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Goel RR, Hardy SC, Brown T

Goel RR, Hardy SC, Brown T.
Surgery for deep venous insufficiency.
Cochrane Database of Systematic Reviews 2021, Issue 9. Art. No.: CD001097.
DOI: 10.1002/14651858.CD001097.pub4.

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[Intervention Review]

Surgery for deep venous insufficiency

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Editorial group: Cochrane Vascular Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 9, 2021.

Citation: Goel RR, Hardy SC, Brown T. Surgery for deep venous insufficiency. *Cochrane Database of Systematic Reviews* 2021, Issue 9. Art. No.: CD001097. DOI: 10.1002/14651858.CD001097.pub4.

ABSTRACT

Background

Chronic deep venous insufficiency is caused by incompetent vein valves, blockage of large-calibre leg veins, or both; and causes a range of symptoms including recurrent ulcers, pain and swelling. Most surgeons accept that well-fitted graduated compression stockings (GCS) and local care of wounds serve as adequate treatment for most people, but sometimes symptoms are not controlled and ulcers recur frequently, or they do not heal despite compliance with conservative measures. In these situations, in the presence of severe venous dysfunction, surgery has been advocated by some vascular surgeons. This is an update of the review first published in 2000.

Objectives

To assess the effects of surgical management of deep venous insufficiency on ulcer healing and recurrence, complications of surgery, clinical outcomes, quality of life (QoL) and pain.

Search methods

The Cochrane Vascular Information Specialist searched the Cochrane Vascular Specialised Register, CENTRAL, MEDLINE, Embase and CINAHL databases, and the WHO ICTRP and ClinicalTrials.gov trials registries to 23 June 2020.

Selection criteria

We considered randomised controlled trials (RCTs) of surgical treatment versus another surgical procedure, usual care or no treatment, for people with deep venous insufficiency.

Data collection and analysis

Two review authors independently assessed trials for inclusion, extracted data and assessed the risk of bias with the Cochrane risk of bias tool. We evaluated the certainty of the evidence using GRADE. We were unable to pool data due to differences in outcomes reported and how these were measured. Outcomes of interest were ulcer healing and recurrence, complications of surgery, clinical changes, QoL and pain.

Main results

We included four RCTs (273 participants) comparing valvuloplasty plus surgery of the superficial venous system with surgery of the superficial venous system for primary valvular incompetence. Follow-up was two to 10 years. All included studies investigated primary valve incompetence. No studies investigated other surgical procedures for the treatment of people with deep venous insufficiency or surgery for secondary valvular incompetence or venous obstruction. The certainty of the evidence was downgraded for risk of bias concerns and imprecision due to small numbers of included trials, participants and events.

None of the studies reported ulcer healing or ulcer recurrence. One study included 27 participants with active venous ulceration at the time of surgery; the other three studies did not include people with ulcers.

There were no major complications of surgery, no incidence of deep vein thrombosis and no deaths reported (very low-certainty evidence).

All four studies reported clinical changes but the data could not be pooled due to different outcome measures and reporting of the data. Two studies assessed clinical changes using subjective and objective measurements, as specified in the clinical, aetiological, anatomical and pathophysiological (CEAP) classification score (low-certainty evidence). One study reported mean CEAP severity scores and one study reported change in clinical class using CEAP. At baseline, the mean CEAP severity score was 18.1 (standard deviation (SD) 4.4) for limbs undergoing external valvuloplasty with surgery to the superficial venous system and 17.8 (SD 3.4) for limbs undergoing surgery to the superficial venous system only. At three years post-surgery, the mean CEAP severity score was 5.2 (SD 1.6) for limbs that had undergone external valvuloplasty with surgery to the superficial venous system and 9.2 (SD 2.6) for limbs that had undergone surgery to the superficial venous system only (low-certainty evidence).

In another study, participants with progressive clinical dynamics over the five years preceding surgery had higher rates of improvement in clinical condition in the treatment group (valvuloplasty plus ligation) compared with the control group (ligation only) (80% versus 51%) after seven years of follow-up. Participants with stable preoperative clinical dynamics demonstrated similar rates of improvement in both groups (95% with valvuloplasty plus ligation versus 90% with ligation only) (low-certainty evidence).

One study reported disease-specific QoL using cumulative scores from a 10-item visual analogue scale (VAS) and reported that in the limited anterior plication (LAP) plus superficial venous surgery group the score decreased from 49 to 11 at 10 years, compared to a decrease from 48 to 36 in participants treated with superficial venous surgery only (very low-certainty evidence).

Two studies reported pain. Within the QoL VAS scale, one item was 'pain/discomfort' and scores decreased from 4 to 1 at 10 years for participants in the LAP plus superficial venous surgery group and increased from 2 to 3 at 10 years in participants treated with superficial venous surgery only. A second study reported that 'leg heaviness and pain' was resolved completely in 36/40 limbs treated with femoral vein external valvuloplasty plus high ligation and stripping of the great saphenous vein (GSV) and percutaneous continuous circumsuture and 22/40 limbs treated with high ligation and stripping of GSV and percutaneous continuous circumsuture alone, at three years' follow-up (very low-certainty evidence).

Authors' conclusions

We only identified evidence from four RCTs for valvuloplasty plus surgery of the superficial venous system for primary valvular incompetence. We found no studies investigating other surgical procedures for the treatment of people with deep venous insufficiency, or that included participants with secondary valvular incompetence or venous obstruction. None of the studies reported ulcer healing or recurrence, and few studies reported complications of surgery, clinical outcomes, QoL and pain (very low- to low-certainty evidence). Conclusions on the effectiveness of valvuloplasty for deep venous insufficiency cannot be made.

PLAIN LANGUAGE SUMMARY

Surgery for deep venous insufficiency

Background

Deep venous insufficiency is a problem in the veins of the legs that can lead to leg ulcers (sores), pain and swelling. It may be caused by a problem with the valves of the vein, by a blockage of the veins or a combination of these events. For most people, wearing special compression stockings and treating the ulcers is enough. When this does not ease the problem, surgery is sometimes tried. It is unclear how much benefit there is from surgery.

Study characteristics and key results

We looked for studies treating deep venous insufficiency with surgery (searched 23 June 2020). We found four studies that randomised 273 participants to treatment or control interventions. All included studies reported on outcomes following surgical repair of venous valves (valvuloplasty). All included studies investigated primary valve incompetence (when valves do not close properly). We found no studies investigating other surgical procedures for treatment or the results of surgery for secondary valvular incompetence (for example, when valves are damaged as a result of deep vein thrombosis and do not close properly), or for venous obstruction. As different outcomes were reported, we could not combine the results of these studies. No studies reported ulcer healing and ulcer recurrence. One study did not investigate this, and the remaining three studies did not include people with ulcers or active ulceration. Three studies reported no major complications of surgery or no incidence of deep vein thrombosis (a blood clot that forms in a deep vein, usually in the leg or pelvis) during follow-up.

We assessed clinical changes using the 'clinical, aetiological, anatomical and pathophysiological' (CEAP) classification score. One study reported an improved CEAP score three years after surgery in both groups, and a greater improvement from before surgery in limbs that had undergone valvuloplasty plus ligation (where a vein is tied off) compared with ligation alone. In another study, participants with worsening deep vein incompetence over the five years before surgery had higher rates of improvement in clinical condition with valvuloplasty plus

ligation compared with ligation only after seven years, but in participants with stable deep vein incompetence, there was no additional benefit from the valvuloplasty.

One study reported improvement in patient-reported quality of life (including pain) in both groups and a greater improvement compared to before surgery in people who had undergone external valvuloplasty using a technique called limited anterior plication at 10 years' follow-up. A second study reported that leg heaviness and pain was resolved completely in 36/40 limbs treated with valvuloplasty plus ligation and 22/40 limbs treated with ligation alone at three years' follow-up.

Reliability of the evidence

The reliability of the evidence was very low or low because there were only four studies with small numbers of participants, and there was a high risk of bias (information regarding how it was decided what treatment a participant received and who knew this was missing in three of the four studies).

Conclusion

There is not enough evidence to determine the effectiveness of surgery on the treatment of people with deep venous insufficiency. The included studies did not include people with severe deep venous insufficiency (venous obstruction). Trials investigating the effects of other surgical procedures on the deep veins are needed.

SUMMARY OF FINDINGS

Summary of findings 1. Valvuloplasty plus surgery of the superficial venous system compared with surgery of the superficial venous system for primary valvular incompetence

Valvuloplasty + surgery of the superficial venous system compared with surgery of the superficial venous system for primary valvular incompetence

Patient or population: people with non-severe primary valvular incompetence

Settings: hospital

Intervention: valvuloplasty[a] + surgery of the superficial venous system

Comparison: surgery of the superficial venous system

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with surgery of the superficial venous system	Risk with valvuloplasty + surgery of the superficial venous system				
Ulcer healing and recurrence	See comment.		—	—	—	No study reported on this outcome.
Complications of surgery (2–10 years)	2 studies reported no major complications of surgery (Belcaro 1993a; Belcaro 1999). 2 studies reported no incidence of DVT during follow-up (Belcaro 1993a; Wang 2006). Wang 2006 reported that there were 0 deaths.		—	105 (3 RCTs)	⊕⊖⊖⊖ **Very low** [b]	It was not possible to pool the results because different outcome measures were used.
Clinical changes (CEAP classification scoring for clinical outcomes after surgery) (3 years)	1 study reported mean CEAP severity scores (Wang 2006). At baseline, mean CEAP severity score was 18.1 (SD 4.4) for limbs undergoing external valvuloplasty + surgery to the superficial venous system and 17.8 (SD 3.4) for limbs undergoing surgery to the superficial venous system only. At 3 years postsurgery mean CEAP severity score was 5.2 (SD 1.6) for limbs that had undergone external valvuloplasty + surgery to the superficial venous system and 9.2 (SD 2.6) for limbs that had undergone surgery to the superficial venous system only. 1 study reported on change in clinical class using CEAP. Makarova 2001 reported that participants with progressive[c] clinical dynamics over the 5 years preceding surgery had higher rates of improvement in clinical condition in the treatment group (valvuloplasty + ligation) compared with the control group (ligation only) (80% vs 51%) after 7 years		—	208 (2 RCTs)	⊕⊕⊖⊖ **Low** [d]	All 4 studies reported on clinical changes but the data could not be pooled due to different outcome measures and reporting. Refer to the Effects of interventions section for more details.

	of follow-up. Participants with stable preoperative clinical dynamics demonstrated similar rates of improvement in both groups (95% valvuloplasty + ligation vs 90% ligation only).				
Health-related quality of life (VAS, ranging from 0 (no problem) to 10 (most severe problem) for each of 10-items, cumulated score) (10 years)	In the LAP + ligation group the CQLS decreased from 49 to 11 at 10 years, compared to a decrease from 48 to 36 in participants treated with ligation only (Belcaro 1999).	—	35 (1 RCT)	⊕⊝⊝⊝ **Very low** [e]	1 study reported health-related quality of life using a VAS devised from interviewing people with 100 venous incompetence prior to the study.
Pain (VAS, ranging from 0 (no problem) to 10 (most severe problem) for 1 of 10-items, pain/discomfort score) (10 years)	Pain/discomfort scores decreased from 4 to 1 at 10 years for participants in the LAP + ligation superficial venous surgery group and increased from 2 to 3 at 10 years in participants treated with ligation only (Belcaro 1999). Wang 2006 reported that all participants had painful leg heaviness at baseline and reported that leg heaviness and pain was resolved completely in 36/40 limbs treated with femoral vein external valvuloplasty + high ligation and stripping of GSV and percutaneous continuous circumsuture and 22/40 limbs treated with high ligation and stripping of GSV and percutaneous continuous circumsuture alone, at 3 years of follow-up.	—	75 (2 RCTs)	⊕⊝⊝⊝ **Very low** [f]	It was not possible to pool the results because they used different outcome measures.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval**; CEAP:** clinical, aetiological, anatomical, and pathophysiological classification score; **CQLS:** cumulative quality of life score; **DVT:** deep venous thrombosis; **GSV:** great saphenous vein; **LAP:** limited anterior plication; **RCT:** randomised controlled trial; **SD:** standard deviation; **VAS:** visual analogue scale.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a] Belcaro 1993a; Belcaro 1999: femoral vein external valvuloplasty using LAP plus ligature of incompetent superficial veins versus ligature of incompetent superficial veins only. Makarova 2001: superficial femoral vein valve correction by internal valvuloplasty plus unilateral GSV stripping and stab avulsions of varicose tributaries versus unilateral GSV

stripping and stab avulsions of varicose tributaries. Phlebographically confirmed incompetent perforating veins subfascially ligated in subgroup of participants in both groups by open long medial vertical approach. Wang 2006: femoral vein external valvuloplasty plus high ligation and stripping of GSV and percutaneous continuous circumsuture versus high ligation and stripping of GSV and percutaneous continuous circumsuture.

[b]Downgraded two levels for risk of bias (two of three studies assessed as high risk of bias in four of five domains) and one level for imprecision due to low number of participants and events.

[c]Changes in the clinical class of the extremity were defined as being of a progressive type of clinical dynamics if the extremity demonstrated an increase of at least one clinical class by the end of the fifth year in comparison with the initial class of the limb. If there was no change in clinical class, the clinical dynamics was defined as the stable type.

[d]Downgraded one level for risk of bias (one of two studies assessed as high risk of bias in four domains) and one level for imprecision due to low number of participants from two RCTs.

[e]Downgraded two levels for risk of bias (one of one study assessed as high risk of bias in four domains) and one level for imprecision due to the low number of participants from one RCT.

[f]Downgraded two levels for risk of bias (one of two studies assessed as high risk of bias in four domains) and one level for imprecision due to low number of participants from two RCTs.

BACKGROUND

Description of the condition

Chronic deep venous insufficiency is a troublesome condition that is associated with a variable range of distressing symptoms such as recurrent ulcers, leg pain and leg swelling. The underlying defect could be valvular incompetence (when the valve does not close tightly and allows blood to leak back into the vein), obstruction of large-calibre veins or a combination of these two events. Valvular incompetence may be primary or secondary. Primary valve incompetence is not associated with post-thrombotic changes, and the defect is sometimes congenital, leading to early development of symptoms. Secondary valve incompetence and the obstructive form of deep venous insufficiency are post-thrombotic phenomena and account for 80% to 95% of cases (Bauer 1948; Browse 1998; Perrin 2004). The obstructive form is less common, affecting 3% to 9% of people (Halliday 1985; Raju 1988).

Description of the intervention

Chronic deep venous insufficiency represents a therapeutic challenge for vascular surgeons. Most surgeons accept that well-fitted graduated compression stockings (GCS) and local care of wounds provide adequate treatment for most people (Lancet 1982). Sometimes symptoms are not controlled and ulcers recur frequently, or they do not heal despite compliance with conservative measures. In these situations, in the presence of severe venous dysfunction, surgery has been advocated by some vascular surgeons (Eriksson 1988; Kistner 1980).

How the intervention might work

Most surgeons accept that primary surgical treatment for concomitant superficial system insufficiency and perforators in the absence of major vein obstruction is essential for good results (Wilson 1991). For people with primary valve insufficiency, a treatment option is valve reconstruction (Chatterjee 2012; Yavuz 2020). Reconstructive surgery of the deep venous system is usually directed towards correcting the underlying defect by bypassing the obstructed segment or by restoring the valve mechanism (O'Donnell 1987). Examples include valvuloplasty, venous segmental transposition, and venous segmental transplantation. The use of prosthetic valve material still has no place in venous surgery in people with venous incompetence; a successful prosthetic venous valve is still to be developed (Bryce 2018; Tien 2017). Postoperative complications include deep venous thrombosis (DVT), pulmonary embolism (PE), venous occlusion and venous incompetence.

Why it is important to do this review

The value of surgery in deep venous insufficiency has still not been fully determined (Gloor 1997). The most recent National Institute for Health and Care excellence (NICE) guidance for lower limb deep valve reconstruction for chronic deep venous incompetence was published in 2007, reassessed in 2010 and it was concluded that NICE will not be updating the guidance at this stage due to a lack of new important evidence (NICE 2007). Results of surgery have not consistently shown long-term improvement in symptoms or in the abnormal venous haemodynamics associated with this condition. This is an update of a review first published in 2000.

OBJECTIVES

To assess the effects of surgical management of deep venous insufficiency on ulcer healing and recurrence, complications of surgery, clinical outcomes, quality of life (QoL) and pain.

METHODS

Criteria for considering studies for this review

Types of studies

We considered all randomised controlled trials (RCTs) of surgical management of deep venous insufficiency in which a surgical procedure was compared with:

- another surgical procedure;
- conventional conservative management; or
- no treatment.

Types of participants

We included participants undergoing treatment for deep venous insufficiency.

Types of interventions

We included RCTs involving any open surgical procedure performed to treat deep venous insufficiency. These included valvuloplasty, venous segmental transposition, venous segmental transplantation or venous bypass surgery and prosthetic valve implantation (including percutaneous insertion). We excluded endovenous procedures. We excluded studies if there was no clear distinction between the types of procedures performed or where perforator ligation was performed without deep vein surgery.

Types of outcome measures

Primary outcomes

- Ulcer healing and recurrence
- Complications of surgery (such as DVT, PE or venous occlusion)

Secondary outcomes

- Clinical changes (CEAP classification scoring)*
- Health-related quality of life (measured using validated questionnaires such as Vascular Quality of Life (VascuQoL))
- Pain (measured using validated scores such as Brief Pain Inventory (BPI))

*as specified by clinical, aetiological, anatomical, and pathophysiological (CEAP) classification scoring for chronic venous disorders and by CEAP classification scoring for clinical outcomes after surgery (Beebe 1996; Porter 1995). This requires vascular laboratory measurements of lower limb haemodynamics before and after surgery. Tests included an overall evaluation of venous function with venous refilling time (VRT) or ambulatory venous pressure (AVP). People undergoing surgery for valvular incompetence should have undergone duplex assessment of venous reflux and possibly radiological investigation of competence and patency. People undergoing surgery for deep venous obstruction should have undergone measurements of maximum venous outflow for assessment of outcome and duplex scanning, or phlebography for assessment of patency and degree of reflux.

Search methods for identification of studies

Electronic searches

For this update, the Cochrane Vascular Information Specialist conducted systematic searches of the following databases for RCTs and controlled clinical trials without language, publication year or publication status restrictions.

- Cochrane Vascular Specialised Register via the Cochrane Register of Studies (CRS-Web searched 24 June 2020);
- Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Register of Studies Online (CRSO 2020, Issue 5);
- MEDLINE (Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE (searched from 1946 to 23 June 2020);
- Embase Ovid (searched 23 June 2020);
- CINAHL EBSCO (searched 24 June 2020).

The Information Specialist modelled search strategies for other databases on the search strategy designed for CENTRAL. Where appropriate, they were combined with adaptations of the highly sensitive search strategy designed by Cochrane for identifying RCTs and controlled clinical trials (as described in the *Cochrane Handbook for Systematic Reviews of Interventions* Chapter 6, Lefebvre 2011). Search strategies for major databases are provided in Appendix 1.

The Information Specialist also searched the following trials registries on 24 June 2020.

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

Searching other resources

We searched the reference lists of relevant articles retrieved by the electronic searches, for additional citations.

Data collection and analysis

Selection of studies

For this update, we used Covidence software for the screening and study selection process (Covidence). Two review authors (SCH and RRG) independently screened the titles and abstracts to identify studies and select trials for possible inclusion in the review. Two review authors (SCH and RRG) obtained the full-text articles where the above inclusion criteria were potentially met and reviewed them. They resolved any disagreements by discussion.

Data extraction and management

For this update, we found no new studies for inclusion. One review author (TB) rechecked and extracted data from previously included studies. This was cross-checked by RRG and SCH. Extracted data included information on participants (age, sex, severity of disease as measured by the CEAP classification scoring system for chronic venous disorders, history of DVT); interventions (type of procedure performed, use of anticoagulants, use of external pneumatic compression stocking, use of GCS after surgery, smoking habits after surgery, use of intermittent leg elevation during the day); and outcomes (as specified in the Criteria for considering studies for this review section).

Assessment of risk of bias in included studies

This updated review included no new studies. For the previous version, two review authors (SCH and RRG) independently assessed the methodological quality of trials using Cochrane's risk of bias tool (Higgins 2011). This tool assesses the risk of bias in each study using seven domains (randomisation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete data, selection bias and any other bias). We resolved disagreements by discussion or by consultation with a third review author (TB) when necessary.

Measures of treatment effect

We analysed continuous outcomes using the same outcome measurement scale using mean differences (MDs) and 95% confidence intervals (CIs). When studies reported the same outcome (i.e. measures of clinical changes) but used different measurement scales, we reported data within the text. We summarised an overall clinical outcome for each study based on the degree of improvement that was reported.

Unit of analysis issues

For outcomes such as lower limb haemodynamics for which bilateral procedures are possible and are reported, each treated limb can be considered as an individual unit of analysis. Therefore, the unit of analysis in the included studies varied, and could be the limb or the participant.

Dealing with missing data

We contacted the authors of studies with missing data, but we received no replies. We intended to use intention-to-treat analysis to pool data when possible.

Assessment of heterogeneity

We assessed heterogeneity clinically on the basis of study descriptions. We also planned to assess heterogeneity between trials using the Chi^2 test and the I^2 statistic if meta-analysis was deemed appropriate. We are aware there can be uncertainty around the value of the I^2 statistic and using thresholds for interpretation, and we intended to also consider the direction and magnitude of effects and degree of overlap between CIs.

Assessment of reporting biases

We assessed reporting bias through review of identified studies. Funnel plots were considered to be inappropriate, as only four studies are included in this review.

Data synthesis

To date, insufficient trials have been conducted to allow pooled statistical analysis. The included trials did not report all outcomes of interest or reported different measurements of clinical change. If more trials are included in future updates, we will undertake meta-analysis when appropriate. For outcomes where we were unable to pool data, we described the results narratively.

Subgroup analysis and investigation of heterogeneity

To date, insufficient data are available to allow subgroup analysis. If appropriate in future updates, subgroup analyses will be carried out according to the surgical intervention.

Sensitivity analysis

Sensitivity analysis will be carried out when appropriate in future updates.

Summary of findings and assessment of the certainty of the evidence

For this update, we prepared a summary of findings table to present the findings from our review for the comparison 'Valvuloplasty plus surgery of the superficial venous system compared with surgery of the superficial venous system for primary valvular incompetence' (Summary of findings 1). We used the GRADE method to evaluate the evidence based on the risk of bias of the individual studies, inconsistency, imprecision, indirectness and publication bias (Schünemann 2021). We evaluated the following outcomes because they were the most clinically relevant.

- Ulcer healing and recurrence.
- Complications of surgery.
- Clinical changes.
- Health-related quality of life.
- Pain.

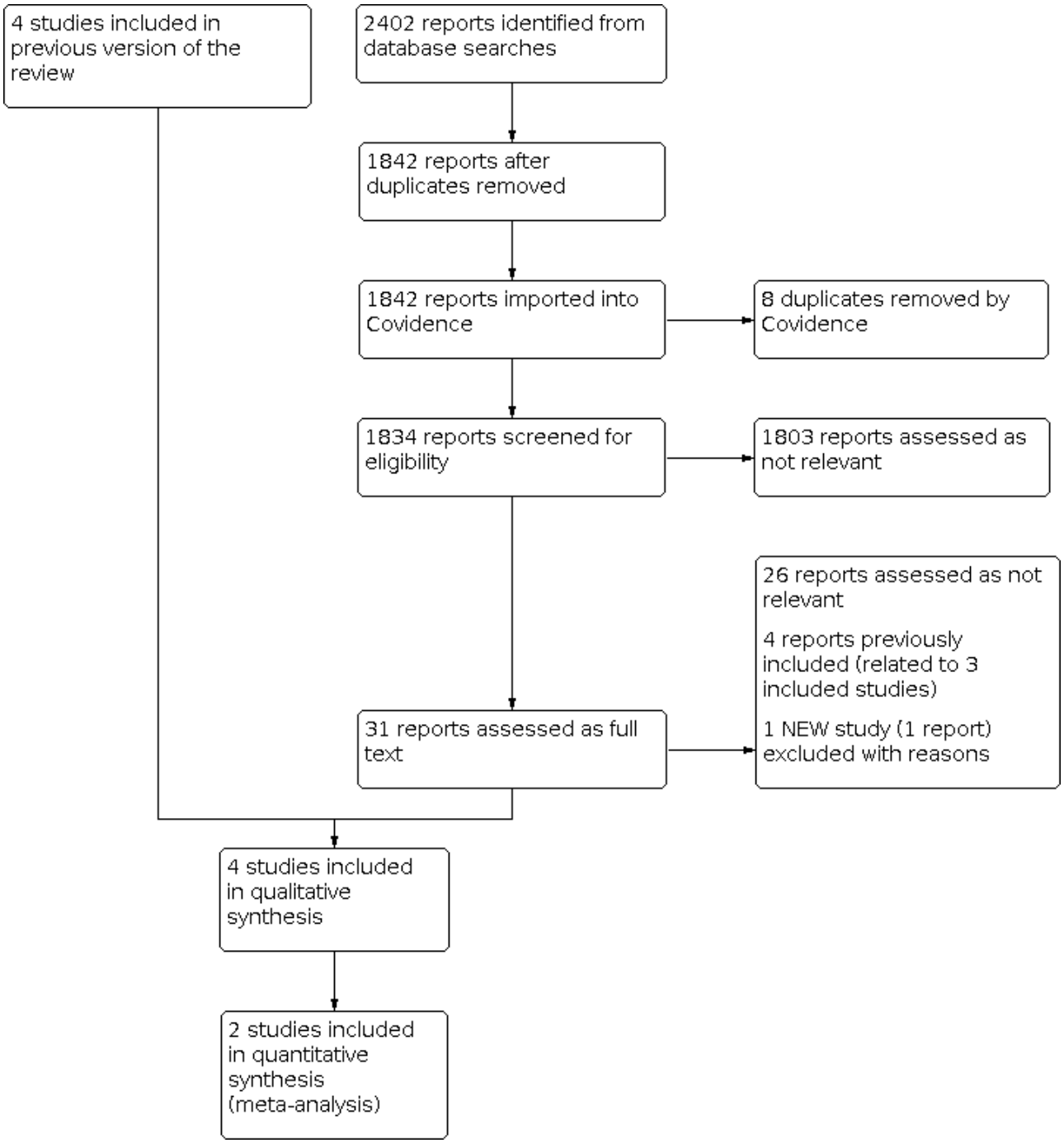
RESULTS

Description of studies

Results of the search

We identified no new studies for inclusion in this update. One study was excluded in this update because it was not an RCT (Maksimović 2008). See Figure 1.

Figure 1. Study flow diagram.



Included studies

The review included four studies with 273 participants (Belcaro 1993a; Belcaro 1999; Makarova 2001; Wang 2006). All four studies were of surgical interventional procedures to treat reflux. We found no trials that investigated the results of surgery for secondary valvular incompetence or the obstructive form of deep venous insufficiency (venous obstruction). Moreover, we identified no trials that compared the results of surgery versus those of conventional conservative measures. Details are given in the Characteristics of included studies table.

Belcaro 1993a and Belcaro 1999: both of these studies compared external valvuloplasty using limited anterior plication (LAP) in combination with ligation of incompetent superficial veins (LAP plus ligation group) versus ligation of incompetent superficial veins (ligation-only group). The number of participants was relatively small. All participants had deep venous insufficiency due to primary valvular incompetence. Criteria for making the diagnosis were referred to in another article published by the same author (Belcaro 1993b). The clinical scores of included participants may be converted to "C4s, Ep, As, d, p, Pr" according to the CEAP classification system (translated as symptomatic skin

changes ascribed to venous disease; chronic venous disorder of undetermined cause; involvement of superficial, deep and perforator veins and underlying pathophysiology of reflux). Inclusion and exclusion criteria are listed in the Characteristics of included studies table. In both trials, the LAP plus ligation group received subcutaneous heparin (dose and frequency not stated) on a daily basis for five days after surgery. In addition, elasticated GCS were used to prevent DVT for five days following surgery in Belcaro 1999. A brief description of LAP is given in the Characteristics of included studies table for each study.

Makarova 2001 compared people with primary valvular incompetence undergoing superficial venous surgery alone versus people having an additional internal valvuloplasty of the superficial femoral vein. In all, 128 participants with CEAP C2 to C4 were initially treated with elasticated compression for five years before entry into the trial. Makarova 2001 stratified participants into two groups according to change in CEAP class during five years of observation: those with "progressive clinical dynamics" (worsening of CEAP class by at least one level) and those with "stable clinical dynamics" (no change in CEAP class). Participants were further stratified according to changing CEAP class, yielding six separate subgroups for random assignment to treatment and control arms of the study. A total of 27 participants had developed active ulceration (CEAP C6), but no healed ulcers (CEAP C5) were reported. All participants had undergone yearly preoperative ultrasound scans to mark out sites of reflux and to measure reflux time (RT) and reflux volume index (RVI). Participants then underwent superficial venous surgery (including subfascial perforator ligation) with or without internal valvuloplasty to the proximal superficial femoral valve. Participants were followed up by an annual duplex scan for seven to eight years after surgery.

Wang 2006 investigated the efficacy of external valvuloplasty of the femoral vein in the treatment of people with primary chronic venous insufficiency (PCVI). The study included 40 participants with bilateral PCVI who were classified as CEAP C2 to C4, with moderate incompetence of the deep vein. The limbs of each participant (total 80 limbs) were randomly assigned to two groups, each consisting of 40 limbs. Group A limbs underwent external valvuloplasty of the femoral vein plus surgery of the superficial venous system; group B limbs underwent surgery to the superficial venous system only. Participants were followed up for three years after surgery was performed. Participants with ulcers were excluded, so no new evidence of ulcer healing was identified.

Excluded studies

We excluded five studies. Reasons for exclusion were:

- participants underwent perforator ligation (Pierik 1997; Sybrandy 2001);
- participants underwent surgery to superficial veins without surgery to deep veins (Rass 2012);
- no control group (Ktenidis 2002);
- not an RCT (Maksimović 2008).

See the Characteristics of excluded studies table.

Risk of bias in included studies

The overall quality of the studies was poor because methods of randomisation and blinding were not reported for three of the four included studies (Belcaro 1993a; Belcaro 1999; Makarova 2001). See Figure 2 and Figure 3.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

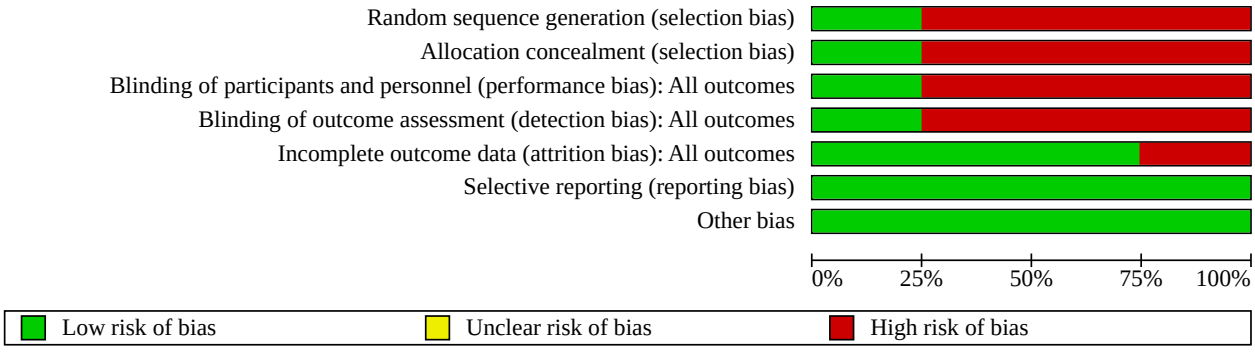
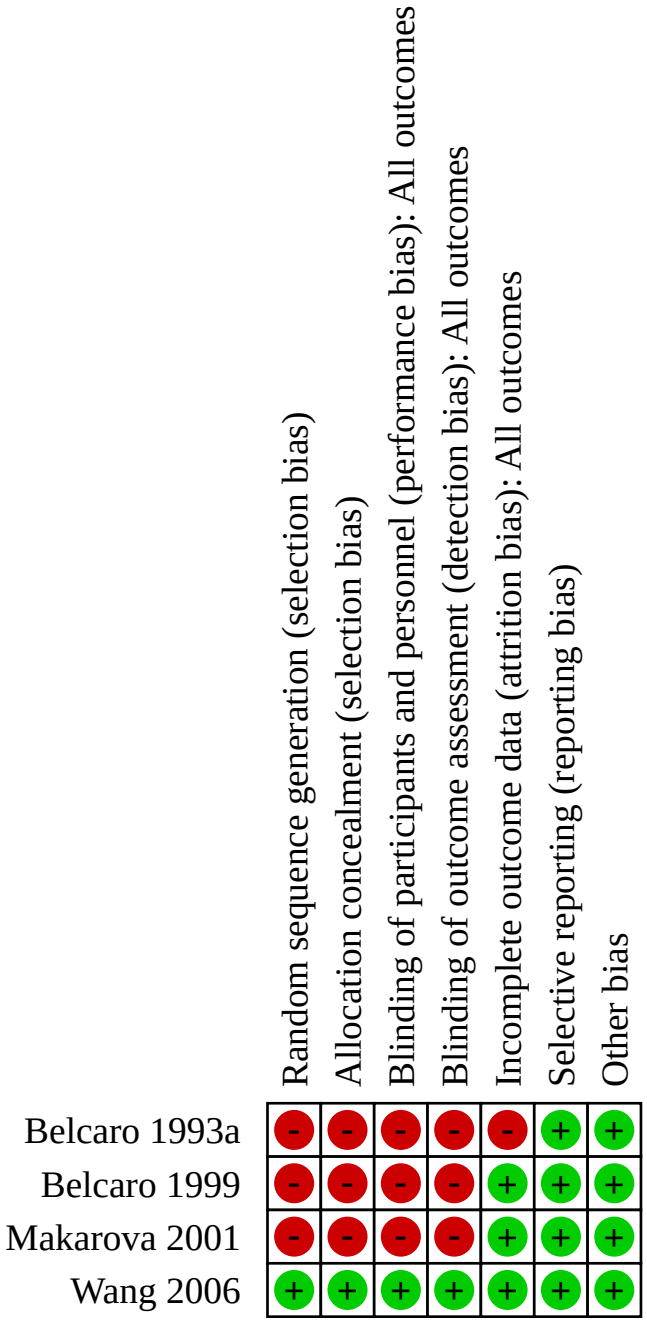


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Wang 2006 conducted randomisation by limb rather than by participant with PCVI. Each of the 40 participants drew lots twice under the observation of researchers. One lot was drawn to determine the operative procedure and the other to determine the leg assigned for the procedure. When one limb was randomly assigned to group A (external valvuloplasty) regardless of whether it was the right or left, the other leg was assigned to group B (control). We judged this at low risk of bias. Belcaro 1993a, Belcaro 1999, and Makarova 2001 randomly assigned participants but the

method of randomisation used was not stated. We judged these at high risk of bias.

Blinding

Three studies did not describe blinding of participants or personnel (Belcaro 1993a; Belcaro 1999; Makarova 2001). We judged these at high risk of bias. In Wang 2006, participants, technical personnel performing air plethysmography (APG), and duplex analysis, and data analysts (but not surgeons) were blinded to the operative procedure performed. Another clinician who did not participate in the surgical procedure determined clinical scores. We judged this study at low risk of bias.

Incomplete outcome data

Belcaro 1993a gave no description for the figures representing the main outcome measures. After discussions with a statistician, the review authors concluded that these figures represented means and standard deviations (SD). The methods used to calculate statistical significance were Mann-Whitney U and Chi^2 tests. We judged this study at high risk of bias.

Nine participants dropped out of Belcaro 1999. We judged this at low risk of bias.

Makarova 2001 stratified 168 CEAP C2 to C4 participants after five years of observation as "progressive" or "stable," depending on the change/stability of their CEAP class over these five years. A total of 40 participants withdrew. Twenty-seven participants had developed venous ulceration but were not considered separately in the study. There was no mention of any participants improving over five years. Inclusion and exclusion criteria were otherwise clearly stated. In all, there were 128 participants in the treatment phase, three of whom subsequently dropped out. The main outcome measures were clinical changes (i.e. deterioration/stability of CEAP class) and duplex scanning for RT and RVI. AVP and VRT were not performed, as they were not planned. Follow-up was yearly for seven to eight years. None of the data were provided in sufficient detail to allow independent statistical analysis. The main method of calculating significance was Chi^2. Valve failure was not analysed through time-based methods. We judged this at low risk of bias.

Three participants declined to draw lots for method of randomisation and procedure and so were excluded from Wang 2006. We judged this at low risk of bias.

Selective reporting

The main outcome measures in Makarova 2001 were clinical changes (i.e. deterioration/stability of CEAP class) and duplex scanning for RT and RVI. Valve failure was not analysed through time-based methods. Belcaro 1993a, Belcaro 1999, and Wang 2006 reported all outcomes. We judged all studies at low risk of bias.

Other potential sources of bias

We identified no other potential sources of bias, so all studies were at low risk of bias.

Effects of interventions

See: **Summary of findings 1** Valvuloplasty plus surgery of the superficial venous system compared with surgery of the superficial venous system for primary valvular incompetence

Surgery for primary valvular incompetence

Ulcer healing and ulcer recurrence

No studies reported ulcer healing and ulcer recurrence. One study reported on active ulceration according to CEAP score baseline and at time of surgery but not postsurgery.

Makarova 2001 included 27 participants with active venous ulceration at the time of surgery: 14 participants in the valvuloplasty plus ligation group and 13 participants in the ligation-only group had active ulceration at the time of surgery (CEAP C6). All participants were C2 to C4 at baseline, and during the first five years of observation (before surgery) four extremities had changed from C2 to C6, three extremities had changed from C3 to C6 and 20 extremities had changed from C4 to C6. Group allocation was not reported. Ulcer healing or recurrence after treatment was not reported.

The three remaining studies did not report ulcer healing or recurrence. Wang 2006 excluded people with CEAP C5 or C6 at baseline. Neither Belcaro 1993a nor Belcaro 1999 included participants with active venous ulceration.

Complications of surgery

The evidence for complications of surgery was of very low certainty, downgraded two levels for risk of bias and one level for imprecision. The studies used different outcome measures and it was not possible to pool the results.

Three studies reported complications of surgery. Belcaro 1993a reported no 'significant' complications and no incidence of DVT. Belcaro 1999 reported that no complications occurred. Wang 2006 reported no incidence of DVT or deaths.

Clinical changes

All four studies reported clinical changes but we were unable to pool data as studies reported different outcomes and used different measurements.

Clinical, aetiological, anatomical, and pathophysiological (CEAP) classification scoring

Two studies assessed clinical changes by subjective and objective measurements, as specified in the CEAP classification score (low-certainty evidence). One study reported mean CEAP severity scores (Wang 2006). At baseline, the mean CEAP severity score was 18.1 (SD 4.4) for limbs that undergoing external valvuloplasty with surgery to the superficial venous system and 17.8 (SD 3.4) for limbs undergoing surgery to the superficial venous system. At three years postsurgery, the mean CEAP severity score was 5.2 (SD 1.6) for limbs that had undergone external valvuloplasty with surgery to the superficial venous system and 9.2 (SD 2.6) for limbs that had undergone surgery to the superficial venous system. Wang 2006 used colour duplex scanning to evaluate deep vein reflux grading. At three-year postoperative assessment, using the CEAP classification, investigators reported 25 limbs in group A (external valvuloplasty of the femoral vein plus surgery of the superficial venous system) graded at 0 to 1, 14 limbs graded at 2 and one limb graded at 3. Within group B (surgery of the superficial venous system), 12 limbs were graded at 2 and 28 limbs were graded at 3 for reflux.

One study reported change in clinical class using CEAP. Makarova 2001 reported that participants with deteriorating clinical dynamics over the five years preceding surgery had higher rates of improvement in clinical condition in the treatment group (valvuloplasty plus ligation) compared with the control group (ligation only) after seven years of follow-up (80% with valvuloplasty plus ligation versus 51% with ligation only). Participants with stable preoperative clinical dynamics demonstrated similar rates of improvement in both groups (95% with valvuloplasty plus ligation versus 90% with ligation only). Among all participants who were clinically stable before surgery (22 in valvuloplasty plus ligation group versus 21 in ligation-only group), only one participant in the ligation-only group showed deterioration compared with none in the valvuloplasty plus ligation group. Among 41 participants who demonstrated deterioration in CEAP class preoperatively (ligation-only group), 14 continued to show deterioration after superficial venous surgery alone, 21 stabilised and six developed recurrent varicose veins. By comparison, progression was halted in participants undergoing a valvuloplasty plus ligation, with only six deteriorating, 33 stabilising and two developed recurrent varicose veins.

Ambulatory venous pressure

Two studies reported AVP (Belcaro 1993a; Belcaro 1999). The mean change at one year was –20 mm Hg in the LAP plus ligation group and –7 mm Hg in the ligation-only group. Changes at two years were –19.0 mm Hg in the LAP plus ligation group and –6 mm Hg in the ligation-only group. The MD between groups was –15.0 mm Hg at one year (95% CI –21.0 to –9.0) and –15.0 mm Hg at two years (95% CI –21.1 to –8.9) (Analysis 1.1). The change in AVP between baseline and 10 years was –21 mm Hg for the 21 in LAP plus ligation group and –3 mm Hg for the ligation-only group. The MD between groups was –18.0 mm Hg (95% CI –21.4 to –14.6; Analysis 1.1).

When a cuff was applied to occlude the superficial system, changes in AVP in the LAP plus ligation group were –16 mm Hg at one year and –14 mm Hg at two years (Belcaro 1993a). Changes in AVP in the ligation-only group were –4 mm Hg at one year and –3 mm Hg at two years. The MD between the two groups was –12.0 mm Hg at one year (95% CI –17.2 to –6.8) and –11.0 mm Hg at two years (95% CI –17.5 to –4.5) (Analysis 1.2). At 10 years in Belcaro 1999, changes in AVP were –19 mm Hg in the LAP plus ligation group and –4 mm Hg in the ligation-only group. The MD was –7.0 mm Hg (95% CI –10.0 to –4.0; Analysis 1.2).

Venous refill time

Two studies reported VRT (Belcaro 1993a; Belcaro 1999). Belcaro 1993a measured VRT before the intervention and at one and two years of follow-up. There was improvement in VRT in both groups at one year (11.7 seconds in the LAP plus ligation group compared with 10 seconds in the ligation-only group) and at two years (11.7 seconds in the LAP plus ligation group compared with 8 seconds in the ligation-only group). The MD at one year was 2.0 seconds (95% CI –2.8 to 6.8) and at two years was 4.0 seconds (95% CI –0.7 to 8.7) (Analysis 1.3). With the application of a cuff, the difference in VRT at one year was 5.5 seconds in the LAP plus ligation group and 4.0 seconds in the ligation-only group. At two years, this was reduced to 4.5 seconds in the LAP plus ligation group and to 2.0 seconds in the ligation-only group. It should be noted that the layout of data in the trial article suggested that these VRT values corresponded to cuff application, although this was not made explicitly clear (Analysis 1.4).

Belcaro 1999 measured VRT at baseline and at 10 years of follow-up. Improvement in VRT: 7 seconds in the LAP plus ligation group compared with 2 seconds in the ligation-only group after 10 years. The MD between the two groups was 4.0 seconds (95% CI 1.9 to 6.1; Analysis 1.3). With the application of a cuff to occlude the superficial venous system, the difference between the two groups was maintained at 10 years with a VRT of 6.0 seconds in the LAP plus ligation group compared with 2.0 seconds in the ligation-only group. The MD between the two groups was 4.0 seconds (95% CI 1.3 to 6.7; Analysis 1.4).

Haemodynamic indices (venous filling index, ejection fraction, reserve volume fraction)

One study reported haemodynamic indices. Wang 2006 reported that haemodynamic indices and muscle pumping indices improved postoperatively in group A limbs (external valvuloplasty of the femoral vein plus surgery of the superficial venous system). In group B limbs (surgery of the superficial venous system), muscle pumping indices did not improve postoperatively. At three years, there was an improvement in reflux volume postoperatively: in group A (external valvuloplasty of the femoral vein plus surgery of the superficial venous system), preoperative values improved from 84.4 (SD 29.2) mL/minute to 43.0 (SD 19.1) mL/minute; in group B (surgery of the superficial venous system), preoperative values improved from 79.2 (SD 4.3) mL/minutes to 68.7 (SD 2.1) mL/minute. Further, there was improvement in venous filling index of 8 mL/minute to 9 mL/minute in group A (external valvuloplasty of the femoral vein plus surgery of the superficial venous system) and 3 mL/minute to 4 mL/minute in group B (surgery of the superficial venous system). There was an improvement in ejection fraction of about 10% in group A (external valvuloplasty of the femoral vein plus surgery of the superficial venous system) and about 2% in group B (surgery of the superficial venous system). Reserve volume fraction improved by about 13% in group A (external valvuloplasty of the femoral vein plus surgery of the superficial venous system) and 4% in group B (surgery of the superficial venous system).

Residual incompetence

All four studies reported residual incompetence. Belcaro 1993a measured residual incompetence in repaired valves using colour duplex scanning. The criteria used were different from those used for inclusion (reflux time longer than three seconds for inclusion, reflux longer than two seconds for follow-up). At two years of follow-up, 2/11 valves repaired were incompetent. As the control group did not undergo valvuloplasty, no figures were given for comparison.

Belcaro 1999 stated that at 10 years, colour duplex indicated no superficial femoral incompetence in the LAP plus ligation group, while all limbs in the ligation-only group showed the same level of femoral incompetence.

Makarova 2001 reported no immediate residual incompetence (RT < 0.5 seconds). In 12/63 participants who had undergone valvuloplasty, reflux reappeared or worsened postoperatively. Changes in RT and RVI (10 participants) were presented graphically by time. However, there were no data on the other participants treated with valvuloplasty or on the controls for comparison.

Wang 2006 reported that competency of the valve was maintained to 90.9% at three years postoperatively (100% at one month) in limbs receiving external valvuloplasty of the femoral vein plus

surgery of the superficial venous system, whereas limbs receiving only surgery of the superficial venous system showed persistent incompetence.

Number of sites of incompetence

Three studies reported on incompetent veins. Belcaro 1993a measured the number of incompetent valves (defined as reflux longer than three seconds) using colour duplex scanning before the intervention, after six months and after two years. The mean number of incompetent valves in the LAP plus ligation group was reduced by 11.9 at six months and 9.9 at two years. The mean number of incompetent valves in the ligation-only group was reduced by 6.0 at six months and 5.0 at two years. The MD between groups was −4.9 at six months (95% CI −6.8 to −3.0) and −3.9 at two years (95% CI −6.5 to −1.4) (Analysis 1.5).

Makarova 2001 reported that among clinically stable participants preoperatively, only 1/22 participant in the valvuloplasty group and 1/21 participants in the control group developed recurrence of varicose veins. In contrast, among participants for whom disease was progressive, 2/41 (5%) of those treated with valvuloplasty developed recurrence, while 6/41 (15%) in the control group developed recurrence.

At 10 years, Belcaro 1999 reported no superficial femoral incompetence in limbs in the LAP plus ligation group, and all limbs in the ligation-only group showed the same level of incompetence.

Overall clinical outcome

We interpreted the data on clinical changes that were reported within the studies to suggest an overall evaluation of the clinical outcome in terms of change in clinical class, on the following basis: +3 (asymptomatic = no symptoms of chronic venous disease, improvement in VRT of at least +5 seconds and improvement in AVP of at least −10 mm Hg), +2 (moderate improvement = mild symptoms with changes in VRT and AVP as in +3), +1 (mild improvement = clinical improvement or improvement in VRT or AVP), 0 (no symptomatic or laboratory changes), −1 (mild worsening = deterioration in symptoms or in VRT or AVP results), −2 (significant worsening = deterioration in symptoms and in VRT or AVP results) and −3 (marked worsening = that seen with −2 accompanied by new or worsening venous claudication). For Belcaro 1993a, the overall score for mean results in the LAP plus ligation group was +2 (moderate improvement). This is represented by mild symptoms of chronic venous insufficiency, improvement in VRT of at least five seconds and improvement in AVP of at least −10 mm Hg. The overall score for the ligation-only group was +1 (mild improvement), represented by clinical improvement or laboratory improvement in VRT or AVP. For Makarova 2001, the overall score for mean results of ligation plus valvuloplasty, whether stable or progressive preoperatively, was +1 (clinical improvement but no physiological pressure data). The overall score for the ligation-only group was +1 among participants who were stable preoperatively 0 or −1 with progressive disease preoperatively. For Wang 2006, there was overall moderate improvement (+2) in both groups. Overall at three years, CEAP severity score showed improvement among 13 in group A (external valvuloplasty of the femoral vein plus surgery of the superficial venous system) and among 8 in group B (surgery of the superficial venous system) (Wang 2006). For Belcaro 1999, the clinical outcome score for the LAP plus ligation group was +2 compared with +1 for the ligation-only group.

Health-related quality of life

The evidence for this outcome was very low certainty, downgraded two levels for risk of bias and one level for imprecision. One study reported health-related QoL. Belcaro 1999 devised a disease-specific QoL measurement score from the 10 most relevant items from 35 items given to 100 similar people with venous incompetence in a questionnaire prior to the study. The 10 items were: pain/discomfort; oedema/swelling; mobility limitation; cosmetic aspects; need to wear stockings; need to see a doctor; expenses; lost working days; other limitations including leisure/sport activities; and social embarrassment. These 10 items were presented as a visual analogue scale (VAS) ranging from 0 (no problem) to 10 (most severe problem) and a cumulative quality of life score (CQLS) was reported at baseline and after 10 years. In the LAP plus ligation group, the CQLS decreased from 49 to 11 (75.5%) in 17 participants at 10 years, compared to a decrease from 48 to 36 (25% reduction) in the 18 participants treated with ligation-only.

Pain

The evidence for pain was very low certainty, downgraded two levels for risk of bias and one level for imprecision. Two studies reported a measure of pain (Belcaro 1999; Wang 2006).

Wang 2006 reported that all participants had painful leg heaviness at baseline and reported that leg heaviness and pain was resolved completely in 36/40 (90%) limbs treated with femoral vein external valvuloplasty plus high ligation and stripping of great saphenous vein (GSV) and percutaneous continuous circumsuture and 22/40 (55%) limbs treated with high ligation and stripping of GSV and percutaneous continuous circumsuture alone at three years follow-up. Belcaro 1999 devised a disease-specific QoL measurement score from the 10 most relevant items from 35 items given to 100 similar people with venous incompetence in a questionnaire prior to the study. One of the 10 items included pain/discomfort, and was presented as a VAS ranging from 0 (no problem) to 10 (most severe problem). Pain/discomfort scores at baseline were 4 for the LAP plus ligation versus 2 for the ligation-only group. Pain/discomfort scores at 10 years were 1 for the LAP plus ligation group versus 3 for the ligation-only group.

Surgery for secondary valvular incompetence

No trials investigated surgery for secondary valvular incompetence.

Surgery for the obstructive form of deep venous insufficiency (venous obstruction)

No trials investigated surgery for the obstructive form of deep venous insufficiency (venous obstruction).

DISCUSSION

Surgery for deep venous insufficiency, mainly caused by venous valve dysfunction, may lead to various problems in the legs such as ulceration. This is usually treated with compression stockings. Failing this and with worsening symptoms, various surgical procedures to rectify incompetent valves have been tried in small groups of cases, usually single-centre studies.

Summary of main results

We found no new studies for this update. The only available RCTs involved performing ligation and valvuloplasty in study

participants with primary valvular incompetence (Belcaro 1993a; Belcaro 1999; Makarova 2001; Wang 2006). This treatment was compared with ligation only. No trials investigated surgical treatment of people with deep venous insufficiency due to secondary valvular incompetence or the obstructive form of deep venous insufficiency (venous obstruction). Moreover, no trials compared the results of surgical procedures versus those of high compression therapy in people with venous ulcers secondary to deep venous insufficiency. The included trials were of small scale. Participants had mild-to-moderate deep venous insufficiency. Many of the measures used in these trials are no longer used in clinical practice.

None of the included studies provided evidence on ulcer healing and ulcer recurrence. Makarova 2001 did not report this outcome, and the remaining three studies did not include people with ulcers or active ulceration (Belcaro 1993a; Belcaro 1999; Wang 2006).

Three studies reported no significant complications of surgery and no incidence of DVT during follow-up (very low-certainty evidence) (Belcaro 1993a; Belcaro 1999; Wang 2006). One study did not report on the occurrence of complications (Makarova 2001).

All four studies reported on clinical changes, but we were unable to pool data as studies reported different outcomes and used different measurements (low-certainty evidence).

Wang 2006 reported that external valvuloplasty of the femoral vein plus surgical repair of the superficial venous system improved the haemodynamic status of the lower limbs, restored valvular function more effectively and achieved better outcomes than surgical repair of the superficial venous system alone. However, the study sample was small (40 participants (80 limbs) with only grade 3 reflux), and did not include people with ulcers.

In people who were deteriorating preoperatively, Makarova 2001 demonstrated sustained mild clinical improvement for seven years among those subjected to valvuloplasty compared with people who had undergone superficial venous surgery alone (0 or –1). However, this benefit was lost when the participant's condition was stable preoperatively.

Sustainable improvement in AVP and VRT was achieved by LAP plus ligation at 10 years which was maintained when AVP and VRT were measured with a cuff while the superficial system was excluded (Belcaro 1999). However, AVP values after surgery remained relatively high, allowing the benefit of surgery to be questioned. Nevertheless, the benefit of valve repair was sustained at 10 years of follow-up (Belcaro 1999).

Belcaro 1993a reported an MD in the number of incompetent valves up to two years in favour of LAP plus ligation (Analysis 1.5); this difference may represent a protective effect of LAP; it may show that more efficient ligation of the superficial incompetent veins was performed in the LAP plus ligation group in comparison with the ligation-only group, or may suggest a combination of the two.

We interpreted the data on clinical changes that were reported within the study publications to suggest an overall evaluation of the clinical outcome in terms of change in clinical class. For Belcaro 1993a, the overall score for mean results in the LAP plus ligation group was +2 (moderate improvement). The overall score for the ligation-only group was +1 (mild improvement). For Makarova 2001, the overall score for mean results of ligation plus valvuloplasty, whether stable or progressive preoperatively, was +1 (clinical improvement but no physiological pressure data). The overall score for the ligation-only group was +1 among participants who were stable preoperatively 0 or –1 with progressive disease preoperatively. For Wang 2006, there was an overall moderate improvement (+2) in both groups. Overall CEAP severity score showed improvement among 13 participants in group A (external valvuloplasty of the femoral vein plus surgery of the superficial venous system) and among eight participants in group B (surgery of the superficial venous system) at three years (Wang 2006). For Belcaro 1999, the clinical outcome score for the LAP plus ligation group was +2 compared with +1 for the ligation-only group.

Overall completeness and applicability of evidence

This review included four small studies that reported clinical outcomes following valvuloplasty. We found no studies investigating other surgical procedures for the treatment of people with deep venous insufficiency. Included studies reported different measures of clinical outcomes. Therefore, meta-analysis was not possible, and we were unable to address all of our objectives. Individually, the studies reported promising results, but they included only participants with mild-to-moderate deep venous insufficiency, and so findings may not be applicable to people with more severe deep venous insufficiency. One small trial showed continuous improvement for three years following external valvuloplasty of the femoral vein, in addition to surgery to the superficial venous system (Wang 2006). This improved the haemodynamic status of lower limbs and restored valvular function more effectively, achieving better outcomes when compared with surgery to the superficial venous system alone showing benefit in a group of patients not usually considered for surgery for deep venous insufficiency (Wang 2006). Results from three additional studies indicated that ligation and valvuloplasty may have produced moderate and sustained improvement for seven to 10 years after surgery among people with mild-to-moderate deep venous insufficiency caused by primary valvular incompetence (Belcaro 1993a; Belcaro 1999; Makarova 2001).

Very little information was available from the included studies on the primary outcome of ulcer healing and recurrence. Three studies excluded people with ulcers or active ulceration, and one study did not report on ulcer healing and recurrence.

Some measures used in the included studies to assess clinical changes, for example, APG and RVI, are no longer used in clinical practice, and consensus has not been reached on how venous haemodynamics should be assessed and quantified. There are very few RCTs investigating this clinically important condition. This could be due to the lack of interest or to a failure in reaching a consensus for venous haemodynamics that could be used to assess the efficacy of these procedures when compared to pre-operative workup. A clinically useful robust measure for the pathophysiology of deep venous insufficiency is needed for future trials.

Quality of the evidence

We included four studies with 273 participants. We were unable to pool any data due to differences in outcomes reported and how they were measured. We assessed the certainty of the evidence using GRADE (Schünemann 2021). We downgraded all outcomes

by one level for imprecision due to few RCTs, few participants and small numbers of events. We downgraded clinical changes by one level for risk of bias concerns and we downgraded two levels for risk of bias concerns for complications of surgery, QoL and pain. See Summary of findings 1.

Potential biases in the review process

We believe that all relevant studies have been identified by our searches, but this review was limited by the number of suitable RCTs and the small numbers of participants treated in these trials. Most participants were treated on an individual basis, and study results should be interpreted with considerable caution.

Agreements and disagreements with other studies or reviews

We are not aware of any other evidence regarding this topic.

AUTHORS' CONCLUSIONS

Implications for practice

We only identified evidence from four randomised controlled trials for valvuloplasty plus surgery of the superficial venous system for primary valvular incompetence. We found no studies investigating other surgical procedures for the treatment of people with deep venous insufficiency, or which included participants with secondary valvular incompetence or venous obstruction. None of the studies reported ulcer healing or recurrence, and very few studies reported complications of surgery, clinical outcomes, quality of life and pain (very low- to low-certainty evidence). Conclusions on the effectiveness of valvuloplasty for deep venous insufficiency cannot be made.

Implications for research

Well-designed, large, randomised trials with long-term follow-up are needed to investigate surgical procedures for the treatment of people with deep venous insufficiency. A clinically useful robust measure for pathophysiology of deep venous insufficiency, that is validated and used consistently, is needed for future trials. In the absence of this, trials should be designed and powered for clinically important outcomes such as ulcer healing, pain scores and quality of life. In particular, trials including participants with venous ulcers secondary to deep venous insufficiency, trials reporting on ulcer healing and ulcer recurrence, and trials comparing surgery with high compression therapy are required. As there are no robust conclusions with current deep venous insufficiency surgical practice, we propose that for future reviews, we would be justified to include other methods of valvular correction or replacement. This could be either be open or percutaneous endovenous replacement, or hybrid procedures.

ACKNOWLEDGEMENTS

The review authors wish to thank Cochrane Vascular for assistance with the literature searches and Mr Ahmed Abidia for his work on the previous version of this review.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Belcaro 1993a

Study characteristics

Belcaro 1993a *(Continued)*

Methods	Study design: randomised, parallel trial Method of randomisation: not stated Blinding: not stated Exclusions after randomisation: not stated Exclusions for failure to consent: not stated Dropouts: 0 Duration of study: 2 years Comparable treatment and control groups
Participants	Country: Italy Number: 21 randomly assigned Age: mean 38 years in treatment group; 37.9 years in control group Sex: 5 males, 6 females in treatment group; 5 males, 5 females in control group Inclusion criteria: primary femoral valve incompetence, signs of venous hypertension (large varicose veins, lipodermatosclerosis, perimalleolar skin changes), deep venous incompetence defined as high AVP only partially affected by exclusion of the superficial system using an ankle tourniquet, significant reflux (on standing) at the common femoral vein defined as reflux lasting > 3 seconds as seen by a colour duplex scan, presence of vein cusps by high-resolution ultrasound Exclusion criteria: none reported
Interventions	Treatment: femoral vein external valvuloplasty using LAP in combination with ligature of incompetent superficial veins. Technique of LAP was described in detail in the published article. In brief, after the long saphenous vein was disconnected, the anterior surface of the common femoral vein was exposed. The anterior surface of the vein was plicated (3 mm in width stitches) longitudinally over the insertion line of the valve cusps for a length of 5 mm. Treatment group also received subcutaneous heparin (dose and frequency not stated) on a daily basis for 5 days after the procedure. No reference was made to the use of compression bandages, elasticated hosiery or intermittent leg elevation after the operation. Control: ligature of incompetent superficial veins only.
Outcomes	Subjective assessment, AVP, VRT, residual incompetence in repaired valves, number of sites of incompetence, common femoral vein diameter, approximation of vein cusps
Funding	Not reported
Declaration of interests	Not reported
Notes	No description was given of the figures representing the main outcome measures. After discussions with a statistician, it was concluded that these figures represented the means and SDs. Methods used to calculate significance level in this trial were not described. Outcome measures were given in a selection of 6 months, 1 year and 2 years, but the data provided in the paper were not complete for each time point.

Risk of bias

Bias	Authors' judgement	Support for judgement

Belcaro 1993a *(Continued)*

Random sequence generation (selection bias)	High risk	No details given.
Allocation concealment (selection bias)	High risk	No details given.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No details given.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No details given.
Incomplete outcome data (attrition bias) All outcomes	High risk	No description given for figures reported, incomplete data reported for each time point.
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Low risk	None.

Belcaro 1999

Study characteristics	
Methods	Study design: randomised, parallel trial Method of randomisation: not reported Blinding: not reported Exclusions after randomisation: not reported Exclusions for failure to consent: 6 Dropouts: 9 Duration of study: 10 years Comparable treatment and control groups
Participants	Country: Italy Number: 44 participants entered, 35 completed 10-year follow-up Age (mean): 41 (SD 8) years in treatment group; 41 (SD 12) years in control group (participants completing the study) Sex: 11 males, 6 females in treatment group; 11 males, 7 females in control group (participants completing the study) Inclusion criteria: primary femoral valve incompetence, signs of venous hypertension (large varicose veins, lipodermatosclerosis, perimalleolar skin changes), deep venous incompetence defined as high AVP > 50 mm Hg and shorter VRT (< 13 seconds) not significantly modified by the application of a below-knee cuff, significant reflux (> 3 seconds) on standing as seen by colour duplex scan, mobile vein cusps on high-resolution ultrasound

Belcaro 1999 *(Continued)*

	Exclusion criteria: not reported
Interventions	Treatment: femoral vein external valvuloplasty using LAP + ligature of incompetent superficial veins. Technique of LAP was described in detail in the published article. In brief, after the long saphenous vein was disconnected, the anterior surface of the common femoral vein was exposed. The anterior surface of the vein was plicated (3 mm in width stitches) longitudinally over the insertion line of the valve cusps for a length of 5 mm. Treatment group also received elasticated graduated compression stockings + daily subcutaneous heparin (dose and frequency not stated) for 5 days after surgery. Control: ligature of incompetent superficial veins only.
Outcomes	Subjective assessment, duplex scanning, venous reflex, CEAP severity scores, APG indices
Funding	Not reported
Declaration of interests	Not reported
Notes	Duplex scanning, venous reflex, CEAP severity scores, APG indices sufficient for inclusion Study suggested possible benefit of valve repair at 10 years

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	No details reported.
Allocation concealment (selection bias)	High risk	No details reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No details reported.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No details reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All data accounted for.
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Low risk	None.

Makarova 2001

Study characteristics	
Methods	Study design: randomised, parallel trial

Makarova 2001 *(Continued)*

	Method of randomisation: not stated. Patients treated by elasticated compression for 5 years before study and divided into stable (unchanging CEAP clinical class) and progressive (deteriorating CEAP class) on entry into study Blinding: not reported Exclusions after randomisation: not reported Exclusions for failure to consent: 40 Dropouts (lost to follow-up): 3 Duration of study (postoperatively): 7 years Comparable treatment and control groups
Participants	Country: Russia Number: 168 participants entered. 149 completed 5-year observation period. 19 refused surgery. 128 entered surgical period. 125 completed 7 years of follow-up (63 in treatment group, 62 in control group) Age: not reported Sex: not reported Inclusion criteria: CEAP C2 to C4, ultrasound reflux in both GSV and SFV Exclusion criteria: history of DVT, episodes of acute oedema of lower extremity, trauma, major surgery, hospital stay with bed rest > 3 days. Ultrasound findings (confirmed on phlebography) of occlusion/stenosis of femoral vein or massive collateral venous pathways
Interventions	Treatment: unilateral GSV stripping and stab avulsions of varicose tributaries. Phlebographically confirmed incompetent perforating veins subfascially ligated in 20 participants by open long medial vertical approach. All 63 participants underwent SFV valve correction by internal valvuloplasty. Control: unilateral GSV stripping and stab avulsions of varicose tributaries. Phlebographically confirmed incompetent perforating veins subfascially ligated in 21 participants by open long medial vertical approach. No reference made to the use of low-dose heparin and graduated compression stockings.
Outcomes	No change in CEAP clinical class (defined as stable improvement) or increase in clinical class (defined as aggravation), recurrent varicose veins RT and RVI were measured yearly by duplex scanning for 7 or 8 years postoperatively
Funding	Not reported
Declaration of interests	Quote: "Competition of interest: nil."
Notes	Complications not mentioned 12 valvuloplasty failures (of 64) mainly during third year postoperatively of follow-up Large quantity of data not suitable for analysis Study suggested possible benefit of valve repair at 7 years

Risk of bias

Bias	Authors' judgement	Support for judgement

Makarova 2001 *(Continued)*

Random sequence generation (selection bias)	High risk	No details reported.
Allocation concealment (selection bias)	High risk	No details reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No details reported.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No details reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	At the end of the fifth year, 19 participants withdrew from the study and were not included in the final data analysis.
Selective reporting (reporting bias)	Low risk	All outcomes reported as planned.
Other bias	Low risk	None.

Wang 2006

Study characteristics	
Methods	Study design: randomised, prospective and self-controlled Method of randomisation: each of 40 participants drew lots under the observation of researchers, randomly assigned according to limb regardless of side Blinding: yes Duration of study: 3 years Comparable treatment and control groups
Participants	Country: China Number: 40 participants entered, 80 limbs Age: < 70 years Inclusion criteria: CEAP C2 to C4 with grade 3 reflux of deep veins, RT time > 0.5 seconds, PCVI of bilateral lower extremities; agreed to undergo simultaneous repair of both extremities, diagnosis confirmed in all cases by colour duplex scanning, APG or venography Exclusion criteria: 3 people declined to draw lots for method of randomisation and procedure and hence were excluded from the study; CEAP C5 or C6; post-thrombotic venous insufficiency; pregnancy; current anticoagulation therapy; serious arterial occlusive disease of lower extremity; malignant tumours and serious cardiac, pulmonary, haematological or central nervous system disease
Interventions	Treatment (group A) (40 limbs), "repaired valve group": femoral vein external valvuloplasty was combined with high ligation and stripping of great saphenous vein and percutaneous continuous circumsuture. Technique of modified external valvuloplasty was described in the published article. In brief, intermittent sutures were replaced with continuous double sutures. Advantage of doing so was ability to

Wang 2006 *(Continued)*

	replicate and reinforce the commissural lines of first valves on venous wall of the femoral vein. Competence was demonstrated during the operation. Control (group B) (40 limbs), "non-repaired valve group": underwent high ligation and stripping of the GSV and percutaneous continuous circumsuture of varicose veins of the legs. Anticoagulation was not given postoperatively and compression stockings were not used.
Outcomes	Subjective assessment, duplex scanning, venous reflex, CEAP severity scores, APG indices; postoperative assessment shows significant improvement in symptoms and venous function in group A compared with group B
Funding	Funding was obtained for the study by 1 of the study authors but no further details reported
Declaration of interests	Quote: "Competition of interest: none."
Notes	Duplex scanning, venous reflex, CEAP severity scores; APG indices show significant differences between groups 3 years postoperatively Study suggested possible benefit of valve repair at 3 years

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Each of the 40 participants drew lots twice under the observation of researchers. 1 lot was drawn to determine the operative procedure, and the other to determine the leg assigned for the procedure.
Allocation concealment (selection bias)	Low risk	When 1 limb was randomly assigned to group A, regardless of whether it was right or left, the other leg was assigned to group B.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants, technical personnel performing APG or colour duplex and another clinician who was not involved in the surgery but measured the clinical score were blinded. The performing surgeon was not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Clinician not involved in surgery measured clinical score and was blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Well reported.
Selective reporting (reporting bias)	Low risk	Comparison of haemodynamic indices was well reported.
Other bias	Low risk	None.

APG: air plethysmography; AVP: ambulatory venous pressure; CEAP: clinical, aetiological, anatomical, and pathophysiological classification score; DVT: deep venous thrombosis; GSV: greater saphenous vein; LAP: limited anterior plication; PCVI: primary chronic venous insufficiency; RT: reflux time; RVI: reflux volume index; SD: standard deviation; SFV: superficial femoral vein; VRT: venous refill time.

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

Study	Reason for exclusion
Ktenidis 2002	No control group.
Maksimović 2008	Not a randomised controlled trial.
Pierik 1997	Participants underwent perforator ligation without surgery to deep veins.
Rass 2012	Participants underwent surgery to superficial veins, not to deep veins.
Sybrandy 2001	Participants underwent perforator ligation without surgery to deep veins.

DATA AND ANALYSES

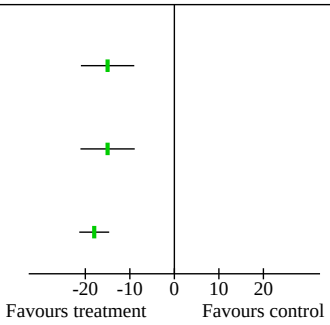
Comparison 1. Intervention versus control: trials on primary valvular incompetence

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Ambulatory venous pressure (AVP)	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1.1 At 1 year	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1.2 At 2 years	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1.3 At 10 years	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.2 AVP with cuff application	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.2.1 At 1 year	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.2.2 At 2 years	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.2.3 At 10 years	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.3 Venous refill time (VRT)	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.3.1 At 1 year	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.3.2 At 2 years	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.3.3 At 10 years	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.4 VRT with cuff	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.4.1 At 1 year	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.4.2 At 2 years	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.4.3 At 10 years	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.5 Number of sites of incompetence	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.5.1 At 6 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.5.2 At 2 years	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

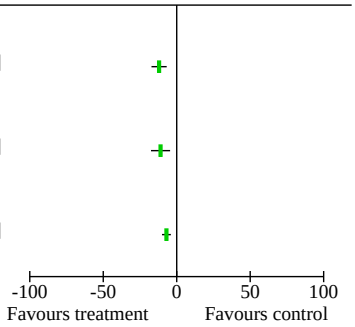
Analysis 1.1. Comparison 1: Intervention versus control: trials on primary valvular incompetence, Outcome 1: Ambulatory venous pressure (AVP)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Mean Difference IV, Fixed, 95% CI
1.1.1 At 1 year							
Belcaro 1993a	44	7	11	59	7	10	-15.00 [-20.99 , -9.01]
1.1.2 At 2 years							
Belcaro 1993a	45	6	11	60	8	10	-15.00 [-21.10 , -8.90]
1.1.3 At 10 years							
Belcaro 1999	44	4	17	62	6	18	-18.00 [-21.36 , -14.64]



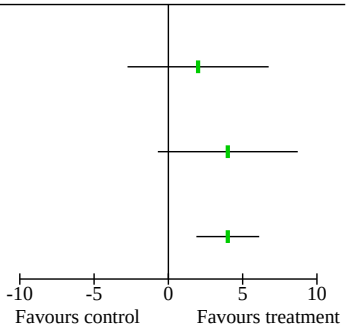
Analysis 1.2. Comparison 1: Intervention versus control: trials on primary valvular incompetence, Outcome 2: AVP with cuff application

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Mean Difference IV, Fixed, 95% CI
1.2.1 At 1 year							
Belcaro 1993a	40	7	11	52	5	10	-12.00 [-17.17 , -6.83]
1.2.2 At 2 years							
Belcaro 1993a	42	9	11	53	6	10	-11.00 [-17.49 , -4.51]
1.2.3 At 10 years							
Belcaro 1999	45	6	17	52	2	18	-7.00 [-10.00 , -4.00]



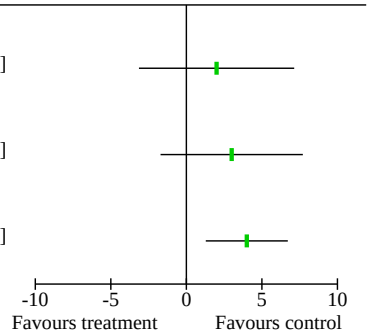
Analysis 1.3. Comparison 1: Intervention versus control: trials on primary valvular incompetence, Outcome 3: Venous refill time (VRT)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Mean Difference IV, Fixed, 95% CI
1.3.1 At 1 year							
Belcaro 1993a	19	5	11	17	6	10	2.00 [-2.75 , 6.75]
1.3.2 At 2 years							
Belcaro 1993a	19	6	11	15	5	10	4.00 [-0.71 , 8.71]
1.3.3 At 10 years							
Belcaro 1999	16	4	17	12	2	18	4.00 [1.89 , 6.11]



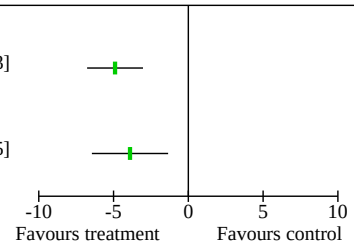
Analysis 1.4. Comparison 1: Intervention versus control: trials on primary valvular incompetence, Outcome 4: VRT with cuff

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Mean Difference IV, Fixed, 95% CI
1.4.1 At 1 year							
Belcaro 1993a	20	6	11	18	6	10	2.00 [-3.14 , 7.14]
1.4.2 At 2 years							
Belcaro 1993a	19	6	11	16	5	10	3.00 [-1.71 , 7.71]
1.4.3 At 10 years							
Belcaro 1999	17	3	17	13	5	18	4.00 [1.29 , 6.71]



Analysis 1.5. Comparison 1: Intervention versus control: trials on primary valvular incompetence, Outcome 5: Number of sites of incompetence

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Mean Difference IV, Fixed, 95% CI
1.5.1 At 6 months							
Belcaro 1993a	1.1	0.3	11	6	3	10	-4.90 [-6.77 , -3.03]
1.5.2 At 2 years							
Belcaro 1993a	3.1	1	11	7	4	10	-3.90 [-6.45 , -1.35]



APPENDICES

Appendix 1. Database searches

Source	Search strategy	Hits retrieved
Cochrane Vascular Specialised Register via CRS-Web	#1 MESH DESCRIPTOR Venous Insufficiency EXPLODE ALL AND INREGISTER #2 CVI AND INREGISTER #3 (femoral or popliteal iliac* or sapheno* or valve or valvular or ven* or vein*) adj4 (insuffici* or insufici* or incompet*) AND INREGISTER #4 #1 OR #2 OR #3 #5 valvuloplasty AND INREGISTER #6 (valve or valvular) adj3 (transplant* or transpos* or reconstruct* or implant*) AND INREGISTER #7 prosthetic valve implantation AND INREGISTER #8 venous bypass surgery AND INREGISTER #9 venous segmental AND INREGISTER #10 (Venous Valves OR Femoral Vein OR Saphenous Vein OR Iliac Vein OR Popliteal Vein) AND (SURGERY OR SURGICAL) AND INREGISTER #11 #5 OR #6 OR #7 OR #8 OR #9 OR #10 #12 #11 AND #4	199
CENTRAL via CRSO	#1 MESH DESCRIPTOR Venous Insufficiency EXPLODE ALL TREES WITH QUALIFIERS SU 90 #2 CVI:TI,AB,KY 230 #3 (((femoral or popliteal iliac* or sapheno* or valve or valvular or ven* or vein*) adj4 (insuffici* or insufici* or incompet*))):TI,AB,KY 2097 #4 MESH DESCRIPTOR Leg EXPLODE ALL TREES 2831 #5 MESH DESCRIPTOR Lower Extremity EXPLODE ALL TREES 6915 #6 #2 OR #3 OR #4 OR #5 8981 #7 MESH DESCRIPTOR Peripheral Vascular Diseases EXPLODE ALL TREES WITH QUALIFIERS SU 166 #8 MESH DESCRIPTOR Venous Valves EXPLODE ALL TREES WITH QUALIFIERS SU 1 #9 MESH DESCRIPTOR Femoral Vein EXPLODE ALL TREES WITH QUALIFIERS SU 53 #10 MESH DESCRIPTOR Saphenous Vein EXPLODE ALL TREES WITH QUALIFIERS SU 240 #11 MESH DESCRIPTOR Iliac Vein EXPLODE ALL TREES WITH QUALIFIERS SU 8 #12 MESH DESCRIPTOR Popliteal Vein EXPLODE ALL TREES WITH QUALIFIERS SU 12	365

(Continued)

	#13 valvuloplasty:TI,AB,KY 192 #14 (venous bypass surgery):TI,AB,KY 2 #15 (prosthetic valve implantation):TI,AB,KY 0 #16 (surgery to the superficial venous system):TI,AB,KY 0 #17 (venous segmental):TI,AB,KY 4 #18 ((valve or valvular) adj3 (transplant* or transpos* or reconstruct* or implant*)):TI,AB,KY 1384 #19 #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 1951 #20 #6 AND #19 342 #21 #1 OR #20 365	
MEDLINE (Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE) from 1946	1 exp Venous Insufficiency/su [Surgery] 2 CVI.ti,ab. 3 ((femoral or popliteal iliac* or sapheno* or valve or valvular or ven* or vein*) adj4 (insuffici* or insufici* or incompet*)).ti,ab. 4 Leg/bs [Blood Supply] 5 Lower Extremity/bs [Blood Supply] 6 or/2-5 7 exp Peripheral Vascular Diseases/su [Surgery] 8 exp Venous Valves/su [Surgery] 9 exp Femoral Vein/su [Surgery] 10 exp Saphenous Vein/su [Surgery] 11 exp Iliac Vein/su [Surgery] 12 exp Popliteal Vein/su [Surgery] 13 valvuloplasty.ti,ab. 14 "venous bypass surgery".ti,ab. 15 "prosthetic valve implantation".ti,ab. 16 "surgery to the superficial venous system".ti,ab. 17 "venous segmental".ti,ab. 18 ((valve or valvular) adj3 (transplant* or transpos* or reconstruct* or implant*)).ti,ab. 19 or/7-18 20 6 and 19 21 1 or 20 22 randomized controlled trial.pt. 23 controlled clinical trial.pt.	791

(Continued)

	24 randomized.ab. 25 placebo.ab. 26 drug therapy.fs. 27 randomly.ab. 28 trial.ab. 29 groups.ab. 30 or/22-29 31 exp animals/ not humans.sh. 32 30 not 31 33 21 and 32	
Embase	1 exp vein insufficiency/su [Surgery] 2 CVI.ti,ab. 3 ((femoral or popliteal iliac* or sapheno* or valve or valvular or ven* or vein*) adj4 (insuffici* or insufici* or incompet*)).ti,ab. 4 exp leg/ 5 or/2-4 6 exp peripheral vascular disease/su [Surgery] 7 exp vein valve/su [Surgery] 8 exp femoral vein/su [Surgery] 9 exp saphenous vein/su [Surgery] 10 exp iliac vein/su [Surgery] 11 exp popliteal vein/su [Surgery] 12 valvuloplasty.ti,ab. 13 "venous bypass surgery".ti,ab. 14 "prosthetic valve implantation".ti,ab. 15 "surgery to the superficial venous system".ti,ab. 16 "venous segmental".ti,ab. 17 ((valve or valvular) adj3 (transplant* or transpos* or reconstruct* or implant*)).ti,ab. 18 or/6-17 19 5 and 18 20 1 or 19 21 randomized controlled trial/ 22 controlled clinical trial/ 23 random$.ti,ab.	902

(Continued)

	24 randomization/ 25 intermethod comparison/ 26 placebo.ti,ab. 27 (compare or compared or comparison).ti. 28 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. 29 (open adj label).ti,ab. 30 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab. 31 double blind procedure/ 32 parallel group$1.ti,ab. 33 (crossover or cross over).ti,ab. 34 ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab. 35 (assigned or allocated).ti,ab. 36 (controlled adj7 (study or design or trial)).ti,ab. 37 (volunteer or volunteers).ti,ab. 38 trial.ti. 39 or/21-38 40 20 and 39	
CINAHL	S35 S19 AND S34 S34 S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 S33 MH "Random Assignment" S32 MH "Triple-Blind Studies" S31 MH "Double-Blind Studies" S30 MH "Single-Blind Studies" S29 MH "Crossover Design" S28 MH "Factorial Design" S27 MH "Placebos" S26 MH "Clinical Trials" S25 TX "multi-centre study" OR "multi-center study" OR "multicentre study" OR "multicenter study" OR "multi-site study" S24 TX crossover OR "cross-over" S23 AB placebo* S22 TX random* S21 TX trial*	111

(Continued)

	S20 TX "latin square" S19 S1 OR S18 S18 S5 AND S17 S17 S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 S16 TX ((valve or valvular) n3 (transplant* or transpos* or reconstruct* or implant*)) S15 TX "venous segmental" S14 TX "surgery to the superficial venous system" S13 TX "prosthetic valve implantation" S12 TX "venous bypass surgery" S11 TX valvuloplasty S10 (MH "Popliteal Vein/SU") S9 (MH "Iliac Vein/SU") S8 (MH "Saphenous Vein/SU") S7 (MH "Femoral Vein/SU") S6 (MH "Peripheral Vascular Diseases+/SU") S5 S2 OR S3 OR S4 S4 (MH "Lower Extremity+/BS") S3 (MH "Leg/BS") S2 TX ((femoral or popliteal iliac* or sapheno* or valve or valvular or ven* or vein*) n4 (insuffici* or insufici* or incompet*)). S1 (MH "Venous Insufficiency+/SU")	
Clinicaltrials.gov	Venous Insufficiency OR venous incompetence OR CVI | SURGERY OR SURGICAL OR valvuloplasty OR prosthetic valve implantation OR venous bypass surgery	34
ICTRP Search Portal		not available

WHAT'S NEW

Date	Event	Description
23 June 2021	New search has been performed	Search updated. No new included studies and one new excluded study identified.
23 June 2021	New citation required but conclusions have not changed	Search updated. No new included studies and one new excluded study identified. New author joined team. Text amended to reflect current Cochrane standards. Summary of findings table added. No change to conclusions.

HISTORY

Protocol first published: Issue 2, 1998
Review first published: Issue 2, 2000

Date	Event	Description
15 October 2014	New search has been performed	New search carried out. One new study included. Three new studies excluded
15 October 2014	New citation required but conclusions have not changed	New search carried out. One new study included. Three new studies excluded. Risk of bias assessed for all included studies and text updated. No changes made to conclusions
3 November 2008	Amended	Converted to new review format
26 May 2004	New citation required but conclusions have not changed	This review has been updated by the addition of 2 new included studies and 1 excluded study. No changes were made to the conclusions of the review

CONTRIBUTIONS OF AUTHORS

RRG: assessed new trials for possible inclusion in the review, provided clinical support, contributed to the discussion and conclusion, and assisted in drafting the review.

SCH: assessed new trials for possible inclusion in the review, contributed to the discussion and conclusion, and checked the draft review.

TB: extracted data, added summary of findings tables and applied GRADE criteria, and drafted the review

DECLARATIONS OF INTEREST

RRG: none.

SCH: has declared that he has received money in support for travel or accommodation to visit other vascular units to observe demonstrations of new venous stent insertions for deep venous obstruction. SH declares he is a Consultant Vascular Surgeon with interest in deep venous disease and its interventional/surgical treatment and also has an interest in the reorganisation of vascular services including the treatment of venous diseases. SH also declares he is Clinical Director of the Cumbria and Lancashire AAA Screening Programme.

TB: none.

SOURCES OF SUPPORT

Internal sources

- No sources of support provided

External sources

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

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

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

2021

We revised the outcomes (but not the other components of the PICO (population, intervention, control and outcomes)) to reflect current clinical practice and clinical importance: health-related quality of life and pain are new secondary outcomes. We added a summary of

findings table and assessed the outcomes presented in the table using GRADE criteria in keeping with Cochrane standards. We amended the title to 'Surgery for deep venous insufficiency' to more accurately reflect the review.

2015

The quality of trials was investigated using the methods of Jadad (Jadad 1996) and Schulz (Schulz 1995). In keeping with updated requirements of The Cochrane Collaboration, quality has now been assessed using the risk of bias tool as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Outcomes and comparisons were reordered for the 2015 update for consistency with both clinical relevance and policies of The Cochrane Collaboration.

INDEX TERMS

Medical Subject Headings (MeSH)

Edema; Saphenous Vein; Stockings, Compression; *Varicose Ulcer [surgery]; *Venous Insufficiency [surgery]

MeSH check words

Humans