Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients (Review)

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TABLE OF CONTENTS

[Intervention Review]

Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients

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ABSTRACT

Background

It has been suggested that combined modalities (methods of treatment) are more effective than single modalities in preventing venous thromboembolism (defined as deep vein thrombosis and pulmonary embolism, or both) in high-risk patients.

Objectives

To assess the efficacy of intermittent pneumatic leg compression combined with pharmacological prophylaxis versus single modalities in preventing venous thromboembolism in high-risk patients.

Search strategy

The Cochrane Peripheral Vascular Diseases (PVD) Group searched their Specialized Register (last searched 17 July 2007) and the Cochrane Central Register of Controlled Trials (CENTRAL) (last searched *The Cochrane Library* 2008, Issue 3). We searched the reference lists of relevant articles to identify additional trials.

Selection criteria

Randomized controlled trials (RCTs) or controlled clinical trials (CCTs) of combined intermittent pneumatic leg compression and pharmacological interventions used to prevent venous thromboembolism in high-risk patients.

Data collection and analysis

Data extraction was undertaken independently by two review authors using data extraction sheets.

Main results

Eleven studies, six of them randomized controlled trials, were identified. The trials included 7431 patients, in total. Compared with compression alone, the use of combined modalities reduced significantly the incidence of both symptomatic pulmonary embolism (PE) (from about 3% to 1%; odds ratio (OR) 0.39, 95% confidence interval (CI) 0.25 to 0.63) and deep vein thrombosis (DVT) (from about 4% to 1%; OR 0.43, 95% CI 0.24 to 0.76). Compared with pharmacological prophylaxis alone, the use of combined modalities significantly reduced the incidence of DVT (from 4.21% to 0.65%; OR 0.16, 95% CI 0.07 to 0.34) but the included studies were underpowered with regard to PE. The comparison of compression plus pharmacological prophylaxis versus compression plus aspirin showed a non-significant reduction in PE and DVT in favor of the former group. Repeat analysis restricted to the RCTs confirmed the above findings.

Authors' conclusions

Compared with compression alone, combined prophylactic modalities decrease significantly the incidence of venous thromboembolism. Compared with pharmacological prophylaxis alone, combined modalities reduce significantly the incidence of DVT but the effect on PE is unknown. The results of the current review support, especially in high-risk patients, the use of combined modalities. More studies on their role in PE prevention, compared with pharmacological prophylaxis alone, are urgently needed.

PLAIN LANGUAGE SUMMARY

Combined intermittent pneumatic leg compression and medication for the prevention of deep vein thrombosis and pulmonary embolism in high-risk patients

Deep vein thrombosis (DVT) and pulmonary embolism, or venous thromboembolism, are possible complications of surgery and trauma. These complications extend hospital stay and are associated with long-term disability and death. Patients undergoing total hip or knee replacement surgery or surgery for colorectal cancer are at high risk of venous thromboembolism. Sluggish venous blood flow, increased blood clotting and blood vessel endothelial injury are contributing factors. Treating more than one of these causes may improve prevention. Mechanical intermittent pneumatic leg compression reduces venous stasis while medications such as aspirin and anticoagulants such as low molecular weight heparin reduce blood clotting. The medications can also increase the risk of bleeding.

The present review showed that combining the two methods was more effective than a single preventative measure. Compared to compression alone, compression plus anticoagulant (combined prophylactic modalities) clearly decreased the incidence of both symptomatic pulmonary embolism (from 2.7% to 1.1%) and DVT (from 4% to 1.6%). Compared with medication with anticoagulants alone, combined compression and medication clearly reduced the incidence of DVT (from 4.21% to 0.65%). The effect on pulmonary embolism could not be determined because of the lack of events in the included

studies.

These conclusions are based on 11 controlled trials involving a total of 7431 surgery patients. The mean age of patients, where reported, was 65.5 years. Most patients had either a high-risk procedure or condition. The surgical procedures were orthopedic surgery in six trials and urological, cardiothoracic, general surgery and gynecology procedures in the other trials. The magnitude of the reduction in venous thromboembolism may be less for patients at moderate risk.

BACKGROUND

The incidence of venous thromboembolism (VTE), defined as deep vein thrombosis (DVT) or pulmonary embolism (PE), or both, is still high despite the use of contemporary prophylactic measures. High-risk patients include those undergoing total hip or knee replacement, or surgery for colorectal cancer (McLeod 2001). Experts in the field have indicated that this and similar observations are the result of failed and also omitted prophylaxis

(Goldhaber 2001; Piazza 2007). For this reason, the most recent consensus guidelines recommend combined pharmacological and mechanical prophylaxis in high-risk groups, in an effort to maximize thromboprophylaxis (Geerts 2004; Nicolaides 2006). It is likely that mechanical methods increase the efficacy of thromboprophylaxis and reduce death and morbidity rates without increasing bleeding risk.

OBJECTIVES

The aim of this review was to assess the efficacy of combined intermittent pneumatic leg compression (IPC) and pharmacological prophylaxis versus single modalities in preventing venous thromboembolism in high-risk patients.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs) and controlled clinical trials (CCTs).

Types of participants

Patients with a high risk of developing VTE including patients undergoing surgery and trauma patients.

Types of interventions

Combined use of IPC and pharmacological prophylaxis (including unfractionated heparin and low molecular weight heparin) compared with IPC or pharmacological prophylaxis alone. We excluded studies that used IPC for a short period of time (that is intraoperatively).

Types of outcome measures

Venous thromboembolism (symptomatic or asymptomatic) was the main outcome measure, with data on DVT and PE extracted as separate endpoints. Outcomes were assessed by: ascending venography, I-125 fibrinogen uptake test, and ultrasound scanning for DVT; and pulmonary angiography or scintigraphy, computed tomography (CT), angiography, and autopsy for PE.

Search methods for identification of studies

The Cochrane Peripheral Vascular Diseases (PVD) Group searched their Specialized Register (last searched 17 July 2007) and the Cochrane Central Register of Controlled Trials (CENTRAL) (last searched *The Cochrane Library* 2008, Issue 3) for publications describing randomized, controlled trials (RCTs) and non-randomized, controlled clinical trials (CCTs) of combined intermittent pneumatic leg compression and pharmacological interventions used to prevent venous thromboembolism in high-risk patients. The PVD Group's Specialized Register contains citations of trials identified through electronic searches of MEDLINE (from 1960 to date), EMBASE (from 1980 to date), CINAHL (1982 to date); and from handsearching journals and conference proceedings.

The full list of journals that have been handsearched as well as the search strategies used to search databases are described in the editorial information about the Cochrane PVD Group in *The Cochrane Library* http://www.mrw.interscience.wiley.com/cochrane/clabout/articles/PVD/frame.html. For details of the search strategies used to search CENTRAL *see* Appendix 1; Appendix 2.

We searched the reference lists of relevant articles to identify additional trials. There was no restriction on language.

Data collection and analysis

Selection of trials

SKK and GG independently searched for studies as specified above to increase retrieval yield. The same two authors independently selected potentially relevant trials.

Quality of trials

SKK and GG independently assessed study quality. We assessed methods of randomization, if used. Complete blinding of treatment is impossible in trials involving leg compression but evidence of independent outcome assessment was sought. The Schultz scale (quality based on concealment of allocation) was used (Schulz 1995).

Data extraction

SKK and GG independently extracted the data. We used a data extraction form to record the type of patient or surgical procedure, total number of participants in the study (including those randomized and those withdrawn), the interventions used, the number of participants who reached an endpoint (DVT or PE) and the methodology used to establish this, and mortality from PE. A third author (JC) arbitrated any disagreements.

Statistical analysis

We used odds ratios (OR) and risk ratio (RR) for assessment of dichotomous outcomes of non-randomized trials and RCTs, respectively. We performed separate analysis for PE, symptomatic DVTs, and all DVTs. We also performed subgroup analysis for intervention type and for RCTs. We used the I^2 statistic to assess heterogeneity.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

A total of 11 studies were identified that met the inclusion criteria. Six were RCTs (Eisele 2007; Ramos 1996; Silbersack 2004; Turpie 2007; Westrich 2006; Woolson 1991) that studied a total of 6273 patients and five were CCTs (Bigg 1992; Borow 1983; Bradley 1993; Sieber 1997; Westrich 2005) that involved a total of 1158 patients.

Eleven other studies were excluded because: use of combined modalities was not concurrent or a different type of pharmacological prophylaxis was given in the two study groups (n = 4) (Eskander 1997; Macdonald 2003; Spinal Cord Injury T; Stannard 2006); IPC use was limited to intraoperative use (n=1) (Roberts 1975); they were controlled before and after studies (n = 3) (Frim 1992; Kamran 1998; Tsutsumi 2000); or they were case-control studies (n = 3) (Ailawadi 2001; Nathan 2006; Winemiller 1999).

The included studies evaluated orthopedic patients (n = 6) (Bradley 1993; Eisele 2007; Silbersack 2004; Westrich 2005; Westrich 2006; Woolson 1991); urology patients (n = 2) (Bigg 1992; Sieber 1997); or general surgery, cardiothoracic and gynecology patients (n = 3) (Borow 1983; Ramos 1996; Turpie 2007). Patient weighted mean age (in the eight studies that reported age, 4082 patients) was 65.5 years (Bigg 1992; Bradley 1993; Ramos 1996; Sieber 1997; Silbersack 2004; Westrich 2005; Westrich 2006; Woolson 1991).

Prophylactic methods in the control group included: IPC in seven studies, either without aspirin (Bigg 1992; Ramos 1996; Sieber 1997; Turpie 2007; Woolson 1991) or with aspirin (Westrich 2005; Westrich 2006; Woolson 1991); and pharmacological prophylaxis in four studies (Bradley 1993; Borow 1983; Eisele 2007; Silbersack 2004). The intervention group in all studies used combined modalities and none included aspirin.

Ultrasound was the main diagnostic modality to diagnose DVT and was used by most studies (Borow 1983; Eisele 2007; Silbersack 2004; Westrich 2005; Westrich 2006; Woolson 1991). PE was diagnosed mainly with scintigraphy scanning (Bigg 1992; Ramos 1996; Turpie 2007; Woolson 1991), a pulmonary angiogram (Ramos 1996; Turpie 2007), or CT scanning (Turpie 2007).

One study did not describe which diagnostic modalities were used to confirm development of symptomatic DVT or PE (Sieber 1997). One study did not report on PE rates (Eisele 2007).

Risk of bias in included studies

The randomization method was not clear in three of the six RCTs (Eisele 2007; Silbersack 2004; Westrich 2006). The studies that provided this information used random tables (Ramos 1996), a centralized computer-generated schedule (Turpie 2007), and sealed envelopes (Woolson 1991).

The five CCTs were classified according to the draft guidelines of the Cochrane Non-Randomised Studies Methods Group (NRSMG). These included two quasi-randomized CCTs (Bigg 1992; Bradley 1993) and three CCTs with concurrent controls (Borow 1983; Sieber 1997; Westrich 2005).

Quality of allocation concealment was unclear in four RCTs (Ramos 1996; Silbersack 2004; Westrich 2006; Woolson 1991). In the fifth study the personnel who performed the DVT screening were not blinded to the treatment regimens (Eisele 2007). The most recent RCT was double-blinded (Turpie 2007). In one CCT the radiologist who read the venograms was blinded to patient allocation (Bradley 1993), while In the remaining four CCTs there was no evidence of any allocation concealment.

A total of 43 patients (0.58%) were excluded. One study excluded eight patients (because of non-compliance, confinement to bed for more than one week, premature transfer to a different institution, or re-operation or discharge from hospital without ultrasonography) (Silbersack 2004). Another study excluded 11 patients because of a protocol violation (discharged before the ultrasound) (n = 6), or because they did not receive the correct study medication (n = 5) (Westrich 2006). A third study excluded 24 patients because inclusion or exclusion criteria were not met, informed consent was withdrawn, adverse events occurred, or for other reasons not stated (Turpie 2007).

One study reported a 26.5% loss to follow up (Westrich 2006), which was 1.0% of the total number of patients in this systematic review; however, short-term data were provided.

Effects of interventions

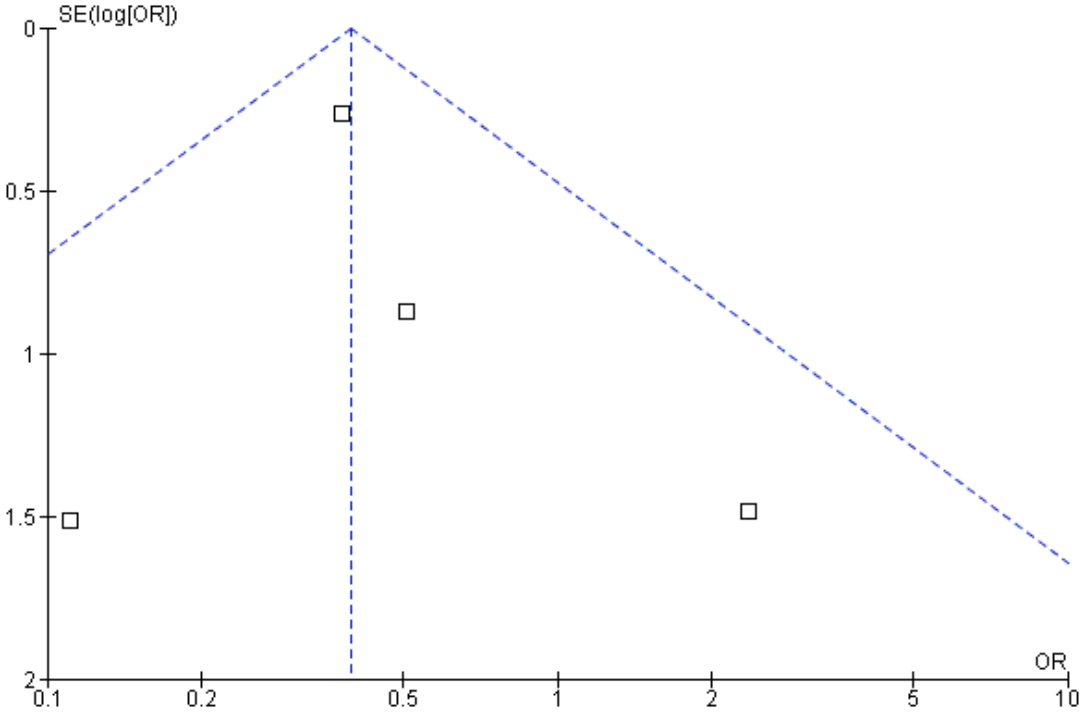
All studies

A. Compression + anticoagulant versus compression

Six of the included studies evaluated the role of combined modalities on the incidence of symptomatic PE (Bigg 1992; Borow 1983;

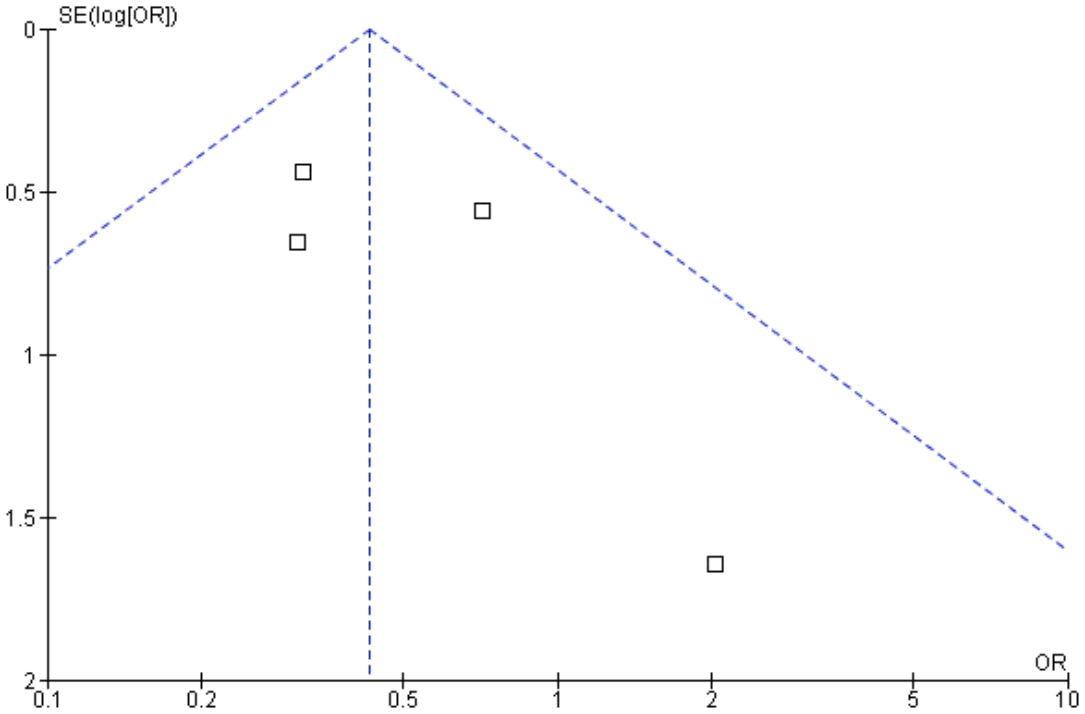
Ramos 1996; Sieber 1997; Turpie 2007; Woolson 1991). These studies showed a reduction in PE from 2.66% (56/2107) in the control group to 1.06% (28/2648) in the treatment group. The odds ratio (OR) was 0.39 (95% confidence interval (CI) 0.25 to 0.63) (Analysis 1/1) Figure 1. Results did not demonstrate heterogeneity or publication bias (I^2 = 0%).

Figure 1. Funnel plot of comparison: 1 Compression + anticoagulant versus compression, outcome: 1.1 Incidence of PE in the treatment and control groups.



Four studies investigated the role of combined modalities on the incidence of DVT (Borow 1983; Sieber 1997; Turpie 2007; Woolson 1991). These studies showed a reduction in DVT from 4.00% (35/875) in the control group to 1.59% (20/1261) in the treatment group (Figure 2). The OR was 0.43 (95% CI 0.24 to 0.76) (Analysis 1/2) Figure 2. Results did not demonstrate heterogeneity or publication bias (I^2 = 0%).

Figure 2. Funnel plot of comparison: 1 Compression + anticoagulant versus compression, outcome: 1.2 Incidence of DVT in the treatment and control groups.

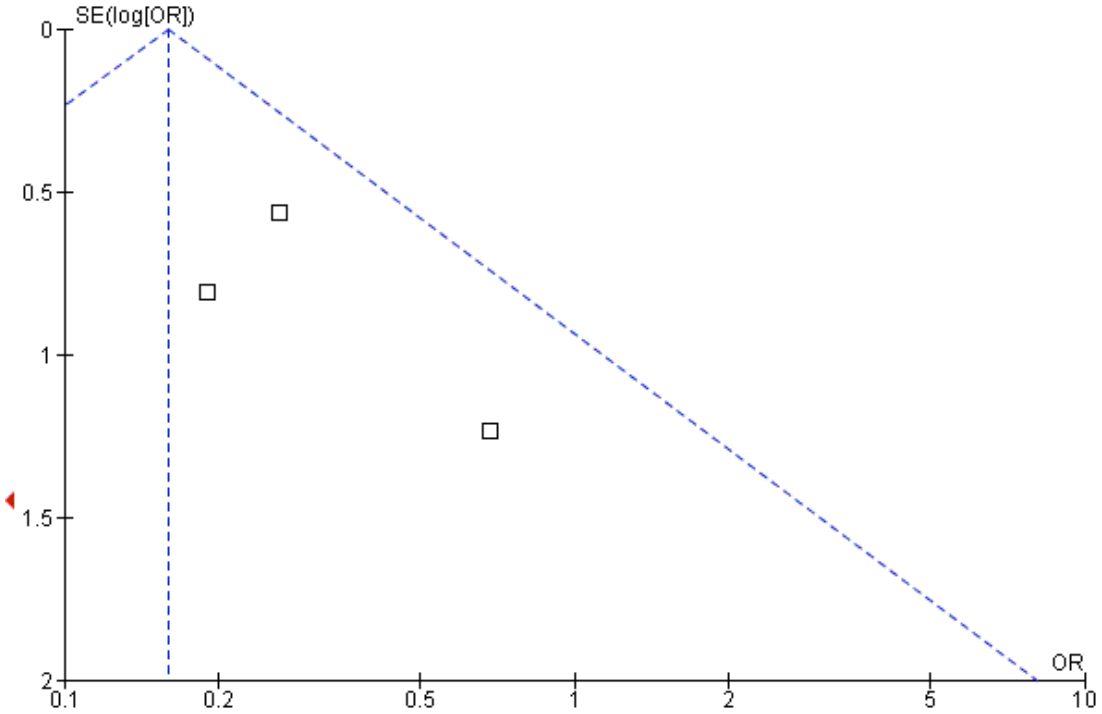


B. Compression + anticoagulant versus anticoagulant

Three studies evaluated the role of combined modalities on the incidence of symptomatic PE (Borow 1983; Bradley 1993; Silbersack 2004). The incidence of PE was 0% in both the control group (0/214) and the treatment group (0/176).

Four studies investigated the role of combined modalities on the incidence of DVT (Borow 1983; Bradley 1993; Eisele 2007; Silbersack 2004). These showed a reduction in DVT from 4.21% (47/1116) in the control group to 0.65% (7/1077) in the treatment group (Figure 3). The OR was 0.16 (95% CI 0.07 to 0.34) (Analysis 2/2) Figure 3. Results were consistent and demonstrated moderate heterogeneity (I^2= 33%).

Figure 3. Funnel plot of comparison: 2 Compression + anticoagulant versus anticoagulant, outcome: 2.2 Incidence of DVT in the treatment and control groups.



C. Compression + anticoagulant versus compression + aspirin

Three studies evaluated the role of these combined modalities on the incidence of symptomatic PE (Westrich 2005; Westrich 2006; Woolson 1991). The studies showed a non-significant reduction in PE from 0.75% (2/268) in the control group to 0% (0/337) in the treatment group.

The same studies investigated the role of combined modalities on the incidence of DVT. They showed a non-significant reduction in DVT from 11.94% (32/268) in the control group to 8.90% (30/337) in the treatment group. The OR was 0.83 (95% CI 0.48 to 1.42) (Analysis 3/2). Results did not demonstrate heterogeneity or publication bias (I^2 = 0%).

Randomized controlled trials

A. Compression + anticoagulant versus compression

Three RCTs evaluated the role of combined modalities on the incidence of symptomatic PE (Ramos 1996; Turpie 2007; Woolson 1991). These trials showed a reduction in PE from 2.71% (52/1918) in the control group to 1.17% (23/2060) in the treatment group. The RR was 0.39 (95% CI 0.24 to 0.64) (Analysis 4/1). Results did not demonstrate heterogeneity or publication bias (I^2 = 0%).

Two studies investigated the role of combined modalities on the incidence of DVT (Turpie 2007; Woolson 1991). These trials showed a reduction in DVT from 4.29% (31/722) in the control group to 1.84% (13/705) in the treatment group. The RR was 0.44 (95% CI 0.23 to 0.82) (Analysis 4/2). Results were consistent and demonstrated moderate heterogeneity (I^2 = 36%).

B. Compression + anticoagulant versus anticoagulant

Only one RCT evaluated the role of combined modalities on the incidence of symptomatic PE; this precluded any statistical analysis (Silbersack 2004).

Two RCTs investigated the role of combined modalities on the incidence of DVT (Eisele 2007; Silbersack 2004). These trials showed a reduction in DVT from 3.42% (33/965) in the control group to 0.41% (4/969) in the treatment group. The RR was 0.13

(95% CI 0.05 to 0.35) (Analysis 5/2). Results were consistent with moderate heterogeneity (I^2 = 66%).

C. Compression + anticoagulant versus compression + aspirin

Two RCTs studies evaluated the role of these combined modalities on the incidence of symptomatic PE (Westrich 2006; Woolson 1991). These trials showed a non-significant reduction in PE from 1.00% (2/201) in the control group to 0% (0/204) in the treatment group). The RR was 0.33 (95% CI 0.03 to 3.17) (Analysis 6/1). Results did not demonstrate heterogeneity or publication bias (I^2 = 0%).

The same trials investigated the role of combined modalities on the incidence of DVT. These showed a non-significant reduction in DVT from 14.92% (30/201) in the control group to 12.25% (25/204) in the treatment group. The RR was 0.81 (95% CI 0.50 to 1.33) (Analysis 6/2). Results did not demonstrate heterogeneity or publication bias (I^2 = 0%).

DISCUSSION

Our review showed that combined modalities are more effective in reducing the incidence of VTE than single modalities. Based on a variety of patient groups in several RCTs and CCTs, both DVT and PE were significantly reduced with the exception of PE in patients using combined modalities and compared with anticoagulant alone. This could be a type II error. The latter also applies to the studies that investigated the combination of compression plus anticoagulant with compression plus aspirin.

The mechanism responsible for the improved effectiveness of combined modalities may be attributed to the fact that DVT is a multifactorial process. Virchow in 1856 suggested that venous stasis, coagulopathy and endothelial injury are all causes of VTE (Virchow 1856). By treating the different causes of VTE it is expected to improve efficacy in DVT prevention. Rosendaal more recently extended Virchow's theory by proposing a model of risk factors, which considered the importance of the additive role and interaction of multiple risk factors (multiple hit model) (Rosendaal 1999). Based on the additive role of mechanical and pharmacological modalities, the results of this review suggest that venous stasis and hypercoagulopathy are truly independent risk factors. Intermittent pneumatic compression reduces venous stasis by producing active flow enhancement (Kakkos 2005) and also increases tissue factor pathway inhibitor (TFPI) plasma levels (Chouhan 1999). Unfractionated and low molecular weight heparin inhibit factor X. These totally different mechanisms of action are most likely responsible for the synergy between these two modality types.

The studies included in this review were carried out in a wide range of patient groups undergoing mainly orthopedic but also urological, cardiothoracic,general surgery and gynecology procedures. Most of the patients had a high-risk procedure or condition and, therefore, the results of this review are not necessarily applicable to different patient groups, including neurosurgical and trauma patients.

Pulmonary embolism risk-reduction rates were mostly consistent across the studies with no heterogeneity, perhaps because symptomatic PE is a clinically significant complication. In contrast, some heterogeneity was noted in the results on DVT reduction. This might have been related to the fact that methodological quality of the assessed studies was low, with allocation concealment usually unclear or not used (Schulz 1995). An alternative explanation is that the heterogeneity of the included patients who underwent various surgical procedures resulted in a variable risk of DVT.

The results of our review endorse the recommendations of the venous thromboembolism prevention guidelines that high-risk patients should receive multimodal prophylaxis (Geerts 2004; Nicolaides 2006). Most patients who received combined modalities in the studies reviewed were at high risk of developing VTE. Although the magnitude of VTE reduction was large in this patient group, the same cannot be extrapolated for patients at moderate risk. Future studies should address this question and also take into account cost-effectiveness issues; looking at benefits in terms of reduced hospital stay, rehabilitation, mortality and long-term complications, for example post-thrombotic syndrome, which add to the burden of disability in the community in the long term. Since the total number of RCTs evaluated in the current review was relatively small, future research using RCTs in other patient groups (such as patients with trauma) and confirmatory RCTs are warranted.

Further research should compare the efficacy of improved single modalities, including more effective schedule changes, with the combinations (Eriksson 2001; Kakkos 2005; King 2007).

AUTHORS' CONCLUSIONS

Implications for practice

Combined modalities should be used in the prevention of venous thromboembolism in the types of high-risk groups studied in the current systematic review.

Implications for research

Cost-effectiveness analysis should be performed in order to define the impact of this policy on health economics in both high-risk and moderate-risk patients.

More studies on the role of combined modalities (as opposed to pharmacological prophylaxis alone) in the prevention of pulmonary embolism are urgently needed.

Further research on the effect of combined use of recently introduced, improved prophylactic modalities is justified.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Bigg 1992

Methods	Study design: controlled clinical trial. Method of randomization: study was planned to be randomized and method of planned randomization was stated as patient order. Concealment of allocation: none stated. Exclusions: none. Losses to follow up: none. Intention-to-treat analysis: yes.
Participants	Country: USA. Number of participants: 68, intervention group 32; control group 36. Age (mean): intervention group 67 years; control group 65 years. Sex: male. Inclusion criteria: radical retropubic prostatectomy with bilateral pelvic prostatectomy for clinically localized prostate cancer. Exclusion criteria: none stated.
Interventions	Intervention group: unfractionated heparin (5000 iu BID, subcutaneously)and sequential compression devices with elastic stockings. Control group: sequential compression devices with elastic stockings.
Outcomes	Symptomatic PE, confirmed with ventilation-perfusion scan.
Notes	The study was planned to be randomized but due to administrative errors the randomization protocol was violated. Sequential compression devices were discontinued at 18 hours postoperatively. Study was discontinued because of bleeding complications associated with heparin use.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	

Borow 1983

Methods	Study design: controlled clinical trial. Method of randomization: none. Concealment of allocation: not reported. Exclusions: none. Losses to follow up: none. Intention-to-treat analysis: yes.
Participants	Country: USA. Number of participants: 272. Age: not reported. Sex: not reported. Inclusion criteria: general, surgery, orthopedics, gynecology, and vascular surgery. Exclusion criteria: genitourinary surgery.
Interventions	Intervention group: sequential compression devices and pharmacological prophylaxis (unfractionated heparin or coumadin). Control group: sequential compression devices or pharmacological prophylaxis (unfractionated heparin or coumadin).
Outcomes	DVT diagnosed with I-125 fibrinogen scanning, IPG, Doppler ultrasound and venography.
Notes	Patients who received aspirin or dextran as an exclusive pharmacological modality or elastic stockings as an exclusive mechanical modality were not included in our review.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	

Bradley 1993

Methods	Study design: controlled clinical trial. Method of randomization: states that patients with an even date of birth were randomized to receive the plantar arteriovenous impulse system on the side to be operated on. Concealment of allocation: not reported other than the radiologist who read the venograms was blinded to patient allocation. Exclusions: none. Losses to follow up: none. Intention-to-treat analysis: yes.
Participants	Country: UK. Number of participants: 74. Age: mean age 70 years. Sex: not reported. Inclusion criteria: unilateral primary THA for osteoarthritis. Exclusion criteria: non-consenting patients.

Bradley 1993 (*Continued*)

Interventions	Intervention group: unfractionated heparin (5000 iu BID, subcutaneously), graduated compression stockings (TEDs), and pneumatic foot compression on the side to be operated on. Control group: unfractionated heparin (5000 iu BID, subcutaneously)and graduated compression stockings (TEDs).
Outcomes	DVT on bilateral lower extremity venography performed post-operative day 12.
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	The radiologist who read the venograms was blinded to patient allocation.

Eisele 2007

Methods	Study design: randomized controlled trial. Method of randomization: not stated. Concealment of allocation: not reported. Exclusions post randomization: none. Losses to follow up: none. Intention-to-treat analysis: yes.
Participants	Country: Germany. Number of participants:1803. Age: not reported. Sex: not reported. Inclusion criteria: total joint arthroplasty (24%); knee ligamentous and meniscal repair; tumor resection; open fixation of traumatic fractures; elective osteotomies to correct deformities of the femur, tibia, foot, and ankle; and to treat high-impact contusion injuries of the lower extremity, pelvis, abdomen, spine, and chest. Exclusion criteria: a surgery location that would interfere with the application of the pneumatic compression calf cuff and existing acute DVT.
Interventions	Intervention group: LMWH, certoparin (3000 iu 12 hours pre-op, 12 post-op then daily, subcutaneously) , compression stockings (18 to 20 mmHg), and rapid-inflation intermittent pneumatic compression. Control group: LMWH, certoparin (3000 iu 12 hours pre-op, 12 post-op then daily, subcutaneously), and compression stockings (18 to 20 mmHg).
Outcomes	Symptomatic DVT and DVT on duplex-color coded ultrasound performed on the day of discharge.
Notes	"The DVT prophylaxis regimen was randomly assigned in the operating theater at the time of completion of surgery and the randomization was stratified by age." No information on PE was provided.

Risk of bias

Eisele 2007 (*Continued*)

Item	Authors' judgement	Description
Allocation concealment?	Unclear	The personnel who performed the DVT screening were not blinded to the treatment regimens.

Ramos 1996

Methods	Study design: randomized controlled trial. Method of randomization: table of random numbers. Concealment of allocation: not reported. Exclusions post randomization: intervention group 57; control group 178. Losses to follow up: yes. Intention-to-treat analysis: no.
Participants	Country: USA. Number of participants: randomized 2786, completed 2551. Age: mean age 63.9 years. Sex: male 1782; female 769. Inclusion criteria: open heart surgery Exclusion criteria: known prior DVT; bleeding complications; intraoperative death; intolerance to IPC; or withdrawal of prophylaxis before full ambulation.
Interventions	Intervention group: unfractionated heparin (5000 iu BID, subcutaneously)and sequential compression devices. Control group: sequential compression devices.
Outcomes	Symptomatic PE, confirmed by ventilation perfusion scan and/or pulmonary angiography.
Notes	

Sieber 1997

Methods	Study design: controlled clinical trial. Method of randomization: none. Exclusions: none. Losses to follow up: none. Intention-to-treat analysis: yes.
Participants	Country: USA. Number of participants: 579. Age: mean age 65 years. Sex: male. Inclusion criteria: patients who had pelvic lymphadenectomy with or without radical retropubic prostatectomy. Exclusion criteria: none.

Sieber 1997 (*Continued*)

Interventions	Intervention group: unfractionated heparin (5000 iu BID, subcutaneously)and sequential compression devices. Control group: sequential compression devices.
Outcomes	Symptomatic DVT or PE.
Notes	Participants were assigned to heparin and control groups by the primary surgeon.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	

Silbersack 2004

Methods	Study design: randomized controlled trial. Method of randomization: not reported. Concealment of allocation: not reported. Exclusions post randomization: 8. Losses to follow up: none. Intention-to-treat analysis: no.
Participants	Country: Germany. Number of participants: 139 randomized. Age: 64 years. Sex: male 47; female 84. Inclusion criteria: primary unilateral THR or TKR. Exclusion criteria: heart failure NYHA class III/IV; stage III chronic renal insufficiency; severe peripheral arterial disease; acute thrombophlebitis; neurological disorders or arthrodeses of the lower limbs; recent anticoagulation; hemorrhagic diathesis; allergy to heparins; or active malignant disease.
Interventions	Intervention group: LMWH, enoxaparin (40 mg daily, subcutaneously)and pneumatic sequential compression. Control group: LMWH, enoxaparin (40 mg daily, subcutaneously)and class-I graduated compression stockings.
Outcomes	Symptomatic and asymptomatic DVT (on ultrasound).
Notes	

Turpie 2007

Methods	Study design: randomized, double-blind, placebo-controlled, superiority trial. Method of randomization: centralized computer-generated schedule (1:1 randomization in blocks of four and stratified by center). Concealment of allocation: yes. Exclusions post randomization: 24. Losses to follow up: none. Intention-to-treat analysis: no.
Participants	Country: USA Number of participants: 1309 randomized, 1285 randomized and treated. Age: median age 59 and 60 years in the control and treatment groups, respectively. Sex: male 635; female 650. Inclusion criteria: abdominal surgery expected to last longer than 45 min in patients aged over 40 years; or patients weighing over 50 kg. Exclusion criteria: vascular surgery with evidence of leg ischemia caused by peripheral vascular disease; unable to receive intermittent pneumatic compression or elastic stockings; pregnant women and women of childbearing age not using effective contraception; life-expectancy < 6 months; clinical signs of DVT and/or history of venous thromboembolism within the previous 3 months; active bleeding; documented congenital or acquired bleeding disorder; active ulcerative gastrointestinal disease (unless it was the reason for the present surgery); hemorrhagic stroke or surgery on the brain, spine or eyes within the previous 3 months; bacterial endocarditis or other contraindications for anticoagulant therapy; planned indwelling intrathecal or epidural catheter for more than 6 hours after surgical closure; unusual difficulty in achieving epidural or spinal anesthesia; known hypersensitivity to fondaparinux or iodinated contrast medium; current addictive disorders; serum creatinine concentration above 2.0 mg/dL in a well-hydrated patient; platelet count below 100 000 mm; or patients requiring anticoagulant therapy or other pharmacologic prophylaxis besides intermittent pneumatic compression.
Interventions	Intervention group: fondaparinux and intermittent pneumatic compression. Control group: intermittent pneumatic compression.
Outcomes	Venous thromboembolism (defined as DVT detected by mandatory screening and/or documented symptomatic DVT or PE, or both) and individual components up to day 10. Symptomatic venous thromboembolism up to day 10 and day 32. Major bleeding detected during the treatment period. Death during the treatment period and up to day 32.
Notes	Study medications were packaged in boxes of identical appearance. Of the 1309 randomized patients, 842 (64.3%) had an evaluable venogram performed and were included in the primary efficacy analysis. Major bleeding occurred in 10 patients (1.6%) and 1 patient (0.2%) of the intervention and control groups, respectively (P = 0.006).

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	

Westrich 2005

Methods	Study design: controlled clinical trial. Method of randomization: none. Concealment of alocation. none. Exclusions: none. Losses to follow up: none. Intention-to-treat analysis: yes.
Participants	Country: USA. Number of participants: 200. Age: mean age 81.3 years. Sex: male 42; female 158. Inclusion criteria: patients older than 60 years who sustained a fragility fracture to the hip; and an ability and willingness to comply with the mechanical and chemical prophylaxis protocol. Exclusion criteria: patients younger than 60 years; history of severe allergy to aspirin or warfarin; refusal to use the pneumatic compression device; multiple trauma injuries; or patients with a hip fracture that did not require surgical treatment.
Interventions	Intervention group: pneumatic sequential compression and warfarin. Control group: pneumatic sequential compression and aspirin.
Outcomes	DVT on ultrasound of the ipsilateral lower external iliac, common femoral, superficial femoral, deep femoral, and popliteal veins.
Notes	No symptomatic VTE was observed. Three patients on warfarin developed bleeding complications.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	Not used

Westrich 2006

Methods	Study design: randomized, controlled trial. Method of randomization: not reported. Concealment of allocation: not reported. Exclusions post randomization: 11. Losses to follow up: 73. Intention-to-treat analysis: no.
Participants	Country: USA. Number of participants: 275. Age: mean age 69 years. Sex: male 99; female 176. Inclusion criteria: unilateral TKA. Exclusion criteria: allergies to aspirin; congenital or acquired bleeding disorders; active ulcerative or angiodysplastic gastrointestinal disease; multiple myeloma or other paraproteinemias; pheochromocytoma; hyperthyroidism; impaired renal function; known hepatic disease; past medical history of stroke; recent brain, spinal, or ophthalmologic

Westrich 2006 (*Continued*)

	surgery; hypersensitivity to enoxaparin; cardiac complications; severe peripheral vascular diseases; chronic heart failure; severe varicose veins; history of DVT and/or PE.
Interventions	Intervention group: pneumatic sequential compression and enoxaparin. Control group: pneumatic sequential compression and aspirin.
Outcomes	DVT on ultrasound before discharge on postoperative days 3 to 5, and 4 to 6 weeks after surgery.
Notes	

Woolson 1991

Methods	Study design: randomized controlled trial. Method of randomization: sealed envelopes. Concealment of allocation: sealed envelopes. Exclusions post randomization: none. Losses to follow up: none. Intention-to-treat analysis: yes.
Participants	Country: USA. Number of participants: 196 patients who had 217 procedures. Age: mean age 65 years. Sex: male 95 procedures; female 122 procedures. Inclusion criteria: primary or revision THA. Exclusion criteria: allergy to aspirin or warfarin; recent peptic ulcer or other bleeding diathesis; receiving any drug that affects platelet function within two weeks before the operation; or patients expected to remain in bed for more than four days after the operation.
Interventions	Intervention group: pneumatic sequential compression, thigh-high graduated elastic compression stockings, and warfarin (one group); or pneumatic sequential compression, thigh-high graduated elastic compression stockings, and aspirin (second group). Control group: pneumatic sequential compression and thigh-high graduated elastic compression stockings.
Outcomes	Proximal DVT on venography, B-mode ultrasonography, or both, on discharge. Symptomatic DVT or PE, objectively diagnosed.
Notes	Warfarin dose was 7.5 or 10 mg orally on the evening before the operation, then titrated to maintain the prothrombin time at 1.2 to 1.3 times the control value. Follow up was at least 3 months for all patients. One patient in each of the three groups had a wound hematoma, that required evacuation in the two intervention group patients but not in the control group. No complications related to the use of the elastic stockings or pneumatic compression were reported.

Risk of bias

Item	Authors' judgement	Description

Woolson 1991 (*Continued*)

Allocation concealment?	Unclear	Does not mention if the sealed envelopes were sequentially numbered and opaque.

BID: twice daily
DVT: deep vein thrombosis
IPC: intermittent pneumatic compression
IPG: impedence plethysmography
iu: international units
LMWH: low molecular weight heparin
mg: milligrams
NYHA: New York Hospital Association
PE: pulmonary embolism
THA: total hip arthroplasty
THR: total hip replacement
TKR: total knee replacement

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

Ailawadi 2001	Retrospective case-control study.
Eskander 1997	Use of combined modalities was not concurrent in the intervention group.
Frim 1992	Controlled before and after study.
Gelfer 2006	Pharmacological prophylaxis was not the same in the two study groups.
Kamran 1998	Controlled before and after study.
Macdonald 2003	Pharmacological prophylaxis was not the same in the two study groups.
Nathan 2006	Prospective case-control study.
Roberts 1975	Pneumatic compression was used only intraoperatively.
Spinal Cord Injury T	Pharmacological prophylaxis was not the same in the two study groups.
Stannard 2006	Use of enoxaparin was not concurrent in the two study groups.
Tsutsumi 2000	Controlled before and after study.
Winemiller 1999	Retrospective case-control study.

DATA AND ANALYSES

Comparison 1. Compression + anticoagulant versus compression

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of PE in the treatment and control groups	6	4755	Odds Ratio (M-H, Fixed, 95% CI)	0.39 [0.25, 0.63]
2 Incidence of DVT in the treatment and control groups	4	2136	Odds Ratio (M-H, Fixed, 95% CI)	0.43 [0.24, 0.76]

Comparison 2. Compression + anticoagulant versus anticoagulant

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of PE in the treatment and control groups	3	390	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
2 Incidence of DVT in the treatment and control groups	4	2193	Odds Ratio (M-H, Fixed, 95% CI)	0.16 [0.07, 0.34]

Comparison 3. Compression + anticoagulant versus compression + aspirin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of PE in the treatment and control groups	3	605	Odds Ratio (M-H, Fixed, 95% CI)	0.33 [0.03, 3.19]
2 Incidence of DVT in the treatment and control groups	3	605	Odds Ratio (M-H, Fixed, 95% CI)	0.83 [0.48, 1.42]

Comparison 4. RCTs on compression + anticoagulant versus compression

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of PE in the treatment and control groups	3	3978	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.24, 0.64]
2 Incidence of DVT in the treatment and control groups	2	1427	Risk Ratio (M-H, Fixed, 95% CI)	0.44 [0.23, 0.82]

Comparison 5. RCTs on compression + anticoagulant versus anticoagulant

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of PE in the treatment and control groups	1	131	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
2 Incidence of DVT in the treatment and control groups	2	1934	Risk Ratio (M-H, Fixed, 95% CI)	0.13 [0.05, 0.35]

Comparison 6. RCTs on compression + anticoagulant versus compression + aspirin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of PE in the treatment and control groups	2	405	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.03, 3.17]
2 Incidence of DVT in the treatment and control groups	2	405	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.50, 1.33]

Analysis 1.1. Comparison 1 Compression + anticoagulant versus compression, Outcome 1 Incidence of PE in the treatment and control groups.

Review: Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients

Comparison: 1 Compression + anticoagulant versus compression

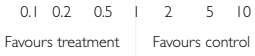
Outcome: 1 Incidence of PE in the treatment and control groups

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
Bigg 1992	0/32	4/36		0.11 [0.01, 2.15]
Borow 1983	0/78	0/52		0.0 [0.0, 0.0]
Ramos 1996	21/1355	48/1196		0.38 [0.22, 0.63]
Sieber 1997	5/478	0/101		2.36 [0.13, 42.98]
Turpie 2007	2/636	4/646		0.51 [0.09, 2.77]
Woolson 1991	0/69	0/76		0.0 [0.0, 0.0]
Total (95% CI)	**2648**	**2107**		**0.39 [0.25, 0.63]**

Total events: 28 (Treatment), 56 (Control)

Heterogeneity: $Chi^2 = 2.27$, df = 3 (P = 0.52); $I^2 = 0.0\%$

Test for overall effect: Z = 3.90 (P = 0.000097)



Analysis 1.2. Comparison 1 Compression + anticoagulant versus compression, Outcome 2 Incidence of DVT in the treatment and control groups.

Review: Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients

Comparison: 1 Compression + anticoagulant versus compression

Outcome: 2 Incidence of DVT in the treatment and control groups

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Borow 1983	1/78	0/52		1.6 %	2.03 [0.08, 50.85]
Sieber 1997	6/478	4/101		17.9 %	0.31 [0.09, 1.11]
Turpie 2007	7/636	22/646		59.1 %	0.32 [0.13, 0.74]
Woolson 1991	6/69	9/76		21.4 %	0.71 [0.24, 2.11]
Total (95% CI)	**1261**	**875**		**100.0 %**	**0.43 [0.24, 0.76]**

Total events: 20 (Treatment), 35 (Control)

Heterogeneity: $Chi^2 = 2.46$, df = 3 (P = 0.48); $I^2 = 0.0\%$

Test for overall effect: Z = 2.88 (P = 0.0039)

Analysis 2.1. Comparison 2 Compression + anticoagulant versus anticoagulant, Outcome 1 Incidence of PE in the treatment and control groups.

Review: Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients

Comparison: 2 Compression + anticoagulant versus anticoagulant

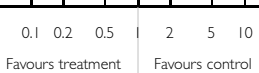
Outcome: 1 Incidence of PE in the treatment and control groups

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
Borow 1983	0/78	0/107		0.0 [0.0, 0.0]
Bradley 1993	0/30	0/44		0.0 [0.0, 0.0]
Silbersack 2004	0/68	0/63		0.0 [0.0, 0.0]
Total (95% CI)	**176**	**214**		**0.0 [0.0, 0.0]**

Total events: 0 (Treatment), 0 (Control)

Heterogeneity: $Chi^2 = 0.0$, df = 0 (P<0.00001); $I^2 = 0.0\%$

Test for overall effect: Z = 0.0 (P < 0.00001)



Analysis 2.2. Comparison 2 Compression + anticoagulant versus anticoagulant, Outcome 2 Incidence of DVT in the treatment and control groups.

Review: Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients

Comparison: 2 Compression + anticoagulant versus anticoagulant

Outcome: 2 Incidence of DVT in the treatment and control groups

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Borow 1983	1/78	2/107		3.7 %	0.68 [0.06, 7.66]
Bradley 1993	2/30	12/44		20.3 %	0.19 [0.04, 0.93]
Eisele 2007	4/901	15/902		33.4 %	0.26 [0.09, 0.80]
Silbersack 2004	0/68	18/63		42.6 %	0.02 [0.00, 0.31]
Total (95% CI)	**1077**	**1116**		**100.0 %**	**0.16 [0.07, 0.34]**
Total events: 7 (Treatment), 47 (Control)					
Heterogeneity: Chi^2 = 4.51, df = 3 (P = 0.21); I^2 =33%					
Test for overall effect: Z = 4.69 (P < 0.00001)					

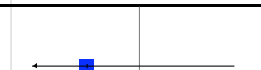
Analysis 3.1. Comparison 3 Compression + anticoagulant versus compression + aspirin, Outcome 1 Incidence of PE in the treatment and control groups.

Review: Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients

Comparison: 3 Compression + anticoagulant versus compression + aspirin

Outcome: 1 Incidence of PE in the treatment and control groups

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
Westrich 2005	0/133	0/67		0.0 [0.0, 0.0]
Westrich 2006	0/135	1/129		0.32 [0.01, 7.83]
Woolson 1991	0/69	1/72		0.34 [0.01, 8.56]
Total (95% CI)	**337**	**268**		**0.33 [0.03, 3.19]**
Total events: 0 (Treatment), 2 (Control)				
Heterogeneity: Chi^2 = 0.00, df = 1 (P = 0.97); I^2 =0.0%				
Test for overall effect: Z = 0.96 (P = 0.34)				



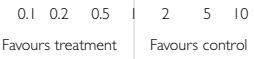
Analysis 3.2. Comparison 3 Compression + anticoagulant versus compression + aspirin, Outcome 2 Incidence of DVT in the treatment and control groups.

Review: Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients

Comparison: 3 Compression + anticoagulant versus compression + aspirin

Outcome: 2 Incidence of DVT in the treatment and control groups

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Westrich 2005	5/133	2/67		8.8 %	1.27 [0.24, 6.72]
Westrich 2006	19/135	23/129		69.6 %	0.75 [0.39, 1.46]
Woolson 1991	6/69	7/72		21.5 %	0.88 [0.28, 2.78]
Total (95% CI)	**337**	**268**		**100.0 %**	**0.83 [0.48, 1.42]**
Total events: 30 (Treatment), 32 (Control)					
Heterogeneity: Chi^2 = 0.34, df = 2 (P = 0.84); I^2 =0.0%					
Test for overall effect: Z = 0.69 (P = 0.49)					



Analysis 4.1. Comparison 4 RCTs on compression + anticoagulant versus compression, Outcome 1 Incidence of PE in the treatment and control groups.

Review: Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients

Comparison: 4 RCTs on compression + anticoagulant versus compression

Outcome: 1 Incidence of PE in the treatment and control groups

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Ramos 1996	21/1355	48/1196		0.39 [0.23, 0.64]
Turpie 2007	2/636	4/646		0.51 [0.09, 2.76]
Woolson 1991	0/69	0/76		0.0 [0.0, 0.0]
Total (95% CI)	**2060**	**1918**		**0.39 [0.24, 0.64]**
Total events: 23 (Treatment), 52 (Control)				
Heterogeneity: Chi^2 = 0.09, df = 1 (P = 0.76); I^2 =0.0%				
Test for overall effect: Z = 3.75 (P = 0.00018)				

Analysis 4.2. Comparison 4 RCTs on compression + anticoagulant versus compression, Outcome 2 Incidence of DVT in the treatment and control groups.

Review: Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients

Comparison: 4 RCTs on compression + anticoagulant versus compression

Outcome: 2 Incidence of DVT in the treatment and control groups

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Turpie 2007	7/636	22/646		71.8 %	0.32 [0.14, 0.75]
Woolson 1991	6/69	9/76		28.2 %	0.73 [0.28, 1.96]
Total (95% CI)	**705**	**722**		**100.0 %**	**0.44 [0.23, 0.82]**
Total events: 13 (Treatment), 31 (Control)					
Heterogeneity: Chi^2 = 1.56, df = 1 (P = 0.21); I^2 =36%					
Test for overall effect: Z = 2.56 (P = 0.011)					

Analysis 5.1. Comparison 5 RCTs on compression + anticoagulant versus anticoagulant, Outcome 1 Incidence of PE in the treatment and control groups.

Review: Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients

Comparison: 5 RCTs on compression + anticoagulant versus anticoagulant

Outcome: 1 Incidence of PE in the treatment and control groups

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Silbersack 2004	0/68	0/63		0.0 [0.0, 0.0]
Total (95% CI)	**68**	**63**		**0.0 [0.0, 0.0]**
Total events: 0 (Treatment), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				

Analysis 5.2. Comparison 5 RCTs on compression + anticoagulant versus anticoagulant, Outcome 2 Incidence of DVT in the treatment and control groups.

Review: Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients

Comparison: 5 RCTs on compression + anticoagulant versus anticoagulant

Outcome: 2 Incidence of DVT in the treatment and control groups

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Eisele 2007	4/901	15/902		43.9 %	0.27 [0.09, 0.80]
Silbersack 2004	0/68	18/63		56.1 %	0.03 [0.00, 0.41]
Total (95% CI)	**969**	**965**		**100.0 %**	**0.13 [0.05, 0.35]**
Total events: 4 (Treatment), 33 (Control)					
Heterogeneity: Chi^2 = 2.96, df = 1 (P = 0.09); I^2 =66%					
Test for overall effect: Z = 4.10 (P = 0.000041)					

Analysis 6.1. Comparison 6 RCTs on compression + anticoagulant versus compression + aspirin, Outcome 1 Incidence of PE in the treatment and control groups.

Review: Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients

Comparison: 6 RCTs on compression + anticoagulant versus compression + aspirin

Outcome: 1 Incidence of PE in the treatment and control groups

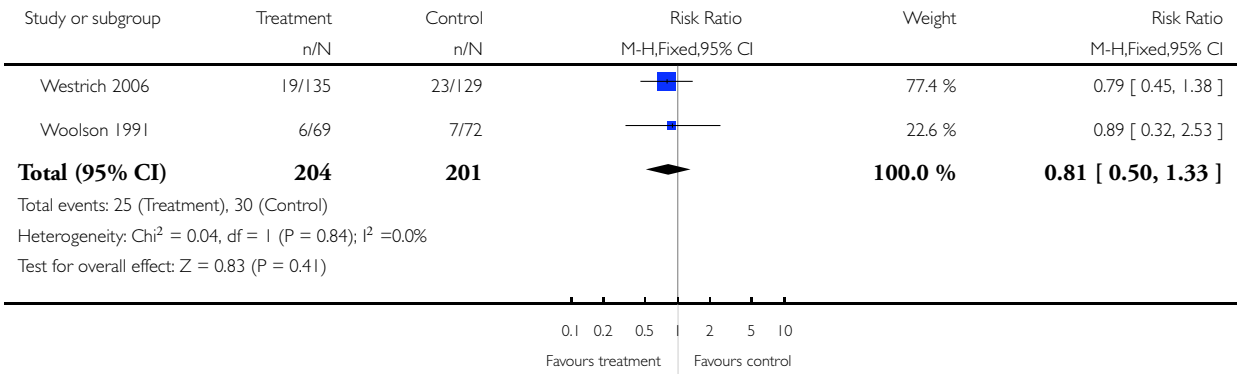
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Westrich 2006	0/135	1/129		51.1 %	0.32 [0.01, 7.75]
Woolson 1991	0/69	1/72		48.9 %	0.35 [0.01, 8.39]
Total (95% CI)	**204**	**201**		**100.0 %**	**0.33 [0.03, 3.17]**
Total events: 0 (Treatment), 2 (Control)					
Heterogeneity: Chi^2 = 0.00, df = 1 (P = 0.97); I^2 =0.0%					
Test for overall effect: Z = 0.96 (P = 0.34)					

Analysis 6.2. Comparison 6 RCTs on compression + anticoagulant versus compression + aspirin, Outcome 2 Incidence of DVT in the treatment and control groups.

Review: Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients

Comparison: 6 RCTs on compression + anticoagulant versus compression + aspirin

Outcome: 2 Incidence of DVT in the treatment and control groups



APPENDICES

Appendix 1. CENTRAL search strategy (Compression versus anticoagulants)

#1	MeSH descriptor Venous Thrombosis explode all trees
#2	MeSH descriptor Thromboembolism explode all trees
#3	MeSH descriptor Thrombosis explode all trees
#4	thromboprophyla* or thrombus* or thrombotic* or thrombolic* or thromboemboli* or thrombos*
#5	dvt* or (deep* near (vein* or ven*) near thromb*) or embol*
#6	(#1 OR #2 OR #3 OR #4 OR #5)
#7	MeSH descriptor Bandages explode all trees
#8	MeSH descriptor Occlusive Dressings explode all trees
#9	stocking* or hosiery* or tights* or sock* or bandage*
#10	bandage* or stocking* or tights* or sock* hosiery

(*Continued*)

#11	compress* near therapy
#12	compress* near treatment
#13	(#7 OR #8 OR #9 OR #10 OR #11 OR #12)
#14	MeSH descriptor Anticoagulants explode all trees
#15	anticoagulant* or heparin*
#16	low next molecular next weight next heparin*
#17	LMWH
#18	unfractionated next heparin*
#19	UFH
#20	(#14 OR #15 OR #16 OR #17 OR #18 OR #19)
#21	(#6 AND #13 AND #20)

Appendix 2. CENTRAL search strategy (Compression versus antiplatelet agents))

#1	MeSH descriptor Venous Thrombosis explode all trees
#2	MeSH descriptor Thromboembolism explode all trees
#3	MeSH descriptor Thrombosis explode all trees
#4	thromboprophyla* or thrombus* or thrombotic* or thrombolic* or thromboemboli* or thrombos*
#5	dvt* or (deep* near (vein* or ven*) near thromb*) or embol*
#6	(#1 OR #2 OR #3 OR #4 OR #5)
#7	MeSH descriptor Bandages explode all trees
#8	MeSH descriptor Occlusive Dressings explode all trees
#9	stocking* or hosiery* or tights* or sock* or bandage*
#10	bandage* or stocking* or tights* or sock* hosiery

(*Continued*)

#11	compress* near therapy
#12	compress* near treatment
#13	(#7 OR #8 OR #9 OR #10 OR #11 OR #12)
#14	MeSH descriptor Platelet Aggregation Inhibitors explode all trees
#15	Platelet near aggregation near inhibit*
#16	antiplatelet*
#17	Ticlopidin* or Clopidogrel or Ketanserin or Dipyridamole or Aspirin
#18	(#14 OR #15 OR #16 OR #17)
#19	(#6 AND #13 AND #18)

WHAT'S NEW

Last assessed as up-to-date: 16 July 2008.

16 June 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 2, 2005

Review first published: Issue 4, 2008

CONTRIBUTIONS OF AUTHORS

SKK and GG selected trials, assessed trial quality, and extracted data.

JC arbitrated disagreements.

AN, DR, and GS contributed to the text of the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

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

INDEX TERMS

Medical Subject Headings (MeSH)

Intermittent Pneumatic Compression Devices; Anticoagulants [therapeutic use]; Combined Modality Therapy [methods]; Controlled Clinical Trials as Topic; Leg [blood supply]; Pulmonary Embolism [*prevention & control]; Venous Thromboembolism [prevention & control]; Venous Thrombosis [*prevention & control]

MeSH check words

Humans