



# Compression Stockings for Preventing the Postthrombotic Syndrome in Patients with Deep Vein Thrombosis

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## ABSTRACT

**OBJECTIVE:** We conducted a systematic review and meta-analysis to address benefits and harms of using elastic compression stockings after lower-extremity deep vein thrombosis.

**METHODS:** We searched 7 electronic databases through January 15, 2015, including randomized controlled trials (RCTs)/quasi-randomized trials reporting on elastic compression stocking efficacy on postthrombotic syndrome incidence, recurrent venous thromboembolism, mortality, and acute pain after deep vein thrombosis. Two reviewers independently screened records, extracted data, assessed risk of bias, and assessed confidence in effect estimates using Grading of Recommendations Assessment, Development, and Evaluation methodology. We applied random-effects meta-analysis models.

**RESULTS:** We included 5 RCTs (n = 1418) reporting on postthrombotic syndrome. The hazard ratio (HR) for postthrombotic syndrome with elastic compression stockings was 0.69 (95% confidence interval [CI], 0.47-1.02). We have very low confidence in this estimate due to heterogeneity and inclusion of unblinded studies at high risk of bias. Excluding high risk of bias studies, a single large RCT at low risk of bias provided moderate-quality evidence of no effect on postthrombotic syndrome (HR 1.00; 95% CI, 0.81-1.24). Moderate-quality evidence including all 5 studies suggests no effect of elastic compression stockings on recurrent venous thromboembolism (relative risk [RR] 0.88; 95% CI, 0.63-1.24) or mortality (RR 1.00; 95% CI, 0.73-1.37, 5 studies). Moderate-quality evidence from one large RCT does not suggest effect on acute pain after deep vein thrombosis.

**CONCLUSIONS:** The highest-quality evidence available suggests no effect of elastic compression stockings on postthrombotic syndrome or pain relief, from a single large RCT. However, results for preventing postthrombotic syndrome differ substantially across studies, and future guideline updates should reflect uncertainty about treatment effects. Elastic compression stockings are unlikely to prevent death or recurrent venous thromboembolism.

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**KEYWORDS:** Compression stockings; Deep vein thrombosis; Meta-analysis; Postthrombotic syndrome

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The application of elastic compression stockings after deep vein thrombosis of the leg to prevent the development of postthrombotic syndrome is a widespread practice, and recommended in several recent guidelines.<sup>1-4</sup>

Although postthrombotic syndrome definitions vary,<sup>5-7</sup> it is generally described as a condition that follows symptomatic deep vein thrombosis and is associated with swelling and

edema of the leg, itching, ectatic veins, feeling of heaviness, cramps, pain, and paresthesias.<sup>5,8-12</sup> Several diagnostic instruments for postthrombotic syndrome exist, including the Ginsberg<sup>5</sup> and Villalta<sup>12,13</sup> scales. The incidence of postthrombotic syndrome following deep vein thrombosis varies widely in different reports, from about 20% to more than 50%<sup>5,12,14-17</sup>; the difference is due at least in part to use of different diagnostic instruments.

Mechanisms of elastic compression stocking effect may include improved venous return through external compression,<sup>18</sup> with associated reduction in edema and swelling in the extremity and improved microcirculation.<sup>12,19</sup> Elastic compression stockings may be individually tailored or off the rack,<sup>8</sup> knee or thigh high, and generally exert a pressure of around 20-40 mm Hg.<sup>9</sup> Although stockings are reportedly well tolerated,<sup>12</sup> they may be cumbersome. Patients may experience treatment durations of years as a significant burden.

Two randomized controlled trials (RCTs) have suggested that elastic compression stockings may reduce the incidence of postthrombotic syndrome by about 50%.<sup>12,20</sup> In a 2010 meta-analysis, Musani et al<sup>21</sup> concluded that venous compression is likely to be effective, although they stated that more research was needed. A recent RCT contradicts this conclusion.<sup>8</sup> We seek to explain the difference in results and provide the best available estimate of effects.

## METHODS

We prespecified eligibility criteria, literature searches, methods of risk-of-bias assessment, and intended analysis methods, including subgroup analyses. The protocol is publicly available in the PROSPERO database.<sup>22</sup>

## Literature Searches

We searched PubMed, Ovid MEDLINE and Ovid EMBASE (including EMBASE Classic), and Cochrane CENTRAL for relevant primary studies through January 15, 2015. We excluded MEDLINE-indexed journals in EMBASE searches. We searched the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, the National Health Service Economic Evaluation Database, and the National Health Service Health Technology Assessment Database for previous reviews on the topic, and screened their bibliographies for relevant primary studies.

We performed searches using population and intervention free-text synonyms and database-specific controlled vocabulary, applying no date, language, or outcome restrictions,

nor any filters. **Appendix Table 1** (available online) presents full search strategies. One author (CFB) developed the search strategies; medical librarians subsequently reviewed them and confirmed their comprehensiveness.

## CLINICAL SIGNIFICANCE

- Elastic compression stockings are applied to prevent postthrombotic syndrome after lower-extremity deep vein thrombosis.
- Treatment with compression stockings may last for years, constituting a significant burden for patients.
- We find that the highest-quality evidence available does not indicate an effect of compression stockings to prevent the postthrombotic syndrome, nor on the recurrence of thrombosis, mortality, or pain in the acute phase of deep vein thrombosis.

## Study Selection

We included RCTs and quasi-randomized trials (ie, based on birth date, order of enrollment into study) with patients having experienced a symptomatic lower-extremity deep vein thrombosis, objectively verified by ultrasonography or another suitable radiographic modality. Patients must either have started treatment with elastic compression stockings within 3 months of the deep vein thrombosis, or if stocking treatment was begun after 3 months, they must have been symptom free at treatment initiation. We included only studies reporting either of the patient-important outcomes postthrombotic syndrome, venous thromboembolism recurrence or death; or one outcome not prespecified in the protocol: pain in the acute phase after deep vein thrombosis.

We de-duplicated search outputs using EndNote X7.<sup>23</sup> In the first round of screening, reviewers (CFB and AK) excluded obviously irrelevant records after independent duplicate examination of title and abstract. We retrieved full texts for citations deemed potentially eligible by at least one reviewer, and screened them in duplicate using the Web-based screening software Covidence.<sup>24</sup> Disagreements were resolved through discussion.

## Data Extraction and Quality Assessment

Reviewers (CFB and either POV or AK) extracted data in duplicate and independently, using standardized forms and resolving disagreements through discussion. We extracted data on participant characteristic, intervention, and control; timing of start of treatment; follow-up time; and statistical data for the prespecified outcomes, important adverse effects, and pain in the acute phase after deep vein thrombosis. Data on postthrombotic syndrome were recorded as dichotomous or survival data, or treatment effects on a relevant diagnostic instrument. For studies not presenting hazard ratios (HRs) for postthrombotic syndrome, we extrapolated these from Kaplan-Meier plots where available using the method of Parmar et al.<sup>25</sup> Two reviewers (CFB and POV) independently assessed risk of bias of each study for each outcome using the Cochrane risk-of-bias tool<sup>26</sup> (**Appendix Table 2**, available online).<sup>5,8,12,20,27-33</sup>

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