

Efficacy of compression stockings on preventing post-thrombotic syndrome: a systematic review and meta-analysis of randomized controlled trials

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Abstract

The effectiveness of elastic compression stockings (ECS) in preventing post-thrombotic syndrome (PTS) following deep vein thrombosis (DVT) remains controversial. A systematic review and meta-analysis was conducted to evaluate whether ECS prevents PTS in DVT patients. A systematic search was performed using PubMed, Scopus, and the Cochrane Library. Risk of bias was assessed using the Cochrane RoB v2 tool, and statistical analysis was conducted with Review Manager 5.4. Of 389 identified articles, 6 studies were included, comprising a total of 1589 participants. A total of 5 randomized controlled trials involving 1490 patients were analyzed. ECS use was associated with a significant reduction in overall PTS risk [odds ratio (OR) 0.45, 95% confidence interval (CI) 0.23-0.86, $p=0.02$] and mild to moderate PTS (OR 0.54, 95% CI 0.34-0.87, $p=0.01$). No significant benefit was observed for severe PTS. ECS may reduce PTS risk, particularly in mild to moderate cases.

Key words: elastic compression stocking, post-thrombotic syndrome, deep vein thrombosis.

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Introduction

Post-thrombotic syndrome (PTS) is a chronic and often progressive complication of deep vein thrombosis (DVT), caused by persistent venous obstruction and reflux.¹ PTS is characterized by symptoms such as limb pain, heaviness, swelling, cutaneous hyperpigmentation, venous ectasia, venous ulceration, and disability.^{2,3} The symptoms usually occur within 3 to 6 months following a thrombotic event, with manifestations ranging from mild to debilitating and dependent on the severity of the condition.

Several scoring systems are used to diagnose and grade PTS severity.⁴ The Villalta score, which was developed in 1994, is the most commonly used.⁵ A PTS diagnosis is confirmed by the presence of a venous ulcer or a Villalta score greater than 5. A score between 5 and 9 denotes mild severity, 10 to 14 denotes moderate severity, and 15 or higher indicates severe PTS.^{6,7}

A recent study reports that 51.1%, 30.7%, and 22.8% of patients suffering from iliofemoral, femoropopliteal, and distal DVT, respectively, are at risk of developing PTS.³ This occurs despite effective anticoagulation treatment for acute venous thromboembolism (VTE). The risk of developing PTS increases with factors such as the presence of a proximal (iliofemoral) DVT, recurrent thrombotic events, obesity, older age, female gender, primary venous insufficiency, residual venous obstruction, and inflammation.⁸⁻¹⁰

Given the limited options for managing PTS, the best approach is to prevent its occurrence. Hence, the appropriate use of pharma-

colytic thromboprophylaxis to prevent VTE in high-risk patients is an effective preventive measure.¹¹⁻¹³ The use of pharmacological thromboprophylaxis, and/or mechanical approaches such as compression devices, reduces the risk of developing blood clots, especially after surgery.¹¹⁻¹³

Graduated or elastic compression stockings (ECS) are a way of preventing PTS events in DVT patients. These medical devices are designed to apply the highest pressure at the ankle with gradually lower pressure proximally. In 1997, the first randomized controlled trial (RCT) was conducted to investigate the effect of ECS on PTS incidence.¹⁴ The study reported a significant (about 50%) reduction in the incidence of PTS after 2 years of wearing ECS with ankle pressure >30 mm Hg, compared with no ECS. In 2004, an RCT by Prandoni *et al.* also found a relative 50% reduction in the risk of developing PTS.¹⁵ A pooled meta-analysis by Musani *et al.* demonstrated a reduced incidence of PTS following ECS, but acknowledged limitations due to between-study variability.¹⁶ In the coming years, major guidelines, such as the American College of Chest Physicians (ACCP) CHEST guidelines and the UK National Institute for Health and Care Excellence (NICE) Clinical Guideline, have suggested graduated compression stockings for patients following proximal DVT.¹⁷⁻¹⁹

However, in 2014, Kahn *et al.* published a large, double-blind, multicenter RCT that contradicted earlier clinical trials and challenged earlier guidelines.²⁰ It was also the first trial to use placebo stockings in the control group instead of no stockings. The study found no significant difference in the incidence of PTS between

patients wearing active or placebo stockings. Following this publication, and a meta-analysis by Subbiah *et al.*, both ACCP and NICE guidelines were updated and revised to recommend against the use of ECS as a prevention strategy for PTS.²¹⁻²⁴ The 2020 guidelines from the American Society of Hematology also recommend against the routine use of ECS to prevent PTS.²⁵ On the other hand, the European Society for Vascular Surgery suggests the use of ECS.²⁶ This recommendation is, however, identified as one where there is conflicting evidence on the efficacy of the preventive measure (the recommendation is labelled as a class IIa).

This conflict in clinical literature and guidelines on the impact of wearing compression stockings is also seen amongst published meta-analysis papers. A review by Subbiah *et al.* reported no significant difference between stocking-wearing and non-socking-wearing DVT patients; however, recent meta-analyses have reported a significant reduction in PTS incidence with compression stockings.^{21,27,28} Currently, there appears to be no agreement on the efficacy of ECS in preventing PTS. This systematic review and meta-analysis aim to analyze results from randomized clinical trials and examine whether the use of compression stockings prevents PTS in DVT patients.

Methods

This systematic review and meta-analysis was conducted according to the guidelines presented in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.²⁹ The study protocol was registered in PROSPERO (CRD420251238883).

Research question

This review aims to examine the impact of compression stockings in the prevention of PTS in patients with DVT. The following PICO format was used and later employed in defining the inclusion criteria.

Population (P): adult patients with confirmed DVT.

Intervention (I): elastic or graduated compression stockings.

Comparison (C): placebo stockings or no stockings.

Outcome (O): PTS as primary outcome, and recurrent VTE and mortality as secondary outcomes.

Database search and study screening

A systematic literature search was conducted to identify relevant studies from inception to November 2025 indexed in PubMed, Scopus, and the Cochrane Library. The identified studies were screened in accordance with the predefined inclusion and exclusion criteria. Title and abstract screenings were conducted first, followed by a full-text review to determine eligibility for inclusion in the systematic review and meta-analysis. The keywords used for search were: “elastic compression stockings”, “graduated compression stockings”, “compression therapy”, “post-thrombotic syndrome”, “deep vein thrombosis”, “DVT”, “venous thrombosis”, and “venous thromboembolism”. These keywords were used together with Boolean operators AND and OR to generate search strings for each database.

Studies identified from the database search were subjected to a study selection process following a predefined set of inclusion criteria. Two independent reviewers, M.A. and F.S., screened titles, abstracts, and full texts. Any conflict concerning the eligibility of a study was resolved through discussion.

Eligibility criteria

For a study to be considered eligible it had to fulfill the following criteria: (i) RCT and included adult patients with confirmed DVT; (ii) patients were wearing ECS compared to placebo or no stocking, (iii) looked at and reported the cases of PTS at end of study period; and (iv) used the Villalta scoring system for assessment of PTS. The exclusion criteria were: (i) studies without a comparator group, (ii) studies comparing the duration of ECS on PTS prevention, and (iii) studies comparing different ECS pressures.

Quality assessment

The methodological quality of included papers was appraised using the Cochrane Risk of Bias Version 2 (RoB v2) tool.³⁰ Traffic light and summary plots were generated using the Robvis online visualization tool.

Data extraction

After the study selection process, data from the included studies were extracted into a predefined Excel sheet. The extracted data included author, publication year, study region, type of study design, total population demographics, treatment group details, ECS characteristics, and follow-up periods.

Statistical analysis

We conducted statistical analysis using Review Manager 5.4. The odds ratio (OR) and risk ratio (RR) were used as effect measures. A p-value of 0.05 was used as the significance threshold. To manage heterogeneity across studies, all analyses employed a random-effects model. The I^2 statistic was employed as a measure of between-study heterogeneity. An I^2 statistic <50% was considered low heterogeneity, <75% was considered moderate heterogeneity, and >75% was considered high heterogeneity.

Sensitivity analysis was performed using the leave-one-out approach, where studies are excluded, one at a time, to see which exclusion leads to a significant change in the effect measure. Additionally, publication bias was assessed by evaluating funnel plot asymmetry.

Results

Search results

The database search produced 347 non-duplicate articles. A total of 329 articles were excluded during title and abstract screening due to topic irrelevance. During full-text screening, 12 of the remaining 18 articles were excluded for various reasons, leaving only 6 studies for inclusion in this systematic review and meta-analysis. This procedure is shown in Figure 1.

Results of risk of bias assessment

A total of 3 studies had a low risk of bias, 1 had a high risk of bias, while 2 showed some concerns. Regarding assessment domains, the domain that presented the highest risk of potential bias was D2 (Bias due to deviations from unattended intervention). This is because 5 of the 6 studies were not double-blinded, meaning that either the participants or the assessors, or both, knew the study group to which the patients were assigned (Figure 2).

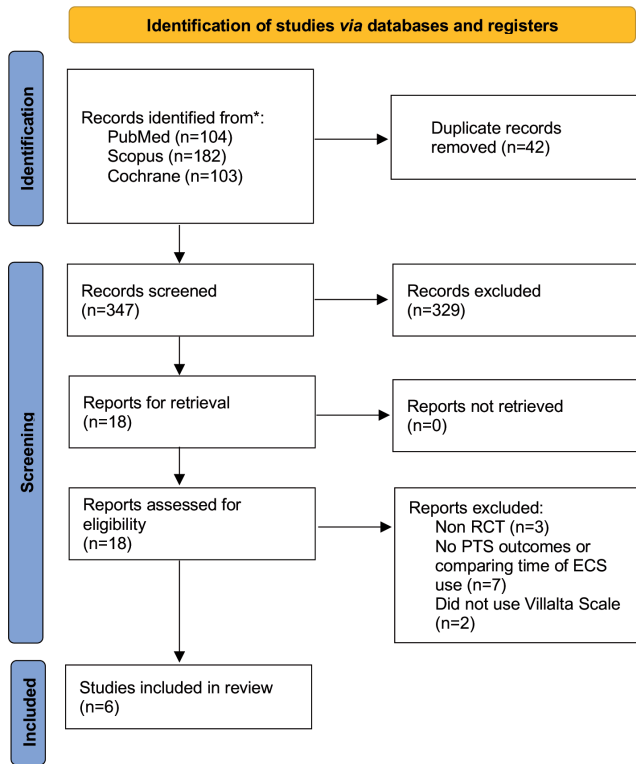


Figure 1. PRISMA flowchart showing study selection process.

Study characteristics

This systematic review included 6 RCTS. The total population was 1589 (*Supplementary Table 1*). All patients suffered from proximal DVT. 800 patients were using active compression stockings, 395 were using no stockings (no-ECS control group), and 394 were using placebo stockings. The details about the application of stockings differed across studies. ECS was adapted earliest after 2 days,³¹ and latest after 4 weeks of DVT confirmation.³² The mean duration of ECS use was 2 years across all studies, except Thapar *et al.*, which reported 1.5 years.³³ This short duration was most likely due to the trial being terminated early because recruitment failed, as it was set to be conducted during the COVID-19 pandemic. ECS compliance was high across studies. The lowest compliance rate (always or most often wore their stockings) was 56%, as reported by Kahn *et al.*²⁰

Post-thrombotic syndrome outcome

Brandjes *et al.* and Prandoni *et al.* reported a 50% reduction in PTS incidence with ECS use.^{14,15} Prandoni *et al.* reported an adjusted hazard ratio (aHR) of 0.49 [95% confidence interval (CI) 0.29 to 0.84; $p=0.011$].¹⁵ Yang *et al.* reported a RR of 0.726 (95% CI 0.547 to 0.964; $p=0.024$), indicating that ECS use is associated with a reduced risk of PTS.³² Thapar *et al.* reported fewer PTS cases in the stocking group (17 cases out of 56 patients) than in the control group (28 cases out of 55 patients).³³ On the other hand, Jayaraj and Meissner reported that the use of ECS did not affect the incidence of PTS.³¹ Kahn *et al.*, when comparing active to placebo stockings, found that ECS use did not prevent PTS (aHR=1.13 (95% CI 0.73 to 1.76; $p=0.58$)).²⁰

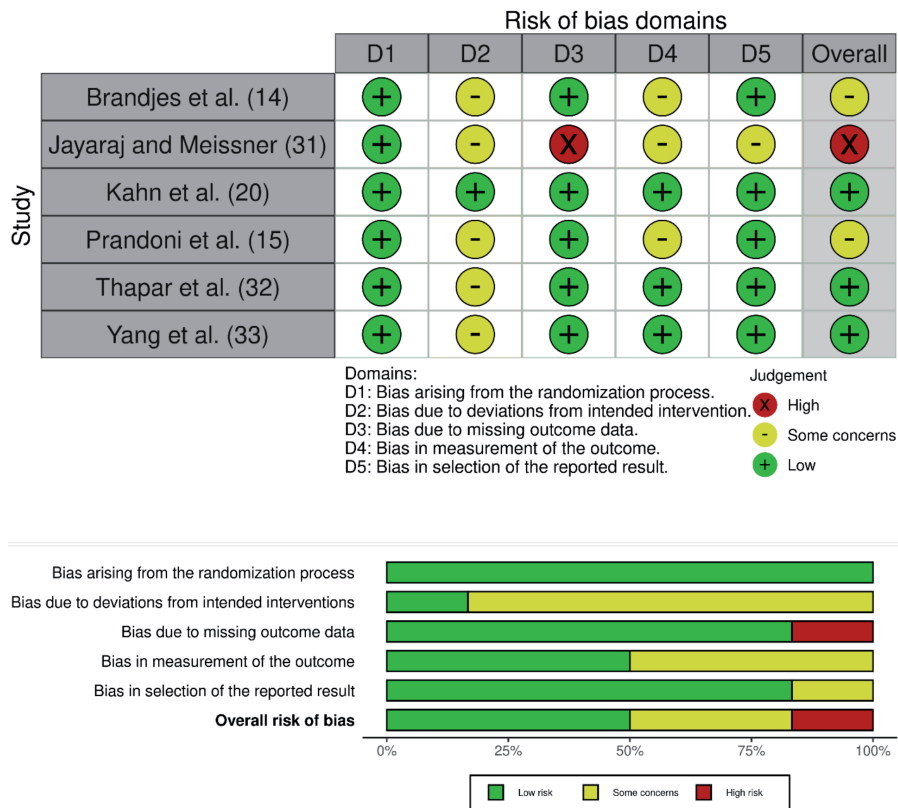


Figure 2. Risk of bias of included studies.

We performed a meta-analysis including 4 of the 5 included studies. The study by Jayaraj and Meissner was excluded from the analysis because it did not report the required data on outcome events.³¹ There were 288 cases of PTS among 751 patients who used ECS, compared with 368 cases among 739 patients who did not use ECS. The results of this meta-analysis showed that the use of ECS after DVT significantly decreased the risk of developing PTS (OR=0.45, 95% CI 0.23 to 0.86, p=0.02) (Figure 3).

We also performed subgroup analyses to examine how the use of ECS would affect the incidence of different severities of PTS. 246

out of 751 ECS users developed mild to moderate PTS (defined by Villalta score of 5 to 14), compared to 309 out of 739 who did not wear compression stockings. The results showed that wearing compression stockings significantly reduced the risk of developing mild to moderate PTS, with an OR of 0.54 (95% CI 0.34 to 0.87), p=0.01 (Figure 4). In the intervention groups, 42 out of 751 patients developed severe PTS; this is compared to 59 out of 739 severe PTS cases in the control groups. Wearing compression stockings was found to non-significantly reduce the risk of developing severe PTS, OR=0.52 (95% CI, 0.23 to 1.18), p=0.12 (Figure 5).

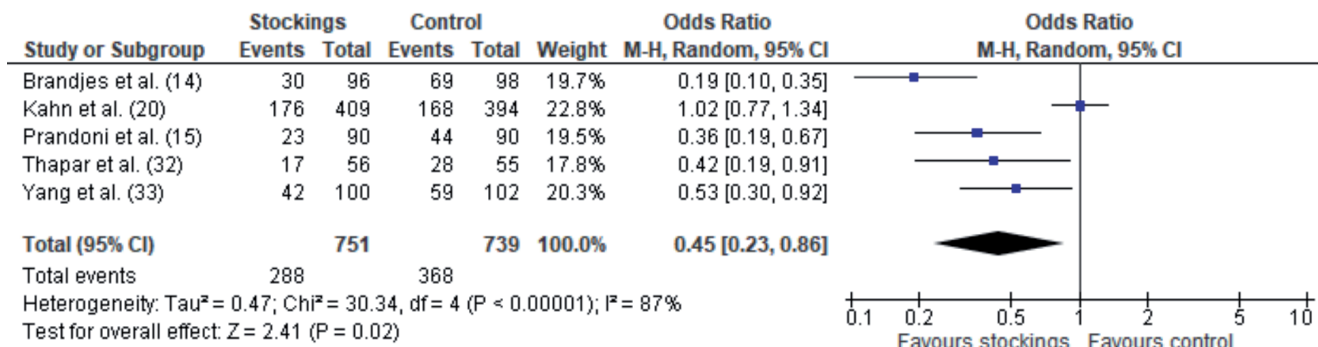


Figure 3. Forest plot on the effect of the use of elastic compression stockings on post-thrombotic syndrome incidence. CI, confidence interval.

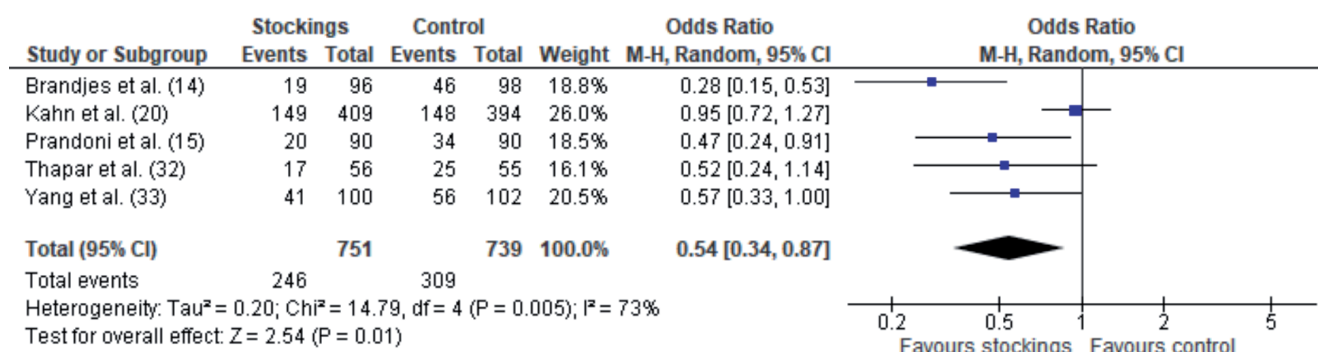


Figure 4. Forest plot on the effect of the use of elastic compression stockings on mild-to-moderate post-thrombotic syndrome incidence. CI, confidence interval.

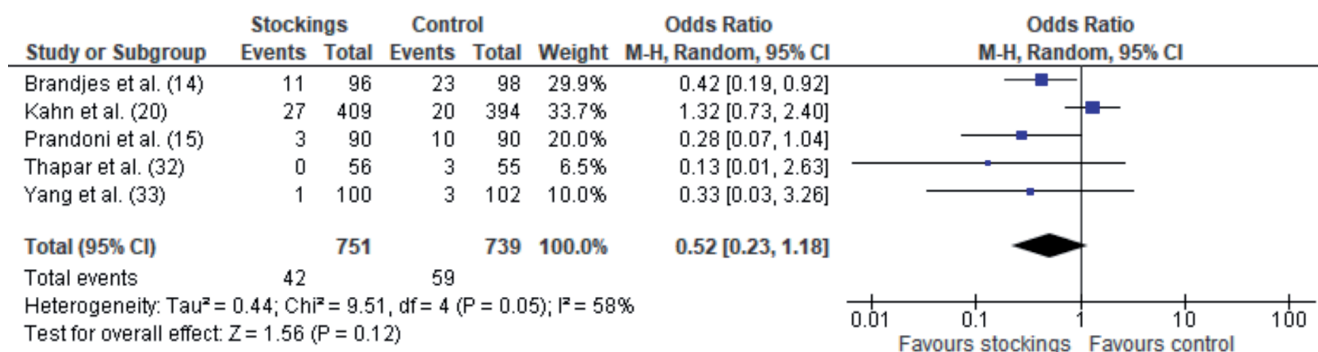


Figure 5. Forest plot on the effect of the use of elastic compression stockings on severe post-thrombotic syndrome incidence. CI, confidence interval.

Publication bias and sensitivity analysis

We also performed a sensitivity analysis of the incidence of PTS (all levels). This was conducted using the leave-one-out approach. The most considerable change in OR occurred when Brandjes *et al.* was excluded.¹⁴ The new OR was 0.56 (95% CI 0.26 to 1.21), indicating no statistically significant evidence that ECS use reduces the risk of PTS. Despite this, the overall OR still showed the protective effect of ECS, thus supporting the robustness of the findings. To assess whether any publication bias was present in our meta-analysis, we plotted a funnel plot. The effect measures (ORs) of the

included studies were symmetrically distributed along the pooled effect measure, indicating little to no publication bias in this meta-analysis (Figure 6).

Secondary outcomes

Recurrent venous thromboembolism

Out of 595 patients wearing compression stockings, 85 developed recurrent VTE, compared to 88 out of 582 in the control group. The use of ECS did not affect the risk of recurrent VTE, with a RR of 0.97 (95% CI 0.75 to 1.25), $p=0.81$ (Figure 7).

Mortality

The use of compression stockings did not affect all-cause mortality (OR=0.94, 95% CI 0.65 to 1.36), $p=0.73$ (Figure 8).

Risk factors for the development of PTS

A total of 3 studies examined the effect of confounding factors on the relationship between ECS use and PTS incidence. In Prandoni *et al.*, recurrent ipsilateral DVT (HR=3.32, 95% CI 1.04 to 10.62; $p=0.04$) and age (HR=1.36, 95% CI 1.15 to 1.60; $p=0.003$) increased the risk of developing PTS.¹⁵ In Yang *et al.*, iliofemoral DVT was a risk factor for PTS (RR=2.25, 95% CI 1.136 to 24.46).³² Jayaraj and Meissner identified obesity as a statistically significant predictor of PTS.³¹

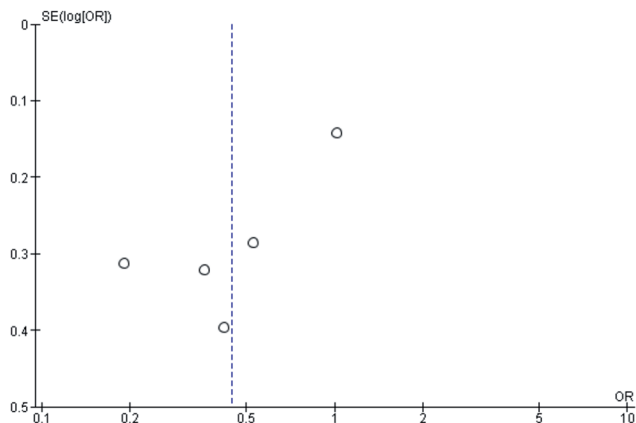


Figure 6. Funnel plot on the outcome of the post-thrombotic syndrome incidence. OR, odds ratio; SE, ...

Discussion

In this systematic review, a pooled analysis across 5 RCTs (n=1490) demonstrated that the use of compression stockings fol-

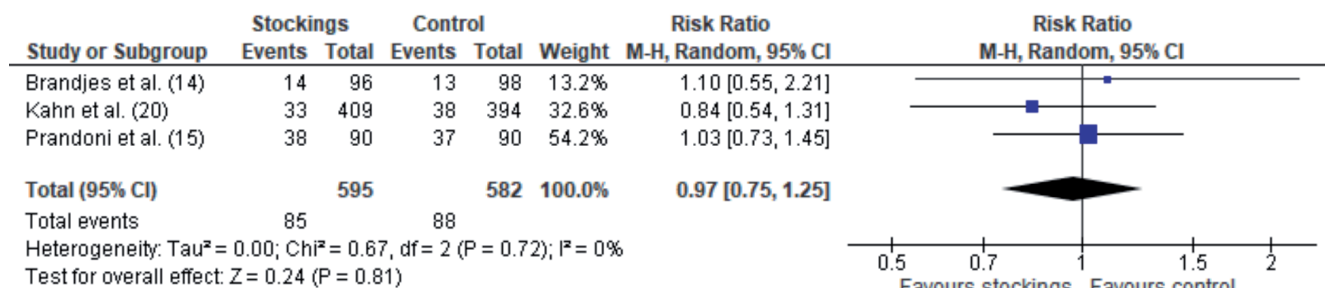


Figure 7. Forest plot on the effect of the use of elastic compression stockings on recurrence of venous thromboembolism. CI, confidence interval.

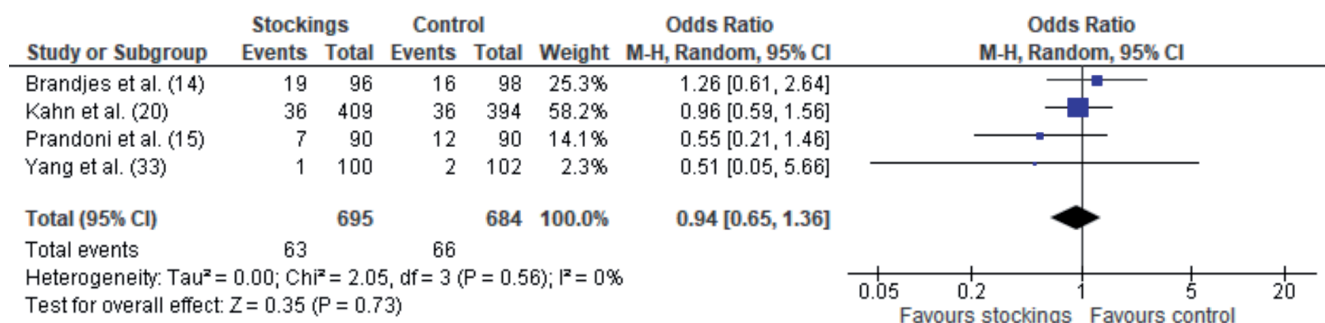


Figure 8. Forest plot for all-cause mortality. CI, confidence interval.

lowing DVT was associated with a statistically significant reduction in the overall risk of PTS (OR=0.45, 95% CI 0.23 to 0.86, $p=0.02$). Subgroup analysis also indicated a significant reduction in risk for mild-moderate PTS (OR=0.54, 95% CI 0.34 to 0.87, $p=0.01$), and a non-significant reduction in risk for severe PTS (OR=0.52, 95% CI 0.23 to 1.18, $p=0.12$). No clear effect of ECS on recurrent VTE or death was observed.

Persistent venous obstruction and valvular damage are two interconnected processes that give rise to PTS.¹ This may result in swelling, capillary leak, and chronic inflammation.^{2,3} Compression stockings are designed to reduce venous pooling and ambulatory venous pressure by applying the greatest external pressure at the ankle, with a gradual decrease up the leg.³⁴ ECS also helps the calf muscle pump more effectively during walking, which is essential for pushing blood out of the leg. They also reduce edema, limit inflammation, and might help prevent excess fluid from leaking into the tissues.^{27,35,36} These effects can interrupt the cycle of venous reflux, chronic inflammation, and fibrosis that eventually leads to PTS.³⁷ Beyond these, various other studies have demonstrated that the use of ECS counteracts venous hypertension, improves lymphatic drainage, and can even enhance tissue oxygenation.^{35,38-40} One study, using near-infrared spectroscopy, found evidence of improved tissue oxygenation in patients who wore graduated compression stockings, with higher levels of compression.³⁸

The results of this research paper are consistent with findings from some earlier meta-analyses. A review by Musani *et al.*, including 5 RCTs, found that use of ECS had a protective effect (RR=0.54, 95% CI 0.44 to 0.67, $p<0.001$) on the incidence of PTS.¹⁶ This protective effect was also reported in Nielsen *et al.* (4 RCTs; OR=0.48, 95% CI 0.36 to 0.63, $p<0.00001$) for mild-moderate PTS and (OR=0.44, 95% CI 0.28 to 0.58, $p=0.0003$) for severe PTS, Meng *et al.* (7 RCTs; RR=0.73, 95% CI 0.53 to 1.00, $p=0.05$), and Appelen *et al.* (5 RCTs; RR=0.62, 95% CI 0.38 to 1.01, $p=0.05$).^{16,27,28,41} Most of these reviews, however, call out the low quality of evidence from studies and the heterogeneity of methods across studies.

Of these 4 meta-analyses, the study by Kahn *et al.* (the first large, placebo-controlled RCT) was only included in Meng *et al.* and Appelen *et al.*^{20,28,41} This inclusion, however, did not appear to substantially alter the protective direction of the overall effect measure in these reviews. It is important to recognize that the results of this trial showed no significant difference in PTS incidence between active stocking and placebo groups (aHR=1.13, 95% CI 0.73 to 1.76; $p=0.58$).²⁰ Nielsen *et al.* did not include the study in their analysis, citing a low compliance rate, since most patients wore stockings for fewer than 4 days per week.²⁷ Kahn *et al.* acknowledged this and performed a subgroup analysis including only patients who reported frequent use.²⁰ Their subgroup analysis results still showed that ECS use did not affect PTS incidence (aHR=0.96, 95% CI 0.53 to 1.74).²⁰ However, they recommend interpreting the subgroup results with caution, since their sample size calculation did not account for subgroup effects.

The SOX trial represents the highest level of evidence due to its double-blind, placebo-controlled design.²⁰ On the other hand, all the other studies included in this meta-analysis are open-label trials, which may introduce biases due to the lack of blinding.

Across literature, there are other meta-analyses papers that report no apparent protective effect of compression stockings. Jin *et al.* reported no effect of ECS on PTS incidence (2 RCTs; OR=0.63, 95% CI 0.23 to 1.74, $p=0.37$) when using the Villalta scale to assess PTS; similarly, Subbiah *et al.*, also reported no effect of ECS (6 RCTs; OR=0.56, 95% CI 0.27 to 1.16, $p=0.12$).^{21,42} From these 2 meta-

analyses, it stands out that both OR values point towards ECS having a protective effect, but neither reached statistical significance.

Several factors can be used to explain the variability in the results of meta-analyses that find or do not find a protective effect for ECS. These include differences in population characteristics, blinding design, period between DVT confirmation and start of ECS use, compliance rate, and differences in ECS stockings (some made-to-fit, and others ready-made, different lengths). A notable factor would be control group design and blinding. The SOX trial was the only one that used a placebo stocking and a double-blind design.²⁰ Many earlier positive trials were open label with no placebo control.

This review includes 6 RCTs from different geographic regions, thus increasing the generalizability of these results. The small number of included studies precluded a reliable assessment of publication bias. The studies were varied in that they included compression stockings with different characteristics, time of adoption, and period of use.

Impact on clinical practice, recommendations, and future research

Our pooled estimate, demonstrating reduced overall and mild-moderate PTS, shows that ECS use may confer benefit for PTS prevention in many patients. However, the presence of a high-quality placebo-controlled trial and the heterogeneity across included studies argue against a one-size-fits-all mandate. We therefore favor selective, patient-centered prescription of ECS. Compression stockings can be made available for symptomatic relief and for patients at higher baseline risk of PTS. Future research should focus on standardizing trial procedures to reduce heterogeneity.

Conclusions

This systematic review and meta-analysis demonstrate that ECS reduces the overall incidence of PTS following DVT, although this benefit is clearest for mild-moderate PTS. The reduction in severe PTS was not statistically significant. However, the direction of effect is consistent, suggesting potential preventive value. Heterogeneity of study methods and a major neutral placebo-controlled trial suggest that general application may not be appropriate for all patients. Compression stockings remain a reasonable option for those with symptoms and for higher-risk patients.

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Online supplementary material:

Supplementary Table 1. Study descriptor table.

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