21) (Analysis 12.4).

Arterial dissection

Arterial dissection was not reported in the Schulz-Schüpke 2014 study.

Arteriovenous fistula

Schulz-Schüpke 2014 reported the incidence of arteriovenous fistula as 0.3% (4/1509) in FemoSeal and 0.5% (8/1506) in ExoSeal participants, respectively (OR 0.50, 95% CI 0.15 to 1.66; P value = 0.26) (Analysis 12.5).

Embolisation resulting in loss of distal pulse

Schulz-Schüpke 2014 did not report on embolisation resulting in loss of distal pulse.

Deep vein thrombosis

Deep vein thrombosis was not reported as an outcome of the Schulz-Schüpke 2014 study.

Limb ischaemia

Schulz-Schüpke 2014 found no cases of limb ischaemia in the FemoSeal nor the ExoSeal group (Analysis 12.6).

Femoral artery thrombosis

Femoral artery thrombosis was not reported as an outcome of the Schulz-Schüpke 2014 study.

Technical failure of VCDs

Schulz-Schüpke 2014 reported that the FemoSeal device failed to close in 5.3% (80/1509) of participants compared with 12.2% (184/1506) of ExoSeal participants, leading to an OR of 0.40 (95% CI 0.31 to 0.53; P value < 0.00001) (Analysis 12.7).

Time spent in angiography suite

Schulz-Schüpke 2014 did not report on time spent in the angiography suite.

Length of hospital stay

Length of hospital stay was not reported as an outcome of the Schulz-Schüpke 2014 study.

Patient satisfaction

Patient satisfaction was not an outcome of the Schulz-Schüpke 2014 study.

Cost of VCD and extrinsic compression

Device cost was not assessed in the included study (Schulz-Schüpke 2014).

Haemostasis after percutaneous EVAR (sheath size ≥ 10 Fr)

One study compared PerClose ProGlide with ProStar XL in participants undergoing percutaneous EVAR (Nelson 2014).

Time to haemostasis

Nelson 2014 measured time to haemostasis between the PerClose ProGlide and ProStar XL devices in participants undergoing percutaneous EVAR. They found no differences between the two devices (MD -3.20 minutes, 95% CI -10.23 to 3.83; P value = 0.37) (Analysis 13.1).

Time to mobilisation

Nelson 2014 also measured time to mobilisation between the PerClose ProGlide and ProStar XL devices in participants undergoing percutaneous EVAR. They found no differences between the two devices (MD 1.00 hour, 95% CI -2.20 to 4.20; P value = 0.54) (Analysis 13.2).

Major adverse event

Nelson 2014 also measured major adverse events between the PerClose ProGlide and ProStar XL devices in participants undergoing percutaneous EVAR. They found no differences in the effectiveness of the devices in preventing death (OR 0.33, 95% CI 0.01 to 8.38; P value = 0.50) nor vascular injury requiring repair (OR 0.33, 95% CI 0.03 to 3.25; P value = 0.34) (Analysis 13.3).

Adverse events

Infection

Nelson 2014 measured infection between the PerClose ProGlide and ProStar XL devices in participants undergoing percutaneous EVAR but found no cases in either group (Analysis 13.4).

Groin haematoma

Nelson 2014 measured groin haematoma between the PerClose ProGlide and ProStar XL devices in participants undergoing percutaneous EVAR but found no cases in either group (Analysis 13.5).

Retroperitoneal haemorrhage

Nelson 2014 did not measure retroperitoneal haemorrhage as an outcome.

Pseudoaneurysm

Nelson 2014 did not measure pseudoaneurysm as an outcome.

Arterial dissection

Arterial dissection was not reported in the Nelson 2014 study.

Arteriovenous fistula

Nelson 2014 measured arteriovenous fistula between the PerClose ProGlide and ProStar XL devices in participants undergoing percutaneous EVAR but found no cases in either group (Analysis 13.6).

Embolisation resulting in loss of distal pulse

Nelson 2014 did not report on embolisation resulting in loss of distal pulse.

Deep vein thrombosis

Nelson 2014 measured deep vein thrombosis between the PerClose ProGlide and ProStar XL devices in participants undergoing percutaneous EVAR and found no differences between the two devices (OR 2.08, 95% CI 0.18 to 23.73; P value = 0.55) (Analysis 13.7).

Limb ischaemia

Nelson 2014 measured limb ischaemia as an outcome but found no differences between the PerClose ProGlide and ProStar XL devices (OR 2.08, 95% CI 0.18 to 23.73; P value = 0.55) (Analysis 13.8).

Femoral artery thrombosis

Nelson 2014 did not measure femoral artery thrombosis as an outcome.

Technical failure of VCDs

Nelson 2014 measured technical failure between the PerClose ProGlide and ProStar XL devices in participants undergoing percutaneous EVAR but found no cases in either group (Analysis 13.9).

Time spent in angiography suite

Nelson 2014 did not measure time spent in angiography suite as an outcome.

Length of hospital stay

Nelson 2014 measured length of hospital stay between the PerClose ProGlide and ProStar XL devices in participants undergoing percutaneous EVAR but found no differences (MD -0.10 hours, 95% CI -0.41 to 0.21; P value = 0.53) (Analysis 13.10).

Patient satisfaction

Patient satisfaction was not reported as an outcome of the Nelson 2014 study.

Cost of VCD and extrinsic compression

Device cost was not assessed in the included study (Nelson 2014).

Haemostasis after EVAR with open exposure of CFA (sheath size ≥ 10 Fr)

One study compared the PerClose ProGlide and ProStar XL devices with surgical suture-based closure in participants undergoing open femoral exposure of the CFA (Nelson 2014).

Time to haemostasis

Nelson 2014 measured time to haemostasis between suture-based devices and surgically mediated closure in participants undergoing EVAR. The suture-based device was associated with shorter time to haemostasis than surgical closure (MD -11.58 minutes, 95% CI -18.85 to -4.31; 101 participants; P value = 0.002) (Analysis 14.1).

Time to mobilisation

Nelson 2014 measured time to mobilisation between suture-based devices and surgically mediated closure in participants undergoing EVAR but found no differences between the two groups (MD: -2.50 hours, 95% CI -7.21 to 2.21) (Analysis 14.2).

Major adverse event

Nelson 2014 measured major adverse events between suture-based devices and surgically mediated closure in participants undergoing EVAR and found no differences between the suture-based device and surgical closure in preventing death (OR 1.51, 95% CI 0.66 to 37.67; P value = 0.80) nor in vascular injury requiring repair (OR 2.02, 95% CI 0.22 to 18.57; P value = 0.53) (Analysis 14.3).

Adverse events

Infection

Nelson 2014 measured infection between suture-based devices and surgically mediated closure in participants undergoing EVAR but found no cases in either group (Analysis 14.4).

Groin haematoma

Nelson 2014 measured groin haematoma between suture-based devices and surgically mediated closure in participants undergoing EVAR but found no cases in either group (Analysis 14.5).

Retroperitoneal haemorrhage

Nelson 2014 did not measure retroperitoneal haemorrhage as an outcome.

Pseudoaneurysm

Nelson 2014 did not measure pseudoaneurysm as an outcome.

Arterial dissection

Arterial dissection was not reported in the Nelson 2014 study.

Arteriovenous fistula

Nelson 2014 measured arteriovenous fistula between suture-based devices and surgically mediated closure in participants undergoing EVAR but found no cases in either group (Analysis 14.6).

Embolisation resulting in loss of distal pulse

Nelson 2014 did not report on embolisation resulting in loss of distal pulse.

Deep vein thrombosis

Nelson 2014 measured deep vein thrombosis between suture-based devices and surgically mediated closure in participants undergoing EVAR and found no differences between the two devices (OR 0.48, 95% CI 0.09 to 2.47; P value = 0.38) (Analysis 14.7).

Limb ischaemia

Nelson 2014 measured limb ischaemia between suture-based devices and surgically mediated closure in participants undergoing EVAR but found no differences between the two groups (OR 0.73, 95% CI 0.12 to 4.54; P value = 0.74) (Analysis 14.8).

Femoral artery thrombosis

Nelson 2014 did not measure femoral artery thrombosis as an outcome.

Time spent in angiography suite

Nelson 2014 did not measure time spent in angiography suite as an outcome.

Length of hospital stay

Length of hospital stay was measured in the Nelson 2014 study, which reported no differences between participants treated with a suture-based device and those who underwent surgical closure following EVAR (MD -10.80 hours, 95% CI -27.20 to 5.60; P value = 0.20).

Patient satisfaction

Patient satisfaction was not an outcome of the Nelson 2014 study.

Cost of VCD and extrinsic compression

Device cost was not assessed in the included study (Nelson 2014).

Subgroup analysis

The first planned subgroup analysis included looking at studies using smaller sheath sizes (5 to 6 Fr) compared with those with larger sheath sizes in participants undergoing EVAR procedures. However, all studies included in this review used sheath size 9 Fr or smaller. As only one study compared the effectiveness of VCDs in participants undergoing EVAR procedures, it was not possible to complete this subgroup analysis.

A second planned subgroup analysis was conducted to compare studies according to whether they used antegrade or retrograde puncture. However, very few studies reported on the direction of puncture used in the procedure; therefore, it was not feasible to conduct this subgroup analysis.

DISCUSSION

Summary of main results

Time to haemostasis

Meta-analysis indicated that collagen-based or plug-based, metal clip-based and suture-based vascular closure devices (VCDs) were all associated with reduced time to haemostasis when compared with manual or mechanical compression. However, considerable heterogeneity could not be explained; therefore, results of the meta-analysis may not be meaningful. Every included study used a strict definition of time to haemostasis, defined as the time from sheath removal to complete cessation of bleeding and absence of palpable haematoma in minutes. Most studies (Ansel 2006; Brachmann 1998; Castañeda 2003; Gerckens 1998; Gwechenberger 1997; Hermiller 2005; Hermiller 2006; Kussmaul 1995; Magosaki 1999; Martin 2008; Perlowski 2011; Reddy 2004; Rickli 2002; Sanborn 1993; SEAL Trial Study Team; Seidelin 1997; Silber 1998; Sun 2009; Tron 2003; Ward 1998; Wetter 2000; Wong 2009; Yadav 2003) measured time to haemostasis in minutes. One study (Juergens 2004) measured time to haemostasis in hours, and another study (Diaz 2001) measured time to haemostasis in seconds. For the purposes of the review, data from Diaz 2001 and Juergens 2004 were converted to minutes. Seven studies (Gerckens 1998; Kussmaul 1995; Sanborn 1993; SEAL Trial Study Team; Sun 2009; Wong 2009; Yadav 2003) presented time to haemostasis for the entire study population and also separately for the subgroup of participants who underwent diagnostic and interventional procedures. Seven studies could not be used in the meta-analysis because standard deviations were not reported (Doneaux 2001; Martin 2008; Ward 1998; Yadav 2003) or because median and interquartile range were presented (Holm 2014; Schulz-Schüpke 2014; SEAL Trial Study Team).

Evidence on the effectiveness of one VCD compared with another VCD is lacking. No study compared time to haemostasis between collagen-based and metal clip-based VCDs. Only one study (Sun 2009) compared one metal clip-based VCD (StarClose) with a suture-based VCD (PerClose) and found that StarClose was associated with shorter time to haemostasis. However, this study was based on 469 participants, and the quality of the study could not be assessed because reporting of methods was insufficient. Two studies (Michalis 2002; Shammas 2002) compared the effectiveness of two collagen devices: AngioSeal and VasoSeal. In Michalis 2002, VasoSeal was associated with shorter time to haemostasis for both diagnostic and interventional procedures. However, when Shammas 2002 was added to the meta-analysis, no difference in time to haemostasis was noted overall between the two devices. Michalis 2002 also provided a third treatment arm with the Duett device. In this study, VasoSeal was associated with shorter time to haemostasis than AngioSeal for both diagnostic and interventional procedures. Similarly the Duett device was associated with shorter time to haemostasis when compared with AngioSeal in both diagnostic and interventional procedures. However, no difference was found in either type of procedure when VasoSeal was compared with the Duett device. Martin 2008 reported that AngioSeal was associated with significantly reduced time to haemostasis compared with PerClose. Nelson 2014 compared ProStar and ProGlide devices in participants undergoing percutaneous EVAR but found no differences in time to haemostasis between the two devices. The same study (Nelson 2014) compared the ProStar and ProGlide devices with surgical suture-based closure following EVAR and found reduced time to haemostasis for the VCDs.

Time to mobilisation

Meta-analysis showed that collagen-based, metal clip-based and suture-based VCDs were all associated with reduced time to mobilisation when compared with manual/mechanical compression. However, considerable heterogeneity could not be explained; therefore, results of the meta-analysis may not be meaningful.

Some studies (Ansel 2006; Brachmann 1998; Carere 2000; Castañeda 2003; Gerckens 1998; Jensen 2008; Martin 2008; Rickli 2002; SEAL Trial Study Team; Seidelin 1997; Ward 1998; Wetter 2000; Wong 2009) encouraged VCD participants to ambulate sooner than manual compression participants. Other studies (Hermiller 2005; Hermiller 2006; Juergens 2004; Legrand 2005; Machnik 2012; Sanborn 1993; Yadav 2003) measuring time to mobilisation did so at the same time intervals regardless of the treatment. Some studies specified a particular distance for time to ambulation (Ansel 2006; Castañeda 2003; Gerckens 1998; Hermiller 2005; Hermiller 2006; Michalis 2002; SEAL Trial Study Team; Wong 2009; Yadav 2003), including 3 to 5 steps, 3 metres, 10 feet, 20 feet and 110 feet; other studies (Brachmann 1998; Carere 2000; Juergens 2004; Legrand 2005; Machnik 2012; Martin 2008; Rickli 2002; Sanborn 1993; Seidelin 1997; Ward 1998; Wetter 2000) simply specified out-of-bed moving or did not define time to mobilisation.

Although it was featured in the study protocol, time to ambulation is usually a clinician-defined occurrence that varies according to local protocols and depends on the procedure undertaken as well as on the method of haemostasis. The authors of this review believe that it is not suitable for use as an outcome measure unless it is used in combination with the occurrence of vascular complications associated with different ambulation times.

Evidence on the effectiveness of one VCD compared with another VCD is lacking. Only one study (Sun 2009) compared time to ambulation between one metal clip-based VCD (StarClose) and a suture-based VCD (PerClose). This study found that StarClose was associated with shorter time to ambulation (0.30 hour) when compared with PerClose. However, the mean difference was very small and the confidence interval was close to zero, suggesting no differences between the two devices. Two studies (Michalis 2002; Shammas 2002) compared the effectiveness of two collagen devices: AngioSeal and VasoSeal. In the study by Michalis 2002, AngioSeal was associated with shorter time to mobilisation for both diagnostic and interventional procedures. However, when Shammas 2002 was added to the meta-analysis, no differences in time to mobilisation were noted between the two devices. Michalis 2002 also included a third treatment arm using the Duett device. AngioSeal was associated with shorter time to mobilisation when compared with the Duett device in diagnostic but not in interventional procedures. Finally, no difference in time to haemostasis was noted for VasoSeal and Duett devices regardless of procedure type. No study compared time to ambulation between collagen-based and metal clip-based VCDs. Martin 2008 reported that AngioSeal was associated with less time to mobilisation when compared with PerClose. Nelson 2014 compared ProStar and ProGlide devices in participants undergoing percutaneous endovascular aortic aneurysm repair (EVAR) but found no differences in time to mobilisation between the two

devices. The same study (Nelson 2014) also compared the VCDs with surgical closure following EVAR but reported no differences in time to mobilisation between the two treatment groups.

Major adverse events and adverse events

Very few studies eligible for inclusion in this review recorded the incidence of major adverse events including mortality and vascular injury requiring repair. When incidence of death was reported in the included studies,no cases of death were described, except when PerClose ProGlide was compared with ProStar XL for percutaneous EVAR (Nelson 2014). For vascular injury repair, meta-analyses demonstrated that neither collagen-based nor clip-based VCDs were more effective than manual compression. Data on the effectiveness of one VCD versus another were lacking. Results showed no differences in effectiveness between ProGlide and ProStar after percutaneous EVAR nor when the same two devices were compared with surgical closure after EVAR.

Infection

Meta-analyses of nine studies showed no difference in the incidence of this outcome between participants treated with a collagen-based VCD and those treated with manual compression. In addition, four studies reported no cases of infection. No differences in the incidence of infection were noted between metal clip-based VCDs nor suture-based VCDs and manual compression. Furthermore, no difference was identified between different types of VCDs. Suture-based devices were compared with each other following percutaneous EVAR, and also with surgical closure following EVAR, but no differences between treatment groups were reported.

Groin haematoma

Collagen VCDs were associated with a lower incidence of groin haematoma when compared with manual compression, but no differences were noted between metal clip-based and suture-based devices and manual compression. The clinical significance of the haematoma was not recorded in these studies, thus it was not possible to distinguish between the incidence of self-limiting and clinically relevant haematoma. Furthermore, no differences between different types of VCDs were identified. Suture-based devices were compared with each other following percutaneous EVAR and also with surgical closure following EVAR, but no differences in the incidence of groin haematoma were noted between treatment groups

The incidence of pseudoaneurysm was lower with collagen-based devices than with manual or mechanical compression. The incidence of all other adverse events including retroperitoneal haemorrhage, arteriovenous fistula, deep vein thrombosis, limb ischaemia and femoral artery thrombosis did not differ by type of VCD nor when VCD was compared with manual or mechanical compression. Suture-based devices were compared with one other following percutaneous EVAR and also with surgical closure following EVAR, but no differences in these outcomes were reported between treatment groups. No study measured arterial dissection nor time spent in angiography suite, and one study reported only distal embolisation and femoral artery thrombosis.

Length of hospital stay

Meta-analysis showed that participants treated with a VCD were discharged from hospital earlier than those undergoing manual compression. Significant heterogeneity demonstrated in the reported data could not be controlled by the use of standard techniques of meta-analysis. Owing to the short duration of stay often expected in patients undergoing percutaneous arterial procedures, the duration of stay could have been influenced mainly by procedural factors, not by the method of haemostasis. Furthermore, time to discharge after the procedure is often locally defined and controlled and may not be suitable as an outcome measure. Length of hospital stay did not differ significantly between suture-based devices following percutaneous EVAR or between suture-based devices and surgical closure following EVAR.

Patient satisfaction

Some studies have shown increased patient satisfaction when a closure device was used over extrinsic compression, but owing to differences in the tools used to assess this, we could not make a formal comparison between different mechanisms of action of VCD.

Cost of VCD and extrinsic compression

Only three studies reported on the cost of VCDs; all found that treatment with a suture-based VCD cost less than manual compression. Study authors' calculations show that this was due to an associated time saving. These costs and calculations vary widely between different centres, and the review authors therefore believe that evidence is insufficient to allow firm conclusions.

Overall completeness and applicability of evidence

As detailed above, we observed heterogeneity in the studies identified including a wide variety of definitions for different outcome measures. The study protocol required that the closure device use must be assessed in diagnostic and interventional procedures. Practice varies between specialities, between centres and between countries, and possible differences between interventional and diagnostic procedures that could influence outcomes (e.g. anticoagulant use, time between procedure end and sheath removal) were not clearly defined in the included studies. Outcome measures such as local arterial damage could be caused by the arteriotomy or by the closure device used, and most of the included studies did not consider this. Arteriovenous fistula formation is a complication of arterial puncture, not of closure device use per se. Some studies did not specifically report whether the device was used in a manner consistent with the manufacturer's instructions for use or did not comment on operator training and experience with the device.

No study measured the pre-defined outcomes of arterial dissection and time spent in the angiography suite, and only one study reported on distal embolisation and femoral artery thrombosis. Furthermore, some studies did not report data in useable format; therefore, we could not include those particular studies in the meta-analysis. In such instances, we attempted to contact the study authors, but we did not receive the requested data.

Quality of the evidence

Very few studies reported on the method of randomisation used or the way in which treatment allocation was concealed. No study reported that participants were blinded. However, we judged that, as most reported outcomes required physical measurements, lack of blinding was unlikely to bias outcome measures. Only eight studies blinded outcome assessors. This is important to note as measures at the puncture site could be influenced by the assessor's

knowledge of allocated treatment. We judged most studies as having low risk of attrition, reporting and other bias. Overall, we determined that the methodological quality of the studies included in this review was moderate to low.

The quality of evidence, defined according to GRADE (Grades of Recommendation, Assessment, Development and Evaluation) (GRADE 2004), was deemed to be low for the primary outcomes of this review: time to haemostasis, time to mobilisation and major adverse events. We downgraded the quality of the outcomes time to haemostasis and time to mobilisation for serious imprecision on the basis of substantial and unexplained heterogeneity between studies. We downgraded the outcome major adverse event to low in the domain of precision because we observed in the meta-analysis a small sample size in relation to the expected effect size and wide confidence intervals. For secondary outcomes including adverse events, technical failure of the device and length of hospital stay, we judged the quality of the evidence as moderate for precision, consistency and directness.

A major limitation of this review is the inclusion of data from the past 20 years. Device and delivery system development throughout this period may have influenced success and complication rates, potentially allowing masking of significant differences. Furthermore, the remit of the review was to evaluate VCDs by mechanism of action (clip-, collagen- or suture-based) rather than by specific device, resulting in limited transferability to clinical practice. Differences between specific devices and their delivery systems may account, at least in part, for the substantial heterogeneity evident within the data set, and this could mask associated benefits or detrimental effects.

Many studies did not state the direction of puncture (as antegrade or retrograde), and many differentiated between diagnostic and interventional procedures without defining the relevant differences in procedure technique (e.g. sheath size, anticoagulant administration, differences in time between end of the procedure and sheath removal). Many studies showed wide variability in the stratification of complications into groups, meaning that a large quantity of the data was unfit for meta-analysis.

It is important to note that other known techniques for closure of the puncture site have not been covered by this review but will be considered for inclusion in future versions of the review.

Potential biases in the review process

None of the authors of this review were involved in any of the included or excluded studies. Furthermore, none of the review authors have commercial or other conflicts of interest. The search was as comprehensive as possible, and two review authors independently assessed all studies for inclusion in the review. We are confident that we have included all relevant studies, and we have attempted to reduce bias in the review process by performing data extraction and assessing study quality independently. However, the possibility remains that studies may have been overlooked by the search methods.

For one study included in this review (Sun 2009), data on time to haemostasis and time to ambulation were presented separately by type of procedure. So these data could be included in a meta-analysis, we combined the mean and standard deviations for the outcomes of time to haemostasis and time to ambulation according to the formula given in Table 7.7.a in Chapter 7 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). For a second study (Nelson 2014), which compared two suture-based devices with surgical closure in participants undergoing EVAR, data on time to haemostasis, time to ambulation and length of hospital stay were presented separately for each device. So these data could be included in a meta-analysis, we combined the mean and standard deviations for these outcomes according to the formula given in Table 7.7.a in Chapter 7 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Agreements and disagreements with other studies or reviews

To date, four (Biancari 2010; Jiang 2015; Koreny 2004; Nikolsky 2004) systematic reviews and meta-analyses have been conducted to investigate the efficacy and safety of VCDs.

Koreny 2004 included 30 randomised controlled trials (RCTs) of VCDs versus manual compression and found that participants treated with a VCD had shorter time to haemostasis (mean difference (MD) 17 minutes, range 14 to 19 minutes), shorter duration of bedrest (MD 10.8 hours, range 8.5 to 13.1 hours) and shorter duration of hospital stay (MD 0.6 days, range 0.1 to 1.1 days) than those treated with manual compression. However, considerable statistical heterogeneity was observed for these efficacy endpoints. With regard to safety outcomes, Koreny 2004 found no differences between VCDs and manual compression for groin haematoma (risk ratio (RR) 1.14, 95% confidence interval (CI) 0.86 to 1.51), bleeding (RR 1.48, 95% CI 0.88 to 2.48) and pseudoaneurysm (RR 1.19, 95% CI 0.75 to 1.88). The authors of the review raised concerns about the quality of the included studies, which they judged as poor to moderate.

Nikolsky 2004 included 30 studies on VCDs versus manual compression. However, only 18 of these were RCTs. Nikolsky 2004 performed device-specific meta-analysis and found no differences in complication rates between AngioSeal and mechanical compression (odds ratio (OR) 0.73, 95% CI 0.38 to 1.39) nor between PerClose ProGlide and mechanical compression (OR 1.00, 95% CI 0.53 to 1.88). The authors of the review did report that VasoSeal was associated with an increase in complications (OR 2.78, 95% CI 1.51 to 5.13); this consistent finding has led to removal of the device from clinical use.

Biancari 2010 included 31 RCTs with a total of 7528 participants randomised to VCD or manual/mechanical compression after diagnostic angiography or interventional procedures. Meta-analysis showed no differences in the incidence of haematoma, bleeding and pseudoaneurysm between the two treatment groups. However, lower limb ischaemia (0.3% vs 0% P value = 0.02), the need for surgery for vascular complications (0.7% vs 0.4%; P value = 0.10) and groin infection (0.6% vs 0.2%; P value = 0.02) were more frequent in the VCD group. Meta-analysis also showed that VCDs were associated with shorter time to haemostasis for participants undergoing both diagnostic (MD 16.64 minutes, range -21.96 to -11.32 minutes) and interventional procedures (MD -37.67 minutes, range -47.94 to -27.40 minutes). However, the authors of the review reported substantial heterogeneity for time to haemostasis outcomes.

Jiang 2015 included 40 RCTs with a total of 16,868 participants and found no differences in the rate of adverse vascular events between

all VCDs combined and manual compression. However, subgroup analysis showed that both FemoSeal and AngioSeal devices were associated with fewer adverse events, in particular, haematoma.

AUTHORS' CONCLUSIONS

Implications for practice

This review has included randomised controlled trials comparing extrinsic compression and VCDs in the closure of femoral arterial punctures and in surgical closure with percutaneous closure after large-calibre arterial access. We have demonstrated no significant differences in the primary endpoints of time to haemostasis and time to mobilisation when VCD use is compared with extrinsic compression, owing to data heterogeneity in the included studies. Furthermore, we found no significant differences in the incidence of vascular injury or mortality when use of VCDs is compared with use of extrinsic compression. Collagen-based VCDs are associated with a lesser incidence of groin haematoma when compared with extrinsic compression but no difference when metal clip-based VCDs or suture-based VCDs were compared with manual or mechanical compression. The incidence of pseudoaneurysm was lower among individuals treated with collagen-based devices than in those treated with manual or mechanical compression, but no difference was evident when metal clip-based VCDs or suture-based VCDs were compared with manual or mechanical compression. For other adverse events, we observed no differences between collagen, clip-based or suture-based. and manual or mechanical compression. With larger-calibre arterial access, percutaneous closure has been shown to be associated with shorter time to haemostasis without an increase in complication rates when compared with surgical closure.

A major limitation of this review is the inclusion of data spanning the past 20 years. Device and delivery system development throughout this period may have influenced success and complication rates, potentially allowing masking of significant differences.Differences between specific devices and their delivery systems may account, at least in part, for the substantial heterogeneity evident within the data set, and this could mask associated benefits or detrimental effects.

Many studies did not state the direction of puncture (as antegrade or retrograde), and many others differentiated between diagnostic and interventional procedures without defining the relevant differences in procedure technique (e.g. sheath size, anticoagulant administration, differences in time between end of the procedure and sheath removal). Many studies showed wide variety in the stratification of complications into groups, meaning that a large quantity of the data was unfit for analysis. This variability in study and reporting methodology means that the findings of thi review are of limited value in specific clinical situations.

Three studies describe cost-savings associated with decreased time to haemostasis. Owing to wide variation in VCD cost and local hospital costs, formal economic analysis should be performed at a local level before VCDs are accepted on the basis of cost-savings alone.

Implications for research

Overall, successful VCD deployment is associated with a reduced incidence of groin hematoma and shorter length of hospital stay, with no increase in local arterial complications or major adverse events. Further work is necessary to evaluate the efficacy of specific devices currently used and to compare these with one other and with extrinsic compression with respect to clearly defined outcome measures. Researchers should evaluate primary and secondary outcomes of different devices in antegrade and retrograde puncture and should evaluate VCD outcome measures with respect to their on-label and off-label uses.

Some studies report increased patient satisfaction with successful VCD deployment. A formal assessment of this could be undertaken.

VCDs are widely used and are convenient for both patients and operators. Large longitudinal data demonstrate their safety and efficacy with low complication rates; thus investigators may resist development of randomised controlled trials of sufficiently robust methodology to truly evaluate their efficacy.

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REFERENCES

References to studies included in this review

Amin 2000 *{published data only}*

Amin FR, Yousufuddin M, Stbales R, Shamim Q, Al-Nasser FM, Coats AJS, et al. Femoral haemostasis after transcatheter therapeutic intervention: a prospective randomised study of the AngioSeal device vs. the FemoStop device. *International Journal of Cardiology* 2000;**76**:235-40.

Amine 1999 *{published data only}*

Amine el S, Teiger E, Aptecar E, Dubois-Randé J-L, Pernès J-M, Dupouy P. Suture percutanée du point de ponction artériel fémoral après coronarographie diagnostique. *Archives des Malaides du Coeur et des Vaisseaux* 1999;**92**(11):1447-53.

Ansel 2006 *{published data only}*

Ansel G, Yakubov S, Neilson C, Allie D, Stoler R, Hall P, et al. Safety and efficacy of staple-mediated femoral arteriotomy closure: results from a randomised multicentre study. *Catheterization and Cardiovascular Interventions* 2006;**67**:546-53.

Behan 2007 *{published data only}*

Behan MWH, Large JK, Patel NR, Lloyd GW, Sulke AN. A randomised controlled trial comparing the routine use of an AngioSeal STS device strategy with conventional femoral haemostasis methods in a district general hospital. *International Journal of Clinical Practice* 2007;**61**(3):367-72.

Brachmann 1998 *{published data only}*

Brachmann J, Asnsah M, Kosinksi EJ, Schuler GC. Imprved clinical effectiveness with a collagen vascular hemostasis device for shortened immobilization time following diagnostic angiography and percutaneous transluminal coronary angioplasty. *The American Journal of Cardiology* 1998;**81**(12):1502-5.

Camenzind 1994 *{published data only}*

Camenzind E, Grossholz M, Urban P, Dorsaz PA, Didier D, Meier B. Collagen application versus manual compression: a prospective randomized trial for arterial puncture site closure after coronary angioplasty. *Journal of the American College of Cardiology* 1994;**24**(3):655-62.

Carere 2000 *{published data only}*

Carere RG, Webb JG, Buller CEH, Wilson M, Rahman T, Spinelli J, et al. Suture closure of femoral arterial puncture sites after coronary angioplasty followed by same-day discharge. *American Heart Journal* 2000;**139**:52-8.

Castañeda 2003 *{published data only}*

Castañeda F, Swischuk JL, Smouse B, Brady T. Gelatin sponge closure device versus manual compression after peripheral arterial catheterization procedures. *Journal of Vascular and Interventional Radiology* 2003;**14**(12):1517-23.

Chen 2013 *{published data only}*

Chen CP, Huang HP, Hsia CH, Chang YM, Lin LS, Lee CL. Short-term safety and efficacy of femoral vascular closure after percutaneous coronary intervention with combination of the BoomerangTM device and intravenous Protamine Sulfate. *Acta Cardiologica Sinica* 2013;**29**(6):531-8.

Deuling 2008 *{published data only}*

Deuling JHH, Jaarsma T, Vermeulen RP, Van Den Heuvel AFM. A randomized controlled trial comparing StarClose and AngioSeal vascular closure devices in a district general hospital. *International Journal of Clinical Practice* 2008;**62**(11):1801. [DOI: 10.1111/j.1742-1241.2008.01865.x]

* Deuling JHH, Vermeulen RP, Anthonio RA, van den Heuvel AFM, Jaarsma T, Jessurun G, et al. Closure of the femoral artery after cardiac catheterization: a comparison of AngioSeal, StarClose and manual compression. *Catheterization and Cardiovascular Interventions* 2008;**71**(4):518-23.

Diaz 2001 *{published data only}*

Diaz De La Llera LS, Fournier Andray JA. Early deambulation following cardiac catheterization by the use of 6 Fr Angio-Seal, a new hemostatic percutaneous puncture closure device. *Revista Espanola de Cardiologia* 2001;**54**(12):1406-10.

Doneaux 2001 *{published data only}*

Doneaux P, Gach O, Martinez CH, Legrand V. Femoral puncture closure devices versus manual compression after percutaneous coronary interventions. *European Heart Journal* 2001;**22**(Suppl):216.

Fargen 2011 *{published data only}*

Fargen KM, Hoh BL, Mocco J. A prospective randomized single-blind trial of patient comfort following vessel closure: extravascular synthetic sealant closure provides less pain than a self-tightening suture vascular compression device. *Journal of Neurointerventional Surgery* 2011;**3**:219-33.

NCT00998023. Patient comfort with vascular closure. http://clinicaltrials gov/show/NCT00998023 (accessed 26 October 2013).

Gerckens 1998 *{published data only}*

Gerckens U, Cattelaens N, Lampe EG, Grube E. Management of arterial puncture site after catheterization procedures: evaluating a suture-mediated closure device. *American Journal of Cardiology* 1999;**83**(12):1658-63.

* Gerckens U, Cattelaens N, Müller R, Lampe E-G, Grube E. Perkutaner nahtverschluß von femoralarteriezugängen nach diagnostischen herzkatheterisierungen oder koronarinterventionen. Sicherheit and effekitivtät einer neuen verschlußtechnik arterieller punktionsstellen. *Herz* 1998;**23**(1):27-34.

Gwechenberger 1997 *{published data only}*

Gwechenberger M, Katzenschlager R, Heinz G, Gottsauner-Wolf M, Probst P. Use of a collagen plug versus manual compression for sealing arterial puncture site after cardiac catheterization. *Angiology* 1997;**48**(2):121-6.

Hattab 2012 *{published data only}*

Hattab M, Hokin M, Carreira VB, Elhadad S. A randomized trial comparing two vascular closure devices: PROGLIDE and the novel EXOSEAL after percutaneous femoral procedures. *Journal of the American College of Cardiology* 2012;**60**(17 Suppl B):B112.

Hermanides 2010 *{published data only}*

Hermanides RS, Ottervanger JP, Dambrink JH, de Boer MJ, Hoorntje JC, Gosselink AT, et al. Closure device or manual compression in patients undergoing percutaneous coronary intervention: a randomized comparison. *Journal of Invasive Cardiology* 2010;**22**(12):562-6.

Hermiller 2005 *{published data only}*

Hermiller J, Simonton C, Hinohara T, Lee D, Cannon L, Mooney M, et al. Clinical experience with a circumferential clip-based vascular closure device in diagnostic catheterization. *Journal of Invasive Cardiology* 2005;**17**(10):504-10.

Hermiller 2006 *{published data only}*

DiDonato K, Jaff M, Hermiller J, Simonton C, Hinohara T, Mooney M. 6 month results for the CLIP trial. Transcatheter Cardiovascular Therapeutics. 2006; Vol. Abstract 479.

* Hermiller JB, Simonton C, Hinohara T, Cannon L, Mooney M, O'Shaughnessy C, et al. The StarClose® vascular closure system: interventional results from the CLIP study. *Catheterization and Cardiovascular Interventions* 2006;**68**(5):677-83.

Jaff MR, Hadley G, Hermiller JB, Simonton C, Hinohara T, Cannon L, et al. The safety and efficacy of the StarClose Vascular CLosure system: the ultrasound substudy of the CLIP study. *Catheterization and Cardiovascular Interventions* 2006;**68**(5):684-9.

Holm 2014 *{published data only}*

Holm NR, Sindberg B, Schou M, Maeng M, Kaltoft A, Bottcher M, et al. Randomised comparison of manual compression and FemoSeal vascular closure device for closure after femoral artery access coronary angiography: the CLOSure dEvices Used in everyday Practice (CLOSE-UP) study. *Eurointervention* 2014;**10**(2):183-90.

Sindberg B, Schou M, Hansen L, Christiansen KJ, Jørgensen KS, Søloft M, et al. Pain and discomfort in closure of femoral access coronary angiography. The CLOSuredEvices Used in everyday Practice (CLOSE-UP) pain substudy. *European Journal of Cardiovascular Nursing* 2014;**13**(3):221-6.

Jensen 2008 *{published data only}*

Jensen J, Saleh N, Jensen U, Svane B, Jönsson A, Tornvall P. The inflammatory response to femoral arterial closure devices: a randomized comparison among FemoStop, AngioSeal, and PerClose. *Cardiovascular and Interventional Radiology* 2008;**31**(4):751-5.

Juergens 2004 *{published data only}*

Juergens CP, Leung DYC, Crozier JA, Wong AM, Robinson JTC, Lo S, et al. Patient tolerance and resource utilisation associated with an arterial closure versus an external compression device after percutaneous coronary intervention. *Catheterization and Cardiovascular Interventions* 2004;**63**:166-70.

Kalsch 2008 *{published data only}*

Kalsch HIM, Eggebrecht H, Mayringer S, Konorza T, Sievers B, Sack S, et al. Randomized comparison of effects of suture-based and collagen-based vascular closure devices on post-procedural leg perfusion. *Clinical Research in Cardiology* 2008;**97**(1):43-8.

Kussmaul 1995 *{published data only}*

Kussmaul WG, Buchbinder M, Whitlow PL, Heuser RR, King SB, Kent KM, et al. Rapid arterial hemostasis and decreased access site complications after cardiac catheterization and angioplasty: results of a randomized trial of a novel hemostatic device. *Journal of the American College of Cardiology* 1995;**25**(7):1685-92.

Legrand 2005 *{published data only}*

Legrand V, Doneux P, Martinez C, Gach O, Bellekens M. Femoral access management: comparison between two different vascular closure devices after percutaneous coronary intervention. *Acta Cardiologica* 2005;**60**(5):482-8.

Machnik 2012 *{published data only}*

Machnik R, Pleniążek, Musiałek P, Przewłocki T, Tekieli Ł, Trystuła M, et al. Control of local haemostasis with the AngioSeal® vascular closure device in peripheral endovascular interventions via 6-9 F femoral artery access. *Postępy w Kardiologii Interwencyjnej* 2012;**8**(1):1-7.

Magosaki 1999 *{published data only}*

Magosaki N, Hosoda S, Kawagishi N, Yamaguchi T, Sakatani H, Haze K, et al. Efficacy of hemostatic puncture closing device for hemostasis and early ambulation after coronary angiography and angioplasty: results of a multicentre trial. *Journal of Cardiology* 1999;**34**:131-8.

Martin 2008 *{published data only}*

Martin JL, Pratsos A, Magargee E, Mayhew K, Pensyl C, Nunn M, et al. A randomized trial comparing compression, PerClose ProGlide™ and AngioSeal VIP™ for arterial closure following percutaneous coronary intervention: the CAP trial. *Catheterization and Cardiovascular Interventions* 2008;**71**(1):1-5.

Michalis 2002 *{published data only}*

Michalis LK, Rees MR, Patsouras D, Katsouras CS, Goudevenos J, Pappas S, et al. A prospective randomized trial comparing the safety and efficacy of three commercially available closure devices (AngioSeal, VasoSeal and Duett). *Cardiovascular and Interventional Radiology* 2002;**25**:423-9.

Nelson 2014 *{published data only}*

Nelson PR, Kracjer MSZ, Kansal N, Rao V. A multicenter, randomized, controlled trial of totally percutaneous access versus open femoral exposure for endovascular aortic aneurysm repair (the PEVAR trial). *Journal of Vascular Surgery* 2014;**59**:1181-94.

Noguchi 2000 *{published data only}*

Noguchi T, Miyazaki S, Yasuda S, Baba T, Sumida H, Morii I, et al. A randomised controlled trial of ProStar-Plus for haemostasis in patients after coronary angioplasty. *European Journal of Vascular and Endovascular Surgery* 2000;**19**(5):451-5.

Park 2005 *{published data only}*

Park Y, Roh HG, Choo SW, Lee SH, Shin SW, Do YS, et al. Prospective comparison of collagen plug (AngioSeal™) and suture-mediated (the Closure S™) closure devices at femoral access sites. *Korean Journal of Radiology* 2005;**6**:248-55.

Perlowski 2011 *{published data only}*

Perlowski A, Jaff M, O'Shaughnessy D, Brueggeman C, Rosenfield K. StarClose device closure of femoral arteriotomy site versus manual compression in patients with peripheral arterial disease: the CLIPIT trial. *Journal of the American College of Cardiology* 2011;**57**(14(Suppl 1)):E1982.

Rastan 2008 *{published data only}*

Rastan A, Sixt S, Schwarzwälder U, Schwarz T, Frank U, Bürgelin K, et al. VIPER-2: a prospective, randomized single-centre comparison of 2 different closure devices with a hemostatic wound dressing for closure of femoral artery access sites. *Journal of Endovascular Therapy* 2008;**15**:83-90.

Reddy 2004 *{published data only}*

Reddy BK, Brewster PS, Walsh T, Burket MW, Thomas WJ, Cooper CJ. Randomized comparison of rapid ambulation using radial, 4 French femoral access, or femoral access with AngioSeal closure. *Catheterization and Cardiovascular Interventions* 2004;**62**:143-9.

Rickli 2002 *{published data only}*

Rickli H, Unterweger M, Sütsch G, Brunner-La Rocca HP, Sagmeister M, Ammann P, et al. Comparison of costs and safety of a suture-mediated closure device with conventional manual compression after coronary artery interventions. *Catheterization and Cardiovascular Interventions* 2002;**57**(3):297-302.

Sanborn 1993 *{published data only}*

Sanborn TA, Gibbs HH, Brinker JA, Knopf WD, Kosinski EK, Roubin GS. A multicentre randomised trial comparing a percutaneous collagen haemostasis device with conventional manual compression after diagnostic angiography and angioplasty. *Journal of the American College of Cardiology* 1993;**22**(5):1273-9.

Schräder 1992 *{published data only}*

Schräder R, Steinbacher ST, Kaltenbach M. Randomisierter vergleich zwischen kollagenpplikation und druckverband zum verschluß der arteriellen punktionsstelle nach koronarangiographie und koronardilatation. *Zeitschrift für Kardiologie* 1992;**81**:507-11.

Schulz-Schüpke 2014 *{published data only}*

Schulz-Schüpke S, Helde S, Gewalt S, Ibrahim T, LinhardtM, Haas K, et al. Comparison of vascular closure devices vs manual compression after femoral artery puncture. The ISAR-CLOSURE randomized clinical trial. *Journal of the American Medical Association* 2014;**312**(19):1981-7.

SEAL Trial Study Team *{published data only}*

* The SEAL Trial Study Team. Assessment of the safety and efficacy of the DUETT vascular hemostasis device: final results of the Safe and Effective Vascular Hemostasis (SEAL) trial. *American Heart Journal* 2002;**143**(4):612-9.

Zhang Z, Mahoney EM, Gershony G, Ellis S, Saucedo JF, Talley JD, et al. Impact of the Duett sealing device on quality of life and hospitalization costs for coronary diagnostic and interventional procedures: results from the Study of Economic and Quality of Life substudy of the SEAL trial. *American Heart Journal* 2001;**142**:982-8.

Seidelin 1997 *{published data only}*

Seidelin PH, Adelman AG. Mobilization within thirty minutes of elective diagnostic coronary angiography: a feasibility study using a hemostatic femoral puncture closure device. *Journal of Interventional Cardiology* 1997;**10**:409-15.

Shammas 2002 *{published data only}*

Shammas NW, Rajendran VR, Alldredge SG, Witcik WJ, Robken JA, Lewis JR, et al. Randomized comparison of VasoSeal and AngioSeal closure devices in patients undergoing coronary angiography and angioplasty. *Catheterization and Cardiovascular Interventions* 2002;**55**:421-5.

Silber 1998 *{published data only}*

Silber S, Björvik A, Mühling H, Rösch A. Usefulness of collagen plugging with VasoSeal® after PTCA as compared to manual compression with identical sheath dwell times. *Catheterization and Cardiovascular Diagnosis* 1998;**43**:421-7.

Sun 2009 *{published data only}*

Sun JJ, Zhang HT, Huang CC, Luo HL, Wang JH, Tan WJ, et al. Three kinds of vascular closure devices StarClose, PerClose and Boomerang in the femoral artery hemostasis applications. *Journal of Clinical Rehabilitative Tissue Engineering Research* 2009;**13**(13):2485-90.

Tron 2003 *{published data only}*

Tron C, Koning R, Eltchaninoff H, Douillet R, Chassaing S, Sanchez-Giron C, et al. A randomized comparison of a percutaneous suture device versus manual compression for femoral artery hemostasis after PTCA. *Journal of Interventional Cardiology* 2003;**16**(3):217-21.

Upponi 2007 *{published data only}*

Upponi SS, Ganeshan AG, Warakaulle DR, Phillips-Hughes J, Boardman P, Uberoi R. AngioSeal versus manual compression for haemostasis following peripheral vascular diagnostic and interventional procedures - A randomized controlled trial. *European Journal of Radiology* 2007;**61**(2):332-4.

Veasey 2008 *{published data only}*

Veasey RA, Large JK, Silberbauer J, Paul G, Taggu Wm Ellery S, Rathore VS, et al. A randomised controlled trial comparing StarClose and AngioSeal vascular closure devices in a district general hospital. *International Journal of Clinical Practice* 2008;**62**(6):912-8.

von Hoch 1995 *{published data only}*

von Hoch F, Neumann F-J, Theiss W, Kastrati A, Schömig A. Efficacy and safety of collagen implants for haemostasis of the vascular access site after coronary balloon angioplasty and

coronary stent implantation: a randomized study. *European Heart Journal* 1995;**16**(5):640-6.

Ward 1998 *{published data only}*

Ward SR, Casale P, Raymond R, Kussmaul WG, Simpfendorfer C for the Angio-Seal Investigators. Efficacy and safety of a hemostatic puncture closure device with early ambulation after coronary angiography. *American Journal of Cardiology* 1998;**81**:569-72.

Wetter 2000 *{published data only}*

Wetter DR, Rickli H, van Smekal A, Amann FW. Early sheath removal after coronary artery interventions with use of a suture-mediated closure device: clinical outcome and results of Doppler US evaluation. *Journal of Vascular and Interventional Radiology* 2000;**11**:1033-7.

Wong 2009 *{published data only}*

Wong SC, Bachinsky W, Cambier P, Stoler R, Aji J, Rogers JH, et al. A randomized comparison of a novel bioabsorbable vascular closure device versus manual compression in the achievement of hemostasis after percutaneous femoral procedures. *Journal of the American College of Cardiology: Cardiovascular Interventions* 2009;**2**(8):785-93.

Yadav 2003 *{published data only}*

Yadav JS, Ziada KM, Almany S, Davis TP, Castaneda F. Comparisons of the QuickSeal femoral arterial closure system with manual compression following diagnostic and interventional catheterization procedures. *American Journal of Cardiology* 2003;**91**:1463-6.

References to studies excluded from this review

Baim 2000 *{published data only}*

Baim DS, Knopf WD, Hinohara T, Schwarten DE, Schatz RA, Pinkerton CA, et al. Suture-mediated closure of the femoral access site after cardiac catheterization: results of the Suture To Ambulate aNd Discharge (STAND I and STAND II) trials. *American Journal of Cardiology* 2000;**85**(7):864-9.

Beyer-Enke 1996 *{published data only}*

Beyer-Enke SA, Soldner J, Zeitler E. Immediate sealing of arterial puncture site following femoropopliteal angioplasty: a prospective randomized trial. *Cardiovascular and Interventional Radiology* 1996;**19**:406-10.

Chalmers 2007 *{published data only}*

Chalmers R, Clement Darling R, Wingard JT, Chetter I, Cutler B, Kern JA, FIBRIN SEALANT PV Investigator Group. A prospective, randomized controlled trial comparing the effects of a fibrin sealant (EVICEL) versus manual compression on hemostatic effectiveness during vascular surgical procedures utilizing polytetrafluorethylene graft material. *Transfusion* 2007;**47**(11(Suppl)):22A.

Chevalier 2000 *{published data only}*

Chevalier B, Henry M, Pillière R, Koning R, Lancelin B, Puel J, et al. Duplex scan assessment of femoral access for coronary stenting: compression versus AngioSeal comparison in the HEMOSTASE trial. *European Heart Journal* 2000;**21**(Abstract Supplement 642):3522.

Chevalier B, Lancelin B, Koning R, Henry M, Gommeaux A, Pilliere R, et al. Effect of a closure device on complication rates in high-local-risk patients: results of a randomized multicenter trial. *Catheterization and Cardiovascular Interventions* 2003;**58**(3):285-91.

Jean-Baptiste 2008 *{published data only}*

Jean-Baptiste E, Hassen-Khodja R, Haudebourg P, Bouillanne PJ, Declemy S, Batt M. Percutaneous closure devices for endovascular repair of infrarenal abdominal aortic aneurysms: a prospective, non-randomized comparative study. *European Journal of Vascular and Endovascular Surgery* 2008;**35**(4):422-8.

Kurşaklioğlu 2008 *{published data only}*

Kurşaklioğlu H, Iyisoy A, Barçin C, Celik T, Nitzan R, Köse S, et al. The experience with the Epiclose-T vascular access closure device: a human study. *Anadolu Kardiyoloju Dergisi* 2008;**8**(1):38-42.

Larzon 2015 *{published data only}*

Larzon T, Roos H, Gruber G, Henrikson O, Magnuson A, Falkenberg M. A randomised controlled trial of the fascia suture technique compared with a suture-mediated closure device for femoral arterial closure after endovascular aortic repair. *European Jouranl of Vascular and Endovascular Surgery* 2015;**49**(2):166-73.

Leinbudgut 2013 *{published data only}*

Leibundgut G, Pache J, Schulz S, Berger PB, Ferenc M, Gick M, et al. Collagen plug vascular closure devices and reduced risk of bleeding with bivalirudin versus heparin plus abciximab in patients undergoing percutaneous coronary intervention for non ST-segment elevation myocardial infarction. *Journal of Interventional Cardiology* 2013;**26**(6):623-9.

Lupi 2012 *{published data only}*

Lupi A, Rognoni A, Secco CG, Lazzero M, Plebani L, Cossa G. Different spectrum of vascular complications after AngioSeal deployment of manual compression. *Journal of Invasive Cardiology* 2012;**24**(3):90-6.

Neudecker 2003 *{published data only}*

Neudecker A, Manke C, Lenhart M, Zorger N, Paetzel C, Feurbach S, et al. Evaluation of a haemostatic device with percutaneous collagen application (VasoSeal) compared to a mechanical compression system (Compressar) after transfemoral catheterization of patients suffering from arterial occlusive disease [Evaluation eines Verschlusssystems mit perkutaner Kollageneinbringung (VasoSeal) im Vergleich zu einem mechanischen Kompressionssystem (Compressar) nach Femoralispunktion bei Patienten mit AVK]. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin* 2003;**175**(5):676-81.

Ratnam 2007 *{published data only}*

Ratnam LA, Raja J, Munneke GJ, Morgan RA, Belli AM. Prospective non-randomized trial of manual compression and

AngioSeal and StarClose arterial closure devices in common femoral punctures. *Cardiovascular and Interventional Radiology* 2007;**30**(2):182-8.

Slaughter 1995 *{published data only}*

Slaughter PM, Chetty R, Flintoft VF, Lewis S, Sykora K, Beattie DM, et al. A single center randomized trial assessing use of a vascular hemostasis device vs. conventional manual compression following PTCA: what are the potential resource savings?. *Catheterization and Cardiovascular Diagnosis* 1995;**34**(3):210-4.

Smilowitz 2012 *{published data only}*

Smilowitz NR, Kirtane AJ, Guiry M, Gray WA, Dolcimascolo P, Querijero M, et al. Practices and complications of vascular closure devices and manual compression in patients undergoing elective transfemoral coronary procedures. *American Journal of Cardiology* 2012;**110**(2):177-82.

Starnes 2003 *{published data only}*

Starnes BW, O'Donnell SD, Gillespie DL, Goff JM, Rosa P, Parker MV, et al. Percutaneous arterial closure in peripheral vascular disease: a prospective randomized evaluation of the PerClose device. *Journal of Vascular Surgery* 2003;**38**(2):263-71.

References to studies awaiting assessment

NCT01297322 *{published data only}*

NCT01297322. RESPECT Trial - (Rapid Extravascular Sealing Via PercutanEous Collagen ImplanT). http://clinicaltrials.gov/showNCT01297322 (accessed 26 October 2013).

References to ongoing studies

ACTRN12611001248954 *{published data only}*

ACTRN12611001248954. Femoral artery closure using the Cardiva VASCADE Vascular Closure System (VCS) to reduce time to hemostasis and reduce time to ambulation and hospital discharge versus manual compression in patients who have undergone diagnostic or interventional endovascular catheterization procedures utilizing 6 Fr or 7 Fr procedural sheaths. http://www anzctr org au/ACTRN12611001248954 (accessed 26 October 2013).

CTRI/2014/09/004946 *{published data only}*

CTRI/2014/09/004946. Impact of femoral access site closure after percutaneous coronary interventions. A comparison between manual compression and the use of vascular closure device (PerClose ProGlide). http://apps.who.int/trialsearch/Trial2.aspx?TrialID=CTRI/2014/09/004946 (accessed 27 May 2015).

DRKS00000802 *{published data only}*

DRKS00000802. A prospective randomized trial to evaluate the complication rate and patient comfort using three different vascular closure strategies following coronary angiography. http://drks-neu.uniklinik-freiburg.de/drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00000802 (accessed 26 October 2013).

NCT00264264 *{published data only}*

NCT00264264. Arterial closure vs direct compression for hemostasis after PCI - ACDC Trial. http://clinicaltrials.gov/show/NCT00264264 (accessed 25 October 2013).

NCT00428155 *{published data only}*

NCT00428155. Arterial Closure Device Comparison Trial II - ACDC Trial II. http://clinicaltrials.gov/show/NCT00428155 (accessed 25 October 2103).

NCT01389375 *{published data only}*

NCT01389375. Instrumental sealing of arterial puncture site closure device versus manual compression trial (ISAR-CLOSURE). http://clinicaltrials.gov/show/NCT01389375 (accessed 26 October 2013).

NCT01600482 *{published data only}*

NCT01600482. Clinical investigation for safety and efficacy study of CELT ACD arterial closure device. http://clinicaltrials.gov/show/NCT01600482 (accessed 26 October 2013).

NCT01669382 *{published data only}*

NCT01669382. AngioSeal® vs. ExoSeal® for closure of arterial puncture sites. http://clinicaltrials.gov/show/NCT01669382 (accessed 26 October 2013).

NCT02061696 *{published data only}*

NCT02061696. A randomized controlled trial to assess safety and efficacy of AXERA (device name) 2 Access System compared to manual compression. https://clinicaltrials.gov/ct2/show/NCT02061696 (accessed 27 May 2015).

NCT02234830 *{published data only}*

NCT02234830. Randomized comparison of ExoSeal® and AngioSeal vascular closure devices: the CLOSE-UP II trial. https://clinicaltrials.gov/ct2/show/NCT02234830 (accessed 27 May 2015).

NCT02237430 *{published data only}*

NCT02237430. Randomized comparison of MynxGrip vascular closure device and manual compression for closure after femoral access angiography. The Closure Devices Used in Every Day Practice Study, CLOSE-UP III Trial. https://clinicaltrials.gov/ct2/show/NCT02237430 (accessed 27 May 2015).

Additional references

Bechara 2010

Bechara CF, Annambhotla S, Lin PH. Access site management with vascular closure devices for percutaneous transarterial procedures. *Journal of Vascular Surgery* 2010;**52**(6):1682-96.

Biancari 2010

Biancari F, D'Andrea V, Di Marco C, Savino G, Tiozzo V, Catania A. Meta-analysis of randomized trials on the efficacy of vascular closure devices after diagnostic angiography and angioplasty. *American Heart Journal* 2010;**159**:518-31.

GRADE 2004

GRADE Working Group. Grading quality of evidence and strength of recommendations. *BMJ* 2004;**328**:1490-4.

Higgins 2011

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. www.cochrane-handbook.org.

Jiang 2015

Jiang J, Zou J, Ma H, Jiao Y, Yang H, Zhang X, et al. Network meta-analysis of randomized trials on the safety of vascular closure devices for femoral arterial puncture site haemostasis. *Scientific Reports* 2015;**5**:13761.

Koreny 2004

Koreny M, Riedmüller E, Nikfardjam M, Siostrzonek P, Müllener M. Arterial puncture closing devices compared with standard manual compression after cardiac catheterization. Systematic review and meta-analysis. *Journal of American Medicine Association* 2004;**291**(3):350-7.

Kurşaklioğlu 2008

Kurşaklioğlu H, Iyisoy A, Barçin C, Celik T, Nitzan R, Köse S, et al. The experience with the Epiclose-T vascular access closure device: a human study. *Anadolu Kardiyoloji Dergisi - The Anatolian Journal of Cardiology* 2008;**8**(1):38-42.

Merriweather 2012

Merriweather N, Sulzbach-Hoke LM. Managing risk of complications at femoral vascular access sites in percutaneous coronary intervention. *Critical Care Nurse* 2012;**32**(5):16-30.

Nikolsky 2004

Nikolsky E, Mehran R, Halkin A, Aymong ED, Mintz GS, Lasic Z, et al. Vascular complications associated with arteriotomy closure devices in patients undergoing percutaneous coronary procedures: a meta-analysis. *Journal of the American College of Cardiology* 2004;**44**(6):1200-9.

Scheinert 2007

Scheinert D, Sievert H, Turco MA, Schmidt A, Hauptmann KE, Mueller R, et al. The safety and efficacy of an extravascular, water-soluble sealant for vascular closure: initial clinical results for Mynx. *Catheterization and Cardiovascular Interventions* 2007;**70**(5):627-33.

Schwartz 2010

Schwartz BG, Burstein S, Economides C, Kloner RA, Shavelle DM, Mayeda GS. Review of vascular closure devices. *Journal of Invasive Cardiology* 2010;**22**(12):599-607.

Sterne 2001

Sterne JA, Egger M. Funnel plots for detecting bias in meta-analysis: guidelines on choice of axis. *Journal of Clinical Epidemiology* 2001;**54**(10):1046-55.

Zahn 1997

Zahn R, Fromm E, Thoma S, Lotter R, Zander M, Wagner S. Local venous thrombosis after cardiac catheterization. *Angiology* 1997;**48**:1-7.

References to other published versions of this review

Hsu 2011

Hsu CCT, Kwan GNC, Rophael JA, Anthony C, van Driel ML. Vascular closure devices for femoral arterial puncture site haemostasis. *Cochrane Database of Systematic Reviews* 2012, Issue 1. [DOI: 10.1002/14651858.CD009541]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Amin 2000

Methods	**Study design** : randomised prospective study
Participants	**Country** : UK **Setting** : hospital **Number of centres** : 1 **Numbers** : AngioSeal 75, FemoStop 75 **Age (mean (SD))** : AngioSeal 58.0 (9.2) years, FemoStop 59.5 (9.6) years **Sex** : AngioSeal 48 M/17 F, FemoStop 49 M/16 F **Inclusion criteria** : patients undergoing intracoronary stent deployment **Exclusion criteria** :

Amin 2000 *(Continued)*

	patients with a history of previous application of AngioSeal within 90 days, peripheral vascular disease, recent acute myocardial infarction, anticoagulation therapy, pre-existing haematoma, formation of haematoma during the procedure or a concomitant femoral venous sheath. Patients in whom the puncture needle had penetrated the posterior wall of the artery during the procedure were also considered for exclusion
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : FemoStop groin compression device **Sheath size** : 8 Fr
Outcomes	**Primary** : composite of bleeding, haematoma formation, bruise, requirement for blood transfusion, clinical indication for ultrasound examination and cross-over to either method at 2 and 24 hours following the procedure; bleeding (defined as significant external blood loss after the application of either device, with significant bleeding defined as blood loss (Hb < 10.0 g/dL) requiring blood transfusion); haematoma (defined as development of a palpable mass over the access site classified as mild (< 5 cm), moderate (5 to 10 cm) or severe (> 10 cm)) **Secondary** : pseudoaneurysm (palpable expansible mass detected by clinical examination and confirmed by ultrasound imaging); groin discomfort (minimal, moderate or severe) **Time of measurement** : 2 and 24 hours after the procedure
Notes	All participants received a bolus dose of 10,000 units of heparin after diagnostic angiograms Antithrombotic agents following the procedure: aspirin 150 mg once daily long term and ticlopidine 250 mg twice daily for 3 weeks Outcomes measured at 2 and 24 hours post procedure, but 9 participants crossed over from AngioSeal to FemoStop because of persistent bleeding despite prolonged manual pressure

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Amine 1999

Methods	**Study design** : randomised study
Participants	**Country** : France **Setting** : hospital **Number of centres** : 1 **Numbers:** Techstar 50, manual compression 50 **Age (mean (SD))** : Techstar 61 (10) years, manual compression 60 (8) years **Sex** : Techstar 72 M/28 F, manual compression 70 M/30 F **Inclusion criteria** : patients undergoing diagnostic coronography **Exclusion criteria** : patients in an acute phase of myocardial infarct, with or without thrombolysis treatment, with known anomalies of coagulation or plaque counting, with severe and uncontrollable arterial hypertension (systolic > 190 mmHg and diastolic >110 mmHg) and inflammation of arthritis of the inferior limbs
Interventions	**Intervention 1** : PerClose **Intervention 2** : manual compression **Sheath size** : 6 Fr
Outcomes	**Primary** : clinical and ultrasound complications during the first 15 days after treatment **Secondary** : time to haemostasis; time to ambulation (defined as time between removal of the closure device and the moment the participant could stand up and walk for 5 metres); success rate of the system Clinical exams at 1 hour and 24 hours looked for signs of ischaemia, haematoma, re-bleeding, pseudo-aneurysm and arteriovenous fistula. Doppler echographic examination at 24 hours looked for signs of haematoma, pseudo-aneurysm, arteriovenous fistula, intra-arterial thrombus or the presence of arterial narrowing at the puncture level
Notes	Coronography with 6 Fr sheath for all participants

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomised in blocks of 4 for the manual compression group and by envelope opened at the end of the coronography procedure for the suture device group" Comment: Envelopes were used, so sequence generation was probably random. Study was judged to be at low risk of selection bias
Allocation concealment (selection bias)	Low risk	Quote: "closed envelope system" Comment: Envelopes were sealed, so the study was judged to be at low risk of selection bias
Blinding of participants and personnel (performance bias)	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding

Amine 1999 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Ansel 2006

Methods	**Study design** : randomised multi-centre study

Participants	**Country** : USA
	
	Setting : hospital
	
	Number of centres : 7
	
	Numbers: Angiolink EVS 243, manual compression 119
	
	Age (mean (SD)) : Angiolink EVS 61.2 (11.3) years, manual compression 62.9 (10.2) years
	
	Sex : Angiolink EVS 137 M/106 F, manual compression 75 M/44 F
	
	Inclusion criteria : patients 18 to 80 years of age undergoing percutaneous femoral access for elective or urgent transfemoral cardiac or peripheral vascular diagnostic or interventional procedures
	
	Exclusion criteria :
	
	• *Pre-procedure exclusion procedure*
	  • Patients already participating in another research protocol; history of a pre-existing autoimmune disease/vasculitis; history of bleeding/platelet disorder; thrombolytic therapy administered within 24 hours; absent pedal pulses of either extremity; use of a closure device in ipsilateral CFA within 6 months; prior femoral vascular surgery at the targeted site; prior stent placement in the vicinity of the arterial puncture site; pre-existing pseudoaneurysm/arteriovenous fistula/haematoma at targeted site; pre-existing terminal illness that would preclude follow up; pre-existing systemic or cutaneous infection or pre-procedure platelet count < 100,000 × 10^3/μL or haematocrit > 28%
	• *Intraprocedural exclusion procedure*
	  • Obesity precluding access with a standard needle; arterial access requiring multiple punctures; failed single wall arterial puncture; bleeding around sheath before sheath removal; use of a sheath < 6 Fr; tortuous vascular anatomy with bends > 90°; chronic limb ischaemia identified by claudication and severe peripheral vascular disease at or immediately adjacent to the access site arteriotomy as determined by femoral angiography; arterial access obtained in or near a vascular graft; cardiogenic shock experienced during or immediately post procedure; systolic blood pressure < 90 mmHg after the start of the procedure; uncontrolled hypertension; unresponsive to pharmaceutical treatment before closure; failure to remove the sheath within the cardiac catheterisation laboratory
	
	Type of procedure : 188 diagnostic (EVS n = 125, compression n = 63), 174 interventional (EVS n = 118, compression n = 56)

Interventions	**Intervention 1** : Angiolink Vascular Closure System (EVS)

Ansel 2006 *(Continued)*

	Intervention 2 : Manual compression **Sheath size** : > 6 Fr

Outcomes	**Primary** : time to haemostasis (defined as time from sheath removal to complete cessation of bleeding); time to ambulation (defined as time from sheath removal to independent ambulation ≥ 20 feet without complication); time to device deployment (defined as the interval from sheath removal to device deployment); combined rate of major complications at 30-day follow-up
	
	Secondary :
	
	• *Major complications*
	  • Requirement for ultrasound-guided compression for pseudoaneurysm; vascular surgery; femoral occlusion; retroperitoneal bleeding; uncontrolled bleeding requiring surgical intervention; groin-related infection requiring IV antibiotics or extended hospitalisation; new neuropathy in the ipsilateral lower extremity or decline ≥ 1 Rutherford class
	• *Minor complications*
	  • Bleeding not requiring transfusion; haematoma ≥ 6 cm; intraluminal staple delivery not requiring surgical intervention; access site wound dehiscence; localised access site infection treated without intravenous antibiotics; pseudoaneurysm treated with thrombin injection or spontaneous resolution; arteriovenous fistula; ipsilateral pedal pulse ≤ 2 grades
	
	Time of measurement : after sheath removal, before hospital discharge and 30 ± 7 days post procedure

Notes	EVS participants who did not receive IIb/IIIa inhibitors were ambulated 1 hour and those treated with IIb and IIIa were ambulated 2 hours post sheath removal. Manual compression participants were ambulated 4 (no IIb/IIIa inhibitors) and 6 hours (IIb/IIIa inhibitors) post sheath removal

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomised weighted 2:1 toward the device" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judge that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Behan 2007

Methods	**Study design** : prospective randomised controlled trial
Participants	**Country** : United Kingdom **Setting** : district general hospital **Number of centres** : 1 **Numbers:** AngioSeal 107, manual compression 99 **Age (mean (SD))** : AngioSeal 66.3 (9.7) years, manual compression 65.4 (8.7) years **Sex** : AngioSeal 61 M/46 F, manual compression 57 M/42 F **Inclusion criteria** : patients undergoing day case cardiac catheterisation **Exclusion criteria** : unstable angina or acute myocardial infarction; significant peripheral vascular disease; previous peripheral vascular surgery or percutaneous intervention; inability to fully consent; pregnancy; age < 18 years; known ASD or VSD; previous femoral artery complication from angiography; patients whose vascular access site was obtained through a vascular graft; patients with uncontrolled hypertension (> 180 mmHg systolic); puncture site in superficial femoral artery, distal to or at the bifurcation of the superficial femoral and profunda femoris arteries, proximal to the inguinal ligament or multiple punctures
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : manual compression **Sheath size** : 6 Fr
Outcomes	**Primary** : bruising; bleeding (defined as the requirement for transfusion); retroperitoneal bleed; pseudoaneurysm; leg ischaemia; vasovagal reaction; access site infection **Secondary** : participant satisfaction (comfort, experience, duration of hospital stay, immobilisation time, pain during and after the procedure and post-procedure bruising)
Notes	Participants randomised to AngioSeal were mobilised within 30 minutes; manual compression participants were mobilised within 2 hours

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Angiogram lists were randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Bruise size measurements were carried out for all the patients by the same trained nurse, who was separate from the group of operators. This person was not blinded to the method of haemostasis used"

Behan 2007 *(Continued)*

		Comment: no blinding or incomplete blinding for bruising, but this was not an outcome of the review; therefore, it does not introduce detection bias
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Seventy-six of 107 (71%) patients in the Angio-Seal group attended for the 1 week follow up as did 71 of the 99 (72%) in the manual compression group. Furthermore the AngioSeal device was deployed in only 74 out of 107 patients randomised to the device. Reasons are stated for 23 patients but the reasons were not recorded in 10 cases"
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Brachmann 1998

Methods	**Study design** : prospective multi-centre randomised trial
Participants	**Country** : Germany **Setting** : hospital **Number of centres** : not stated **Numbers** : VasoSeal 306, manual compression 204 **Age (mean (SD))** : VasoSeal (angiography) 61 (12) years, VasoSeal (PTCA) 62 (11) years, manual compression (angiography) 61 (10) years, manual compression (PTCA) 61 (10) years **Sex:** VasoSeal 224 M/82 F, manual compression 153 M/51 F **Inclusion criteria** : patients 18 to 80 years of age who were acceptable candidates for diagnostic angiography and percutaneous transluminal coronary angioplasty (PTCA) procedures and manual compression after intervention **Exclusion criteria:** patients who were morbidly obese (body mass index > 40); with bleeding disorders; with a clinically significant haematoma (> 6 cm) present before sheath removal; admitted for emergency angioplasty; with known allergies to beef or collagen products; with elevated blood pressure (> 140/90 mmHg) that could not be controlled by medical therapy; pregnant women
Interventions	**Intervention 1** : VasoSeal **Intervention 2** : manual compression **Sheath size** : 6 to 8 Fr
Outcomes	**Primary** : time to haemostasis; time to mobilisation (defined as time from sheath pull to getting out of bed and moving about as necessary) **Secondary** : vascular repair; transfusion; infection prolonging hospital stay; haematoma > 6 cm; bleeding requiring > 30 minutes to re-achieve haemostasis; pseudoaneurysm requiring mechanical compression; deep vein thrombosis; arteriovenous fistula; infection not prolonging hospital stay; retroperitoneal bleed; thromboembolism; failure to deploy collagen **Time of measurement** : immediately after sheath pull, 24 hours and 30 days post procedure
Notes	PTCA participants were randomised to VasoSeal normal (2 hours after sheath pull) and immediate (immediately after sheath pull) 21 participants removed from the analysis for time to mobilisation because of prior illness

Brachmann 1998 *(Continued)*

	Initial mobilisation was attempted at 1 hour after sheath pull in VasoSeal participants and 6 hours post sheath pull in manual compression participants

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information about the sequence generation process to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No blinding, but review authors judge that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Camenzind 1994

Methods	**Study design** : randomised study
Participants	**Country** : The Netherlands **Setting** : hospital **Number of centres** : 1 **Numbers** : VasoSeal 62, manual compression 62 **Age (mean (SD))** : VasoSeal 59 (12) years, manual compression 60 (11) years **Sex** : VasoSeal 50 M/12 F, manual compression 53 M/9 F **Inclusion criteria** : patients undergoing percutaneous transluminal coronary angioplasty performed with a 6F guiding catheter and full-dose heparinisation for > 12 hours or coronary angioplasty with 7F or 8F guiding catheters and optional subsequent herparinisation **Exclusion criteria** : pre-existing local haematoma and known allergy to collagen products
Interventions	**Intervention 1** : VasoSeal **Intervention 2** : manual compression

Camenzind 1994 *(Continued)*

	Sheath size : 8 Fr
Outcomes	**Primary** : immediate haemostasis **Secondary** : haematoma; pseudoaneurysm; arteriovenous fistula; venous thrombosis; arterial occlusion
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information about the sequence generation process to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Two physicians interpreted the ultrasound examinations without knowledge of treatment assignment" Comment: Blinding of outcome assessors was done. Study was judged to be at low risk of performance bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Study outcomes clearly reported
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Carere 2000

Methods	**Study design** : randomised controlled trial
Participants	**Country** : Canada **Setting** : hospital **Number of centres** : 1 **Numbers** : ProStar-Plus 50, C-Clamp 50 **Age (mean (SD))** : ProStar-Plus 62 (11) years, C-Clamp 59 (12) years **Sex** : ProStar-Plus 44 M/6 F, C-Clamp: 39 M/11 F **Inclusion criteria** : patients with elective or urgent coronary angioplasty with or without stenting in whom same-day discharge was reasonable

Carere 2000 *(Continued)*

	Exclusion criteria : clinical evidence of peripheral arterial disease, pre-existing femoral haematoma, serum creatinine > 150 mmol/L, blood pressure > 180/100 mmHg, participating in another research project
Interventions	**Intervention 1** : ProStar-Plus **Intervention 2** : C-Clamp **Sheath size** : 8 Fr
Outcomes	**Primary** : time to mobilisation; time to discharge **Secondary** : insertion failure; need for vascular surgery; external bleeding after initial haemostasis; an ooze of blood; haematomas (small < 5 cm, medium 5 to 10 cm, large > 10 cm); blood transfusion; participant satisfaction; cost per participant
Notes	Participants randomised to ProStar were mobilised after 4 hours; manual compression participants were mobilised 6 hours after sheath removal

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly allocated" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free of other sources of bias

Castañeda 2003

Methods	**Study design** : randomised trial
Participants	**Country** : United States of America **Setting** : hospital **Number of centres** : 1

Castañeda 2003 *(Continued)*

	Numbers : QuickSeal 85, manual compression 56 **Age (mean (SD))** : QuickSeal 62 (11.4) years, manual compression mean 65 (10.8) years **Sex** : QuickSeal 54 M/31 F, manual compression 31 M/25 F **Inclusion criteria** : patients 18 to 80 years of age undergoing percutaneous diagnostic or interventional procedure via the common femoral artery **Exclusion criteria** : pre-existing autoimmune disease; punctures through a vascular graft; puncture depth < 3 cm or > 7.5 cm; haematoma present before sheath removal; significant bleeding or platelet disorders; uncontrolled hypertension; ipsilateral arterial site closure with QuickSeal within 6 weeks; closure with manual compression within 6 weeks, or closure with another device within 180 days; pregnant or breastfeeding women. Intraprocedural exclusion criteria included bleeding before sheath removal, suspected contamination of access site, multiple or double wall punctures, ipsilateral venous sheath, palpable haematoma before sheath removal and intraprocedural therapeutic thrombolysis
Interventions	**Intervention 1** : QuickSeal **Intervention 2** : manual compression **Sheath size** : ≤ 8 Fr
Outcomes	**Primary** : time to haemostasis (time between sheath pull and haemostasis); time to ambulation (defined as time between end of the procedure and the participant walking 10 feet); rate of major complications (need for medical intervention beyond that of standard procedure (haematoma requiring transfusion, severe vessel damage or infection) and that required extended hospitalisation, transfusion or unanticipated surgery); rate of minor complications (haematoma, ecchymosis, bleeding and minor pseudoaneurysm requiring no intervention) **Secondary** : time to hospital discharge
Notes	Ambulation was attempted at 1 hour, followed by subsequent checks at hourly intervals, in the QuickSeal group. The first check for ambulation in the manual compression group was attempted at 4 hours in participants undergoing diagnostic procedures and at 6 hours among participants undergoing interventional procedures

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomised according to a 3:2 ratio. Randomization was also stratified to type of procedure" Comment: random aspect of sequence generation. Study judged to be at low risk of bias
Allocation concealment (selection bias)	Low risk	Quote: "Opaque envelopes containing the random assignment that specified the method for achieving haemostasis were used to randomise patients" Comment: adequate concealment of allocation, so study judged to be at low risk of selection bias
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk

Castañeda 2003 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Chen 2013

Methods	**Study design** : randomised study
Participants	**Country** : Taiwan **Setting** : hospital **Number of centres** : 1 **Numbers** : Boomerang 30, PerClose 30 **Age (mean (SD))** : Boomerang 63.1 (9.9) years, PerClose mean 69.8 (10.6) years **Sex** : QuickSeal 21 M/9 F, manual compression 20 M/10 F **Inclusion criteria** : patients undergoing percutaneous interventional procedure via the common femoral artery **Exclusion criteria** : patients with “double wall” arterial punctures, intraluminal thrombi, pseudoaneurysms, haematomas, arteriovenous (AV) fistulas or infection in the target artery lesion; history of protamine allergy; previous injections of neutral protamine hagedorn (NPH). We also excluded patients who required a long sheath (> 23 cm)
Interventions	**Intervention 1** : Boomerang **Intervention 2** : PerClose **Sheath size** : 7 Fr
Outcomes	**Primary** : procedure success; device success; device deployment time; device dwell time; manual compression time; time to ambulation; major complications **Secondary** : pain score; minor complications
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk

Chen 2013 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Deuling 2008

Methods	**Study design** : prospective randomised trial
Participants	**Country:** The Netherlands **Setting:** hospital **Number of centres** : 1 **Numbers** : AngioSeal 150, StarClose 150, manual compression 150 **Age (mean (SD))** : AngioSeal 62.7 (11.8) years, StarClose 64.1 (10.8) years, manual compression 62.9 (12.5) years **Sex** : AngioSeal 102 M/48 F, StarClose 109 M/41 F, manual compression 110 M/40 F **Inclusion criteria** : patients admitted for elective diagnostic or interventional cardiac catheterisation procedures who were eligible for femoral access **Exclusion criteria** : high or low arterial puncture
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : StarClose **Intervention 3** : manual compression **Sheath size** : 6 Fr
Outcomes	**Primary:** success of haemostasis; oozing; haemoglobin change during hospital admission; complications (haematoma, need for blood transfusion, surgical intervention at access site, infection) **Secondary:** participant comfort
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Deuling 2008 *(Continued)*

Random sequence generation (selection bias)	High risk	Quote: "Patients received a device or manual compression based on order of presentation" Comment: non-random sequence generation. Study judged to be at high risk of selection bias
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Diaz 2001

Methods	**Study design** : quasi-randomised controlled trial
Participants	**Country** : Spain **Setting** : hospital **Number of centres** : 1 **Numbers** : AngioSeal 75, manual compression 75 **Age (mean (SD))** : AngioSeal 59 (9.5) years, manual compression 60 (9) years **Sex** : AngioSeal 65 M/10 F, manual compression 64 M/11 F **Inclusion criteria** : patients aged over 18 years undergoing coronary angiography and/or percutaneous transluminal coronary angioplasty (PTCA) via the femoral artery with or without implantation of stent **Exclusion criteria** : the drilling of the posterior wall of the artery during puncture, presence of a femoral murmur, history of aortic vascular surgery or lower limb and the presence of haematoma before randomisation
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : manual compression **Sheath size** : 6 Fr
Outcomes	**Primary** : time to haemostasis; time to ambulation

Diaz 2001 *(Continued)*

	Secondary : Hhaematoma
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Sequence generated by odd and even numbers
Allocation concealment (selection bias)	High risk	Allocation based on alternation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No missing data
Selective reporting (reporting bias)	Unclear risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Doneaux 2001

Methods	**Study design** : randomised comparison
Participants	**Country** : Belgium **Setting** : hospital **Number of centres** : not stated **Numbers** : AngioSeal 58, manual compression 63 **Age** : not stated **Sex** : not stated **Inclusion criteria** : patients undergoing percutaneous coronary intervention **Exclusion criteria** : not stated
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : manual compression **Sheath size** : not stated

Doneaux 2001 *(Continued)*

Outcomes	**Primary** : device success; time to compression; duration of compression; time to ambulation; participant satisfaction **Secondary** : large haematoma (> 5 cm); pseudoaneurysm; groin discomfort; subcutaneous bleeding
Notes	Study is published as an abstract only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomised" Comment: insufficient information about the sequence generation process to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judge that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Fargen 2011

Methods	**Study design** : blinded randomised controlled trial
Participants	**Country** : United States of America **Setting** : hospital **Number of centres** : 1 **Numbers** : AngioSeal 32, Mynx 32 **Age (mean (SD))** : Mynx 55.0 (1.9) years, AngioSeal 58.5 (2.6) years **Sex** : Mynx 11 M/21 F, AngioSeal 13 M/19 F **Inclusion criteria** : adult patients undergoing diagnostic cerebral angiography via femoral access **Exclusion criteria** : patients undergoing angiography through any non-femoral artery percutaneous access site; those with documented psychiatric disorders, altered mental status or necessitating conscious sedation during their procedures; those reporting a baseline chronic pain rating ≥ 4 on the visu-

Fargen 2011 *(Continued)*

	al analogue scale (VAS) before closure device deployment; patients in which the puncture was distal to the bifurcation of the superficial femora and profunda femoris arteries; puncture site proximal to the inguinal ligament; puncture through a vascular graft; multiple punctures required to obtain arterial access; patients with clinically significant peripheral vascular disease; uncontrolled hypertension (systolic blood pressure > 180 mmHg); femoral artery size < 5 mm
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : Mynx M5 **Sheath size** : not stated
Outcomes	**Primary** : change in pain from baseline (pre-closure) to post closure, assessed by VAS **Secondary** : participant reporting of the most painful portion of the procedure from a multiple choice selection. Major complications (access site-related surgical vascular repair; amputation related to access closure complication; permanent access site-related nerve injury; access site-related bleeding requiring transfusion; new ipsilateral lower extremity ischaemia by exam, Doppler or angiography requiring non-surgical intervention; local access site-related infection, inflammation or generalised infection due to the procedure requirement of intravenous antibiotics or prolonged hospitalisation); minor complications (arteriovenous fistula documented by ultrasound not requiring treatment; pseudoaneurysm not requiring treatment or treated with thrombin injection; access site haematoma ≥ 6 cm; access site bleeding requiring ≥ 30 minutes to achieve haemostasis; late (pre- or post-discharge) access site-related bleeding; ipsilateral deep vein thrombosis; transient access site-related nerve injury; local access-site related infection or inflammation requiring oral antibiotics)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomization was performed utilizing pre study-created, randomly allotted, sealed envelopes containing the name of the VCD to be used" Comment: insufficient information regarding random sequence generation to permit judgement of high or low risk
Allocation concealment (selection bias)	Low risk	Quote: "Randomization was performed utilizing pre study-created, randomly allotted, sealed envelopes containing the name of the VCD to be used" Comment: adequate concealment of allocation. Study judged to be at low risk of selection bias
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The patients, nurses administering the questionnaire and study coordinators were blinded to the VCD treatment used" Comment: Blinding of participants and personnel was done. Study was judged to be at low risk of performance bias
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The patients, nurses administering the questionnaire and study coordinators were blinded to the VCD treatment used" Comment: Blinding of outcome assessors was done. Study was judged to be at low risk of performance bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data

Fargen 2011 *(Continued)*

Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Gerckens 1998

Methods	**Study design** : single-centre randomised trial
Participants	**Country** : Germany **Setting** : hospital **Number of centres** : 1 **Numbers** : suturing device 298, manual compression 292 **Age (mean (SD))** : suturing device 60 (9) years, manual compression 62 (8) years **Sex** : suturing device 206 M/92 F, manual compression 207 M/85 F **Inclusion criteria** : patients who were possible candidates for same-day ambulation and who had undergone a catheterisation procedure via the common femoral artery through a 5.5 Fr to 8 Fr introducer sheath **Exclusion criteria** : patients with suspected significant peripheral vascular disease; those in whom contralateral or bilateral arterial access site was punctured; previous vascular complication or repair; small common femoral artery; back wall of common femoral artery was punctured; multiple puncture attempts were made; patient's anatomy made successful device deployment unlikely
Interventions	**Intervention 1** : Techstar or ProStar Plus **Intervention 2** : manual compression **Sheath size** : 6 Fr or 8 Fr
Outcomes	**Primary** : incidence of major vascular complications; time to haemostasis; time to ambulation (elapsed time between randomisation and time the participant walked 3 meters) **Secondary** : surgery; untreated pseudoaneurysm; infection requiring oral antibiotics; arteriovenous fistula; peripheral ischaemia; haematoma > 4 cm
Notes	Guidelines for ambulation allowed the participant to walk within 1 hour after the suture-mediated closure procedure in the diagnostic subset and within 4 hours in the interventional subset. Ambulation for compression participants was based on hospital standards (usually 4 hours after diagnotic procedures and 6 hours after achievement of haemostasis after interventional procedures)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomisation process" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk

Gerckens 1998 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Gwechenberger 1997

Methods	**Study design** : randomised study
Participants	**Country** : Austria **Setting** : hospital **Number of centres** : 1 **Numbers:** VasoSeal 33, manual compression 33 **Age (mean (SD))** : VasoSeal 59.8 (8.1) years, manual compression 56.9 (10.8) years **Sex** : VasoSeal 31 M/2 F, manual compression 24 M/5 F **Inclusion criteria** : patients undergoing diagnostic or therapeutic percutaneous transluminal coronary angioplasty **Exclusion criteria** : not stated
Interventions	**Intervention 1** : VasoSeal **Intervention 2** : manual compression **Sheath size** : not stated
Outcomes	**Primary** : time to haemostasis **Secondary** : complications (arteriovenous fistula, pseudoaneurysm, bleeding, haematoma > 6 cm in diameter)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomised"

Gwechenberger 1997 *(Continued)*

		Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Unclear risk	Study outcomes are not clearly reported
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Hattab 2012

Methods	**Study design** : prospective randomised study
Participants	**Country** : France **Setting** : hospital **Number of centres** : 1 **Numbers:** ExoSeal 50, ProGlide 50 **Age** : not stated **Sex** : not stated **Inclusion criteria** : patients undergoing PCI and endovascular peripheral procedures via retrograde femoral artery access **Exclusion criteria** : not stated
Interventions	**Intervention 1** : ExoSeal **Intervention 2** : PerClose ProGlide **Sheath size** : 6 Fr
Outcomes	**Primary** : immediate total haemostasis **Secondary** : incidence of vascular complications (haematoma, blood transfusion)
Notes	
Risk of bias	

Hattab 2012 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly assigned" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Hermanides 2010

Methods	**Study design** : single-centre retrospective randomised study
Participants	**Country** : The Netherlands **Setting** : hospital **Number of centres** : 1 **Numbers:** AngioSeal 313, manual compression 314 **Age (mean (SD))** : AngioSeal 64.5 (11.3) years, manual compression 64.0 (11.0) years **Sex** : AngioSeal 238 M/75 F, manual compression 239 M/75 F **Inclusion criteria** : patients undergoing PCI via femoral artery access **Exclusion criteria** : age < 18 years; serious co-morbidity such as cancer; advanced cerebrovascular disease; unwilling or unable to sign the consent form for participation; females of childbearing age not using medically prescribed contraceptives; unsuitable access site (severe peripheral vascular disease, poor location)
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : manual compression **Sheath size** : 6 Fr
Outcomes	**Primary** : combined incidence of (1) severe haematoma > 5 cm at the puncture site or groin bleeding resulting in prolonged hospital stay, transfusion and/or surgical intervention at the puncture site; (2) arteriovenous fistula formation at the puncture site and/or surgical intervention at the puncture site

Hermanides 2010 *(Continued)*

	Secondary : decrease in haemoglobin 1 day after inclusion; hospital admission duration
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was performed by means of a computer program in blocks (randomly changing block size)" Comment: random sequence generation. Study was judged to be at low risk of selection bias
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "A blinded independent clinical endpoint committee adjudicated all clinical endpoints" Comment: Blinding of outcome assessors was done. Study was judged to be at low risk of performance bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Hermiller 2005

Methods	**Study design** : prospective randomised multi-centre trial (CLIP trial). Substudy of diagnostic arm
Participants	**Country** : United States of America **Setting** : hospital **Number of centres** : 17 **Numbers** : StarClose 136, manual compression 72 **Age (mean (SD))** : StarClose 62.07 (12.12) years, manual compression 60.85 (11.11) years **Sex** : StarClose 93 M/43 F, manual compression 46 M/26 F **Inclusion criteria** : patients undergoing diagnostic angiography; arterial puncture site in an appropriate vessel; suitable as a candidate for vascular surgery; ability to complete required clinical follow-up **Exclusion criteria** : patients with uncontrolled hypertension, clinically severe peripheral vascular disease (including calcification at the arteriotomy), obesity (BMI > 35) or a history of bleeding diathesis

Hermiller 2005 *(Continued)*

Interventions	**Intervention 1** : StarClose **Intervention 2** : manual compression **Sheath size** : 6 Fr
Outcomes	**Primary** : major vascular complications (composite of vascular injury requiring repair, new ipsilateral distal ischaemia requiring revascularisation, access site nerve injury requiring intervention, access site bleeding requiring transfusion and access site infection requiring intravenous antibiotics or prolonged hospital stay); time to haemostasis (defined as time between sheath removal and first observed clinical haemostasis) **Secondary** : device success; procedure success; time to ambulation (defined as time from sheath pull to participant walking 20 feet without bleeding); time to discharge **Follow-up** : 30 days post procedure
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information to permit judgement of low or high risk
Allocation concealment (selection bias)	Unclear risk	Comment: insufficient information to permit judgement of low or high risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to permit judgement of low or high risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Hermiller 2006

Methods	**Study design** : prospective randomised multi-centre trial (CLIP trial). Substudy of interventional arm
Participants	**Country** : United States of America **Setting** : hospital **Number of centres** : 17

Hermiller 2006 *(Continued)*

	Numbers: StarClose 184, manual compression 91 **Age** : 62.8 (9.9) years **Sex** : 221 M/54 F **Inclusion criteria** : patients undergoing interventional catheterisation procedures; arterial puncture site in an appropriate vessel; suitability as a candidate for vascular surgery with ability to complete required clinical follow-up **Exclusion criteria** : patients with uncontrolled hypertension; clinically severe peripheral vascular disease (including calcification at the arteriotomy); obesity (BMI > 35);history of bleeding diathesis
Interventions	**Intervention 1** : StarClose **Intervention 2** : manual compression **Sheath size** : 6 Fr
Outcomes	**Primary** : major vascular complications (composite of vascular injury requiring repair, new ipsilateral distal ischaemia requiring revascularisation, access site nerve injury requiring intervention, access site bleeding requiring transfusion and access site infection requiring intravenous antibiotics or prolonged hospital stay); time to haemostasis (defined as time between sheath removal and first observed clinical haemostasis) **Secondary** : device success; procedure success; time to ambulation (defined as time from sheath pull to participant walking 20 feet without bleeding); time to discharge
Notes	All participants received anticoagulation medication (heparin, aspirin, clopidogrel, glycoprotein IIb/IIIa inhibitors)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Subjects were randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Holm 2014

Methods	**Study design** : prospective randomised non-blinded single-centre trial (CLOSE-UP trial)
Participants	**Country** : Denmark **Setting** : hospital **Number of centres** : 1 **Numbers:** FemoSeal 500, manual compression 501 **Age (mean (SD))** : FemoSeal 64.3 (11) years, manual compression 65.2 (11) years **Sex** : FemoSeal 310 M/190 F, manual compression 311 M/190 F **Inclusion criteria** : patients > 18 years of age eligible for femoral access and scheduled for elective diagnostic coronary angiography **Exclusion criteria** • Patients with expected life span < 1 year • Coronary angiography within the past month or subsequent coronary angiography within 14 days • Presence of groin haematoma before closure procedure • Known pseudoaneurysm at the femoral artery • Sheath size other than 6 Fr • Known stenosis of > 50% in the femoral or iliac artery • INR above 3.0 • Platelet count < 120×19^9/L • Thrombolysis within 24 hours • Femoral disease • Pregnancy • Systolic blood pressure > 200 mmHg and/or diastolic pressure > 110 mmHg • Patients with femoral vein access during the same procedure
Interventions	**Intervention 1** : FemoSeal **Intervention 2** : manual compression **Sheath size** : 6 Fr
Outcomes	**Primary** • In-hospital incidence of access site haematoma > 5 cm **Secondary** • 14-Day major bleeding • Retroperitoneal bleeding • Pseudoaneurysm • Arteriovenous fistula • Infection • Other complications necessitating surgery • Time to haemostasis • Time to ambulation • Device deployment failure • Need for repeat manual compression after haemostasis was obtained • Vasovagal response

Holm 2014 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomisation was performed 1:1 by telephone call to a voice prompt stand-alone computer-based system" Comment: random sequence generation. Study was judged to be at low risk of selection bias
Allocation concealment (selection bias)	Low risk	Quote: "Randomisation was performed 1:1 by telephone call to a voice prompt stand-alone computer-based system" Comment: adequate concealment of allocation. Study was judged to be at low risk of selection bias
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Jensen 2008

Methods	**Study design** : prospective randomised single-centre study
Participants	**Country** : Sweden **Setting** : hospital **Number of centres** : 1 **Numbers** : AngioSeal 22, PerClose 22, FemoStop 24 **Age (mean (SD))** : AngioSeal 63 (11) years, PerClose 62 (9) years, FemoStop 61 (9) years, **Sex** : AngioSeal 15 M/7 F, PerClose 16 M/6 F, FemoStop 21 M/3 F **Inclusion criteria** : Patients undergoing planned coronary angiography because of stable angina pectoris were able to complete the required clinical follow-up and provide informed consent **Exclusion criteria** : patients with unstable angina pectoris, ongoing infection, known inflammatory disease, previous PCI or coronary bypass grafting or other major surgery within 12 months and during follow-up, and ongoing treatment with warfarin, steroids or non-steroid anti-inflammatory drugs

Jensen 2008 *(Continued)*

Interventions	**Intervention 1** : AngioSeal **Intervention 2** : PerClose **Intervention 3** : FemoStop **Sheath size** : 6 Fr
Outcomes	**Primary** : inflammatory markers **Secondary** : immediate haemostasis; vascular injury; bleeding; haematoma
Notes	FemoStop participants were ambulated after 2 hours; those who received AngioSeal or PerClose were ambulated after 1 hour

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised to one of the following devices" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Unclear risk	Number of side effects not reported
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk.

Juergens 2004

Methods	**Study design** : randomised trial
Participants	**Country** : Australia **Setting** : hospital **Number of centres** : 1 **Numbers** : 58 AngioSeal, 57 FemoStop **Age (mean (SD))** : AngioSeal 59 (11) years, FemoStop 59 (10) years

Juergens 2004 *(Continued)*

	Sex : AngioSeal 44 M/14 F, FemoStop 46 M/11 F **Inclusion criteria** : patients undergoing percutaneous coronary intervention, clean (single puncture through the anterior wall only) arterial access with a 7 Fr sheath and guiding system, no development of haematoma during the procedure **Exclusion criteria** : patients in whom repeat femoral access through the same side was likely within the ensuing 90 days
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : FemoStop **Sheath size** : 7 Fr
Outcomes	**Primary** : patient tolerance and resource utilisation (cost of disposals, amount of medical and nursing time spent attending to the femoral access site) **Secondary** : time to removal of participant from angiography suite; time to haemostasis; time to ambulation; time to hospital discharge; incidence of vascular complications
Notes	First outcome assessments were made at 4 hours, at 8 hours and on the morning after the procedure

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised at the end of the procedure" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Patients underwent a duplex ultrasound reported by a vascular surgeon who was blinded to treatment assignment" Comment: outcome assessors blinded to treatment. Study was judged to be at low risk of detection bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Kalsch 2008

Methods	**Study design** : prospective single-centre randomised study

Kalsch 2008 *(Continued)*

Participants	**Country** : Germany **Setting** : hospital **Number of centres** : 1 **Numbers** : AngioSeal 214, PerClose 152 **Age (mean (SD))** : AngioSeal 64 (11) years, PerClose 65 (10) years **Sex** : AngioSeal 151 M/61 F, PerClose 111 M/43 F **Inclusion criteria** : patients undergoing diagnostic cardiac catheterisation (n = 224) or interventional coronary procedures (n = 144) **Exclusion criteria** : patients < 18 years, pre-existing large haematoma, known allergy to bovine products or reabsorbable suture material
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : PerClose **Sheath size** : 6 Fr or 8 Fr
Outcomes	**Primary** : ankle-brachial index; incidence of major complications during the in-hospital period **Secondary** : successful technical deployment of the device; successful +haemostasis without additional treatment
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised to..." Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Kussmaul 1995

Methods	**Study design** : randomised multi-centre trial
Participants	**Country** : United States of America **Setting** : hospital **Number of centres** : 8 **Numbers** : AngioSeal 218, manual compression 217 **Age (mean (SD))** : AngioSeal 61 (11) years, manual compression 62 (11) years **Sex** : AngioSeal 159 M/59 F, manual compression 156 M/61 F **Inclusion criteria** : patients undergoing cardiac catheterisation or angioplasty **Exclusion criteria** : patients < 18 or > 80 years; bleeding diathesis; warfarin therapy; thrombolytic therapy within 24 hours of or during catheterisation; acute myocardial infarction; marked obesity; uncontrolled hypertension and known allergy to bovine collagen or reabsorbable suture material; clinical or ultrasound evidence of significant peripheral vascular disease; history of claudication or vascular surgery; absent pedal pulses; femoral artery bruit; ankle/brachial systolic blood pressure index < 0.9; significant (> 20% occlusive) anterior atherosclerosis seen on ultrasound of the common femoral artery
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : manual compression **Sheath size** : 8 Fr
Outcomes	**Primary** : time to haemostasis (defined as time between sheath removal and no bleeding) **Secondary** : complications (bleeding (any external blood loss after device deployment, ≥ 30 minutes of manual pressure required or any late bleeding, whether or not a measurable decrease in hematocrit occurred or transfusion was necessary); haematoma (any palpable mass); pseudoaneurysm (periarterial mass detected by physical examination or ultrasound-containing Doppler-detected flow); loss of pulse; infection; clinical evidence of leg ischaemia)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomisation procedure ensured that equal numbers of patients would be randomised to groups I and II by using a block scheme with six patients per block" Comment: random sequence generation. Study was judged to be at low risk of selection bias
Allocation concealment (selection bias)	Low risk	Quote: "The results of randomisation were place in sealed, sequential envelopes to be opened at each site as needed" Comment: adequate concealment of allocation. Study was judged to be at low risk of selection bias
Blinding of participants and personnel (performance bias)	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding

Kussmaul 1995 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Of the 435 participants randomised, 115 underwent interventional procedures. However, data on only 109 interventional participants are reported. Therefore, 6 participants are missing from this analysis, and it is not stated why
Selective reporting (reporting bias)	Unclear risk	Study outcomes not clearly pre-specified
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Legrand 2005

Methods	**Study design** : randomised trial
Participants	**Country** : Belgium **Setting** : hospital **Number of centres** : 1 **Numbers** : AngioSeal 100, manual compression 102 **Age (mean (SD))** : AngioSeal 62.6 (10.3) years, manual compression 62.1 (13.0) years **Sex** : AngioSeal 79 M/21 F, manual compression 77 M/25 F **Inclusion criteria** : patients undergoing coronary intervention through a femoral 6 Fr access sheath **Exclusion criteria** : uncontrolled hypertension (> 200 mmHg); platelet count < 75,000; septicaemia; acute myocardial infarction; cardiogenic shock; severe acute non-cardiac systemic disease or terminal illness; sheath in place longer than 24 hours; multiple femoral punctures; significant femoral disease and/or vascular tortuosity in the region of the puncture; vessel diameter < 5 mm; arterial puncture performed in the profunda femoris or close to the bifurcation; access through a femoral prosthesis; access sheath in the femoral vein; presence of a palpable haematoma at the end of the procedure
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : manual compression **Sheath size** : 6 Fr
Outcomes	**Primary** : freedom from puncture site-related complications (vasovagal response requiring atropine and fluid administration; large haematoma defined as any palpable mass > 5 cm diameter; pseudoaneurysm detected by Doppler ultrasound with significant bleeding after an initial period of haemostasis; loss of pulse; vessel occlusion; deep vein thrombosis; retroperitoneal haemorrhage; infection; arteriovenous fistula; crural nerve compression) **Secondary** : time to haemostasis; time to ambulation (defined as time between the end of PCI and cessation of bedrest); nursing time; participant satisfaction
Notes	

Risk of bias

Legrand 2005 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The computer assisted randomisation procedure ensured that approximately 100 patients would be included in each group" Comment: random sequence generation. Study was judged to be at low risk of selection bias
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Machnik 2012

Methods	**Study design** : randomised study
Participants	**Country** : Poland **Setting** : hospital **Number of centres** : 1 **Numbers** : AngioSeal 91, manual compression 110 **Age (mean (SD))** : AngioSeal 66.9 (8) years, manual compression 66.7 (8) years **Sex** : AngioSeal 53 M/38 F, manual compression 66 M/44 F **Inclusion criteria** : patients undergoing percutaneous interventions on carotid, vertebral or peripheral arteries **Exclusion criteria** : not stated
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : manual compression **Sheath size** : 6 Fr and 8 Fr
Outcomes	**Primary** : complications (large haematomas (> 10 cm), acute lower limb ischaemia requiring surgical intervention, pseudoaneurysm, arteriovenous fistula)

Machnik 2012 *(Continued)*

	Secondary : time to mobilisation; duration of post-procedural hospitalisation
Notes	All participants were receiving dual antiplatelet therapy (aspirin 75 mg + clopidogrel 75 mg). Unfractionated heparin was used during the procedure to achieve activated coagulation time > 250 seconds. Oral anticoagulant therapy was stopped before the procedure in all participants receiving long-term treatment with acenocoumarol/warfarin to obtain INR < 1.4, allowing an elective percutaneous intervention. Subcutaneous injections of low molecular weight heparin were stopped for ≥ 12 hours before the procedure and after the procedure for all participants receiving this type of therapy

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Unclear risk	Study outcomes are not clearly pre-specified
Other bias	Low risk	Study appears to be free from other sources of bias

Magosaki 1999

Methods	**Study design** : propsective randomised trial
Participants	**Country** : Japan **Setting** : hospital **Number of centres** : 4 **Numbers** : AngioSeal 120, manual compression 120 **Age (mean (SD))** : AngioSeal 61.1 (10.9) years, manual compression 60.9 (9.9) years **Sex** : AngioSeal 93 M/27 F, manual compression 90 M/30 F **Inclusion criteria** : patients undergoing diagnostic angiography or coronary angioplasty **Exclusion criteria** : not stated

Magosaki 1999 *(Continued)*

Interventions	**Intervention 1** : AngioSeal **Intervention 2** : manual compression **Sheath size** : 5 to 8 Fr
Outcomes	**Primary** : time to haemostasis; time to ambulation; complications **Secondary** : activated clotting time; successful placement of device
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Martin 2008

Methods	**Study design** : prospective randomised trial
Participants	**Country** : United States of America **Setting** : hospital **Number of centres** : 1 **Numbers** : AngioSeal 70, PerClose ProGlide 63, manual compression 67 **Age (mean (SD))** : AngioSeal 63 (12) years, PerClose 66 (12) years, manual compression 68 (11) years **Sex** : AngioSeal 50 M/20 F, PerClose 40 M/23 F, manual compression 50 M/17 F **Inclusion criteria** : patients undergoing PCI using a 6 Fr femoral sheath

Martin 2008 *(Continued)*

	Exclusion criteria : arterial insertion site not in the common femoral artery; more than minimal arterial calcification or common femoral artery < 6 mm in diameter; patients with INR > 1.4 or who had prior arterial access at the same femoral site within 30 days
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : PerClose **Intervention 3** : manual compression **Sheath size** : not stated
Outcomes	**Primary** : major and minor bleeding; time to haemostasis (defined as time at which no compression was required to control bleeding at the arteriotomy site) **Secondary** : time to ambulation; vascular complications (retroperitoneal haemorrhage, pseudoaneurysm, thrombosis, arteriovenous fistula); participant satisfaction
Notes	Ambulation was allowed 3 hours after PerClose or AngioSeal and 6 hours after compression

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "A patient questionnaire was administered at hospital discharge by study personnel blinded to treatment assignment" Comment: Study personnel assessing participant satisfaction were blinded to treatment allocation. However, it is not clear whether assessors measuring other study outcomes such as time to haemostasis, time to mobilisation and complications were blinded to treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Michalis 2002

Methods	**Study design** : prospective randomised single-centre trial
Participants	**Country** : Greece

Michalis 2002 *(Continued)*

	Setting : hospital **Number of centres** : 1 **Numbers** : AngioSeal 290, VasoSeal 280, Duett 281 **Age (mean (SD))** : AngioSeal 62.7 (14.3) years, VasoSeal 64.1 (10.2) years, Duett 62.4 (12.6) years **Sex** : AngioSeal 200 M/90 F, VasoSeal 196 M/84 F, Duett 205 M/76 F **Inclusion criteria** : patients undergoing coronary angiography and/or angioplasty who were deemed appropriate for immediate sheath removal **Exclusion criteria** : patients in whom the sheath was retained for prolonged access
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : VasoSeal **Intervention 3** : Duett **Sheath size** : 6 Fr
Outcomes	**Primary** : successful deployment of the device; time of device deployment; time to haemostasis (defined as time between completion of the device insertion procedure to achievement of haemostasis by compression); time to ambulation (measured from end of the catheterisation procedure until participant was able to stand and walk 3 to 5 steps unaided) **Secondary** : major complications (haematoma > 5 cm in diameter; haematoma or bleeding requiring transfusion; pseudoaneurysm; arteriovenous fistula; retroperitoneal haemorrhage; plug embolism; groin infection; death); minor complications (bleeding from the puncture site that did not require transfusion and/or vascular surgery; haematoma < 5 cm in diameter; pain at the puncture site; skin allergic reaction related to the device)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were prospectively randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data

Michalis 2002 *(Continued)*

Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Nelson 2014

Methods	**Study design** : prospective multi-centre randomised controlled trial
Participants	**Country** : America **Setting** : hospital **Number of centres** : 20 **Numbers** : ProGlide 50, ProStar XL 51 **Age (mean (SD))** : ProGlide (70 (6.6)) years, ProStar XL (74 (11)) years **Sex (M/F)** : ProGlide 47 M/3 F, ProStar XL 44 M/7 F **Inclusion criteria** : patients ≥ 18 years old with an abdominal aortic aneurysm (AAA) of maximum diameter ≥ 5 cm, or in the range of 4 to 5 cm, which has increased by ≥ 0.5 cm in the past 6 months; suitable ipsilateral common femoral artery for percutaneous access using a 'PreClose' technique as detailed in the protocol **Exclusion criteria** • Life expectancy < 1 year as judged by the investigator • Psychiatric or other condition that may interfere with the study • Participation in the enrolment or 30-day follow-up phase of another clinical study • Known allergy to any device component • Coagulopathy or uncontrolled bleeding disorder • Ruptured, leaking or mycotic aneurysm • Serum creatinine (S-Cr) level > 1.7 mg/dL • Traumatic vascular injury • Active systemic or localised groin infection • Connective tissue disease (e.g. Marfan's syndrome) • Renal transplant patient • Recent (within prior 3 months) cerebrovascular accident or myocardial infarction • Planned major intervention or surgery within 30 days following the EVAR procedure • Requirement for an arterial conduit at the access site • Morbid obesity (BMI ≥ 40) • Calcification throughout the CFA target area anterior wall or circumferentially, or over > 50% of the posterior wall • Femoral artery aneurysm, arteriovenous fistula or pseudoaneurysm • Evidence of prior common femoral artery surgery (e.g. groin incision) • Prior clip-based vascular closure device placement in either arterial access site • Collagen-based vascular closure device placement in either arterial access site within the prior 90 days • Femoral artery needle puncture in either arterial access site within the prior 30 days • Haematoma at the ipsilateral arterial access site • Significant scarring at the ipsilateral arterial access site
Interventions	**Intervention 1** : ProGlide

Nelson 2014 *(Continued)*

	Intervention 2 : ProStar XL **Sheath size** : ProGlide 8 Fr, ProStar XL 10 Fr
Outcomes	**Primary** : treatment success defined as the composite of procedural technical success, absence of vascular complications and absence of major adverse events **Secondary** : all serious and non-serious adverse events; stent graft patency and integrity; health-related quality of life survey; clinical utility measures
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was conducted by study site, using two block sizes (3 or 6) with random choice of block size order" Comment: random sequence generation. Study was judged to be at low risk of selection bias
Allocation concealment (selection bias)	Low risk	Quote: "One set of sealed randomization envelopes was provided to each site after completion of roll-in cases and on sponsor approval to initiate the randomized trial. On screening eligibility confirmation, the next sequential randomization envelope was opened and the assignment was immediately allocated" Comment: adequate concealment of allocation. Study was judged to be at low risk of selection bias
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Noguchi 2000

Methods	**Study design** : prospective randomised controlled trial
Participants	**Country** : Japan **Setting** : hospital **Number of centres** : 1

Noguchi 2000 *(Continued)*

	Numbers : ProStar 30, manual compression 30 **Age (mean (SD))** : ProStar 63 (10) years, manual compression 61 (12) years **Sex** : ProStar 27 M/3 F, manual compression 25 M/5 F **Inclusion criteria** : patients undergoing angioplasty or stenting **Exclusion criteria** : arterial access at a site other than the right or left femoral artery; emergency procedure; continued use of warfarin before the procedure; haematoma formation during the procedure; history of claudication due to arteriosclerosis obliterans or vascular surgery that involved the groin area such as aortofemoral bypass surgery; unwillingness or inability to provide written informed consent
Interventions	**Intervention 1** : ProStar **Intervention 2** : manual compression **Sheath size** : 8 Fr
Outcomes	**Primary** : time to haemostasis; time to ambulation; time to discharge **Secondary** : surgical repair; infection; arteriovenous fistula; pseudoaneurysm; distal embolisation; haematoma; participant comfort; hospital costs
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information about the sequence generation process to permit judgement of high or low risk
Allocation concealment (selection bias)	Low risk	Quote: "Randomisation was carried out using consecutive sealed envelopes" Comment: Envelopes were sealed, so the study was judged to be at low risk of selection bias
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Study outcomes are clearly reported
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Park 2005

Methods	**Study design** : prospective randomised study
Participants	**Country** : Korea **Setting** : hospital **Number of centres** : 1 **Numbers** : AngioSeal 961, Closure S 715 **Age (mean)** : AngioSeal 56.8 years, Closure S 51.1 years **Sex** : AngioSeal 727 M/234 F, Closure S 435 M/280 F **Inclusion criteria** : patients undergoing diagnostic angiography or endovascular interventional treatment **Exclusion criteria** : difficulty in puncturing the artery; severe peripheral vascular disease; marked obesity; age < 15 years; arterial sheath size < 4 Fr or > 8 Fr; patient's refusal to provide written informed consent
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : Closure S **Sheath size** : 6 Fr or 8 Fr
Outcomes	**Primary** : immediate haemostasis; successful vascular device closure (defined as immediate haemostasis without complications) **Secondary** : major complications (need for vascular surgery; haemorrhage requiring transfusion; pseudoaneurysm; arteriovenous fistula; arterial occlusion or distal arterial embolism; infection necessitating treatment with intravenous antibiotics or surgical debridement); minor complications (haemorrhage from the puncture site that was controlled via conservative management without transfusion (i.e. additional manual compression, sandbag placement or prolonged bedrest); infection that could be treated with oral antibiotics). All complications were categorised as early (< 24 hours of the procedure) and late (≥ 24 hours after the procedure)
Notes	This study included participants with several femoral artery punctures. Outcomes are based on the number of punctures rather than on the number of individual participants. After personal communication with the study author, it was decided that although this study was relevant and met the inclusion criteria, we would not include data in the analyses, as they were not comparable with data based on individuals from the other included studies

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised"
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding

Park 2005 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Perlowski 2011

Methods	**Study design** : single-centre prospective randomised trial
Participants	**Country** : United States of America **Setting** : hospital **Number of centres** : 1 **Numbers** : StarClose 39, manual compression 42 **Age** : not stated **Sex** : not stated **Inclusion criteria** : patients with confirmed peripheral arterial disease undergoing percutaneous endovascular and coronary procedures **Exclusion criteria** : not stated
Interventions	**Intervention 1** : StarClose **Intervention 2** : manual compression **Sheath size** : not stated
Outcomes	**Primary** : vascular complications (pseudoaneurysm, arteriovenous fistula) **Secondary** : time to haemostasis; procedural success; device success; death
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised to" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk

Perlowski 2011 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Rastan 2008

Methods	**Study design** : prospective single-centre randomised controlled trial
Participants	**Country** : Switzerland **Setting** : hospital **Number of centres** : 1 **Numbers** : AngioSeal 285, StarClose 286 **Age (mean (SD))** : AngioSeal 67.6 (9.3) years, StarClose 66.1 (10.3) years **Sex** : AngioSeal 201 M/84 F, StarClose 204 M/82 F **Inclusion criteria** : patients undergoing a percutaneous transluminal procedure through a 5 Fr or 6 Fr femoral sheath **Exclusion criteria** : patients with a history of vascular surgery at the intended access site; treatment with glycoprotein IIb/IIIa inhibitors or fibrinolytic therapy; history of bleeding diathesis or documented puncture of the superficial or deep femoral artery near the femoral artery bifurcation
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : StarClose **Sheath size** : 5 Fr or 6 Fr
Outcomes	**Primary** : composite incidence of access site pseudoaneurysm, major bleeding requiring transfusion, in-hospital access site vascular surgery or catheter intervention or in-hospital death from all causes **Secondary** : incidence of arteriovenous fistula; device failure (defined as access site bleeding requiring adjunctive therapy such as prolonged manual compression and/or pressure bandage); groin haematoma ≥ 5 cm in diameter
Notes	
Risk of bias	

Rastan 2008 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomization was by envelope" Comment: insufficient information regarding random sequence generation to permit judgement of high or low risk
Allocation concealment (selection bias)	Low risk	Quote: "Randomization was by sealed envelope" Comment: adequate concealment of allocation. Study was judged to be at low risk of selection bias
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Reddy 2004

Methods	**Study design** : prospective randomised study
Participants	**Country** : United States of America **Setting** : hospital **Number of centres** : 1 **Numbers** : AngioSeal 25, manual compression 25 **Age (mean (SD))** : AngioSeal 64 (3) years, manual compression 61 (3) years **Sex** : AngioSeal 15 M/10 F, manual compression 14 M/11 F **Inclusion criteria** : patients undergoing diagnostic cardiac catheterisation; ≥ 18 years of age; easily palpable femoral and radial pulses; a normal Allen's test **Exclusion criteria** : vascular disease of the upper or lower extremities precluding access at the femoral or radial artery; prior femoral artery graft surgery; unstable coronary syndromes; unstable patients with myocardial infarction who require an intervention within 7 days; patients for whom additional procedures were planned at the same setting or during the same hospital stay; those who were unable or unwilling to provide informed consent
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : manual compression

Reddy 2004 *(Continued)*

	Sheath size : 6 Fr
Outcomes	**Primary** : quality of life **Secondary** : cardiovascular and major vascular complications
Notes	All participants were ambulated within 1 hour

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were prospectively randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Rickli 2002

Methods	**Study design** : single-centre multiple-operator prospective study
Participants	**Country** : Switzerland **Setting** : hospital **Number of centres** : 1 **Numbers** : PerClose 96, manual compression 97 **Age (mean (SD))** : PerClose 62 (11) years, manual compression 59 (10) years **Sex** : PerClose 71 M/25 F, manual compression 81 M/16 F **Inclusion criteria** : patients undergoing percutaneous coronary intervention by 6 Fr or 7 Fr femoral access **Exclusion criteria** : not stated

Rickli 2002 *(Continued)*

Interventions	**Intervention 1** : PerClose **Intervention 2** : manual compression **Sheath size** : 6 Fr and 7 Fr
Outcomes	**Primary** : major (need for surgical intervention; local infection; need for blood transfusion); minor complications (pseudoaneurysm; local haematoma > 1 mL assessed by ultrasound); time to haemostasis; time to ambulation; time to discharge **Secondary** : participant discomfort; costs
Notes	Participants treated with PerClose were allowed to ambulate 4 hours after the procedure, but manual compression participants were ambulated the morning after the procedure

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Sanborn 1993

Methods	**Study design** : prospective multi-centre randomised trial
Participants	**Country** : United States of America **Setting** : hospital **Number of centres** : not stated **Numbers** : VasoSeal 246 (90 diagnostic catheterisation, 156 coronary angioplasty), manual compression 209 (75 diagnostic catheterisation, 134 coronary angioplasty)

Sanborn 1993 *(Continued)*

	Age (mean (SD)) : VasoSeal diagnostic catheterisation 62.4 (10.8) years, VasoSeal coronary angioplasty without heparin 58.6 (9.8) years, VasoSeal coronary angioplasty with heparin 60.8 (9.8) years, manual compression diagnostic catheterisation 62.8 (10.7) years, manual compression coronary angioplasty 61.3 (11.0) years **Sex** : VasoSeal 181 M/65 F, manual compression 141 M/68 F **Inclusion criteria** : patients undergoing diagnostic cardiac catheterisation or balloon angioplasty; > 20 years of age; ability to give written consent and understand the obligation for a follow-up study **Exclusion criteria** : patients who were markedly obese; known platelet dysfunction; uncontrolled hypertension; haematoma during catheterisation or angioplasty procedure. Patients undergoing atherectomy or intracoronary stent placement were not enrolled because the interventions required larger sheaths or greater anticoagulant regimens
Interventions	**Intervention 1** : VasoSeal **Intervention 2** : manual compression **Sheath size** : 6 to 9 Fr
Outcomes	**Primary** : time to haemostasis (defined as time elapsed from initial compression and removal of pre-existing sheath until completion of compression); time to ambulation (calculated as total time from start of the procedure until ambulation) **Secondary** : peripheral vascular complications requiring vascular surgical repair for bleeding; large pseudoaneurysm; arteriovenous fistula; thrombosis or loss of distal pulse; transfusion due to bleeding at puncture site; deep vein thrombosis; infection at the puncture site requiring intravenous antibiotics; bleeding from the puncture site; small pseudoaneurysm treated medically; haematomas 2 to 6 cm and > 6 cm **Follow-up** : in hospital, 3 days and 30 days after sheath removal
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information to provide judgement on low or high risk of bias
Allocation concealment (selection bias)	Unclear risk	Insufficient information to provide judgement on low or high risk of bias
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to provide judgement on low or high risk of bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data

Sanborn 1993 *(Continued)*

Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Schräder 1992

Methods	**Study design** : randomised single-centre study
Participants	**Country** : Germany **Setting** : hospital **Number of centres** : 1 **Numbers:** VasoSeal 50, manual compression 50 **Age (mean (SD))** : VasoSeal 58.5 (10.2) years, manual compression 58.5 (9.2) years **Sex** : VasoSeal 43 M/7 F, manual compression 45 M/5 F **Inclusion criteria** : patients undergoing femoral artery catheterisation for coronary angiography or coronary artery dilation **Exclusion criteria** : patients taking vitamin K antagonists; thrombyte disorders; allergy to collagen products
Interventions	**Intervention 1** : VasoSeal **Intervention 2** : pressure dressing
Outcomes	**Primary** : compression time; time to ambulation **Secondary** : bleeding; haematoma **Follow-up** : not reported
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information to provide judgement on low or high risk of bias
Allocation concealment (selection bias)	Unclear risk	Insufficient information to provide judgement on low or high risk of bias
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias)	Unclear risk	Insufficient information to provide judgement on low or high risk of bias

Schräder 1992 *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to provide judgement on low or high risk of bias
Selective reporting (reporting bias)	Unclear risk	Insufficient information to provide judgement on low or high risk of bias
Other bias	Unclear risk	Insufficient information to provide judgement on low or high risk of bias

Schulz-Schüpke 2014

Methods	**Study design** : randomised large-scale multi-centre open-label clinical trial
Participants	**Country** : Germany **Setting** : hospital **Number of centres** : 4 **Numbers:** FemoSeal 1509, ExoSeal 1506, manual compression 1509 **Age (mean (range))** : FemoSeal 66.6 (57.8 to 74.3) years, ExoSeal 68.1 (59.3 to 74.9) years, manual compression 68.4 (59.5 to 74.8 years) **Sex** : FemoSeal 1040 M/469 F, ExoSeal 1058 M/448 F, manual compression 1031 M/478 F **Inclusion criteria** : Patients were eligible for enrolment if they provided written informed consent and were undergoing diagnostic coronary angiography (without subsequent percutaneous coronary intervention) with a 6 Fr sheath through the common femoral artery, which had to have a diameter > 5 mm (proven by angiography) **Exclusion criteria** : Major exclusion criteria were implantation of a VCD within the last 30 days, symptomatic leg ischaemia, prior thromboendarteriectomy (TEA) or patch plastic of the common femoral artery, planned invasive diagnostic or interventional procedure in the following 90 days, a heavily calcified vessel, active bleeding or bleeding diathesis, severe arterial hypertension (> 220/110 mmHg), local infection, autoimmune disease, allergy to resorbable suture and pregnancy
Interventions	**Intervention 1** : FemoSeal **Intervention 2** : ExoSeal **Intervention 3** : manual compression **Sheath size** : 6 Fr
Outcomes	**Primary** : incidence of vascular access site complications (i.e. the composite of haematoma measuring ≥ 5 cm, pseudoaneurysm, arteriovenous fistula, access site–related major bleeding, acute ipsilateral leg ischaemia, need for vascular surgical or interventional treatment or local infection at 30 days after randomisation **Secondary** : time to haemostasis; repeat manual compression; VCD failure **Follow-up** : 30 days
Notes	
Risk of bias	

Schulz-Schüpke 2014 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Sealed opaque envelopes containing a computer-generated sequence were used" Comment: random sequence generation. Study was judged to be at low risk of selection bias
Allocation concealment (selection bias)	Low risk	Quote: "Sealed opaque envelopes containing a computer-generated sequence were used" Comment: adequate concealment of allocation. Study was judged to be at low risk of selection bias
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "All events were adjudicated and classified by an event adjudication committee in which members were unaware of the assigned treatment" Comment: Outcome assessors were blinded to treatment allocation. Study was judged to be at low risk of detection bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

SEAL Trial Study Team

Methods	**Study design** : multi-centre randomised study
Participants	**Country** : United States of America **Setting** : hospital **Number of centres** : 16 **Numbers** : Duett 392, manual compression 238 **Age (mean (SD))** : Duett 62 (11) years, manual compression 63 (12) years **Sex** : Duett 309 M/83 F, manual compression 165 M/73 F **Inclusion criteria** : patients >18 years undergoing a diagnostic (n = 209) or interventional (n = 421) cardiac procedure with femoral arterial access who could provide written informed consent **Exclusion criteria** : arterial sheath < 5 Fr or > 9 Fr or longer than 10 cm; presence of a ≥ 6 cm diameter haematoma before initial sheath removal; presence of clinically severe peripheral vascular disease manifested by claudication at < 100 feet; weak or absent pulses in the affected limb; ankle brachial index < 0.5 at rest; known stenosis ≥ 50% in the iliac or femoral artery on the affected side; prior vascular bypass surgery or stent placement involving the affected femoral artery; suspected posterior femoral artery puncture or puncture distal to the common femoral artery bifurcation; known bleeding disor-

SEAL Trial Study Team *(Continued)*

	der including platelet count < 100,000 or receipt of thrombolytic therapy within the previous 24 hours; haemoglobin < 10 g/dL; international normalised ratio > 1.5; activated clotting time > 400 seconds at the conclusion of the catheterisation procedure; suspected pregnancy; life expectancy < 1 year; Q wave myocardial infarction within 72 hours; uncontrolled severe hypertension (systolic blood pressure > 180 mmHg or diastolic blood pressure > 110 mmHg); medical indication for continued intravenous heparin therapy after the procedure; known allergy to bovine-derived products; estimated femoral artery diameter < 6 mm on the basis of femoral angiography results
Interventions	**Intervention 1** : Duett **Intervention 2** : manual compression + FemoStop or C-Clamp **Sheath size** : 5 to 9 Fr
Outcomes	**Primary** : time to haemostasis; time to ambulation (defined as time from the end of sheath removal to time when the participant had gotten out of bed and walked 110 feet without loss of haemostasis); incidence of major complications (vascular surgery; ultrasound scan-guided compression to treat a pseudoaneurysm; bleeding requiring transfusion; infection of the puncture site requiring extended hospitalisation; antibiotic administration within 30 days) **Secondary** : device success rate; time to discharge; composite of the primary endpoints divided by diagnostic and interventional procedures **Follow-up** : 30 days
Notes	Participants randomised to the Duett device were ambulated 2 to 4 hours after the procedure according to manufacturer guidelines. Participants randomised to standard compression were ambulated according to the institution's practice

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly allocated to 1 of the 2 treatment groups with a closed envelope system and permuted block design supplied by the coordinating centre" Comment: random sequence generation. Study was judged to be at low risk of selection bias
Allocation concealment (selection bias)	Low risk	Quote: "Closed envelope system" Comment: adequate concealment of allocation. Study was judged to be at low risk of selection bias
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Treatment masked analysis of ultrasound examination tape" Comment: Outcome assessors were blinded to treatment allocation. Study was judged to be at low risk of detection bias
Incomplete outcome data (attrition bias) All outcomes	High risk	Only 227 of 392 Duett participants completed 7-day and 30-day follow-up examinations in the quality of life substudy. No explanation for incomplete data was provided by the study authors

SEAL Trial Study Team *(Continued)*

Selective reporting (reporting bias)	High risk	Under Results, study authors reported 7-day and 30-day follow-up examinations in the quality of life substudy participant group to measure participant discomfort, but this is not specified as an outcome of the study
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Seidelin 1997

Methods	**Study design** : randomised pilot trial
Participants	**Country** : Canada **Setting** : hospital **Number of centres** : 1 **Numbers:** AngioSeal 24, manual compression 26 **Age (mean (SD))** : AngioSeal 55 (10) years, manual compression 56 (9) years **Sex** : AngioSeal 18 M/6 F, manual compression 19 M/7 F **Inclusion criteria** : patients < 75 years of age referred for elective coronary angiography **Exclusion criteria** : patients with a femoral bruit; reduced femoral pulses; previous vascular surgery of the aorta or lower limb arteries; history or evidence of peripheral vascular disease; history of puncture site complications from prior percutaneous procedures; known allergy to materials in the device; current anticoagulant therapy; known hypercoagulation or hypocoagulation conditions; presence of severe acute non-cardiac systemic disease or terminal illness; female of child-bearing potential; evidence of systemic bacterial or cutaneous infection
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : manual compression **Sheath size** : 7 Fr
Outcomes	**Primary** : time to haemostasis (defined as time elapsed from sheath removal to time haemostasis was first confirmed); time to mobilisation (defined as time elapsed from sheath removal to time the participant was mobilised) **Secondary** : groin complications (re-bleeding after initial haemostasis (3 categories): insignificant oozing requiring further compression or requiring transfusion); swelling; haematoma (minor ≤ 3 cm, moderate 3 to 6 cm, large > 6 cm); pseudoaneurysm; need for blood transfusion; need for vascular surgery; other groin complications not pre-specified **Follow-up** : at 30 minutes, at 2 hours, at 4 hours, at discharge, at 7 days after the procedure
Notes	Participants treated with the AngioSeal device were mobilised within 5 minutes of tamper removal, but manual compression participants were placed on bedrest for 4 to 6 hours before mobilisation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly allocated" Comment: insufficient information to permit judgement of high or low risk

Seidelin 1997 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Shammas 2002

Methods	**Study design** : single-centre randomised study
Participants	**Country** : United States of America **Setting** : hospital **Number of centres** : 1 **Numbers** : AngioSeal 79, VasoSeal 78 **Age (mean (SD))** : AngioSeal 60 (11.4) years, VasoSeal 60 (10.9) years **Sex** : AngioSeal 37 M/42 F, VasoSeal 42 M/36 F **Inclusion criteria** : patients undergoing cardiac catheterisation or percutaneous interventional procedures **Exclusion criteria** : arteriotomy larger than 8 Fr; any suspicion that the introducer has been placed through the superficial femoral artery and the profunda femoris, or at the bifurcation of these 2 vessels; the presence of significant vascular disease as judged by the cardiologist; uncontrolled hypertension at the time of deployment of the device; allergy to beef product, collagen or polyglycolic or polylactic acid polymers; emergency cases; therapeutic thrombolysis; vascular graft puncture; bleeding disorder; pregnant or lactating females; previous device placed within 6 weeks in the same common femoral artery; pre-existing autoimmune disease; morbid obesity; hematoma before the procedure; < 18 or > 80 years of age
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : VasoSeal **Sheath size** : 8 Fr
Outcomes	**Primary** : time to haemostasis; time to ambulation

Shammas 2002 *(Continued)*

	Secondary : major complications (pseudoaneurysm; arteriovenous fistula; thrombosis of common femoral artery;retroperitoneal bleed; infection; bleeding from the puncture site requiring transfusion; death)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Comment: insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Silber 1998

Methods	**Study design** : prospective randomised study
Participants	**Country** : Germany **Setting** : hospital **Number of centres** : 1 **Numbers** : VasoSeal 74, manual compression 76 **Age (mean (SD))** : VasoSeal 59.8 (9.0) years, manual compression 58.0 (9.2) years **Sex** : VasoSeal 58 M/16 F, manual compression 58 M/18 F **Inclusion criteria** : patients undergoing PTCA **Exclusion criteria** : prolonged duration PTCA patients requiring an additional bolus of heparin; patients with need for overnight heparin infusion or coumadin; inadvertent penetration of the dorsal arterial wall within the puncture needle; previous application of collagen sealing of the femoral access site; known allergy to collagen; peripheral artery disease; patients with acute myocardial infarction; status post thrombolytic therapy; known coagulation defects or known platelet dysfunction; severe uncon-

Silber 1998 *(Continued)*

	trolled arterial hypertension (systolic > 220 mmHg or diastolic > 120 mmHg); pre-existing haematoma; haematoma developed during the procedure; patients with a venous femoral sheath
Interventions	**Intervention 1** : VasoSeal **Intervention 2** : manual compression **Sheath size** : 8 Fr
Outcomes	**Primary** : time to haemostasis; groin discomfort; haematoma (small < 7 cm, medium 7 to 15 cm, large > 15 cm) **Secondary** : major complications (thrombosis; loss of distal pulses; large pseudoaneurysm; arteriovenous fistula; bleeding with need for transfusion or any vascular surgery); minor complications (bleeding from the puncture site not requiring transfusion; vascular surgery and small pseudoaneurysm treated medically) **Follow-up** : 24 hours after sheath pull
Notes	As time to ambulation was not an endpoint of the study, participants had to stay in bed until the morning after the procedure

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly assigned" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Sun 2009

Methods	**Study design** : randomised comparative study
Participants	**Country** : China **Setting** : hospital

Sun 2009 *(Continued)*

	Number of centres : 1 **Numbers** : StarClose 286, PerClose 183, manual compression 271 **Age (mean (SD))** : StarClose CAG 62.0 (10.5) years, StarClose PCI 63.9 (12.1) years, PerClose CAG 61.9 (11.1) years, StarClose PCI 64.0 (10.1) years, manual compression CAG 61.7 (10.5) years, manual compression PCI 64.1 (12.3) years **Sex** : StarClose 179 M/107 F, PerClose 115 M/68 F, manual compression 158 M/113 F **Inclusion criteria** : patients undergoing coronary angiography (CAG) and percutaneous coronary intervention (PCI) **Exclusion criteria** : not reported
Interventions	**Intervention 1** : StarClose **Intervention 2** : PerClose **Intervention 3** : Boomerang **Sheath size** : not reported
Outcomes	**Primary** : haemostasis operation time; immobilisation time; incidence of vascular complications **Secondary** : device failures **Follow-up** : not stated
Notes	Data presented by diagnosis/intervention

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized" Insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Tron 2003

Methods	**Study design** : randomised study
Participants	**Country** : France **Setting** : hospital **Number of centres** : 1 **Numbers** : PerClose 91, manual compression 76 **Age (mean (SD))** : PerClose 59 (10) years, manual compression 59 (11) years **Sex** : PerClose 85 M/6 F, manual compression 76 M/0 F **Inclusion criteria** : patients undergoing successful PTCA through the femoral artery with a 6 Fr or 8 Fr sheath **Exclusion criteria** : difficulty in puncturing the artery; peripheral vascular disease; marked obesity; age > 80 years; acute myocardial infarction; ilio-femoral tortuosities; presence of a venous sheath; arterial sheath already inserted the day before PTCA; > 3 previous punctures in the same artery; refusal to give written informed consent
Interventions	**Intervention 1** : PerClose **Intervention 2** : manual compression **Sheath size** : 6 Fr or 8 Fr
Outcomes	**Primary** : success rate; time to haemostasis; haematoma (defined as a palpable mass at the puncture site); blood oozing; length of hospital stay **Secondary** : participant pain **Follow-up** : 2 days post procedure
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data

Tron 2003 *(Continued)*

Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Upponi 2007

Methods	**Study design** : prospective randomised study
Participants	**Country** : United Kingdom **Setting** : hospital **Number of centres** : 1 **Numbers:** AngioSeal 50, manual compression 50 **Age (mean (SD))** : AngioSeal 68.9 years, manual compression 70.1 years **Sex** : AngioSeal 33 M/17 F, manual compression 35 M/15 F **Inclusion criteria** : patients undergoing retrograde femoral arterial puncture **Exclusion criteria** : not stated
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : manual compression **Sheath size** : 5 Fr to 7 Fr
Outcomes	**Primary** : minor complications (haematoma < 6 cm); major complications (false aneurysm; arterio-venous fistula; vessel occlusion; those requiring further percutaneous or surgical intervention) **Secondary** : none **Follow-up** : up to 6 weeks post procedure
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "50 patients were randomised to each group" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk

Upponi 2007 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Unclear risk	Outcomes are not clearly stated
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Veasey 2008

Methods	**Study design** : randomised single-blind prospective trial
Participants	**Country** : United Kingdom **Setting** : district general hospital **Number of centres** : 1 **Numbers:** AngioSeal 208, StarClose 193 **Age (mean (SD))** : AngioSeal 65.3 (10.6) years, StarClose 66.5 (10.8) years **Sex** : AngioSeal 115 M/93 F, StarClose 107 M/86 F **Inclusion criteria** : patients undergoing elective day-case diagnostic coronary angiography with immediate post-procedure mobilisation **Exclusion criteria** : patients with a diagnosis of unstable angina or acute myocardial infarction; significant peripheral vascular disease; previous peripheral vascular surgery; pregnant; unable to give written informed consent; younger than 18 years; previous femoral artery complication from coronary angiography
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : StarClose **Sheath size** : 5 Fr
Outcomes	**Primary** : complications (induration; haematoma; bleeding; retroperitoneal bleed; pseudoaneurysm; leg ischaemia; access site infection) **Secondary** : participant satisfaction; pain scores **Follow-up** : 1 week post procedure
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised to" Comment: insufficient information to permit judgement of high or low risk

Veasey 2008 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Outcomes are not clearly stated
Selective reporting (reporting bias)	Unclear risk	Outcomes are not clearly stated
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

von Hoch 1995

Methods	**Study design** : prospective randomised study
Participants	**Country** : Germany **Setting** : hospital **Number of centres** : 1 **Numbers:** VasoSeal 154, manual compression 155 **Age (median (IQR))** : VasoSeal 63 (54 to 70) years, manual compression 60 (53 to 70) years **Sex** : VasoSeal 125 M/29 F, 118 M/37 F **Inclusion criteria** : patients requiring emergency coronary stenting or elective percutaneous coronary angioplasty **Exclusion criteria** : patients with known allergies to collagen or other animal products; any haemostatic disorder; previous catheterisation from the right femoral artery within 1 week before the qualifying procedure; acute myocardial infarction
Interventions	**Intervention 1** : VasoSeal **Intervention 2** : manual compression **Sheath size** : not stated
Outcomes	**Primary** : complications at the vascular access site (pseudoaneurysm; arteriovenous fistula; local bleeding requiring blood transfusion or surgical treatment; groin infection; occlusion of the femoral artery) **Secondary** : time to haemostasis
Notes	

von Hoch 1995 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly assigned to" Insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Ward 1998

Methods	**Study design** : randomised multi-centre study
Participants	**Country** : United States of America **Setting** : hospital **Number of centres** : 8 **Numbers:** AngioSeal 202, manual compression 102 **Age (mean (SD))** : AngioSeal 61.7 (12) years, manual compression 64.7 (10) years **Sex** : AngioSeal 140 M/62 F, manual compression 72 M/30 F **Inclusion criteria** : patients undergoing diagnostic catheterisation via the femoral approach with an 8 Fr sheath or smaller **Exclusion criteria** : patients with severe systemic or terminal illness, systemic or cutaneous infection, platelet count < 75,000 cells/µL, use of an intra-aortic balloon pump, thrombolytic therapy within previous 24 hours, fibrinogen count < 100 mg/dL, sheath in place > 36 hours, presence of haematoma before sheath removal, suspected profunda femoris puncture, younger than 18 years or unable to give informed consent
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : manual compression

Ward 1998 *(Continued)*

	Sheath size : 5 Fr to 8 Fr
Outcomes	**Primary** : time to haemostasis (defined as elapsed time between sheath removal and first observed haemostasis); time to ambulation; time to discharge **Secondary** : vascular injury (need for vascular repair or pseudoaneurysm); bleeding complications (bleeding requiring transfusion; haematoma < 6 cm; haematoma ≥ 6 cm; late bleeding) **Follow-up** : 14 days and 30 days after hospital discharge
Notes	Participants randomised to AngioSeal were ambulated at 1 hour; manual compression participants were ambulated 4 to 6 hours after sheath removal

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Wetter 2000

Methods	**Study design** : prospective randomised study
Participants	**Country** : Switzerland **Setting** : hospital **Number of centres** : 1 **Numbers:** PerClose 50, manual compression 50 **Age (mean (SD))** : PerClose 58.5 (10.5) years, manual compression 59.9 (9.7) years **Sex** : not stated

Wetter 2000 *(Continued)*

	Inclusion criteria : patients who had undergone elective percutaneous transluminal coronary angioplasty **Exclusion criteria** : patients not ambulatory on the day of the intervention
Interventions	**Intervention 1** : PerClose **Intervention 2** : manual compression **Sheath size** : 6 Fr or 7 Fr
Outcomes	**Primary** : time to haemostasis (measured from insertion of device until application of bandage); time to mobilisation **Secondary** : haematoma; pseudoaneurysm; arteriovenous fistula **Follow-up** : 4 hours post procedure
Notes	PerClose participants had 4 hours of bedrest; manual compression participants were kept in bed until the morning after the procedure

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement of high or low risk

Wong 2009

Methods	**Study design** : randomised non-blinded trial
Participants	**Country** : United States of America **Setting** : hospital

Wong 2009 *(Continued)*

	Number of centres : 17 **Numbers:** ExoSeal 267, manual compression 134 **Age (mean (SD))** : ExoSeal 63.3 (11.1) years, manual compression 61.4 (10.5) years **Sex** : ExoSeal 182 M/85 F, manual compression 83 M/51 F **Inclusion criteria** : patients 18 to 84 years of age scheduled to undergo a diagnostic or interventional coronary or peripheral procedure via arterial puncture of a > 5 mm lumen diameter common femoral artery **Exclusion criteria** : patients who had sustained a myocardial infarction with ST-segment elevation < 48 hours before the catheterisation procedure; uncontrolled hypertension at time of closure; symptomatic leg ischaemia in the target vessel limb or prior femoral vascular surgery or placement of a vascular graft at the target site; history of bleeding or platelet disorder or previous treatment with a thrombin-specific anticoagulant or low molecular wegiht heparin < 24 hours before the catheterisation procedure; required puncture of both femoral arteries; prior closure of the target artery with any vascular closure device; pre-existing systemic or cutaneous infection
Interventions	**Intervention 1** : ExoSeal **Intervention 2** : manual compression **Sheath size** : 6 Fr
Outcomes	**Primary** : time to haemostasis (defined as time from sheath removal to time haemostasis was achieved); time to ambulation (defined as time from sheath removal to time the participant was able to walk > 20 feet without recurrence of bleeding) **Secondary** : time to eligibility for hospital discharge; time to hospital discharge; procedure success; major adverse event (need for vascular repair by surgical or non-surgical techniques; bleeding requiring a blood transfusion; infection requiring antibiotics; new-onset ischaemia of the ipsilateral lower extremity; permanent access site-related nerve injury); device success; post-procedural complications (recurrent local bleeding requiring a haemostatic intervention or a > 6 cm haematoma or ecchymosis; pseudoaneurysm; arterio-venous fistula; vascular laceration or retroperitoneal bleeding; ipsilateral manifestations of vascular insufficiency or embolisation including loss of distal pulse, total arterial occlusion or deep vein thrombosis, infection and nerve injury) **Follow-up** : 30 days post procedure
Notes	ExoSeal participants were ambulated at 1 hour (received no glycoprotein IIb/IIIa inhibitors), 2 hours (received glycoprotein IIb inhibitor) and 6 hours (received glycoprotein IIIa inhibitors); manual compression participants were ambulated no later than 4 hours post haemostasis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Assignment was based on a computer-generated treatment list, which balanced the randomisation by centre and type of procedure performed" Comment: random sequence generation. Study was judged to be at low risk of selection bias
Allocation concealment (selection bias)	Low risk	Quote: "Patients were randomly assigned using sealed envelopes" Comment: allocation of treatment was concealed. Study was judged to be at low risk of selection bias

Wong 2009 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Nonblinded" Comment: no blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

Yadav 2003

Methods	**Study design** : randomised multi-centre controlled clinical investigation
Participants	**Country** : United States of America **Setting** : hospital **Number of centres** : 9 **Numbers:** QuickSeal 240, manual compression 158 **Age (mean (SD))** : QuickSeal 62 (10.4) years, manual compression 61 (11.2) years **Sex** : QuickSeal 156 M/84 F, manual compression 102 M/56 F **Inclusion criteria** : patients 18 to 80 years of age who provided written informed consent and underwent a percutaneous diagnostic or interventional procedure by way of the common femoral artery **Exclusion criteria** : patients with pre-existing autoimmune disease; ipsilateral arterial site closure with the QuickSeal device or manual compression within previous 6 weeks; closure utilising another device within 180 days; pregnant or lactating women; significant bleeding or platelet disorders; platelet count < 100,000; haemoglobin < 10 mg/dL; hematocrit < 30%; blood pressure > 170/100 mmHg
Interventions	**Intervention 1** : QuickSeal **Intervention 2** : manual compression **Sheath size** : 5 to 8 Fr
Outcomes	**Primary** : time to haemostasis (defined as time between end of the procedure and haemostasis); time to ambulation (defined as time between end of the procedure and participant ambulation > 10 feet); incidence of major complications (vascular repair; bleeding requiring transfusion and/or intervention; infection requiring intravenous antibiotics and/or extended hospitalisation) **Secondary** : time to discharge; minor complications (haematoma; ecchymosis; bleeding and pseudoaneurysm) **Follow-up** : 30 days after discharge

Yadav 2003 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised" Comment: insufficient information to permit judgement of high or low risk
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement of high or low risk
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding, but review authors judged that outcomes and outcome measurements are not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement of high or low risk
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Data on pre-specified outcomes reported
Other bias	Low risk	Study appears to be free from other sources of bias

ASD: atrial septal defect
BMI: body mass index
CAG: coronary angiography
CFA: common femoral artery
INR: international normalised ratio
PCI: percutaneous coronary intervention
PTCA: percutaneous transluminal coronary angioplasty
SD: standard deviation
VAS: visual analogue scale
VCD: vascular closure device
VSD: ventricular septal defect

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

Study	Reason for exclusion
Baim 2000	ProStar-Plus device was used with an 8 Fr or 10 Fr sheath size, but data are not presented separately. We contacted study authors twice but received no response
Beyer-Enke 1996	Could not confirm with study authors that access for the procedure was attained through the femoral artery
Chalmers 2007	EVICEL is not a vascular closure device
Chevalier 2000	Data on review outcomes were not presented in the study report (abstract)

Study	Reason for exclusion
Jean-Baptiste 2008	Not a randomised controlled trial
Kurşaklioğlu 2008	Cannot confirm that this is a randomised controlled trial and that access was attained via the femoral artery
Larzon 2015	Did not use a vascular closure device
Leinbudgut 2013	Participants were randomised by drug received to prevent bleeding rather than by vascular closure device (VCD)
Lupi 2012	Not a randomised controlled trial
Neudecker 2003	Not a randomised controlled trial
Ratnam 2007	Not a randomised controlled trial
Slaughter 1995	Cost-effectiveness analysis. No relevant data
Smilowitz 2012	Not a randomised controlled trial
Starnes 2003	Arteriography participants who were treated with 7 Fr to 10 Fr sheaths. Data are not presented according to sheath size. Attempts to contact the study author for specific data were unsuccessful

Characteristics of studies awaiting assessment *[ordered by study ID]*

NCT01297322

Methods	**Study design** : randomised open-label trial **Country** : United States of America **Setting** : hospital **Number of centres** : 21
Participants	**Inclusion criteria** • Patients 18 to 80 years of age • Undergoing an elective, non-emergent diagnostic or interventional endovascular procedure via the common femoral artery with a 6 Fr or 7 Fr introducer sheath **Exclusion criteria** • Advanced refusal of blood transfusion, if necessary • Active systemic or cutaneous infection or inflammation • Pre-existing immunodeficiency disorder and/or long-term use of systemic steroids • Known, significant history of bleeding diathesis, coagulopathy, von Willebrand's disease or current platelet count < 100,000 cells/mm^3 • Baseline international normalised ratio (INR) ≥ 1.8, or fibrinogen level < 150 mg/dL (if received a fibrinolytic agent within previous 24 hours) • Severe co-existing morbidities • Life expectancy < 30 days • Ipsilateral femoral arteriotomy within previous 30 days • Previous ipsilateral femoral artery closure with a permanent implant-based closure device • Previous vascular grafts or surgery at the target vessel access site

NCT01297322 *(Continued)*

- History of symptomatic peripheral arterial disease
- Revascularisation or deep vein thrombosis in the ipsilateral limb
- Unilateral or bilateral lower extremity amputation
- Renal insufficiency
- Females who are pregnant, planning to become pregnant within 3 months of the procedure or lactating
- Extreme morbid obesity (body mass index (BMI) > 45 kg/m^2) or underweight (BMI < 20 kg/m^2)
- Known allergy/adverse reaction to bovine derivatives, sodium hyaluronate or hyaluronan preparations
- Administration of low molecular weight heparin within 8 hours of the procedure

Interventions	**Intervention 1** : VASCADE Vascular Closure System **Intervention 2** : manual compression
Outcomes	**Primary** • Time to haemostasis and rate of access site-relayed major complications including access site-related bleeding requiring transfusion, vascular injury requiring repair (via surgery, ultrasound-guided compression, transcatheter embolisation or stent graft) • New ipsilateral lower extremity ischaemia causing a threat to the viability of the limb and requiring surgical or additional percutaneous intervention. This compromised blood flow is documented by participant symptoms, physical exam and/or decreased or absent blood flow on lower extremity angiogram • Access site-related infection requiring intravenous antibiotics and/or extended hospitalisation • New-onset access site-related neuropathy in the ipsilateral lower extremity requiring surgical repair • Permanent access site-related nerve injury **Secondary** • Time to ambulation • Time to discharge eligibility • Time to hospital discharge • Device success • Procedure success • Rate of minor access site-related complications including access site-related bleeding requiring > 30 minutes to achieve haemostasis • Access site-related hematoma > 6 cm • Late access site-related bleeding (after hospital discharge) • Ipsilateral lower extremity arterial emboli • Ipsilateral deep vein thrombosis • Access site-related vessel laceration • Access site wound dehiscence • Localised access site infection treated with intramuscular or oral antibiotics • Arteriovenous fistula not requiring treatment • Pseudoaneurysm requiring thrombin injection or fibrin adhesive injection • Pseudoaneurysm not requiring treatment • New-onset access site-related neuropathy in the ipsilateral lower extremity not requiring surgical repair • Ipsilateral pedal pulse diminished by 2 grades or transiently lost
Notes	This study was published just after the searches were run and will be included in a future update

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

ACTRN12611001248954

Trial name or title	ACTRN12611001248954
Methods	**Study design** : open-label randomised multi-centre controlled trial **Country** : United States of America **Setting** : hospital **Number of centres** : multi-centre
Participants	**Inclusion criteria** • Patients 18 to 80 years of age • Clinically indicated for an elective, non-emergent diagnostic or interventional endovascular procedure via the common femoral artery with a 6 Fr or 7 Fr introducer sheath. **Exclusion criteria** • Active systemic or cutaneous infection • Pre-existing immunodeficiency disorder and/or long-term use of systemic steroids • Ipsilateral femoral arteriotomy within previous 30 days • Planned endovascular procedure within next 30 days • Unilateral or bilateral lower extremity amputation(s) • Extreme morbid obesity (BMI > 45 kg/m^2) or underweight (BMI < 22 kg/m^2) • Difficult insertion of procedural sheath or needle stick problems at onset of the procedure (e.g. multiple stick attempts, "back-wall stick") • Fluoroscopically visible calcium • Atherosclerotic disease • Stent within 1 cm of the puncture site
Interventions	**Intervention 1** : VASCADE Vascular Closure System **Intervention 2** : manual compression
Outcomes	**Primary** • 30-Day rate of combined access site-related major complications (major complications include access site-related bleeding requiring transfusion; assessment of site-related bleeding was performed via direct observation; excessive blood loss would be determined via Institutional guidelines) • Vascular injury requiring repair: Prolonged bleeding would require further assessment for vascular injury by techniques such as ultrasound imaging • New ipsilateral lower extremity ischaemia causing a threat to the viability of the limb and requiring surgical or additional percutaneous intervention: Compromised blood flow is documented by participant symptoms, physical exam and/or decreased or absent blood flow on lower extremity angiogram • Access site-related infection: assessment based on participant symptoms and physical exam • New-onset access site-related neuropathy in the ipsilateral lower extremity requiring surgical repair: assessment based on participant symptoms and physical exam • Permanent access site-related nerve injury (> 30 days): based on participant symptoms and physical exam **Secondary**

ACTRN12611001248954 *(Continued)*

- Time to ambulation: defined as elapsed time between device removal for Cardiva VASCADE VCS and sheath removal for manual compression and when participant stands and walks 20 feet without evidence of arterial re-bleeding from the access site
- Time to discharge eligibility: defined as elapsed time between device removal for Cardiva VASCADE VCS and sheath removal for manual compression and when participant is medically able to be discharged based solely on access site assessment
- Time to hospital discharge: defined as elapsed time between device removal for Cardiva VASCADE VCS and sheath removal for manual compression and when participant actually is discharged from the hospital, as recorded on the discharge

Starting date	December 2011
Contact information	charles_maroney@cardivamedical.com
Notes	

CTRI/2014/09/004946

Trial name or title	Closure of puncture site in the groin after coronary stenting
Methods	**Study design** randomised parallel-group active controlled trial **Country** : India **Setting** : hospital **Number of centres** : 1
Participants	**Inclusion criteria** • Patients 18 to 85 years of age • Acceptable candidates for elective PCI through common femoral artery (CFA) with 6 Fr to 8 Fr procedural sheath • Voluntary participation as per signed, informed consent by the participant **Exclusion criteria** • Patient requiring emergency or primary PCI • Anaemia with pre-procedure haemoglobin < 10 g • History of bleeding diathesis • Pregnancy, suspected pregnant or lactating mothers • Previous deployment of VCD in ipsilateral femoral artery at any time • Peripheral vascular disease of ipsilateral limb defined as history of claudication, weak or absent pulse or lower extremity vascular graft • Active systemic infection • Local access site cutaneous infection or inflammation • Patient known or determined to require treatment that will extend his/her hospitalisation (requiring CABG, staged PCI, etc) • Presence of clinically significant hematoma > 5 cm, pseudoaneurysm or arterio-venous fistula in ipsilateral access site as detected clinically and confirmed by Doppler ultrasound • Placement of arterial access sheath with < 6 Fr or > 8 Fr • Placement of both arterial and venous sheaths during PCI • Difficulty inserting the introducer sheath at the start of the PCI due to vessel scarring, tortuosity, stenosis, etc, as judged by the operator • Intraprocedural bleeding and/or haematoma at the access site

CTRI/2014/09/004946 *(Continued)*

- Sheath angiography reveals anatomical unsuitability for device closure, which is defined as
  - the site of arterial puncture distal or at common femoral artery bifurcation
  - the site of arterial puncture above the inguinal ligament, which is typically defined by the inferior border of the inferior epigastric artery or the upper third of the femoral head by plain fluoroscopy
  - the arterial lumen diameter at the access site < 5 mm by visual estimate
  - angiographic evidence of calcified lesions at the access site

Interventions	**Intervention 1** : PerClose ProGlide **Intervention 2** : manual compression
Outcomes	**Primary** • Haematoma at access site < 5 cm • Access site-related re-bleeding • Localised access site-related infection requiring oral antibiotics • Haematoma at access site > 5 cm • Pseudoaneurysm • Arterio-venous fistula • Retroperitoneal haematoma • Any access site-related major bleeding • Ipsilateral lower extremity ischaemia • Access site-related infection requiring intravenous antibiotics • Access site-related nerve injury **Secondary** • Time to haemostasis: average time to stop arterial bleeding • Flat time: average time participant has to lie flat on bed with movement restriction • Time to ambulate: average time between arterial sheath pull and first observed ambulation of 10 feet in the ward without occurrence of bleeding at the access site • Patient satisfaction questionnaire: recorded at 24 hours post PCI or at discharge (if sooner)
Starting date	01/09/2014
Contact information	drssandeep@hotmail.com
Notes	

DRKS00000802

Trial name or title	VCD trial
Methods	**Study design** : prospective, randomised clinical trial **Country** : Germany **Setting** : hospital **Number of centres** : multi-centre
Participants	**Inclusion criteria** • Patients 18 years of age or older

DRKS00000802 *(Continued)*

	• Undergoing diagnostic angiography or coronary intervention with a 5 Fr or 6 Fr introducer sheath via femoral artery puncture **Exclusion criteria** • Uncontrolled blood pressure > 180/110 mmHg • Previous vascular surgery or femoral bypass surgery • Previous femoral or iliac vascular intervention • Former femoral vascular closure with internal closure system (e.g. AngioSeal, CoStar) • Heavily calcified or atheromatous modified femoral artery
Interventions	**Intervention 1** : ExoSeal **Intervention 2** : Safeguard **Intervention 3:** manual compression
Outcomes	**Primary** • Combined endpoint of complications after puncture of the femoral artery (haematoma ≥ 5 cm, aneurysm spurium, bleeding with haemoglobin decrease ≥ 2 mg/dL, transfusion requirement, retroperitoneal haemorrhage, pressure ulcer ≥ grade 2, ischaemia of the ipsilateral lower extremity, nerve injury within 48 hours, after 7 days and 31 days **Secondary** • Haematoma < 5 cm • Bleeding with haemoglobin drop < 2 mg/dL • Abrasion of the skin • Pressure ulcer grade 1 • Prolonged tourniquet time • Prolonged hospitalisation • Fever within 24 hours after surgery • Local infection of the puncture • Pain • User satisfaction
Starting date	May 2011
Contact information	stefan.köberich at uniklinik-freiburg.de marc.kollum at hbh-kliniken.de
Notes	

NCT00264264

Trial name or title	ACDC trial
Methods	**Study design** : randomised parallel-assignment double-blind trial **Country** : Canada **Setting** : hospital **Number of centres** : 1

NCT00264264 *(Continued)*

Participants	**Inclusion criteria** • Patients older than 20 years of age • Undergoing elective PCI procedures in whom femoral anatomy is favourable for placement of a closure device **Exclusion criteria** • Patients undergoing emergency PCI • End-stage renal disease • Haemoglobin level < 100 g/L • Fish allergy • Known allergy to protamine • Use of low molecular weight heparin within previous 12 hours • Prior closure device use within 90 days • Symptomatic peripheral vascular disease • Femoral artery calcification on fluoroscopy • Arterial puncture of the superficial femoral artery • Double wall puncture (puncture of anterior and posterior wall of femoral artery) • Placement of intra-aortic balloon pump • Placement of a femoral venous sheath • Coronary dissection • Thrombus or perforation not resolved by the end of the case
Interventions	**Intervention 1** : vascular closure device **Intervention 2** : direct compression
Outcomes	**Primary** • Composite of major vascular complications (device failure, bleeding, haematoma, infection, pseudoaneurysm, arterio-venous fistula and vascular repair) **Secondary** • Time to haemostasis • Ambulation time • Quality of life • Composite of minor vascular complications (bleeding, repeat compression, failure to ambulate per protocol) • Post-procedural infarction • Death • MI
Starting date	July 2006
Contact information	Asim Cheema, St Michael's Hospital, Toronto
Notes	

NCT00428155

Trial name or title	ACDC trial II

NCT00428155 *(Continued)*

Methods	**Study design** : randomised single-group assignment single-blind trial **Country** : Canada **Setting** : hospital **Number of centres** : 1
Participants	**Inclusion criteria** • Patients older than 25 years of age • Undergoing non-emergent PCI procedures with a 6 Fr arterial sheath, with femoral artery favourable for placement of an arterial closure device **Exclusion criteria** • Patients undergoing emergency PCI • End-stage renal disease • Prior arterial closure device use within 90 days • Symptomatic peripheral vascular disease • Arterial puncture of the superficial femoral artery • Suspected double wall puncture (puncture of anterior and posterior wall of femoral artery) • Placement of intra-aortic balloon pump • Placement of femoral venous sheath
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : StarClose
Outcomes	**Primary** • Composite of major vascular complications (device failure, bleeding, haematoma, infection) **Secondary** • Time to haemostasis • Lack of ambulation per protocol • Need for additional measures to achieve haemostasis (manual pressure, FemoStop use, etc) • Minor vascular complication (minor bleeding, analgesic use) • Post-procedural myocardial infarction • 30-Day incidence of death • MI • Participant discomfort • Quality of life measurements at discharge and at 4 weeks • Nurse resource utilisation at discharge
Starting date	January 2007
Contact information	Asim Cheema, St Michael's Hospital, Toronto; cheemaa@smh.toronto.on.ca
Notes	

NCT01389375

Trial name or title	Instrumental sealing of arterial puncture site closure device versus manual compression trial

NCT01389375 *(Continued)*

Methods	**Study design** : prospective randomised open-label trial **Country** : Germany **Setting** : hospital **Number of centres** : not stated
Participants	**Inclusion criteria** • Patients between 18 and 85 years of age • Undergoing femoral access coronary angiography **Exclusion criteria** • Peripheral arterial occlusive disease • Prior peripheral artery surgery • Percutaneous coronary intervention • Femoral access device closure in previous 30 days • Scheduled coronary angiography/intervention within 90 days • Critical limb ischaemia • Uncontrolled hypertension > 220/110 mmHg • Coagulopathy (bleeding disorder) • Local infection • Common femoral artery lumen diameter < 5 mm • Allergy to absorbable suture • Autoimmune disease • Pregnancy
Interventions	**Intervention 1** : ExoSeal **Intervention 2** : FemoSeal **Intervention 3** : manual compression
Outcomes	**Primary** • Composite of arterial access-related complications, defined as the composite of rate of ipsilateral groin haematomas with largest diameter exceeding 5 cm, pseudoaneurysm, arteriovenous fistula, major bleeding, critical limb ischaemia, local infection, surgical repair and revascularisation **Secondary** • Time to haemostasis (from sheath removal to complete haemostasis) • Device deployment failure • Need for repeated manual compression after end of closure procedure • Cost/benefit analysis
Starting date	July 2011
Contact information	Maryam Linhardt, Deutsches Herzzentrum München, Klinik für Herz-und Kreislauferkrankungen
Notes	

NCT01600482

Trial name or title	Clinical investigation for safety and efficacy study of CELT ACD arterial closure device
Methods	**Study design** : randomised multi-centre open-label study **Countries** : United States of America, Germany and Ireland **Setting** : hospital **Number of centres** : multi-centre
Participants	**Inclusion criteria** • Patients older than 18 years • Willingness to give informed consent • Clinical indication for an intra-arterial procedure involving access through the common femoral artery and conducted through an access sheath size between 6 Fr and 7 Fr inclusive **Exclusion criteria** • Patients with known allergy to any materials used in the device • Severe acute non-cardiac systemic disease or terminal illness with life expectancy < 1 year • Evidence of systemic bacterial or cutaneous infection, including groin infection, definitive or potential coagulopathy or platelet count < 100,000/µL • Use of systemic thrombolytic agents within 24 hours before or during the catheterisation procedure that cause the concentration of fibrinogen to be < 100 mg/dL, or when post-thrombolytic fibrinogen (in case of thrombolysis within 24 hours or intraprocedural) cannot be measured • Patients in whom an introducer sheath smaller than 6 Fr or greater than 7 Fr has been used • Currently participating in another investigational device or drug study • Severe claudication • Iliac or femoral artery diameter stenosis > 50% • Previous bypass surgery or stent placement in the vicinity of the access site • Indication that puncture has been made in the profunda femoris artery or the superficial femoral artery, or adjacent to the bifurcation • Common femoral artery lumen diameter <an 5 mm • Any amputation from an access site limb • Patients who have undergone a percutaneous procedure performed with a vascular closure device for haemostasis within the previous 30 days or those treated with manual/mechanical pressure for haemostasis within the previous 30 days in the same leg • Systolic blood pressure < 90 mmHg • Active haematoma, arteriovenous fistula or pseudoaneurysm • A very superficial artery in which the depth from skin to the artery surface at the access site is less than 4 mm • Morbidly obese patients (BMI > 35 kg/m^2) • A stent ≤ 1 cm of the puncture site that would interfere with placement of the device implant • Patients known or suspected to be pregnant or lactating • Patients with an antegrade puncture • Difficulty in obtaining vascular access resulting in multiple arterial punctures and/or posterior arterial wall puncture • Patients who have undergone prior or recent use of an intra-aortic balloon pump through the arterial access site • Uncontrolled hypertension (BP ≥ 180/110 mmHg) at time of vascular closure • Acute ST-elevation myocardial infarction ≤ 48 hours before catheterisation procedure • Cardiogenic shock (haemodynamic instability requiring intravenous medication or mechanical support) experienced during or immediately post catheterisation • Inability to ambulate at baseline • Patients known to require an extended hospitalisation (e.g. patient undergoing cardiac surgery)

NCT01600482 *(Continued)*

	• Patient who has already participated in the trial or is unavailable for follow-up
Interventions	**Intervention 1** : CELT ACD **Intervention 2** : manual compression
Outcomes	**Primary** • Combined rate of major complications and time to haemostasis, both within 30 ± 7 days following the PCI procedure **Secondary** • Combined rate of minor complications • Time to ambulation • Time to dischargeability • Procedure success • Device successes, all within 30 ± 7 days following the procedure
Starting date	May 2012
Contact information	Turi-Zoltan@CooperHealth.edu scwong@med.cornell.edu michael.laule@charite.de
Notes	

NCT01669382

Trial name or title	ACCESS
Methods	**Study design** : randomised multi-centre single-blinded trial **Country** : Germany **Setting** : hospital **Number of centres** : multi-centre
Participants	**Inclusion criteria** • Patients 18 years of age and older • Receive coronary angiography/intervention with a 6 Fr sheath **Exclusion criteria** • Severe calcification of the access vessel • Severe peripheral artery disease • Puncture in the origin of the profound femoral artery • Non-femoral sheath insertion • Marked tortuosity of the femoral or iliac artery • Marked obesity or cachexia (BMI > 40 kg/m^2 or < 20 kg/m^2) • Patients on continuous medication with oral anticoagulants
Interventions	**Intervention 1** : ExoSeal

NCT01669382 *(Continued)*

	Intervention 2 : AngioSeal
Outcomes	**Primary** • Bleeding • Need for vascular surgery • Device failure **Secondary** • Occurrence of false aneurysms • Severe pain (Borg scale ≥ 5) • Haematoma ≥ 5 cm
Starting date	January 2012
Contact information	johannes.brachmann@klinikum-coburg.de harald.rittger@uk-erlangen.de holger.nef@innere.med.uni-giessen.de
Notes	

NCT02061696

Trial name or title	A randomised controlled trial to assess safety and efficacy of AXERA (device name) 2 Access System compared with manual compression
Methods	**Study design** : randomised parallel-assignment open-label **Country** : United States of America **Setting** : hospital **Number of centres** : multi-centre
Participants	**Inclusion criteria** • Between 18 and 85 years of age • Cardiac catheterisation procedure indicated involving access through a 5 Fr or 6 Fr introducer in the femoral artery • Ability to ambulate without assistance before the procedure and expected to ambulate (20 feet) post procedure • Participant or legally authorised representative has signed informed consent **Exclusion criteria** • Inability to routinely ambulate 20 feet without assistance (e.g. requires a walker or wheelchair to mobilise, has paralysis) • Active systemic or cutaneous infection or inflammation (e.g. septicaemia) at the time of the procedure • Emergent or urgent cardiac catheterisation for acute myocardial infarction • Extensive calcification of the femoral artery as seen on fluoroscopy • Systemic hypertension unresponsive to treatment (> 180 mmHg systolic and > 110 mmHg diastolic) • Thrombolytic therapy within the 72 hours before catheterisation

NCT02061696 *(Continued)*

	• Known bleeding disorder, such as Factor 5 deficiency, idiopathic thrombocytopenic purpura (ITP), thrombasthaenia, von Willebrand's disease • Taking warfarin with an international normalised ratio (INR) of 1.5 • Platelet count < 100,000 • Anaemia (haemoglobin < 10 g/dL or haematocrit < 30%) • Compromised femoral artery access site • Procedure requires an introducer sheath size > 6 Fr • Prior vascular surgery or vascular grafts at the femoral artery access site • Presentation with haemodynamic instability or in need of emergent surgery • Femoral artery closure on the target access vessel with a collagen/PEG closure device within 90 days • Pre-existing severe non-cardiac systemic disease or illness that results in life expectancy < 1 year • Participation in an investigational drug or another device research study that interferes with current research study endpoints • Pregnant or lactating women
Interventions	**Intervention 1** : AXERA 2 Access System **Intervention 2** : manual compression
Outcomes	**Primary** • Observation of any site-related major adverse events • Observation of any major access site-related complications **Secondary** • AXERA 2 Access System success • Time to haemostasis . • Time to discharge eligibility • Time to actual discharge • Time to ambulation • Ability to sit up at a 45-degree angle • Minor access site-related complications • Participant satisfaction • Pain score
Starting date	30 January 2014
Contact information	frank.saltiel@borgess.com vishal.gupta@borgess.com
Notes	

NCT02234830

Trial name or title	CLOSE-UP II trial
Methods	**Study design** : randomised parallel-assignment open-label **Country** : Denmark **Setting** : hospital

NCT02234830 *(Continued)*

	Number of centres : multi-centre
Participants	**Inclusion criteria** • Ability to provide valid informed signed consent • PCI procedure including treatment by balloon and/or stent • PCI indicated by silent ischaemia, stable angina pectoris, non-ST elevation myocardial infarction (NSTEMI) or ST elevation myocardial infarction (STEMI) **Exclusion criteria** • Only coronary angiography • Multiple punctures • Active infection • Groin haematoma before the closure procedure • Sheath size > 7 Fr • Known pseudoaneurysm or arterio-venous (AV) fistula in the ipsilateral groin • Prior arterial surgery in abdomen and/or lower extremities • Cardiogenic shock • Life expectancy < 1 year • Female of childbearing potential with possible pregnancy or positive pregnancy test within 7 days before index procedure, or lactating • Simultaneous or planned subsequent femoral vein access • Allergy to any of the components in the closure material left in the groin • Puncture of same site < 30 days • Peripheral artery disease patients can be included at operator's discretion except if heavy calcification is present at the access site, which at the operator's discretion precludes insertion of the VCD
Interventions	**Intervention 1** : AngioSeal **Intervention 2** : ExoSeal
Outcomes	**Primary** • Incidence at 30 days of the composite endpoint of access site-related major adverse vascular events. This includes major bleeding and/or bleeding necessitating blood transfusion, pseudoaneurysm with indication for treatment, arteriovenous fistula, groin surgery and/or possible related vascular surgery and infection needing antibiotic **Secondary** • Time to haemostasis from removal of the sheath (AngioSeal) or insertion of the device (ExoSeal) until haemostasis • Device failure • Vasovagal reaction until 5 minutes after end of closure procedure • Need for new onset of manual compression • Pain and discomfort related to the closure procedure • Time to mobilisation • In-hospital large groin haematoma • Bleeding according to BARC definitions • Major bleeding and/or bleeding necessitating blood transfusion • Pseudoaneurysm with indication for treatment • Arteriovenous fistula • Groin surgery and/or possible related vascular surgery • Infection needing antibiotics

NCT02234830 *(Continued)*

	• Need for medical evaluation of possible closure procedure-related symptom(s)
Starting date	December 2012
Contact information	hellbarg@rm.dk niels.holm@clin.au.dk
Notes	

NCT02237430

Trial name or title	CLOSE-UP III trial
Methods	**Study design** : randomised parallel-assignment open-label **Country** : Denmark **Setting** : hospital **Number of centres** : multi-centre
Participants	**Inclusion criteria** • > 18 years of age • Ability to provide valid informed signed consent • CAG, possibly including intracoronary measurement (FFR) or intracoronary imaging (IVUS, optical coherence tomography (OCT), NIRS) **Exclusion criteria** • Percutaneous coronary intervention (PCI) procedure and/or implantation of stents • ST-elevation myocardial infarction (STEMI) • Multiple punctures • Active infection • Groin haematoma before the closure procedure • Known pseudoaneurysm or arterio-venous (AV) fistula in the ipsilateral groin • Cardiogenic shock • Prior peripheral arterial surgery in abdomen or lower extremities • Sheat size > 7 Fr • Life expectancy < 1 year • Possible pregnancy or positive pregnancy test or breastfeeding women • Simultaneous or planned subsequent femoral vein access • Allergy to any of the components in the closure material left in the groin • Puncture or closure with closure device at same site < 30 days • Puncture or closure with manual compression at same site < 5 days • Patients with peripheral artery disease can be included at operator's discretion, except if heavy calcification is present at the access site, which at the operator's discretion precludes insertion of the closure device
Interventions	**Intervention 1** : Mynx **Intervention 2** : manual compression
Outcomes	**Primary**

NCT02237430 *(Continued)*

- Incidence at 30 days of the composite endpoint of access site-related major adverse vascular events, including major bleeding and/or bleeding necessitating blood transfusion, pseudoaneurysm with indication for treatment, arteriovenous fistula, groin surgery and/or possible related vascular surgery, infection needing antibiotic

Secondary

- Time to haemostasis from removal of the sheath (AngioSeal) or insertion of the device (ExoSeal) until haemostasis
- Device failure
- Vasovagal reaction until 5 minutes after end of closure procedure
- Need for new onset of manual compression
- Pain and discomfort related to the closure procedure
- Time to mobilisation
- In-hospital large groin haematoma
- Bleeding according to BARC definitions
- Major bleeding and/or bleeding necessitating blood transfusion
- Pseudoaneurysm with indication for treatment
- Arteriovenous fistula
- Groin surgery and/or possible related vascular surgery
- Infection needing antibiotics
- Need for medical evaluation of possible closure procedure-related symptom(s)

Starting date	June 2014
Contact information	niels.holm@clin.au.dk evald.christiansen@dadlnet.dk
Notes	

AV: arterio-venous
BARC: Bleeding Academic Research Consortium
BMI: body mass index
BP: blood pressure
CABG: coronary artery bypass graft
CAG: coronary angiography
CFA: common femoral artery
cm: centimetres
FFR: fractional flow reserve
Hct: haematocrit
Hgb: haemoglobin
INR: International normalised ratio
ITP: idiopathic thrombocytopenic purpura
IV: intravenous
IVUS: intravascular ultrasound
MI: myocardial infarction
mm: millimetres
NIRS: near infrared spectroscopy
NSTEMI: non-ST elevation myocardial infarction
OCT: optical coherence tomography
PCI: percutaneous coronary intervention
PEG: polyethylene glycol
STEMI: ST elevation myocardial infarction
VCD: vascular closure device

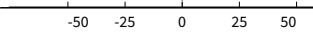
DATA AND ANALYSES

Comparison 1. Collagen-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Time to haemostasis (minutes)	12		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Time to mobilisation (hours)	13		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Major adverse event (any time)	6		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Mortality	1	141	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Vascular injury requiring vascular repair by surgical or non-surgical techniques	5	5731	Odds Ratio (M-H, Fixed, 95% CI)	2.81 [0.47, 16.79]
4 Infection	9	7616	Odds Ratio (M-H, Fixed, 95% CI)	2.14 [0.88, 5.22]
5 Groin haematoma	25	10247	Odds Ratio (M-H, Fixed, 95% CI)	0.46 [0.40, 0.54]
6 Retroperitoneal haemorrhage	3	744	Odds Ratio (M-H, Fixed, 95% CI)	1.58 [0.22, 11.42]
7 Pseudoaneurysm	21	9342	Odds Ratio (M-H, Fixed, 95% CI)	0.74 [0.55, 0.99]
8 Arterio-venous fistula	8	6153	Odds Ratio (M-H, Fixed, 95% CI)	0.98 [0.43, 2.21]
9 Deep vein thrombosis	3	629	Odds Ratio (M-H, Fixed, 95% CI)	2.41 [0.46, 12.50]
10 Limb ischaemia	3	4970	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Femoral artery thrombosis	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
12 Length of hospital stay (hours)	6		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1 Collagen-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 1 Time to haemostasis (minutes).

Study or subgroup	VCD		Compression		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Brachmann 1998	89	7.6 (4.1)	99	19.1 (5.9)	+	-11.5[-12.94,-10.06]
Brachmann 1998	100	6.4 (4.2)	99	13.2 (5.1)	+	-6.8[-8.1,-5.5]
Castañeda 2003	85	8.2 (4.1)	56	14.1 (5.4)	+	-5.9[-7.56,-4.24]
Diaz 2001	75	2 (3.5)	75	22.5 (6.2)	+	-20.5[-22.11,-18.89]
Gwechenberger 1997	33	9.6 (2)	29	23.6 (16.4)	+	-14[-20.01,-7.99]
Juergens 2004	58	24 (66)	57	384 (102)	◀	-360[-391.46,-328.54]



Favours VCD — Favours compression

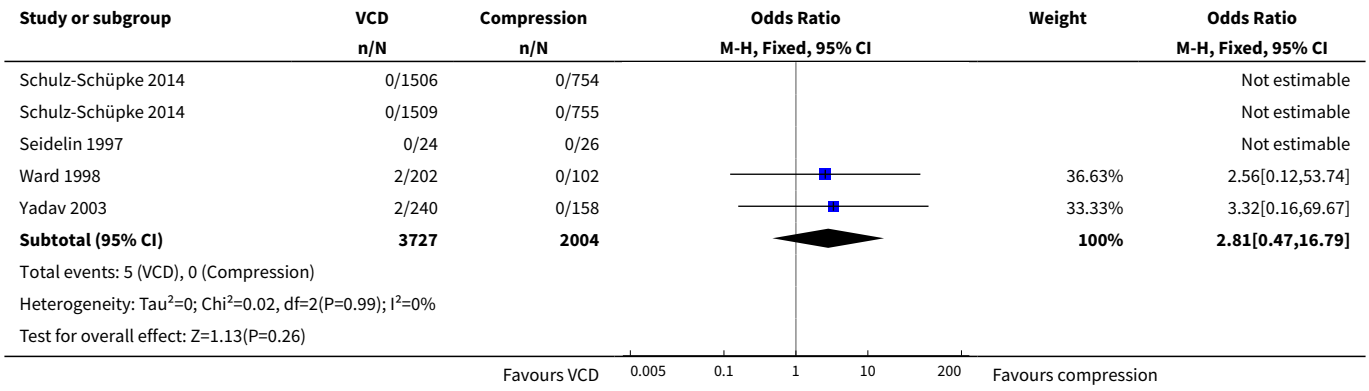
Study or subgroup	VCD		Compression		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Kussmaul 1995	218	2.5 (15.2)	217	15.3 (11.7)		-12.8[-15.35,-10.25]
Magosaki 1999	120	0.8 (3.2)	120	12.2 (5.3)		-11.4[-12.51,-10.29]
Reddy 2004	25	8.2 (16.7)	25	16.1 (11.6)		-7.9[-15.87,0.07]
Sanborn 1993	90	4.1 (2.8)	75	17.6 (9.2)		-13.5[-15.66,-11.34]
Sanborn 1993	71	4.3 (3.7)	134	33.6 (24.2)		-29.3[-33.49,-25.11]
Seidelin 1997	24	0.5 (1.4)	26	43 (21)		-42.5[-50.59,-34.41]
Silber 1998	74	3 (3)	76	17.4 (7)		-14.4[-16.12,-12.68]
Wong 2009	267	4.4 (11.6)	131	20.1 (22.5)		-15.7[-19.8,-11.6]
				Favours VCD	-50 -25 0 25 50	Favours compression

Analysis 1.2. Comparison 1 Collagen-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 2 Time to mobilisation (hours).

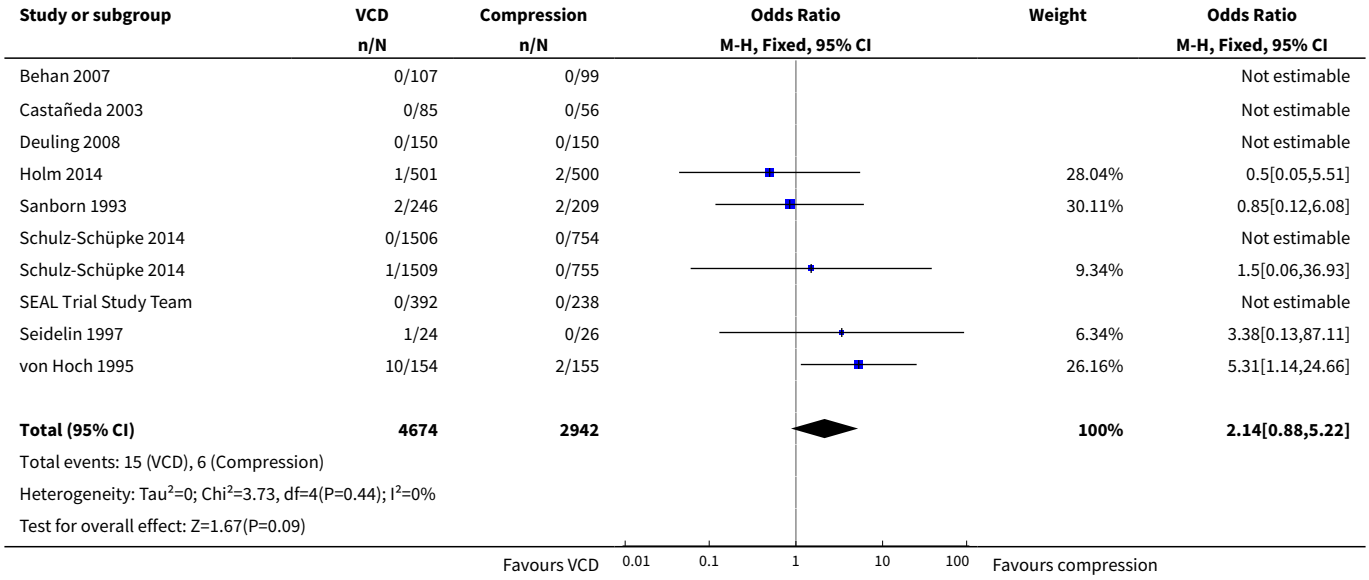
Study or subgroup	VCD		Compression		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Behan 2007	107	1.5 (0.7)	99	2.4 (0.3)		-0.94[-1.09,-0.79]
Brachmann 1998	88	8.1 (4.2)	101	13.4 (5.3)		-5.3[-6.66,-3.94]
Brachmann 1998	99	3.3 (8.8)	99	6.3 (5)		-3[-4.99,-1.01]
Castañeda 2003	85	2.8 (2.5)	56	7.2 (3.4)		-4.44[-5.47,-3.41]
Diaz 2001	75	3.1 (0.4)	75	12.3 (3.1)		-9.2[-9.91,-8.49]
Holm 2014	501	1.5 (0.6)	500	1.4 (0.9)		0.08[-0.02,0.18]
Juergens 2004	58	17 (8)	57	22 (13)		-5[-8.95,-1.05]
Legrand 2005	100	4.5 (2)	102	12.2 (1.5)		-7.7[-8.19,-7.21]
Machnik 2012	91	2.9 (2.4)	110	14.2 (2.3)		-11.3[-11.95,-10.65]
Magosaki 1999	120	5.3 (3.7)	120	10.9 (5.1)		-5.6[-6.73,-4.47]
Sanborn 1993	90	13.3 (12.1)	75	19.1 (17.8)		-5.8[-10.54,-1.06]
Sanborn 1993	71	23 (11.1)	134	32.7 (18.8)		-9.7[-13.8,-5.6]
Schräder 1992	50	6.4 (2.2)	50	21.6 (5.4)		-15.2[-16.82,-13.58]
Seidelin 1997	24	0.5 (0.1)	26	5.4 (0.7)		-4.85[-5.12,-4.58]
Wong 2009	264	2.5 (5)	129	6.2 (13.3)		-3.7[-6.07,-1.33]
				Favours VCD	-20 -10 0 10 20	Favours compression

Analysis 1.3. Comparison 1 Collagen-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 3 Major adverse event (any time).

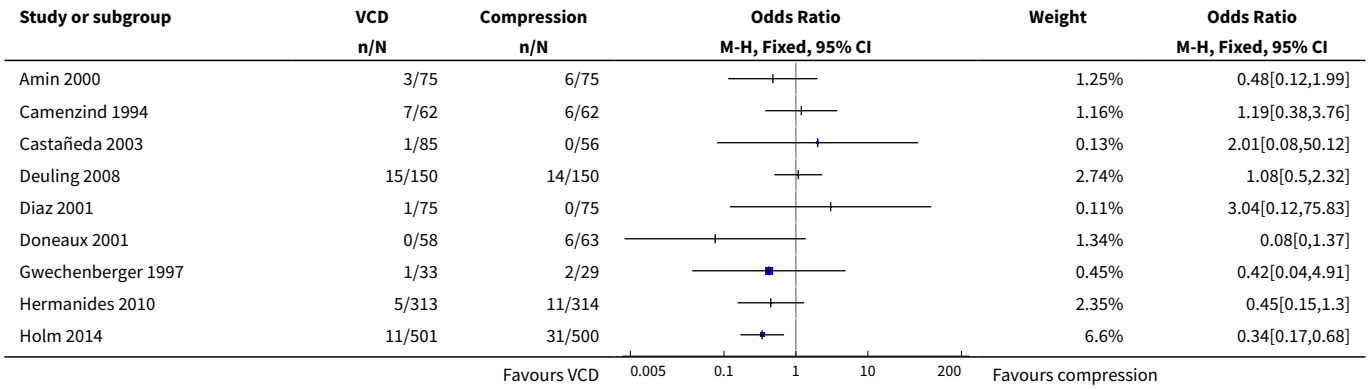
Study or subgroup	VCD	Compression	Odds Ratio	Weight	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI
1.3.1 Mortality					
Castañeda 2003	0/85	0/56			Not estimable
Subtotal (95% CI)	**85**	**56**			**Not estimable**
Total events: 0 (VCD), 0 (Compression)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.3.2 Vascular injury requiring vascular repair by surgical or non-surgical techniques					
Sanborn 1993	1/246	0/209		30.03%	2.56[0.1,63.18]
		Favours VCD	0.005 0.1 1 10 200		Favours compression

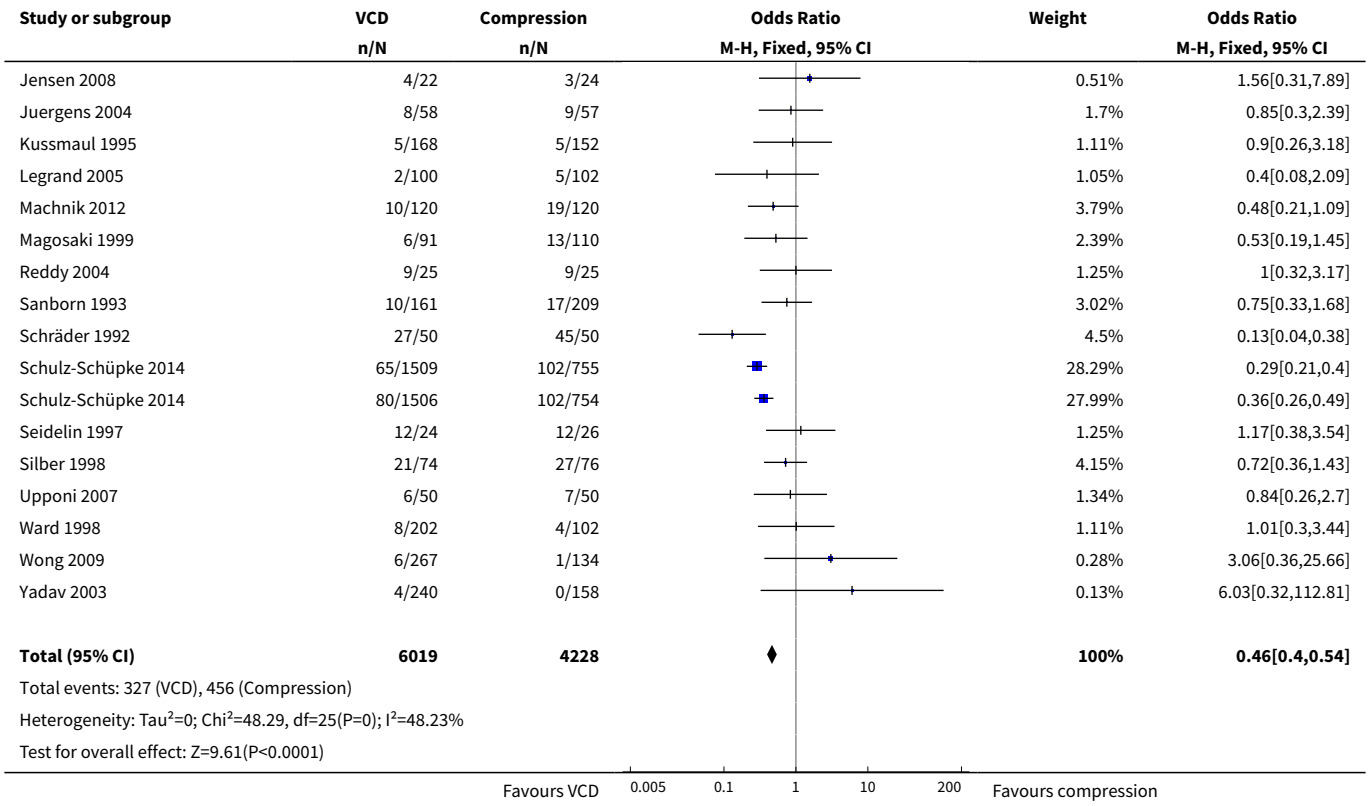


Analysis 1.4. Comparison 1 Collagen-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 4 Infection.

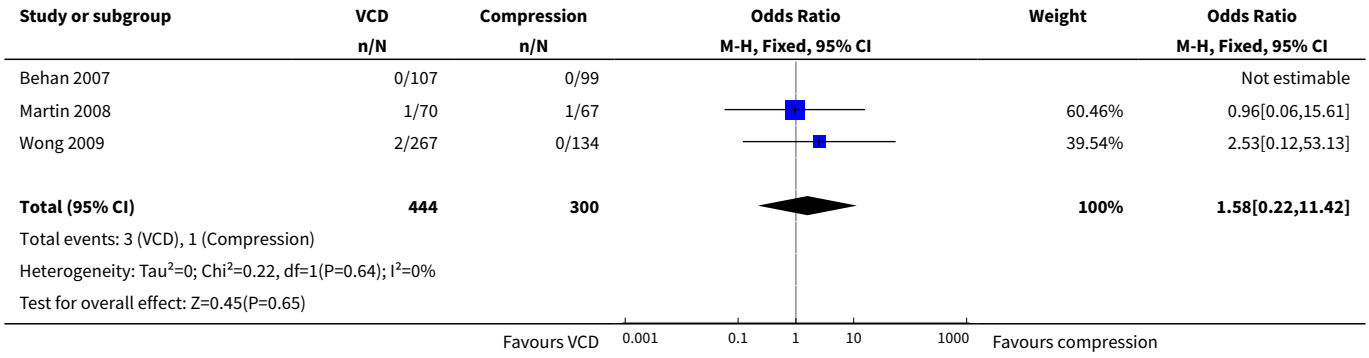


Analysis 1.5. Comparison 1 Collagen-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 5 Groin haematoma.

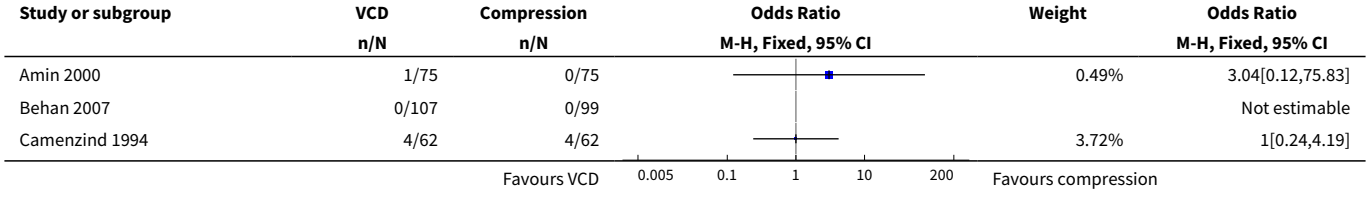


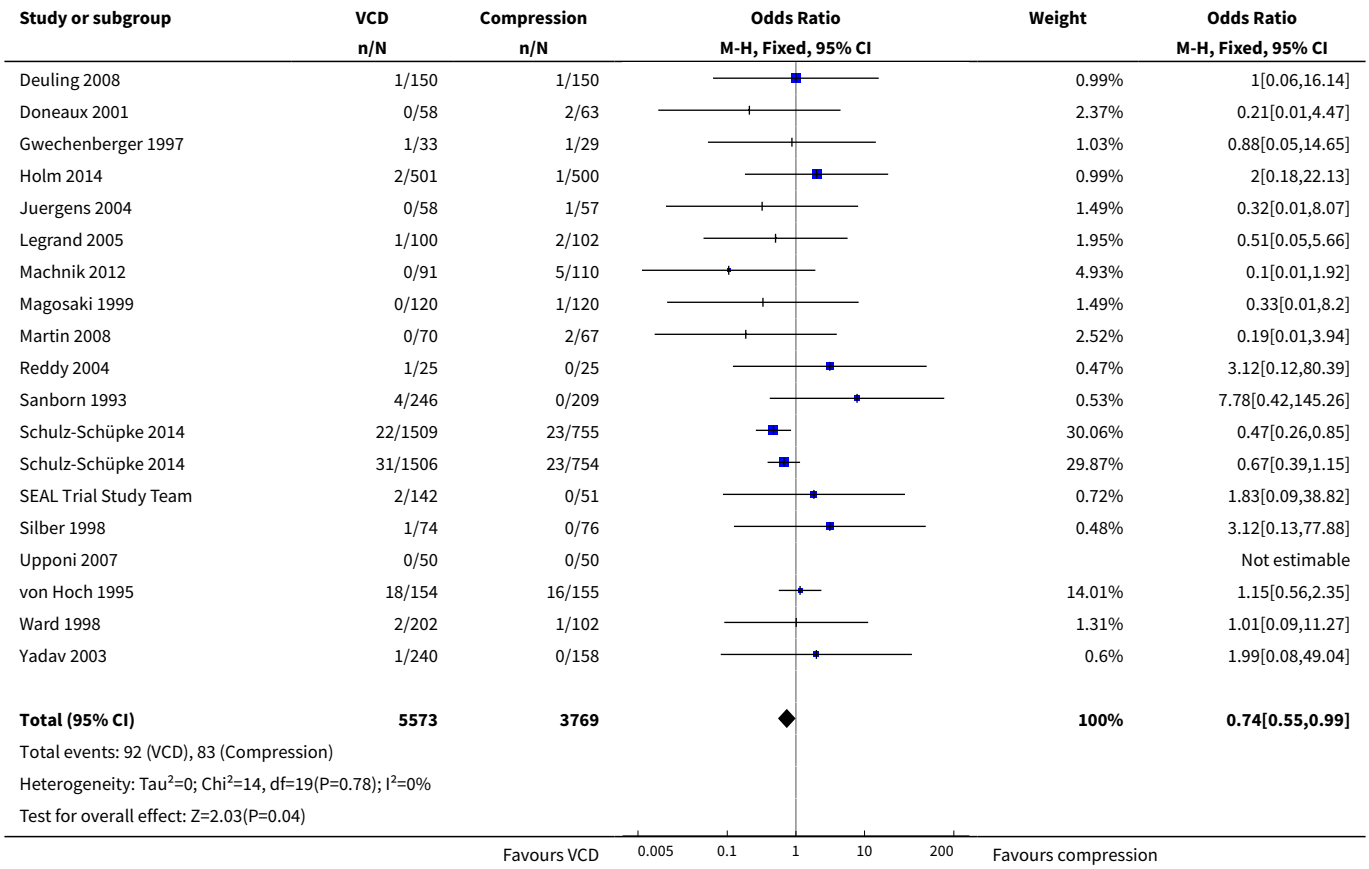


Analysis 1.6. Comparison 1 Collagen-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 6 Retroperitoneal haemorrhage.

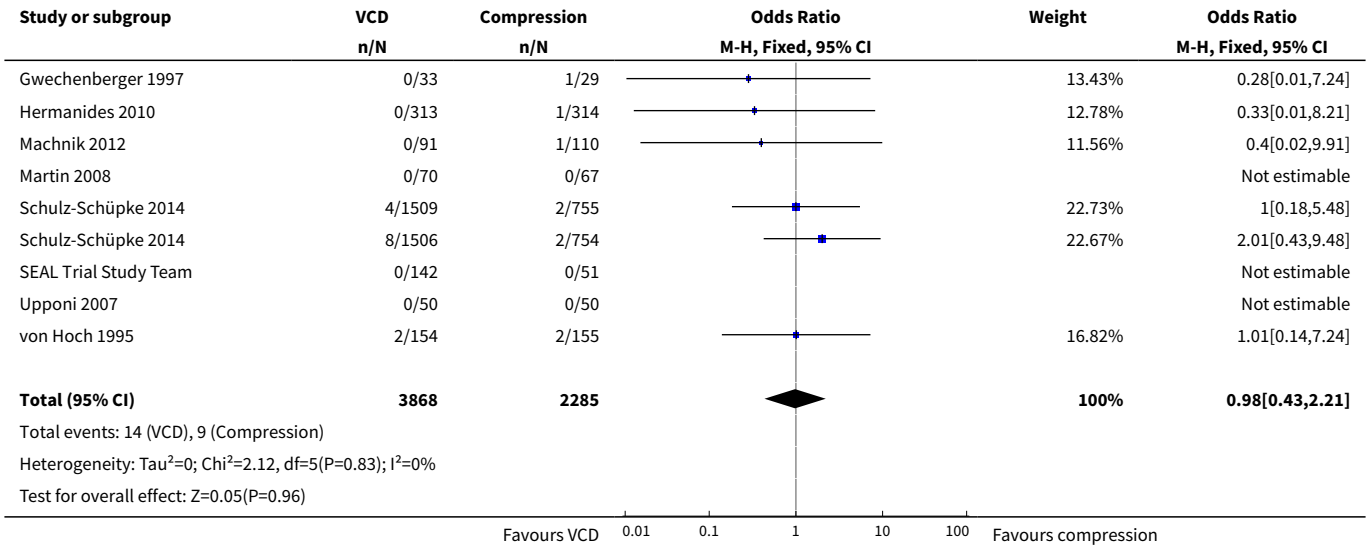


Analysis 1.7. Comparison 1 Collagen-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 7 Pseudoaneurysm.



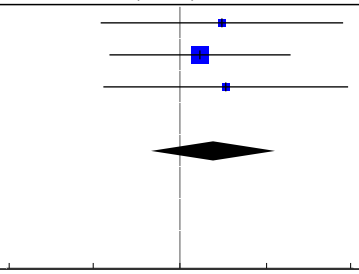


Analysis 1.8. Comparison 1 Collagen-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 8 Arterio-venous fistula.



Analysis 1.9. Comparison 1 Collagen-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 9 Deep vein thrombosis.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Camenzind 1994	1/62	0/62		24.25%	3.05[0.12,76.3]
Sanborn 1993	2/246	1/209		53.29%	1.7[0.15,18.94]
Seidelin 1997	1/24	0/26		22.46%	3.38[0.13,87.11]
Total (95% CI)	**332**	**297**		**100%**	**2.41[0.46,12.5]**
Total events: 4 (VCD), 1 (Compression)					
Heterogeneity: Tau^2=0; Chi^2=0.14, df=2(P=0.93); I^2=0%					
Test for overall effect: Z=1.05(P=0.3)					



Favours VCD — Favours compression

Analysis 1.10. Comparison 1 Collagen-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 10 Limb ischaemia.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Behan 2007	0/107	0/99			Not estimable
Machnik 2012	0/120	0/120			Not estimable
Schulz-Schüpke 2014	0/1506	0/754			Not estimable
Schulz-Schüpke 2014	0/1509	0/755			Not estimable
Total (95% CI)	**3242**	**1728**			**Not estimable**
Total events: 0 (VCD), 0 (Compression)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

Favours VCD — Favours compression

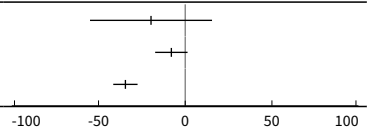
Analysis 1.11. Comparison 1 Collagen-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 11 Femoral artery thrombosis.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Upponi 2007	0/50	0/50		Not estimable

Favours VCD — Favours compression

Analysis 1.12. Comparison 1 Collagen-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 12 Length of hospital stay (hours).

Study or subgroup	VCD N	VCD Mean(SD)	Compression N	Compression Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Castañeda 2003	85	23.9 (53.4)	56	43.6 (127.1)		-19.73[-54.91,15.45]
Juergens 2004	58	32 (20)	57	40 (30)		-8[-17.34,1.34]
Machnik 2012	91	33.6 (14.2)	110	68.1 (34.1)		-34.5[-41.51,-27.49]



Favours VCD — Favours compression

Study or subgroup	VCD N	VCD Mean(SD)	Compression N	Compression Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Magosaki 1999	120	105.6 (129.6)	120	110.4 (124.8)		-4.8[-36.99,27.39]
Silber 1998	74	98.4 (100.8)	76	124.8 (165.6)		-26.4[-70.14,17.34]
Wong 2009	264	16.8 (19.8)	133	19.4 (29.2)		-2.6[-8.11,2.91]

Favours VCD -100 -50 0 50 100 Favours compression

Comparison 2. Metal clip-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Time to haemostasis (minutes)	5	1665	Mean Difference (IV, Random, 95% CI)	-14.81 [-16.98, -12.63]
2 Time to mobilisation (hours)	3		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Major adverse event (any time)	4		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Mortality	3	564	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Vascular injury requiring vascular repair by surgical or non-surgical techniques	3	783	Odds Ratio (M-H, Fixed, 95% CI)	0.49 [0.03, 7.95]
4 Infection	3	783	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Groin haematoma	4	1523	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.46, 1.34]
6 Pseudoaneurysm	6	1966	Odds Ratio (M-H, Fixed, 95% CI)	0.76 [0.20, 2.89]
7 Arterio-venous fistula	3	564	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Deep vein thrombosis	2	483	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Limb ischaemia	2	483	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 2.1. Comparison 2 Metal clip-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 1 Time to haemostasis (minutes).

Study or subgroup	VCD N	VCD Mean(SD)	Compression N	Compression Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Ansel 2006	125	3.3 (2.6)	63	19.3 (5.7)		21.4%	-16[-17.48,-14.52]
Ansel 2006	118	5.5 (5.1)	56	22.3 (9.9)		17.22%	-16.8[-19.55,-14.05]
Hermiller 2005	135	1.5 (4.5)	72	15.5 (11.4)		17.23%	-14.01[-16.76,-11.26]
Hermiller 2006	184	8 (28.2)	91	20.1 (35.3)		5.31%	-12.11[-20.43,-3.79]
Perlowski 2011	39	3 (5.8)	42	19.5 (8.7)		15.68%	-16.55[-19.75,-13.35]
Sun 2009	469	3.2 (1.9)	271	15.5 (5.8)		23.16%	-12.26[-12.97,-11.55]

Favours VCD -20 -10 0 10 20 Favours compression

Study or subgroup	VCD N	VCD Mean(SD)	Compression N	Compression Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Total ***	**1070**		**595**			**100%**	**-14.81[-16.98,-12.63]**
Heterogeneity: Tau²=5.19; Chi²=31.53, df=5(P<0.0001); I²=84.14%							
Test for overall effect: Z=13.33(P<0.0001)							

Favours VCD -20 -10 0 10 20 Favours compression

Analysis 2.2. Comparison 2 Metal clip-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 2 Time to mobilisation (hours).

Study or subgroup	VCD N	VCD Mean(SD)	Compression N	Compression Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Ansel 2006	125	2.4 (3.3)	63	6 (5.2)		-3.6[-5.01,-2.19]
Ansel 2006	118	3.4 (4.5)	56	7.6 (7)		-4.2[-6.21,-2.19]
Hermiller 2005	131	2.7 (1.7)	70	4.5 (2.3)		-1.77[-2.38,-1.16]
Sun 2009	469	4.8 (1.6)	271	20.3 (6.5)		-15.46[-16.25,-14.67]

Favours VCD -20 -10 0 10 20 Favours compression

Analysis 2.3. Comparison 2 Metal clip-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 3 Major adverse event (any time).

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
2.3.1 Mortality					
Hermiller 2005	0/136	0/72			Not estimable
Hermiller 2006	0/184	0/91			Not estimable
Perlowski 2011	0/39	0/42			Not estimable
Subtotal (95% CI)	**359**	**205**			**Not estimable**
Total events: 0 (VCD), 0 (Compression)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.3.2 Vascular injury requiring vascular repair by surgical or non-surgical techniques					
Deuling 2008	0/150	0/150			Not estimable
Hermiller 2005	0/136	0/72			Not estimable
Hermiller 2006	1/184	1/91		100%	0.49[0.03,7.95]
Subtotal (95% CI)	**470**	**313**		**100%**	**0.49[0.03,7.95]**
Total events: 1 (VCD), 1 (Compression)					
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%					
Test for overall effect: Z=0.5(P=0.62)					

Favours VCD 0.001 0.1 1 10 1000 Favours compression

Analysis 2.4. Comparison 2 Metal clip-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 4 Infection.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Deuling 2008	0/150	0/150			Not estimable
Hermiller 2005	0/136	0/72			Not estimable
Hermiller 2006	0/184	0/91			Not estimable
Total (95% CI)	**470**	**313**			**Not estimable**
Total events: 0 (VCD), 0 (Compression)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

Analysis 2.5. Comparison 2 Metal clip-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 5 Groin haematoma.

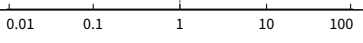
Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Deuling 2008	17/150	14/150		41.09%	1.24[0.59,2.62]
Hermiller 2005	1/136	1/72		4.3%	0.53[0.03,8.53]
Hermiller 2006	8/184	7/91		29.66%	0.55[0.19,1.55]
Sun 2009	4/469	6/271		24.96%	0.38[0.11,1.36]
Total (95% CI)	**939**	**584**		**100%**	**0.79[0.46,1.34]**
Total events: 30 (VCD), 28 (Compression)					
Heterogeneity: Tau^2=0; Chi^2=3.24, df=3(P=0.36); I^2=7.39%					
Test for overall effect: Z=0.87(P=0.38)					

Analysis 2.6. Comparison 2 Metal clip-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 6 Pseudoaneurysm.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Ansel 2006	3/243	0/119		13.71%	3.48[0.18,67.88]
Deuling 2008	1/150	1/150		20.62%	1[0.06,16.14]
Hermiller 2005	0/136	0/72			Not estimable
Hermiller 2006	0/184	0/91			Not estimable
Perlowski 2011	0/39	0/42			Not estimable
Sun 2009	0/469	2/271		65.67%	0.11[0.01,2.4]
Total (95% CI)	**1221**	**745**		**100%**	**0.76[0.2,2.89]**
Total events: 4 (VCD), 3 (Compression)					
Heterogeneity: Tau^2=0; Chi^2=2.53, df=2(P=0.28); I^2=20.91%					
Test for overall effect: Z=0.4(P=0.69)					

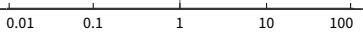
Analysis 2.7. Comparison 2 Metal clip-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 7 Arterio-venous fistula.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Hermiller 2005	0/136	0/72			Not estimable
Hermiller 2006	0/184	0/91			Not estimable
Perlowski 2011	0/39	0/42			Not estimable
Total (95% CI)	**359**	**205**			**Not estimable**
Total events: 0 (VCD), 0 (Compression)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



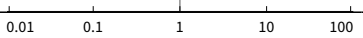
Analysis 2.8. Comparison 2 Metal clip-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 8 Deep vein thrombosis.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Hermiller 2005	0/136	0/72			Not estimable
Hermiller 2006	0/184	0/91			Not estimable
Total (95% CI)	**320**	**163**			**Not estimable**
Total events: 0 (VCD), 0 (Compression)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



Analysis 2.9. Comparison 2 Metal clip-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 9 Limb ischaemia.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Hermiller 2005	0/136	0/72			Not estimable
Hermiller 2006	0/184	0/91			Not estimable
Total (95% CI)	**320**	**163**			**Not estimable**
Total events: 0 (VCD), 0 (Compression)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



Comparison 3. Suture-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr)

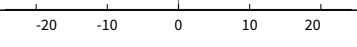
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Time to haemostasis (minutes)	7	1664	Mean Difference (IV, Random, 95% CI)	-14.58 [-16.85, -12.32]
2 Time to mobilisation (hours)	7		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Major adverse event (any time)	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
3.1 Mortality	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Vascular injury requiring vascular repair	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infection	3	750	Odds Ratio (M-H, Fixed, 95% CI)	1.66 [0.22, 12.71]
5 Groin haematoma	6	1350	Odds Ratio (M-H, Fixed, 95% CI)	0.65 [0.41, 1.02]
6 Retroperitoneal haemorrhage	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
7 Pseudoaneurysm	6	1527	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.25, 2.53]
8 Arterio-venous fistula	4	880	Odds Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 8.02]
9 Embolisation	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
10 Limb ischaemia	2	720	Odds Ratio (M-H, Fixed, 95% CI)	1.02 [0.14, 7.22]
11 Length of hospital stay (hours)	3	327	Mean Difference (IV, Random, 95% CI)	-11.66 [-20.46, -2.85]

Analysis 3.1. Comparison 3 Suture-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 1 Time to haemostasis (minutes).

Study or subgroup	VCD N	VCD Mean(SD)	Compression N	Compression Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Amine 1999	50	6 (10)	50	20 (6)		13.41%	-14[-17.23,-10.77]
Gerckens 1998	298	7.8 (4.8)	292	19.6 (13.2)		16.87%	-11.8[-13.41,-10.19]
Noguchi 2000	30	10 (3)	30	27 (9)		13.04%	-17[-20.39,-13.61]
Rickli 2002	96	7.1 (3.4)	97	22.9 (14)		14.23%	-15.8[-18.67,-12.93]
Sun 2009	183	4.6 (1.8)	271	15.5 (5.8)		18.08%	-10.89[-11.63,-10.15]
Tron 2003	91	8 (6)	76	25 (11)		14.47%	-17[-19.76,-14.24]
Wetter 2000	50	7.3 (3.2)	50	25.7 (17.4)		9.9%	-18.4[-23.3,-13.5]
Total * **	**798**		**866**			**100%**	**-14.58[-16.85,-12.32]**

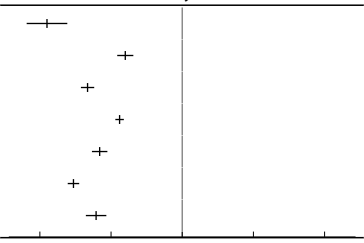
Heterogeneity: Tau^2=7.27; Chi^2=44.39, df=6(P<0.0001); I^2=86.48%

Test for overall effect: Z=12.6(P<0.0001)



Analysis 3.2. Comparison 3 Suture-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 2 Time to mobilisation (hours).

Study or subgroup	VCD N	VCD Mean(SD)	Compression N	Compression Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Amine 1999	50	5 (9)	50	24 (5)		-19[-21.85,-16.15]
Carere 2000	50	7 (1.2)	50	15 (3.9)		-8[-9.13,-6.87]
Gerckens 1998	298	4.5 (6.5)	292	17.8 (5)		-13.3[-14.23,-12.37]
Noguchi 2000	30	2.2 (0.9)	30	11 (1.4)		-8.8[-9.4,-8.2]
Rickli 2002	96	6.8 (5)	97	18.4 (2.1)		-11.6[-12.68,-10.52]
Sun 2009	183	5 (1.6)	271	20.3 (6.5)		-15.28[-16.09,-14.47]
Wetter 2000	50	6.2 (4.7)	50	18.3 (2.2)		-12.1[-13.54,-10.66]

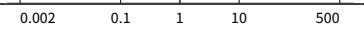


Analysis 3.3. Comparison 3 Suture-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 3 Major adverse event (any time).

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
3.3.1 Mortality				
Noguchi 2000	0/30	0/30		Not estimable
3.3.2 Vascular injury requiring vascular repair				
Noguchi 2000	0/30	0/30		Not estimable

Analysis 3.4. Comparison 3 Suture-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 4 Infection.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Amine 1999	0/50	0/50			Not estimable
Gerckens 1998	1/298	1/292		67.91%	0.98[0.06,15.74]
Noguchi 2000	1/30	0/30		32.09%	3.1[0.12,79.23]
Total (95% CI)	**378**	**372**		**100%**	**1.66[0.22,12.71]**
Total events: 2 (VCD), 1 (Compression)					
Heterogeneity: Tau^2=0; Chi^2=0.28, df=1(P=0.6); I^2=0%					
Test for overall effect: Z=0.49(P=0.63)					

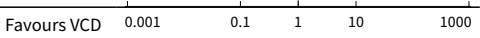


Analysis 3.5. Comparison 3 Suture-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 5 Groin haematoma.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Amine 1999	5/50	4/50		7.71%	1.28[0.32,5.07]
Carere 2000	8/50	10/50		17.99%	0.76[0.27,2.12]
Gerckens 1998	11/298	21/292		43.77%	0.49[0.23,1.05]
Jensen 2008	3/22	1/24		1.77%	3.63[0.35,37.83]
Noguchi 2000	4/30	10/30		18.57%	0.31[0.08,1.13]
Sun 2009	3/183	6/271		10.19%	0.74[0.18,2.98]
Total (95% CI)	**633**	**717**		**100%**	**0.65[0.41,1.02]**
Total events: 34 (VCD), 52 (Compression)					
Heterogeneity: Tau^2=0; Chi^2=4.91, df=5(P=0.43); I^2=0%					
Test for overall effect: Z=1.86(P=0.06)					

Analysis 3.6. Comparison 3 Suture-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 6 Retroperitoneal haemorrhage.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Martin 2008	0/63	1/67		0.35[0.01,8.73]

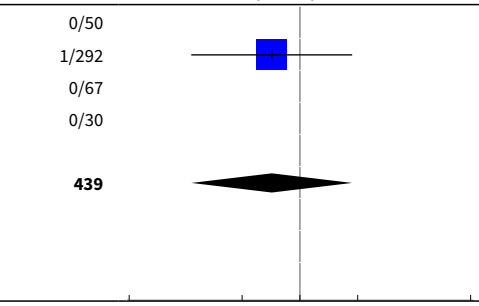


Analysis 3.7. Comparison 3 Suture-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 7 Pseudoaneurysm.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Gerckens 1998	1/298	1/292		15.53%	0.98[0.06,15.74]
Martin 2008	1/63	2/67		29.43%	0.52[0.05,5.93]
Noguchi 2000	0/30	0/30			Not estimable
Rickli 2002	1/96	1/97		15.19%	1.01[0.06,16.39]
Sun 2009	1/183	2/271		24.74%	0.74[0.07,8.21]
Wetter 2000	1/50	1/50		15.12%	1[0.06,16.44]
Total (95% CI)	**720**	**807**		**100%**	**0.79[0.25,2.53]**
Total events: 5 (VCD), 7 (Compression)					
Heterogeneity: Tau^2=0; Chi^2=0.19, df=4(P=1); I^2=0%					
Test for overall effect: Z=0.39(P=0.7)					

Analysis 3.8. Comparison 3 Suture-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 8 Arterio-venous fistula.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Amine 1999	0/50	0/50			Not estimable
Gerckens 1998	0/298	1/292		100%	0.33[0.01,8.02]
Martin 2008	0/63	0/67			Not estimable
Noguchi 2000	0/30	0/30			Not estimable
Total (95% CI)	**441**	**439**		**100%**	**0.33[0.01,8.02]**
Total events: 0 (VCD), 1 (Compression)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.69(P=0.49)					

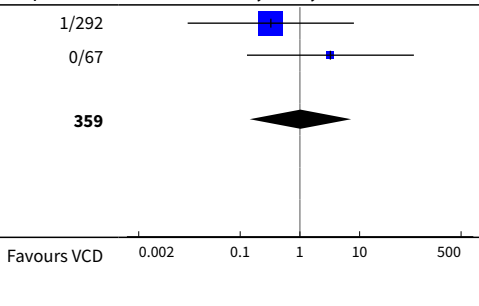


Analysis 3.9. Comparison 3 Suture-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 9 Embolisation.

Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Noguchi 2000	0/30	0/30		Not estimable

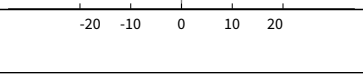
Analysis 3.10. Comparison 3 Suture-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 10 Limb ischaemia.

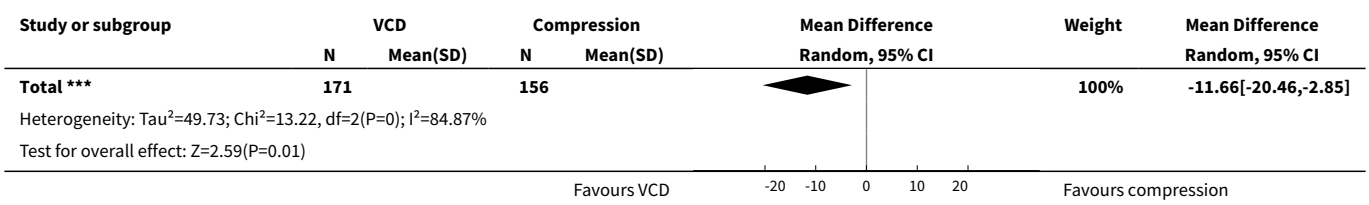
Study or subgroup	VCD n/N	Compression n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Gerckens 1998	0/298	1/292		76.16%	0.33[0.01,8.02]
Martin 2008	1/63	0/67		23.84%	3.24[0.13,81.01]
Total (95% CI)	**361**	**359**		**100%**	**1.02[0.14,7.22]**
Total events: 1 (VCD), 1 (Compression)					
Heterogeneity: Tau^2=0; Chi^2=0.98, df=1(P=0.32); I^2=0%					
Test for overall effect: Z=0.02(P=0.98)					



Analysis 3.11. Comparison 3 Suture-based VCD versus manual or mechanical compression (sheath size ≤ 9 Fr), Outcome 11 Length of hospital stay (hours).

Study or subgroup	VCD N	VCD Mean(SD)	Compression N	Compression Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Carere 2000	50	11 (6.2)	50	22 (3.8)		39.74%	-11[-13.02,-8.98]
Noguchi 2000	30	52.8 (9.6)	30	74.4 (16.8)		32.45%	-21.6[-28.52,-14.68]
Tron 2003	91	39 (40)	76	40 (20)		27.81%	-1[-10.37,8.37]

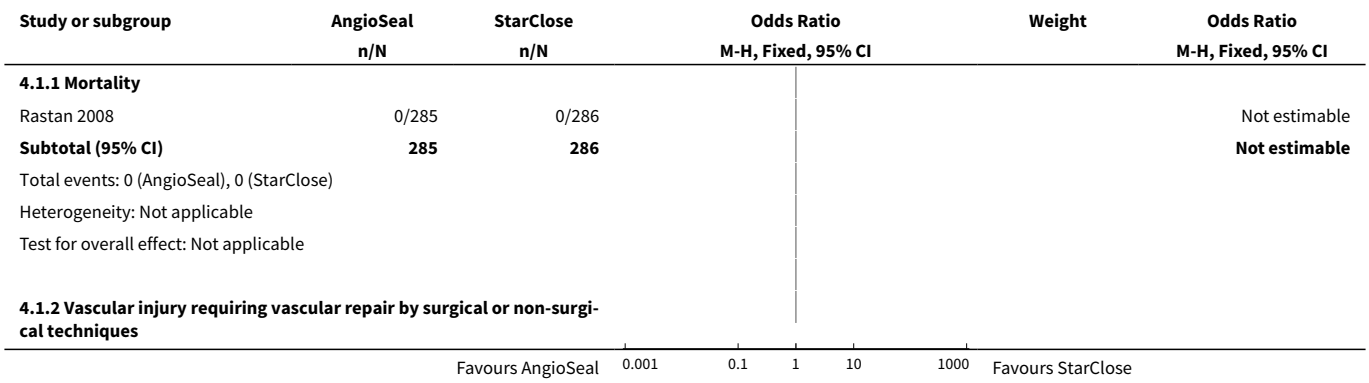


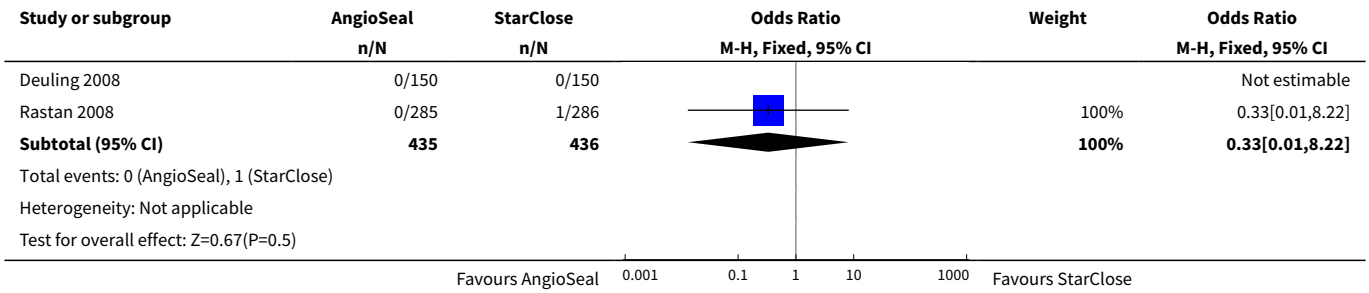


Comparison 4. Collagen-based VCD versus metal clip-based VCD: AngioSeal versus StarClose

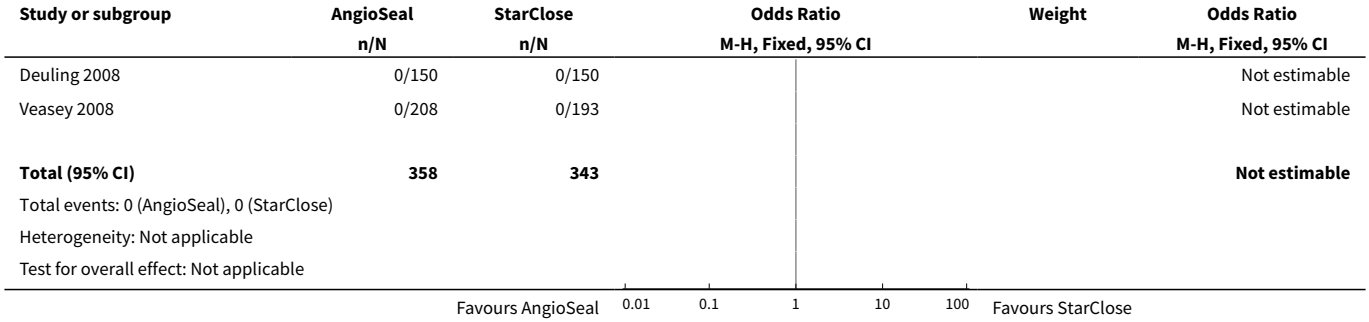
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Major adverse event (any time)	2		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Mortality	1	571	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Vascular injury requiring vascular repair by surgical or non-surgical techniques	2	871	Odds Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 8.22]
2 Infection	2	701	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Groin haematoma	2	871	Odds Ratio (M-H, Fixed, 95% CI)	0.84 [0.43, 1.65]
4 Retroperitoneal haemorrhage	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
5 Pseudoaneurysm	3	1272	Odds Ratio (M-H, Fixed, 95% CI)	0.50 [0.15, 1.66]
6 Arterio-venous fistula	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
7 Limb ischaemia	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
8 Technical failure of VCD	3	1272	Odds Ratio (M-H, Fixed, 95% CI)	0.38 [0.23, 0.64]

Analysis 4.1. Comparison 4 Collagen-based VCD versus metal clip-based VCD: AngioSeal versus StarClose, Outcome 1 Major adverse event (any time).

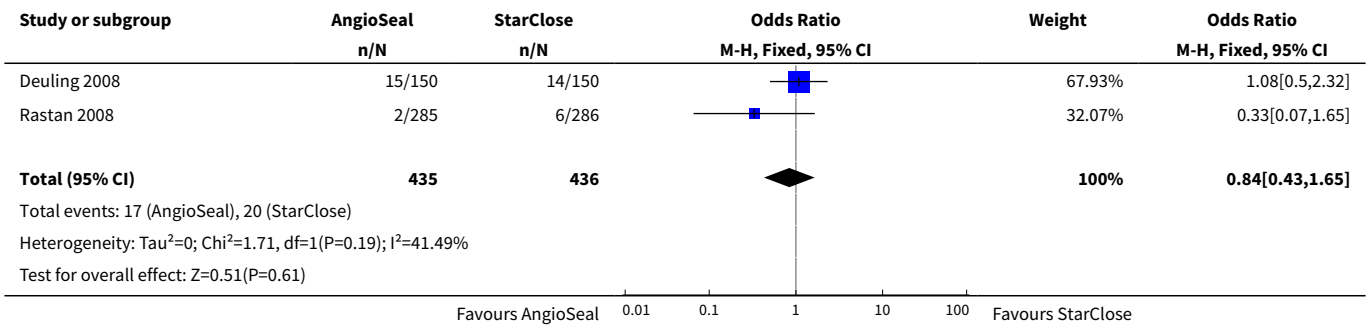




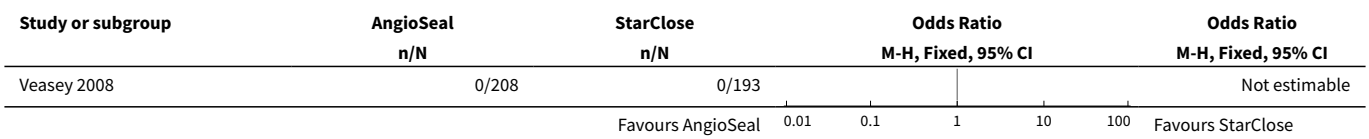
Analysis 4.2. Comparison 4 Collagen-based VCD versus metal clip-based VCD: AngioSeal versus StarClose, Outcome 2 Infection.



Analysis 4.3. Comparison 4 Collagen-based VCD versus metal clip-based VCD: AngioSeal versus StarClose, Outcome 3 Groin haematoma.

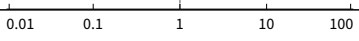


Analysis 4.4. Comparison 4 Collagen-based VCD versus metal clip-based VCD: AngioSeal versus StarClose, Outcome 4 Retroperitoneal haemorrhage.



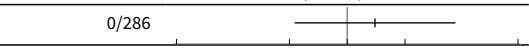
Analysis 4.5. Comparison 4 Collagen-based VCD versus metal clip-based VCD: AngioSeal versus StarClose, Outcome 5 Pseudoaneurysm.

Study or subgroup	AngioSeal n/N	StarClose n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Deuling 2008	1/150	1/150		12.56%	1[0.06,16.14]
Rastan 2008	3/285	7/286		87.44%	0.42[0.11,1.66]
Veasey 2008	0/208	0/193			Not estimable
Total (95% CI)	**643**	**629**		**100%**	**0.5[0.15,1.66]**
Total events: 4 (AngioSeal), 8 (StarClose)					
Heterogeneity: Tau^2=0; Chi^2=0.3, df=1(P=0.59); I^2=0%					
Test for overall effect: Z=1.14(P=0.26)					



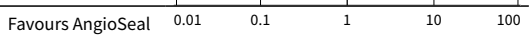
Analysis 4.6. Comparison 4 Collagen-based VCD versus metal clip-based VCD: AngioSeal versus StarClose, Outcome 6 Arterio-venous fistula.

Study or subgroup	AngioSeal n/N	StarClose n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Rastan 2008	1/285	0/286		3.02[0.12,74.47]



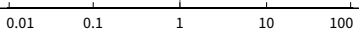
Analysis 4.7. Comparison 4 Collagen-based VCD versus metal clip-based VCD: AngioSeal versus StarClose, Outcome 7 Limb ischaemia.

Study or subgroup	AngioSeal n/N	StarClose n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Veasey 2008	0/208	0/193		Not estimable



Analysis 4.8. Comparison 4 Collagen-based VCD versus metal clip-based VCD: AngioSeal versus StarClose, Outcome 8 Technical failure of VCD.

Study or subgroup	AngioSeal n/N	StarClose n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Deuling 2008	2/150	9/150		17.33%	0.21[0.04,1]
Rastan 2008	14/285	34/286		63%	0.38[0.2,0.73]
Veasey 2008	6/208	10/193		19.67%	0.54[0.19,1.53]
Total (95% CI)	**643**	**629**		**100%**	**0.38[0.23,0.64]**
Total events: 22 (AngioSeal), 53 (StarClose)					
Heterogeneity: Tau^2=0; Chi^2=1, df=2(P=0.61); I^2=0%					
Test for overall effect: Z=3.65(P=0)					

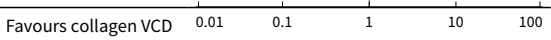


Comparison 5. Collagen-based VCD versus suture-based VCD (sheath size ≤ 9 Fr)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Infection	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
2 Groin haematoma	3	510	Odds Ratio (M-H, Fixed, 95% CI)	1.26 [0.71, 2.22]
3 Retroperitoneal haemorrhage	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
4 Pseudoaneurysm	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
5 Arterio-venous fistula	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
6 Technical failure of VCD	3	510	Odds Ratio (M-H, Fixed, 95% CI)	0.24 [0.08, 0.69]

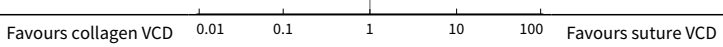
Analysis 5.1. Comparison 5 Collagen-based VCD versus suture-based VCD (sheath size ≤ 9 Fr), Outcome 1 Infection.

Study or subgroup	Collagen VCD n/N	Suture VCD n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Kalsch 2008	0/212	0/154		Not estimable



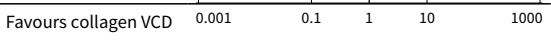
Analysis 5.2. Comparison 5 Collagen-based VCD versus suture-based VCD (sheath size ≤ 9 Fr), Outcome 2 Groin haematoma.

Study or subgroup	Collagen VCD n/N	Suture VCD n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Hattab 2012	5/50	3/50		12.56%	1.74[0.39,7.71]
Jensen 2008	4/22	3/22		11.41%	1.41[0.28,7.18]
Kalsch 2008	25/212	16/154		76.03%	1.15[0.59,2.24]
Total (95% CI)	**284**	**226**		**100%**	**1.26[0.71,2.22]**
Total events: 34 (Collagen VCD), 22 (Suture VCD)					
Heterogeneity: Tau^2=0; Chi^2=0.27, df=2(P=0.88); I^2=0%					
Test for overall effect: Z=0.79(P=0.43)					



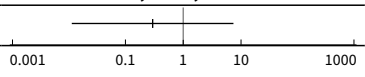
Analysis 5.3. Comparison 5 Collagen-based VCD versus suture-based VCD (sheath size ≤ 9 Fr), Outcome 3 Retroperitoneal haemorrhage.

Study or subgroup	Collagen VCD n/N	Suture VCD n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Martin 2008	1/70	0/63		2.74[0.11,68.51]



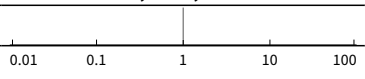
Analysis 5.4. Comparison 5 Collagen-based VCD versus suture-based VCD (sheath size ≤ 9 Fr), Outcome 4 Pseudoaneurysm.

Study or subgroup	Collagen VCD n/N	Suture VCD n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Martin 2008	0/70	1/63		0.3[0.01,7.39]



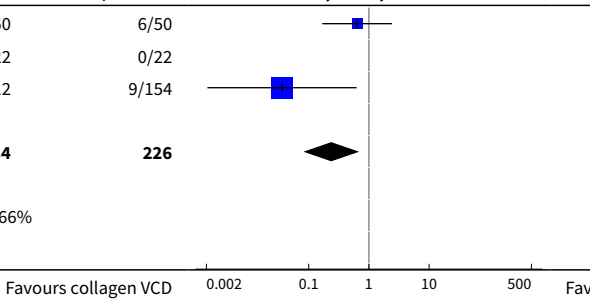
Analysis 5.5. Comparison 5 Collagen-based VCD versus suture-based VCD (sheath size ≤ 9 Fr), Outcome 5 Arterio-venous fistula.

Study or subgroup	Collagen VCD n/N	Suture VCD n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Martin 2008	0/70	0/63		Not estimable



Analysis 5.6. Comparison 5 Collagen-based VCD versus suture-based VCD (sheath size ≤ 9 Fr), Outcome 6 Technical failure of VCD.

Study or subgroup	Collagen VCD n/N	Suture VCD n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Hattab 2012	4/50	6/50		33.47%	0.64[0.17,2.41]
Jensen 2008	0/22	0/22			Not estimable
Kalsch 2008	0/212	9/154		66.53%	0.04[0,0.62]
Total (95% CI)	**284**	**226**		**100%**	**0.24[0.08,0.69]**
Total events: 4 (Collagen VCD), 15 (Suture VCD)					
Heterogeneity: Tau^2=0; Chi^2=3.8, df=1(P=0.05); I^2=73.66%					
Test for overall effect: Z=2.64(P=0.01)					

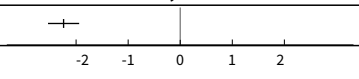


Comparison 6. Metal clip-based VCD versus suture-based VCD: StarClose versus PerClose

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Time to haemostasis	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Time to mobilisation	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Groin haematoma	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
4 Pseudoaneurysm	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
5 Technical failure of VCD	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 6.1. Comparison 6 Metal clip-based VCD versus suture-based VCD: StarClose versus PerClose, Outcome 1 Time to haemostasis.

Study or subgroup	StarClose N	StarClose Mean(SD)	PerClose N	PerClose Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Sun 2009	286	2.3 (1.2)	183	4.6 (1.8)		-2.24[-2.54,-1.94]

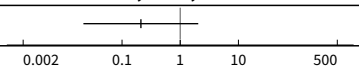


Analysis 6.2. Comparison 6 Metal clip-based VCD versus suture-based VCD: StarClose versus PerClose, Outcome 2 Time to mobilisation.

Study or subgroup	StarClose N	StarClose Mean(SD)	PerClose N	PerClose Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Sun 2009	286	4.7 (1.6)	183	5 (1.6)		-0.3[-0.59,-0.01]

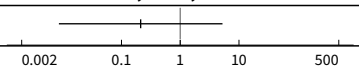
Analysis 6.3. Comparison 6 Metal clip-based VCD versus suture-based VCD: StarClose versus PerClose, Outcome 3 Groin haematoma.

Study or subgroup	StarClose n/N	PerClose n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Sun 2009	1/286	3/183		0.21[0.02,2.04]



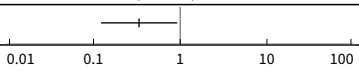
Analysis 6.4. Comparison 6 Metal clip-based VCD versus suture-based VCD: StarClose versus PerClose, Outcome 4 Pseudoaneurysm.

Study or subgroup	StarClose n/N	PerClose n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Sun 2009	0/286	1/183		0.21[0.01,5.24]



Analysis 6.5. Comparison 6 Metal clip-based VCD versus suture-based VCD: StarClose versus PerClose, Outcome 5 Technical failure of VCD.

Study or subgroup	StarClose n/N	PerClose n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Sun 2009	6/286	11/183		0.34[0.12,0.92]

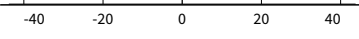


Comparison 7. Disc-based VCD versus suture-based VCD: Boomerang versus PerClose

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Time to haemostasis (minutes)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Time to mobilisation (hours)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Groin haematoma	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
4 Technical failure of VCD	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

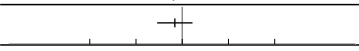
Analysis 7.1. Comparison 7 Disc-based VCD versus suture-based VCD: Boomerang versus PerClose, Outcome 1 Time to haemostasis (minutes).

Study or subgroup	Boomerang		PerClose		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Chen 2013	30	40.1 (4)	30	8 (7.2)		32.05[29.09,35.01]



Analysis 7.2. Comparison 7 Disc-based VCD versus suture-based VCD: Boomerang versus PerClose, Outcome 2 Time to mobilisation (hours).

Study or subgroup	Boomerang		PerClose		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Chen 2013	29	2.1 (0.2)	29	2.1 (0.2)		-0.04[-0.14,0.06]

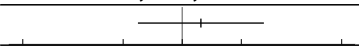


Analysis 7.3. Comparison 7 Disc-based VCD versus suture-based VCD: Boomerang versus PerClose, Outcome 3 Groin haematoma.

Study or subgroup	Boomerang	PerClose	Odds Ratio	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Chen 2013	4/30	0/30		10.36[0.53,201.45]

Analysis 7.4. Comparison 7 Disc-based VCD versus suture-based VCD: Boomerang versus PerClose, Outcome 4 Technical failure of VCD.

Study or subgroup	Boomerang	PerClose	Odds Ratio	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Chen 2013	2/30	1/30		2.07[0.18,24.15]



Comparison 8. Collagen-based VCD versus collagen-based VCD: AngioSeal versus VasoSeal

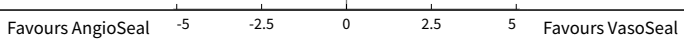
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Time to haemostasis (minutes)	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Time to mobilisation (hours)	2	720	Mean Difference (IV, Random, 95% CI)	-0.13 [-0.63, 0.37]
3 Major adverse event (any time)	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Mortality	1	150	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Vascular injury requiring vascular repair by surgical or non-surgical techniques	1	150	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infection	1	150	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Groin haematoma	2	720	Odds Ratio (M-H, Fixed, 95% CI)	0.49 [0.16, 1.47]
6 Retroperitoneal haemorrhage	2	720	Odds Ratio (M-H, Fixed, 95% CI)	0.36 [0.01, 9.09]
7 Pseudoaneurysm	1	150	Odds Ratio (M-H, Fixed, 95% CI)	0.31 [0.01, 7.71]
8 Arterio-venous fistula	1	150	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Technical failure of VCD	1	570	Odds Ratio (M-H, Fixed, 95% CI)	0.68 [0.37, 1.26]

Analysis 8.1. Comparison 8 Collagen-based VCD versus collagen-based VCD: AngioSeal versus VasoSeal, Outcome 1 Time to haemostasis (minutes).

Study or subgroup	AngioSeal		VasoSeal		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Michalis 2002	243	18.1 (5.8)	228	7 (3.2)		11.1[10.26,11.94]
Michalis 2002	47	19.8 (7.7)	52	7.8 (3.6)		12[9.59,14.41]
Shammas 2002	49	20.5 (4.4)	46	18.6 (11.6)		1.92[-1.64,5.48]
Shammas 2002	28	24.2 (12.7)	27	19.6 (2.3)		4.66[-0.12,9.44]
				Favours AngioSeal	-10 -5 0 5 10	Favours VasoSeal

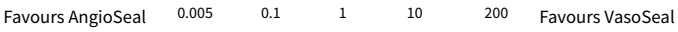
Analysis 8.2. Comparison 8 Collagen-based VCD versus collagen-based VCD: AngioSeal versus VasoSeal, Outcome 2 Time to mobilisation (hours).

Study or subgroup	AngioSeal N	AngioSeal Mean(SD)	VasoSeal N	VasoSeal Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Michalis 2002	47	2.9 (1)	52	3.4 (0.8)		32.92%	-0.48[-0.85,-0.11]
Michalis 2002	243	1.9 (0.5)	228	2.4 (0.7)		39.35%	-0.48[-0.59,-0.37]
Shammas 2002	49	2.4 (2.1)	46	1.8 (1)		24%	0.6[-0.05,1.25]
Shammas 2002	28	10.1 (5.7)	27	8.1 (3.3)		3.72%	2.01[-0.46,4.48]
Total ***	**367**		**353**			**100%**	**-0.13[-0.63,0.37]**
Heterogeneity: Tau^2=0.16; Chi^2=14.2, df=3(P=0); I^2=78.87%							
Test for overall effect: Z=0.5(P=0.62)							



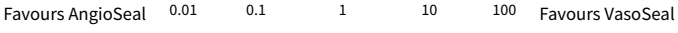
Analysis 8.3. Comparison 8 Collagen-based VCD versus collagen-based VCD: AngioSeal versus VasoSeal, Outcome 3 Major adverse event (any time).

Study or subgroup	AngioSeal n/N	VasoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
8.3.1 Mortality					
Shammas 2002	0/28	0/27			Not estimable
Shammas 2002	0/49	0/46			Not estimable
Subtotal (95% CI)	**77**	**73**			**Not estimable**
Total events: 0 (AngioSeal), 0 (VasoSeal)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
8.3.2 Vascular injury requiring vascular repair by surgical or non-surgical techniques					
Shammas 2002	0/28	0/27			Not estimable
Shammas 2002	0/49	0/46			Not estimable
Subtotal (95% CI)	**77**	**73**			**Not estimable**
Total events: 0 (AngioSeal), 0 (VasoSeal)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



Analysis 8.4. Comparison 8 Collagen-based VCD versus collagen-based VCD: AngioSeal versus VasoSeal, Outcome 4 Infection.

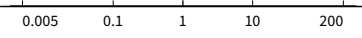
Study or subgroup	AngioSeal n/N	VasoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Shammas 2002	0/49	0/46			Not estimable
Shammas 2002	0/28	0/27			Not estimable
Total (95% CI)	**77**	**73**			**Not estimable**
Total events: 0 (AngioSeal), 0 (VasoSeal)					
Heterogeneity: Not applicable					



Study or subgroup	AngioSeal n/N	VasoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Test for overall effect: Not applicable					

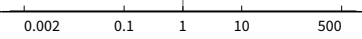
Analysis 8.5. Comparison 8 Collagen-based VCD versus collagen-based VCD: AngioSeal versus VasoSeal, Outcome 5 Groin haematoma.

Study or subgroup	AngioSeal n/N	VasoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Michalis 2002	2/47	5/52		47.15%	0.42[0.08,2.26]
Michalis 2002	3/243	5/228		52.85%	0.56[0.13,2.36]
Shammas 2002	0/28	0/27			Not estimable
Shammas 2002	0/49	0/46			Not estimable
Total (95% CI)	**367**	**353**		**100%**	**0.49[0.16,1.47]**
Total events: 5 (AngioSeal), 10 (VasoSeal)					
Heterogeneity: Tau^2=0; Chi^2=0.06, df=1(P=0.8); I^2=0%					
Test for overall effect: Z=1.27(P=0.2)					



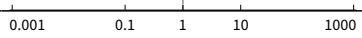
Analysis 8.6. Comparison 8 Collagen-based VCD versus collagen-based VCD: AngioSeal versus VasoSeal, Outcome 6 Retroperitoneal haemorrhage.

Study or subgroup	AngioSeal n/N	VasoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Michalis 2002	0/47	1/52		100%	0.36[0.01,9.09]
Michalis 2002	0/243	0/228			Not estimable
Shammas 2002	0/49	0/46			Not estimable
Shammas 2002	0/28	0/27			Not estimable
Total (95% CI)	**367**	**353**		**100%**	**0.36[0.01,9.09]**
Total events: 0 (AngioSeal), 1 (VasoSeal)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.62(P=0.54)					



Analysis 8.7. Comparison 8 Collagen-based VCD versus collagen-based VCD: AngioSeal versus VasoSeal, Outcome 7 Pseudoaneurysm.

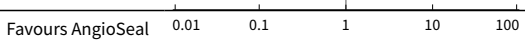
Study or subgroup	AngioSeal n/N	VasoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Shammas 2002	0/49	1/46		100%	0.31[0.01,7.71]
Shammas 2002	0/28	0/27			Not estimable
Total (95% CI)	**77**	**73**		**100%**	**0.31[0.01,7.71]**



Study or subgroup	AngioSeal n/N	VasoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Total events: 0 (AngioSeal), 1 (VasoSeal)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.72(P=0.47)					

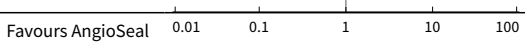
Analysis 8.8. Comparison 8 Collagen-based VCD versus collagen-based VCD: AngioSeal versus VasoSeal, Outcome 8 Arterio-venous fistula.

Study or subgroup	AngioSeal n/N	VasoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Shammas 2002	0/28	0/27			Not estimable
Shammas 2002	0/49	0/46			Not estimable
Total (95% CI)	**77**	**73**			**Not estimable**
Total events: 0 (AngioSeal), 0 (VasoSeal)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



Analysis 8.9. Comparison 8 Collagen-based VCD versus collagen-based VCD: AngioSeal versus VasoSeal, Outcome 9 Technical failure of VCD.

Study or subgroup	AngioSeal n/N	VasoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Michalis 2002	2/47	4/52		14.69%	0.53[0.09,3.06]
Michalis 2002	17/243	22/228		85.31%	0.7[0.36,1.36]
Total (95% CI)	**290**	**280**		**100%**	**0.68[0.37,1.26]**
Total events: 19 (AngioSeal), 26 (VasoSeal)					
Heterogeneity: Tau^2=0; Chi^2=0.09, df=1(P=0.77); I^2=0%					
Test for overall effect: Z=1.23(P=0.22)					



Comparison 9. Collagen-based VCD versus collagen-based VCD: AngioSeal versus Mynx

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Major adverse event (any time)	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Vascular injury requiring vascular repair by surgical or non-surgical techniques	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 Infection	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
3 Groin haematoma	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 9.1. Comparison 9 Collagen-based VCD versus collagen-based VCD: AngioSeal versus Mynx, Outcome 1 Major adverse event (any time).

Study or subgroup	AngioSeal n/N	Mynx n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
9.1.1 Vascular injury requiring vascular repair by surgical or non-surgical techniques				
Fargen 2011	0/32	0/32		Not estimable

Favours AngioSeal 0.005 0.1 1 10 200 Favours Mynx

Analysis 9.2. Comparison 9 Collagen-based VCD versus collagen-based VCD: AngioSeal versus Mynx, Outcome 2 Infection.

Study or subgroup	AngioSeal n/N	Mynx n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Fargen 2011	0/32	0/32		Not estimable

Favours AngioSeal 0.01 0.1 1 10 100 Favours Mynx

Analysis 9.3. Comparison 9 Collagen-based VCD versus collagen-based VCD: AngioSeal versus Mynx, Outcome 3 Groin haematoma.

Study or subgroup	Favours AngioSeal n/N	Mynx n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Fargen 2011	0/32	0/32		Not estimable

Favours AngioSeal 0.005 0.1 1 10 200 Favours Mynx

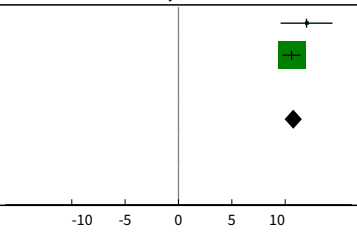
Comparison 10. Collagen-based VCD versus collagen-based VCD: AngioSeal versus Duett

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Time to haemostasis (minutes)	1	571	Mean Difference (IV, Fixed, 95% CI)	10.75 [9.95, 11.56]
2 Time to mobilisation (hours)	1	571	Mean Difference (IV, Fixed, 95% CI)	-0.39 [-0.50, -0.29]
3 Groin haematoma	1	571	Odds Ratio (M-H, Fixed, 95% CI)	0.97 [0.28, 3.40]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 Retroperitoneal haemorrhage	1	571	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Technical failure of VCD	1	571	Odds Ratio (M-H, Fixed, 95% CI)	0.54 [0.30, 0.99]

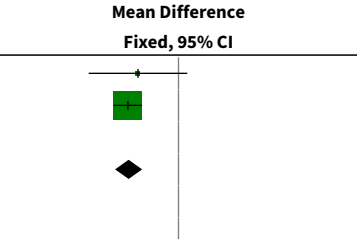
Analysis 10.1. Comparison 10 Collagen-based VCD versus collagen-based VCD: AngioSeal versus Duett, Outcome 1 Time to haemostasis (minutes).

Study or subgroup	AngioSeal N	AngioSeal Mean(SD)	Duett N	Duett Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Michalis 2002	47	19.8 (7.7)	47	7.8 (3.6)		11.04%	12[9.57,14.43]
Michalis 2002	243	18.1 (5.8)	234	7.5 (3.5)		88.96%	10.6[9.74,11.46]
Total ***	**290**		**281**			**100%**	**10.75[9.95,11.56]**
Heterogeneity: Tau²=0; Chi²=1.13, df=1(P=0.29); I²=11.84%							
Test for overall effect: Z=26.1(P<0.0001)							



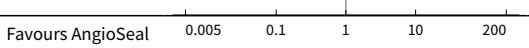
Analysis 10.2. Comparison 10 Collagen-based VCD versus collagen-based VCD: AngioSeal versus Duett, Outcome 2 Time to mobilisation (hours).

Study or subgroup	AngioSeal N	AngioSeal Mean(SD)	Duett N	Duett Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Michalis 2002	47	2.9 (1)	47	3.2 (0.9)		7.55%	-0.32[-0.71,0.07]
Michalis 2002	243	1.9 (0.5)	234	2.3 (0.7)		92.45%	-0.4[-0.51,-0.29]
Total ***	**290**		**281**			**100%**	**-0.39[-0.5,-0.29]**
Heterogeneity: Tau²=0; Chi²=0.15, df=1(P=0.7); I²=0%							
Test for overall effect: Z=7.22(P<0.0001)							



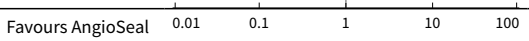
Analysis 10.3. Comparison 10 Collagen-based VCD versus collagen-based VCD: AngioSeal versus Duett, Outcome 3 Groin haematoma.

Study or subgroup	AngioSeal n/N	Duett n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Michalis 2002	2/47	1/47		19.22%	2.04[0.18,23.35]
Michalis 2002	3/243	4/234		80.78%	0.72[0.16,3.25]
Total (95% CI)	**290**	**281**		**100%**	**0.97[0.28,3.4]**
Total events: 5 (AngioSeal), 5 (Duett)					
Heterogeneity: Tau²=0; Chi²=0.51, df=1(P=0.47); I²=0%					
Test for overall effect: Z=0.04(P=0.97)					



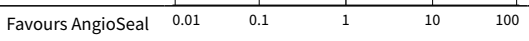
Analysis 10.4. Comparison 10 Collagen-based VCD versus collagen-based VCD: AngioSeal versus Duett, Outcome 4 Retroperitoneal haemorrhage.

Study or subgroup	AngioSeal n/N	Duett n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Michalis 2002	0/243	0/234			Not estimable
Michalis 2002	0/47	0/47			Not estimable
Total (95% CI)	**290**	**281**			**Not estimable**
Total events: 0 (AngioSeal), 0 (Duett)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



Analysis 10.5. Comparison 10 Collagen-based VCD versus collagen-based VCD: AngioSeal versus Duett, Outcome 5 Technical failure of VCD.

Study or subgroup	AngioSeal n/N	Duett n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Michalis 2002	17/243	27/234		84.24%	0.58[0.31,1.09]
Michalis 2002	2/47	5/47		15.76%	0.37[0.07,2.03]
Total (95% CI)	**290**	**281**		**100%**	**0.54[0.3,0.99]**
Total events: 19 (AngioSeal), 32 (Duett)					
Heterogeneity: Tau^2=0; Chi^2=0.22, df=1(P=0.64); I^2=0%					
Test for overall effect: Z=2.01(P=0.04)					

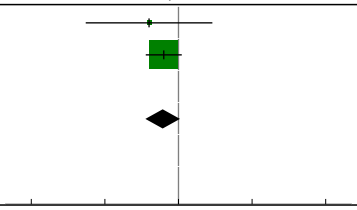


Comparison 11. Collagen-based VCD versus collagen-based VCD: VasoSeal versus Duett

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Time to haemostasis (minutes)	1	561	Mean Difference (IV, Fixed, 95% CI)	-0.54 [-1.13, 0.05]
2 Time to mobilisation (hours)	1	561	Mean Difference (IV, Fixed, 95% CI)	0.09 [-0.03, 0.21]
3 Groin haematoma	1	561	Odds Ratio (M-H, Fixed, 95% CI)	2.00 [0.67, 5.95]
4 Retroperitoneal haemorrhage	1	561	Odds Ratio (M-H, Fixed, 95% CI)	2.77 [0.11, 69.59]
5 Technical failure of VCD	1	561	Odds Ratio (M-H, Fixed, 95% CI)	0.80 [0.46, 1.38]

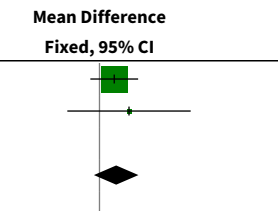
Analysis 11.1. Comparison 11 Collagen-based VCD versus collagen-based VCD: VasoSeal versus Duett, Outcome 1 Time to haemostasis (minutes).

Study or subgroup	VasoSeal N	VasoSeal Mean(SD)	Duett N	Duett Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Michalis 2002	52	7.8 (3.6)	47	8.8 (6.7)		7.47%	-1[-3.15,1.15]
Michalis 2002	228	7 (3.2)	234	7.5 (3.5)		92.53%	-0.5[-1.11,0.11]
Total ***	**280**		**281**			**100%**	**-0.54[-1.13,0.05]**
Heterogeneity: Tau^2=0; Chi^2=0.19, df=1(P=0.66); I^2=0%							
Test for overall effect: Z=1.79(P=0.07)							



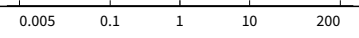
Analysis 11.2. Comparison 11 Collagen-based VCD versus collagen-based VCD: VasoSeal versus Duett, Outcome 2 Time to mobilisation (hours).

Study or subgroup	VasoSeal N	VasoSeal Mean(SD)	Duett N	Duett Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Michalis 2002	228	2.4 (0.7)	234	2.3 (0.7)		86.95%	0.08[-0.05,0.21]
Michalis 2002	52	3.4 (0.8)	47	3.2 (0.9)		13.05%	0.16[-0.17,0.49]
Total ***	**280**		**281**			**100%**	**0.09[-0.03,0.21]**
Heterogeneity: Tau^2=0; Chi^2=0.19, df=1(P=0.66); I^2=0%							
Test for overall effect: Z=1.47(P=0.14)							



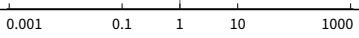
Analysis 11.3. Comparison 11 Collagen-based VCD versus collagen-based VCD: VasoSeal versus Duett, Outcome 3 Groin haematoma.

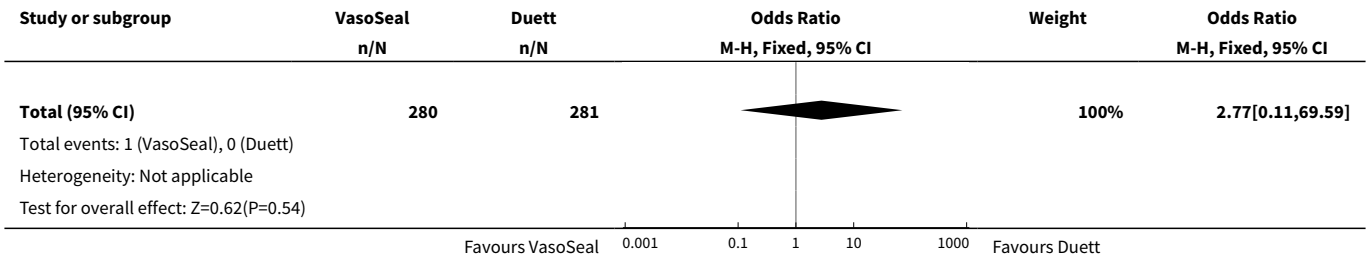
Study or subgroup	VasoSeal n/N	Duett n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Michalis 2002	5/228	4/234		80.26%	1.29[0.34,4.86]
Michalis 2002	5/52	1/47		19.74%	4.89[0.55,43.52]
Total (95% CI)	**280**	**281**		**100%**	**2[0.67,5.95]**
Total events: 10 (VasoSeal), 5 (Duett)					
Heterogeneity: Tau^2=0; Chi^2=1.06, df=1(P=0.3); I^2=6.06%					
Test for overall effect: Z=1.25(P=0.21)					



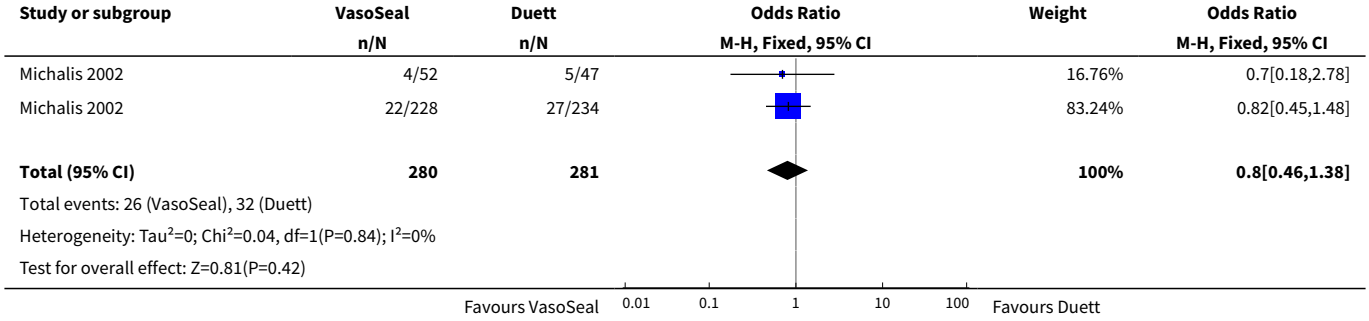
Analysis 11.4. Comparison 11 Collagen-based VCD versus collagen-based VCD: VasoSeal versus Duett, Outcome 4 Retroperitoneal haemorrhage.

Study or subgroup	VasoSeal n/N	Duett n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Michalis 2002	1/52	0/47		100%	2.77[0.11,69.59]
Michalis 2002	0/228	0/234			Not estimable





Analysis 11.5. Comparison 11 Collagen-based VCD versus collagen-based VCD: VasoSeal versus Duett, Outcome 5 Technical failure of VCD.



Comparison 12. Collagen-based VCD versus collagen-based VCD: FemoSeal versus ExoSeal

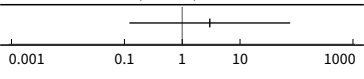
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Major adverse event (any time)	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Vascular injury requiring vascular repair by surgical or non-surgical techniques	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Infection	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
3 Groin haematoma	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
4 Pseudoaneurysm	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
5 Arteriovenous fistula	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
6 Limb ischaemia	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
7 Technical failure of VCD	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 12.1. Comparison 12 Collagen-based VCD versus collagen-based VCD: FemoSeal versus ExoSeal, Outcome 1 Major adverse event (any time).

Study or subgroup	FemoSeal n/N	ExoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
12.1.1 Vascular injury requiring vascular repair by surgical or non-surgical techniques				
Schulz-Schüpke 2014	0/1506	0/1509		Not estimable

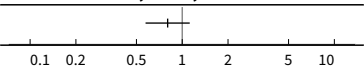
Analysis 12.2. Comparison 12 Collagen-based VCD versus collagen-based VCD: FemoSeal versus ExoSeal, Outcome 2 Infection.

Study or subgroup	FemoSeal n/N	ExoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Schulz-Schüpke 2014	1/1509	0/1506		3[0.12,73.6]



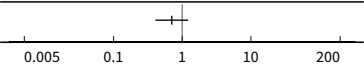
Analysis 12.3. Comparison 12 Collagen-based VCD versus collagen-based VCD: FemoSeal versus ExoSeal, Outcome 3 Groin haematoma.

Study or subgroup	FemoSeal n/N	ExoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Schulz-Schüpke 2014	65/1509	80/1506		0.8[0.57,1.12]



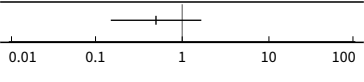
Analysis 12.4. Comparison 12 Collagen-based VCD versus collagen-based VCD: FemoSeal versus ExoSeal, Outcome 4 Pseudoaneurysm.

Study or subgroup	FemoSeal n/N	ExoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Schulz-Schüpke 2014	22/1509	31/1506		0.7[0.41,1.22]



Analysis 12.5. Comparison 12 Collagen-based VCD versus collagen-based VCD: FemoSeal versus ExoSeal, Outcome 5 Arteriovenous fistula.

Study or subgroup	FemoSeal n/N	ExoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Schulz-Schüpke 2014	4/1509	8/1506		0.5[0.15,1.66]



Analysis 12.6. Comparison 12 Collagen-based VCD versus collagen-based VCD: FemoSeal versus ExoSeal, Outcome 6 Limb ischaemia.

Study or subgroup	FemoSeal n/N	ExoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Schulz-Schüpke 2014	0/1509	0/1506		Not estimable

Favours FemoSeal 0.01 0.1 1 10 100 Favours ExoSeal

Analysis 12.7. Comparison 12 Collagen-based VCD versus collagen-based VCD: FemoSeal versus ExoSeal, Outcome 7 Technical failure of VCD.

Study or subgroup	FemoSeal n/N	ExoSeal n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Schulz-Schüpke 2014	80/1509	184/1506		0.4[0.31,0.53]

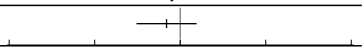
Favours FemoSeal 0.1 0.2 0.5 1 2 5 10 Favours ExoSeal

Comparison 13. PerClose ProGlide versus ProStar XL after percutaneous EVAR

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Time to haemostasis (minutes)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Time to mobilisation (hours)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Major adverse event (any time)	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
3.1 Mortality	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Vascular injury requiring vascular repair by surgical or non-surgical techniques	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infection	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
5 Groin haematoma	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
6 Arterio-venous fistula	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
7 Deep vein thrombosis	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
8 Limb ischaemia	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
9 Technical failure of VCD	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
10 Length of hospital stay (hours)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 13.1. Comparison 13 PerClose ProGlide versus ProStar XL after percutaneous EVAR, Outcome 1 Time to haemostasis (minutes).

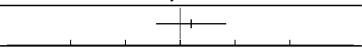
Study or subgroup	ProGlide		ProStar		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Nelson 2014	50	9.8 (17)	51	13 (19)		-3.2[-10.23,3.83]



Favours ProGlide — Fabours ProStar

Analysis 13.2. Comparison 13 PerClose ProGlide versus ProStar XL after percutaneous EVAR, Outcome 2 Time to mobilisation (hours).

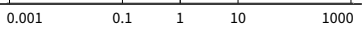
Study or subgroup	ProGlide		ProStar		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Nelson 2014	50	17 (7.2)	51	16 (9.1)		1[-2.2,4.2]



Favours ProGlide — Fabours ProStar

Analysis 13.3. Comparison 13 PerClose ProGlide versus ProStar XL after percutaneous EVAR, Outcome 3 Major adverse event (any time).

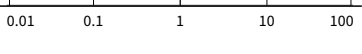
Study or subgroup	ProGlide	ProStar	Odds Ratio	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
13.3.1 Mortality				
Nelson 2014	0/50	1/51		0.33[0.01,8.38]
13.3.2 Vascular injury requiring vascular repair by surgical or non-surgical techniques				
Nelson 2014	1/50	3/51		0.33[0.03,3.25]



Favours ProGlide — Fabours ProStar

Analysis 13.4. Comparison 13 PerClose ProGlide versus ProStar XL after percutaneous EVAR, Outcome 4 Infection.

Study or subgroup	ProGlide	ProStar	Odds Ratio	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Nelson 2014	0/50	0/51		Not estimable



Favours ProGlide — Fabours ProStar

Analysis 13.5. Comparison 13 PerClose ProGlide versus ProStar XL after percutaneous EVAR, Outcome 5 Groin haematoma.

Study or subgroup	ProGlide	ProStar	Odds Ratio	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Nelson 2014	0/50	0/51		Not estimable

Favours ProGlide — Fabours ProStar

Analysis 13.6. Comparison 13 PerClose ProGlide versus ProStar XL after percutaneous EVAR, Outcome 6 Arterio-venous fistula.

Study or subgroup	ProGlide n/N	ProStar n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Nelson 2014	0/50	0/51		Not estimable

Favours ProGlide 0.01 0.1 1 10 100 Fabours ProStar

Analysis 13.7. Comparison 13 PerClose ProGlide versus ProStar XL after percutaneous EVAR, Outcome 7 Deep vein thrombosis.

Study or subgroup	ProGlide n/N	ProStar n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Nelson 2014	2/50	1/51		2.08[0.18,23.73]

Favours ProGlide 0.001 0.1 1 10 1000 Fabours ProStar

Analysis 13.8. Comparison 13 PerClose ProGlide versus ProStar XL after percutaneous EVAR, Outcome 8 Limb ischaemia.

Study or subgroup	ProGlide n/N	ProStar n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Nelson 2014	2/50	1/51		2.08[0.18,23.73]

Favours ProGlide 0.001 0.1 1 10 1000 Fabours ProStar

Analysis 13.9. Comparison 13 PerClose ProGlide versus ProStar XL after percutaneous EVAR, Outcome 9 Technical failure of VCD.

Study or subgroup	ProGlide n/N	ProStar n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Nelson 2014	0/50	0/51		Not estimable

Favours ProGlide 0.01 0.1 1 10 100 Fabours ProStar

Analysis 13.10. Comparison 13 PerClose ProGlide versus ProStar XL after percutaneous EVAR, Outcome 10 Length of hospital stay (hours).

Study or subgroup	ProGlide N	ProGlide Mean(SD)	ProStar N	ProStar Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Nelson 2014	50	1.3 (0.7)	51	1.4 (0.9)		-0.1[-0.41,0.21]

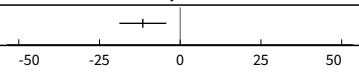
Favours ProGlide -100 -50 0 50 100 Fabours ProStar

Comparison 14. PerClose ProGlide ProStar XL versus suture-based closure after EVAR with open exposure of CFA

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Time to haemostasis (minutes)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Time to mobilisation (hours)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Major adverse event (any time)	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
3.1 Mortality	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Vascular injury requiring vascular repair by surgical or non-surgical techniques	1		Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infection	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
5 Groin haematoma	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
6 Arterio-venous fistula	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
7 Deep vein thrombosis	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
8 Limb ischaemia	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
9 Length of hospital stay (hours)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

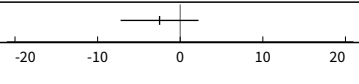
Analysis 14.1. Comparison 14 PerClose ProGlide ProStar XL versus suture-based closure after EVAR with open exposure of CFA, Outcome 1 Time to haemostasis (minutes).

Study or subgroup	VCD		Suture-based closure		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Nelson 2014	101	11.4 (17.9)	50	23 (23)		-11.58[-18.85,-4.31]



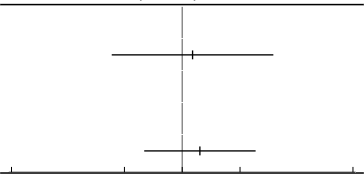
Analysis 14.2. Comparison 14 PerClose ProGlide ProStar XL versus suture-based closure after EVAR with open exposure of CFA, Outcome 2 Time to mobilisation (hours).

Study or subgroup	VCD		Suture-based closure		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Nelson 2014	101	16.5 (8.2)	50	19 (16)		-2.5[-7.21,2.21]



Analysis 14.3. Comparison 14 PerClose ProGlide ProStar XL versus suture-based closure after EVAR with open exposure of CFA, Outcome 3 Major adverse event (any time).

Study or subgroup	VCD n/N	Suture-based closure n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
14.3.1 Mortality				
Nelson 2014	1/101	0/50		1.51[0.06,37.67]
14.3.2 Vascular injury requiring vascular repair by surgical or non-surgical techniques				
Nelson 2014	4/101	1/50		2.02[0.22,18.57]

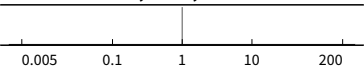


Analysis 14.4. Comparison 14 PerClose ProGlide ProStar XL versus suture-based closure after EVAR with open exposure of CFA, Outcome 4 Infection.

Study or subgroup	VCD n/N	Suture-based closure n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Nelson 2014	0/101	0/50		Not estimable

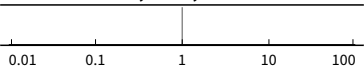
Analysis 14.5. Comparison 14 PerClose ProGlide ProStar XL versus suture-based closure after EVAR with open exposure of CFA, Outcome 5 Groin haematoma.

Study or subgroup	VCD n/N	Suture-based closure n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Nelson 2014	0/101	0/50		Not estimable



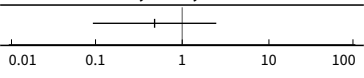
Analysis 14.6. Comparison 14 PerClose ProGlide ProStar XL versus suture-based closure after EVAR with open exposure of CFA, Outcome 6 Arterio-venous fistula.

Study or subgroup	VCD n/N	Suture-based closure n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Nelson 2014	0/101	0/50		Not estimable



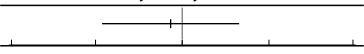
Analysis 14.7. Comparison 14 PerClose ProGlide ProStar XL versus suture-based closure after EVAR with open exposure of CFA, Outcome 7 Deep vein thrombosis.

Study or subgroup	VCD n/N	Suture-based closure n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Nelson 2014	3/101	3/50		0.48[0.09,2.47]



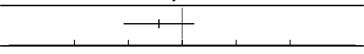
Analysis 14.8. Comparison 14 PerClose ProGlide ProStar XL versus suture-based closure after EVAR with open exposure of CFA, Outcome 8 Limb ischaemia.

Study or subgroup	VCD n/N	Suture-based closure n/N	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Nelson 2014	3/101	2/50		0.73[0.12,4.54]



Analysis 14.9. Comparison 14 PerClose ProGlide ProStar XL versus suture-based closure after EVAR with open exposure of CFA, Outcome 9 Length of hospital stay (hours).

Study or subgroup	VCD N	VCD Mean(SD)	Suture-based closure N	Suture-based closure Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Nelson 2014	101	32.4 (19.2)	50	43.2 (57.6)		-10.8[-27.2,5.6]



ADDITIONAL TABLES

Table 1. Types of vascular closure devices

Types of vascular closure devices (VCD) classified according to their mechanism to achieve haemostasis	Name	Recommended sheath size (Fr)	Extravascular haemostatic agent	Intravascular component
Balloon-based device	Epiclose-T	6	Temporary extravascular haemostatic balloon, which is withdrawn at the end of the procedure	Temporary anchor balloon, which is withdrawn at the end of the procedure
Disc-based device	Cardiva Catalyst II	4 to 10		Temporary nitinol-based wire with a nitinol braided mesh disc, which is removed at the end of the procedure
Plug-based device	AngioSeal VIP, AngioSeal STS-Plus, AngioSeal Evolution	6, 8	Bovine collagen plug and an absorbable traction suture	Absorbable intra-arterial anchor (co-polymers of polylactic and polyglycolic acids, absorbed within 30 days)
	VasoSeal VHD, ED, Elite	5 to 8	Purified bovine collagen-based plug	-
	VasoSeal Low Profile	4, 5	Purified bovine collagen-based plug	-
	Duett Pro, Duett	5 to 9	Thrombin with platelet activation of collagen	Temporary anchor balloon, which is withdrawn at the end of the procedure

Table 1. Types of vascular closure devices *(Continued)*

	6/7F Mynx, Mynx M5	5 to 7	Water-soluble, freeze-dried polyethylene glycol (PEG) material	Temporary anchor balloon, which is withdrawn at the end of the procedure
	ExoSeal		PGA (polyglycolic acid), a trusted non-collagen plug material	-
Metal clip-based device	StarClose	5, 6	Nitinol clip	-
	StarClose SE	5, 6	Nitinol clip	-
	Angiolink EVS	6 to 8	Titanium staple	-
Suture-based device	PerClose AT	5 to 8	Braided polyester suture	-
	PerClose ProGlide	5 to 8	Monofilament polypropylene suture	-
	ProStar XL	8.5 to 10	Braided polyester suture	-
	X-Site	5, 6	Braided polyester suture	-
	SuperStitch	6 to 12	Polypropylene suture	-

- Balloon-based device (Epiclose-T) (Kurşaklioğlu 2008): A temporary balloon-positioning catheter is inflated inside the arterial puncture site, while a larger haemostasis balloon is inflated directly on the outer surface of the arteriotomy. The balloon applies direct pressure on the arteriotomy site, thus allowing natural coagulation to occur. After a few minutes of device deployment, the anchor balloon is pulled back into the distal end of the shaft, while the haemostasis balloon remains pressing against the arteriotomy site. At the end of the haemostasis waiting period, the haemostasis balloon is deflated and the device is removed, leaving no foreign body in the intraluminal nor the extraluminal space.
- Disc-based closure device (Cardiva Catalyst II) (Schwartz 2010): conformable nitinol-based wire with a temporary nitinol braided mesh disc on a tether, which is deployed inside the artery to achieve haemostasis. Temporary placement of a low-profile, conformable disc against the intima creates site-specific compression of both the arteriotomy and the tract. The haemostatic mechanism is based on the natural elastic recoil of the arteriotomy site back to its pre-dilated state, around the wire. In addition, a biocompatible coating on the Catalyst II Wire assists the body's natural haemostatic process and promotes ease of removal. After a few minutes of device deployment, the nitinol mesh disc and wire are removed, thus leaving no foreign body in the intraluminal nor extraluminal space.
- Plug-based device (predominantly of collagen in composition) consisting of an extraluminal sealant with or without an intraluminal anchor (VasoSeal VHD, ED, Elite, VasoSeal Low Profile) (Bechara 2010). The intra-arterial anchor can be a temporary balloon-positioning catheter that is removed at the end of the procedure (Duett Pro, Duett, 6/7F Mynx, Mynx M5) (Bechara 2010; Scheinert 2007) or an absorbable intra-arterial anchor that is absorbed by the body in 30 days (AngioSeal VIP, AngioSeal STS Plus, AngioSeal Evolution). Collagen-based devices without an intra-arterial anchor can undergo repeated puncture for angiography. A commonly used extra-arterial sealant is a bovine biodegradable product that triggers a haemostatic cascade and physical expansion to tamponade the puncture site and tissue tract.
- Metal clip-based device (StarClose, StarClose SE, Angiolink EVS) (Bechara 2010): devices that utilise metal clip-based technology and deploy metal staple or clip that penetrates the vessel wall to achieve haemostasis. Upon deployment, the metal clip or staple remains in situ over the vessel wall and forms a geometric configuration that approximates adventitial vessel layers to close the arterial hole. The metallic clips or staples do not undergo a bioresorption reaction, which therefore does not trigger significant soft tissue inflammatory response. Repeat puncture or surgical exploration of the artery can be done safely.
- Suture-based device (PerClose AT, PerClose ProGlide, ProStar XL, X-Site, SuperStitch) (Bechara 2010): Arterial haemostasis is achieved by deploying sutures to form a knot to close the arteriotomy. The knot is tied by a built-in mechanism within the closure device or is tied manually. No proteinaceous biomaterial is left behind in the puncture tract; therefore, no inflammatory soft tissue reaction is associated with this closure technology. Consequently, repeat arterial access or surgical exploration of the same artery can be performed safely.

APPENDICES

Appendix 1. CRS search strategy

Search run on Fri Apr 8 2015		
#1	MESH DESCRIPTOR Endovascular Procedures EXPLODE ALL TREES	5490
#2	MESH DESCRIPTOR Angiography EXPLODE ALL TREES	5510
#3	MESH DESCRIPTOR Catheterization EXPLODE ALL TREES	8520
#4	MESH DESCRIPTOR Femoral Artery	723
#5	MESH DESCRIPTOR Groin	88
#6	MESH DESCRIPTOR Punctures	288
#7	vascular	23798
#8	vessel	5372
#9	catheter* :TI,AB,KY	13346
#10	cannulat*:TI,AB,KY	1002
#11	endovascular:TI,AB,KY	920
#12	percutan*:TI,AB,KY	7724
#13	PTA or PTCA	1339
#14	angiograph*:TI,AB,KY	9659
#15	angioplasty:TI,AB,KY	5639
#16	arteriotom*:TI,AB,KY	52
#17	femoral:TI,AB,KY	5807
#18	groin:TI,AB,KY	487
#19	punctur*:TI,AB,KY	2580
#20	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19	57621
#21	MESH DESCRIPTOR Wound Closure Techniques EXPLODE ALL TREES	1506
#22	MESH DESCRIPTOR Surgical Instruments EXPLODE ALL TREES	537
#23	compres*:TI,AB,KY	4491
#24	clamp*:TI,AB,KY	3663

(Continued)

#25	press*:TI,AB,KY	79983
#26	plug*:TI,AB,KY	367
#27	closure:TI,AB,KY	4668
#28	closing:TI,AB,KY	511
#29	weight*:TI,AB,KY	49193
#30	clip*:TI,AB,KY	876
#31	seal*:TI,AB,KY	2741
#32	mynx:TI,AB,KY	1
#33	(starclose or star-close or prostar or tecstar or perclose or boomerang or angioseal or proglide or vasoseal or duett):TI,AB,KY	65
#34	MESH DESCRIPTOR Hemostasis	697
#35	hemostasis:TI,AB,KY	2687
#36	haemostasis:TI,AB,KY	615
#37	#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	137390
#38	#20 AND #37	16375
#39	(arterial or artery):TI,AB,KY	44222
#40	closure:TI,AB,KY	4668
#41	#39 AND #40	553
#42	#38 OR #41	16635
#43	* NOT SR-PVD:CC	910030
#44	#42 AND #43	15550

Appendix 2. Glossary

Ambulation: mobilisation
Arteriotomy: procedure in which a hole is made in an artery wall by a knife or a needleArteriovenous fistula: abnormal connection between an artery and a vein
EVAR: endovascular aneurysm repair
Haematoma: bruise
Haemostasis: process that causes bleeding to stop
Percutaneous: through the skin
Pseudoaneurysm: haematoma that occurs as a result of a leaking hole in an artery
6 to 8 Fr: French catheter scale used to measure the size of the sheath or catheter

CONTRIBUTIONS OF AUTHORS

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LR selected studies for inclusion in the review, extracted data, assessed risk of bias for included studies, inputted studies into Review Manager, performed analysis and wrote the review.
AA selected studies for inclusion, extracted data, assessed risk of bias, checked data entry and commented on the review.
FC provided clinical advice and wrote the review.
RJ provided advice on clinical aspects of the review and reviewed the manuscript.

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LR: none known.
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FC: travel/accommodation/meeting expenses: Gore Medical training (product training/aortic intervention, October 2014), Cook Medical training (Vista Education programme) (product training in embolisation, September 2014), Medtronic Aortic University (aortic stent grafting training, 2015), Vascutek (Terumo) (sponsorship for BSIR meeting, November 2014; sponsorship for LINC meeting, January 2015).
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INDEX TERMS

Medical Subject Headings (MeSH)

*Punctures; *Vascular Closure Devices [adverse effects]; Collagen; Endovascular Procedures; Femoral Artery [*surgery]; Hemostasis, Surgical [*instrumentation] [methods]; Length of Stay; Pressure; Randomized Controlled Trials as Topic; Surgical Instruments

MeSH check words

Humans