Meta-analysis of thromboembolic prophylaxis after total knee arthroplasty
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Authors' objectives
To assess the efficacy of four common regimes for thromboembolic prophylaxis after total knee arthroplasty (TKA): aspirin, warfarin, low molecular weight heparin (LMWH) and pneumatic compression.

Searching
MEDLINE was searched from January 1980 to December 1997 using the search criteria 'thrombosis' or 'embolism'. The authors also searched the references of retrieved papers, the proceedings and abstracts from Orthopaedic Transactions, and the haematological abstracts in Thrombosis and Haemostasis.

Study selection
Study designs of evaluations included in the review
Whilst the authors did not state a study design for inclusion a priori, they did include randomised controlled trials (RCTs), reviews, and prospective studies with single groups.

Specific interventions included in the review
Thromboembolic prophylaxis using:

1. Aspirin, at a daily dose between 325 and 650 mg.
2. Warfarin (5 or 10 mg) on the evening before or night of operation, with daily doses on the first or second day after operation with the prothrombin time kept at 1.3 to 1.5 of normal.
3. LMWH.
4. Intermittent pneumatic compression started during or after the operation, with boots or sleeves removed only for walking and physiotherapy.

Participants included in the review
Patients undergoing TKA were included.

Outcomes assessed in the review
The incidence of deep-vein thrombosis (DVT) was the primary outcome measure. Secondary outcome measures were the incidence of symptomatic and asymptomatic pulmonary embolism (PE).

Studies were excluded if they did not using routine venography and a lung scan or angiography to detect DVT and PE.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The authors devised a grading system for methodological quality, which was similar to that used by Hommes et al. (see Other Publications of Related Interest no.1), based on the following eight criteria: a prospective study, a randomised study, an adequate description of patients, blinding of the radiologist, outcome assessment of all patients, adequate description of all drop-outs, adequate prophylaxis, and adequate outcome assessment. Each study was given a score for each criterion with higher scores indicating stronger methodology; the maximum score attainable was 15 points. The authors do not state how the papers were assessed for quality, or how many of the reviewers performed the
quality assessment.

**Data extraction**
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Data were extracted for the categories of: study identification, type of study, the total number of patients, type of prophylaxis and the corresponding number of patients, and quality score. The authors of the primary studies were contacted for additional information where appropriate.

**Methods of synthesis**

*How were the studies combined?*

Pooled odds ratios (ORs) with 95% confidence intervals (CIs) and p-values were calculated using the Mantel-Haenszel method.

*How were differences between studies investigated?*

The authors do not report any tests for assessing heterogeneity.

**Results of the review**

Twenty-three studies with 6,001 participants were included in the review.

The incidence of DVT was 53% (1,701 out of 3,214 participants) in the aspirin group, 45% (541 out of 1,203 participants) in the warfarin group, 29% (311 out of 1,075 participants) in the LMWH group, and 17% (86 out of 509 participants) in the pneumatic compression group.

Intermittent pneumatic compression devices were statistically significantly better than warfarin or aspirin in preventing DVT: the OR values were 1.9 (95% CI: 1.6, 2.3, p=0.003) and 3.2 (95% CI: 2.7, 3.8, p<0.0001), respectively.

LMWH was statistically significantly better than warfarin or aspirin in preventing DVT: the OR values were 2.05 (95% CI: 1.76, 2.39, p<0.0001) and 3.47 (95% CI: 3.04, 3.96, p<0.0001), respectively.

There was no significant difference between warfarin and aspirin (OR 1.7, 95% CI: 1.5, 1.9, p=0.4), or between LMWH and intermittent pneumatic compression (OR 1.09, 95% CI: 0.9, 1.33, p=0.4).

The incidence of asymptomatic PE was 11.7% in the aspirin group (222 out of 1,901 participants), 8.2% in the warfarin group (101 out of 1,229 participants), and 6.3% in the pneumatic compression group (24 out of 378 participants). No studies with LMWH used routine lung scans.

Pneumatic compression was statistically significantly better than aspirin and warfarin in preventing asymptomatic PE: the OR values were OR 2.5 (95% CI: 1.7, 3.8, p=0.0002) and 1.7 (95% CI: 1.1, 2.6, p=0.0003), respectively.

There was no significant difference between warfarin and aspirin (OR 1.2, 95% CI: not noted, p=0.5).

The incidence of symptomatic PE was 1.3% (23 out of 1,800 participants) in the aspirin group, 0.4% (2 out of 559 participants) in the warfarin group, 0.5% (2 out of 416 participants) in the LMWH group, and 0% (0 out of 177 participants) in the pneumatic compression group.

No statistically-significant differences between groups were noted for symptomatic PE: for warfarin compared with aspirin, the OR was 2.1 (95% CI 0.9, 4.8, p=1.0); for LMWH compared with aspirin and warfarin, the ORs were 2.7 (95% CI: 0.5, 14, p=0.9) and 1.8 (95% CI: 0.2, 14, p=0.2), respectively; and for pneumatic compression compared with aspirin, warfarin and LMWH, the ORs were 6.5 (95% CI: 0.4, 106, p=0.2), 3.0 (95% CI: 0.2, 53, p=0.6) and 2.4 (95% CI: 0.1, 59, p=0.03), respectively.
Authors' conclusions
The authors state that pneumatic compression had the lowest incidence of thromboembolism and is an acceptable form of prophylaxis in TKA. Aspirin alone was inadequate. Warfarin alone is used routinely in many institutions, but it too had a greater incidence of associated thromboembolism than LMWH and pneumatic compression. Although the LMWHs appear to give a reduction in thromboembolism, complications are ubiquitous in all published studies and include haemorrhagic problems as well as thrombocytopenia. Prophylaxis for thromboembolic disease in TKA may have to include a combination of some of the above regimes to incorporate their advantages. It should be noted, however, that the authors did not examine the adverse effects of the interventions in this review, but only examined the incidence of embolism as a complication of LMWH.

CRD commentary
The author has stated the research question and inclusion and exclusion criteria. The literature search was limited by only searching one database and it is unclear whether the search was restricted to English language publications. There were no tests for publication bias and it is possible that additional relevant studies may have been missed.

The quality of the included studies was formally assessed, but was not used in further analyses in the review. The authors have not reported how the articles were selected, or who performed the selection and data extraction.

The data extraction is reported in tables and discussed in the text of the review. Additional detail on patient characteristics would have been useful. The studies were statistically combined, but there were no further tests for heterogeneity and it was not stated whether fixed-effect or random-effects models were used in the analysis.

The authors' conclusions appear to follow from the results, but should be viewed with caution because of limitations in the quality of the review process.

Implications of the review for practice and research
Practice: The authors state only that prophylaxis for thromboembolic disease in TKA may have to include a combination of the regimes studied (i.e. aspirin, warfarin, LMWH and pneumatic compression) in order to incorporate their advantages.

Research: The authors state that they are combining the use of a pneumatic compression device with warfarin or aspirin to determine if there is an additive or synergistic effect with combined therapy, but further research is required to assess this effect fully.

Bibliographic details

Original Paper URL
http://www.jbjs.org.uk

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Anticoagulants /therapeutic use; Arthroplasty, Replacement. Knee /adverse effects; Aspirin /therapeutic use; Bandages
/standards; Combined Modality Therapy; Hemorrhage /chemically induced; Heparin, Low-Molecular-Weight /therapeutic use; Incidence; Odds Ratio; Phlebography; Platelet Aggregation Inhibitors /therapeutic use; Research Design /standards; Thromboembolism /diagnosis /epidemiology /etiology /prevention & control; Treatment Outcome; Warfarin /therapeutic use

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**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.