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Effectiveness of Intermittent Pneumatic Compression Devices for Venous Thromboembolism Prophylaxis in High-Risk Surgical Patients: A Systematic Review

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A B S T R A C T

Background: Thromboprophylaxis regimens include pharmacologic and mechanical options such as intermittent pneumatic compression devices (IPCDs). There are a wide variety of IPCDs available, but it is uncertain if they vary in effectiveness or ease of use. This is a systematic review of the comparative effectiveness of IPCDs for selected outcomes (mortality, venous thromboembolism [VTE], symptomatic or asymptomatic deep vein thrombosis, major bleeding, ease of use, and adherence) in postoperative surgical patients.
Methods: We searched MEDLINE (via PubMed), Embase, CINAHL, and Cochrane CENTRAL from January 1, 1995, to October 30, 2014, for randomized controlled trials, as well as relevant observational studies on ease of use and adherence.
Results: We identified 14 eligible randomized controlled trials (2633 subjects) and 3 eligible observational studies (1724 subjects); most were conducted in joint arthroplasty patients. Intermittent pneumatic compression devices were comparable to anticoagulation for major clinical outcomes (VTE: risk ratio, 1.39; 95% confidence interval, 0.73-2.64). Limited data suggest that concurrent use of anticoagulation with IPCD may lower VTE risk compared with anticoagulation alone, and that IPCD compared with anticoagulation may lower major bleeding risk. Subgroup analyses did not show significant differences by device location, mode of inflation, or risk of bias elements. There were no consistent associations between IPCDs and ease of use or adherence.
Conclusions: Intermittent pneumatic compression devices are appropriate for VTE thromboprophylaxis when used in accordance with current clinical guidelines. The current evidence base to guide selection of a specific device or type of device is limited.

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Venous thromboembolism (VTE), which encompasses deep vein thrombosis (DVT) and pulmonary embolism (PE), is a leading cause of morbidity and mortality in high-risk surgical patients [1–3]. Joint arthroplasty in particular is associated with an increased risk of VTE [4,5]. Without prophylaxis, the incidence of 35-day symptomatic VTE events after joint arthroplasty is high, with an estimated baseline rate of 4.3% [6]. Although the risk of symptomatic VTE is highest in the first 6 weeks after surgery, this risk can remain elevated for up to 3 months after surgery [7].

Clinical practice guidelines generally recommend *either* pharmacologic *or* mechanical VTE prophylaxis. Pharmacologic options include anticoagulation (eg, low-molecular-weight heparin [LMWH], new oral anticoagulants, or warfarin) and aspirin, but several of these may increase the risk of bleeding [8,9]. Mechanical prophylaxis with

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intermittent pneumatic compression devices (IPCDs) is recommended, particularly in populations at high risk for bleeding [6,10,11], due to the decreased risk of major bleeding and surgical site bleeding associated with IPCDs [12–14].

It is hypothesized that IPCDs prevent DVT formation through 2 mechanisms, namely, by decreasing venous stasis and activating fibrinolysis [15–17]. There are a wide variety of IPCDs currently available that differ in anatomical location of the sleeve garment, number and location of air bladders, patterns of compression cycles, and duration and rapidity of inflation time and deflation time [18,19]. In general, IPCDs can be categorized into either single-chamber or multichamber devices, constant pressure or sequential pressure devices, slow-gradual or rapid inflation devices, and portable or nonportable devices. Although some clinical guidelines recommend certain device features such as portability [6], in general, guidelines do not make recommendations for or against specific IPCDs or device categories. Therefore, it remains unclear which of these approaches works best for specific patient populations.

The objective of this report is to evaluate the comparative effectiveness of IPCDs in postoperative surgical patients. There is a major gap in the existing literature on which specific populations will benefit from IPCD prophylaxis, and whether IPCDs vary importantly in VTE outcomes, adherence, and ease of use. This study addresses these gaps with a methodologically sophisticated systematic review.

Methods

We followed a standard protocol for this review (PROSPERO registration CRD42014015157). Each step was pilot tested to train and calibrate study investigators. A technical report that fully details our methods and results is available online [20]. The questions addressed are as follows:

1. In hospitalized surgical patients at high risk for VTE,
   a. what is the comparative effectiveness of VTE prophylaxis with IPCDs vs VTE prophylaxis with pharmacologic agents for VTE events, VTE-related mortality, and adverse events?
   b. what is the comparative effectiveness of different IPCDs when compared with one another for preventing VTE events?
2. When used for VTE prophylaxis, do different IPCDs differ in ease of use or adherence?

Search Strategy

We searched MEDLINE, Embase, CINAHL, and Cochrane CENTRAL from January 1, 1995, to October 30, 2014, for peer-reviewed, English-language randomized controlled trials (RCTs) for question 1. We used Medical Subject Heading terms and selected free-text terms for IPCDs and the conditions of interest, along with validated search terms for RCTs [21]. For question 2, we also used terms to identify relevant observational studies (Appendix A). We reviewed bibliographies of included trials and systematic reviews [18,22–31] for missed publications. To assess for possible publication bias, we searched ClinicalTrials.gov (www.clinicaltrials.gov) to identify completed but unpublished studies meeting our eligibility criteria.

Study Selection

Using prespecified inclusion and exclusion criteria, 2 trained investigators assessed titles and abstracts. The full text of potentially eligible studies was retrieved for further review. We included RCTs that compared an IPCD to pharmacologic prophylaxis or another IPCD in adults undergoing hip or joint arthroplasty, and other surgical patients at increased risk for VTE (for full criteria, see Appendix B). Eligible studies reported VTE outcomes at 4 weeks or longer from randomization or study enrollment. We also included comparative quasi-experimental or cohort studies to address ease of use and adherence outcomes. Disagreements on inclusion, exclusion, or the major reason for exclusion were resolved by discussion or by a third investigator.

Data Abstraction and Quality Assessment

Data abstractions were performed by a trained investigator and confirmed by a second. We abstracted patient descriptors; setting, features, and dose of the intervention (including timing and duration for IPCDs); characteristics of the comparator; outcomes; and risk of bias elements. When data were incomplete or missing, we contacted authors to request the data.

We assessed the quality (risk of bias) of each study and summarized the overall risk of bias for each study as low, moderate, or high. We used the key risk of bias criteria described in the Agency for Healthcare Research and Quality's *Methods Guide for Effectiveness and Comparative Effectiveness Reviews* [32] (Appendix C). Detailed quality ratings for each included study are described in Appendix C.

Data Synthesis and Strength of Evidence

We grouped studies into those that enrolled participants undergoing joint arthroplasty and other surgery. We used R (R Foundation for Statistical Computing, Vienna, Austria) with the metafor package [33] to calculate summary risk ratios (RRs). We used a random-effects model, and because of the relatively small number of studies, we used the Knapp and Hartung method to adjust the standard errors of the estimated coefficients [34,35]. We evaluated for statistical heterogeneity in treatment effects using Cochran Q and I^2 statistics. We used subgroup analyses to explore potential sources of heterogeneity, specifying a priori: foot, calf, or thigh location of the IPCD; concurrent use of anticoagulation; and risk of bias elements. In some instances, planned subgroup analyses could not be performed because subgroups did not meet the prespecified minimum of 3 studies per subgroup. When there were at least 3 studies at low or moderate risk of bias, we performed sensitivity analyses to compute summary estimates after excluding studies at high risk for bias. Publication bias was assessed using findings from a search of ClinicalTrials.gov. Funnel plots were not used because analyses did not meet the minimum threshold of at least 10 studies for meaningful analysis.

Where quantitative synthesis was not feasible, we analyzed the data qualitatively. We gave more weight to evidence from higher quality studies. We focused on identifying patterns in the efficacy and safety of the interventions and finding potential reasons for inconsistency in treatment effects.

Using the GRADE approach, we evaluated the overall strength of evidence (SOE) for selected outcomes (mortality, VTE, symptomatic or asymptomatic DVT, and major bleeding) as high, moderate, low, or insufficient using the following domains: risk of bias, directness, consistency of treatment effects, precision of treatment effects, and risk of publication bias [36]. These domains were considered qualitatively, and a summary rating of high, moderate, low, or insufficient SOE was assigned after discussion by 2 investigators. We calculated risk differences for outcomes with SOE ratings of low or higher. We used the pooled estimate of effect and baseline event rates from the literature (VTE, 4.3% [6]) or from the event rate in the anticoagulation arms of the included studies (DVT).

Results

From 1461 unique citations screened, 17 unique studies (14 RCTs and 3 observational studies) met the eligibility criteria after full text review (Fig. 1). A search of ClinicalTrials.gov revealed no additional or completed but unpublished trials. Fourteen RCTs (2633 subjects), conducted primarily in patients undergoing joint arthroplasty, compared the effectiveness of IPCDs to anticoagulation ($n = 10$) or other IPCDs ($n = 4$; Appendices D and E).