Benefits of antithrombotic therapy after infrainguinal bypass grafting: a meta-analysis

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CRD summary
A meta-analysis to determine the benefits of antithrombotic therapy on infrainguinal bypass graft patency found that the risk of graft occlusion in the treated group was about half that in the control or placebo group. This effect persisted at 24 months' follow-up. The authors' conclusions follow from the evidence presented, but the quality of the included studies renders the results potentially unreliable.

Authors' objectives
To determine the benefits of antithrombotic therapy for maintaining vascular graft patency following infrainguinal bypass grafts.

Searching
MEDLINE (1966 to 2000) and the Cochrane Library were searched; the MeSH terms used were listed. In addition, the authors conducted a manual search of the contents of the Journal of Vascular Surgery (1988 to 2000) and the bibliographies of retrieved articles. The search was limited to papers published in the English language.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies that compared peri-operative antithrombotic (antiplatelet or anticoagulant) therapy with control (no treatment) or placebo were eligible for inclusion. The included studies used one or more of the following: ticlodipine, phenprocoumon, aspirin, dipyridamole, dicumarol and coumarin. The combinations and dosages varied; specific regimens were detailed in the review. The duration of treatment, where reported, ranged from 10 days to 10 years.

Participants included in the review
Studies of patients undergoing primary lower extremity bypass operations were eligible for inclusion. The included studies used saphenous and/or prosthetic graft material. In the included studies, the average age was 65 years, 75% of the patients were male, 45% smoked, 21% had diabetes, 35% had hypertension and 43% had intermittent claudication.

Outcomes assessed in the review
The primary outcome was graft occlusion, with or without the need for revascularisation or amputation. The secondary outcomes of interest were all-cause mortality, cerebrovascular accident, myocardial infarction, lower extremity occlusion and bleeding.

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

Assessment of study quality
Studies were assessed on basis of the independence of outcome assessment for graft occlusion, but no other assessment of validity was made. Two authors independently judged validity. It was not stated how disagreements were resolved.

Data extraction
Two authors independently extracted the data onto specially designed data abstraction forms. It was not stated how disagreements were resolved. The odds ratio (OR) for graft occlusion in the treated versus control groups was calculated.
for each study. Where one of the cells of the 2x2 table was zero, 0.5 was added to each cell.

Methods of synthesis
How were the studies combined?
Summary ORs were computed using the random-effects model of DerSimonian and Laird. Publication bias was assessed using Begg's test.

How were differences between studies investigated?
Statistical heterogeneity was investigated by summing the weighted squared deviations of each OR from the summary OR with the weights of the reciprocals of the study variances. Comparisons of the primary outcome were made for predefined subgroups (graft type, location of graft, length of follow-up and treatment type).

Results of the review
Ten RCTs involving 1,750 patients were included. The secondary outcomes were based on fewer than 10 studies.

In terms of study quality, no results on the independence of the outcome assessment were presented.

There was no evidence of publication bias.

The overall risk of graft occlusion was lower in the treated group than in the control or placebo group; the OR was 0.46 (95% CI: 0.32, 0.66). This was also the case when studies reporting 12- and 24-month follow-up were pooled separately; the ORs were 0.50 (95% CI: 0.29, 0.87) and 0.58 (95% CI: 0.39, 0.88), respectively.

The beneficial effect of treatment was stronger in the studies that compared antiplatelet drugs with placebo (OR 0.43, 95% CI: 0.27, 0.67) than in those that compared anticoagulant treatment with placebo (OR 0.54, 95% CI: 0.28, 1.04). In the analyses of antiplatelet drugs versus placebo, the significant heterogeneity was removed with the exclusion of one study, and the beneficial effect remained (OR 0.38, 95% CI: 0.24, 0.59).

The beneficial effect of antithrombotic treatment compared with control or placebo was stronger in those studies in which prosthetic grafts were used (OR 0.25, 95% CI: 0.11, 0.57) than in those studies in which saphenous vein grafts were used (OR 0.55, 95% CI: 0.41, 0.73). There was no significant beneficial effect of antithrombotic treatment in the studies in which both prosthetic and saphenous vein material was used (OR 0.64, 95% CI: 0.23, 1.81).

The beneficial effect of antithrombotic treatment compared with control or placebo was present in studies of patients with above the knee and below the knee grafts; the ORs were 0.29 (95% CI: 0.16, 0.53) and 0.46 (95% CI: 0.32, 0.66), respectively.

All-cause mortality was lower in patients who received antithrombotic treatment than in the control or placebo group (OR 0.70, 95% CI: 0.51, 0.95). In terms of adverse events, there was no statistically significant difference between the treated and control groups for cerebrovascular accident, myocardial infarction, lower extremity amputation or bleeding, though there was a trend towards an increased risk of bleeding.

Authors’ conclusions
Antithrombotic therapy decreases the risk of graft occlusion in patients undergoing lower limb bypass operations by about 50% at 12 months, and is still protective at 24 months after the operation.

CRD commentary
The authors had a clear review question and inclusion/exclusion criteria in terms of the study design and participants. A range of relevant sources was searched, but it is possible that some pertinent trials might have been omitted since the search strategy was limited to papers in English and there were no specific attempts to locate unpublished studies. The methods used to select studies, extract the data and assess validity were not described in detail, but it appears that some efforts were made to reduce errors and bias in the review process (duplicate data extraction onto standardised forms).
Only one aspect of study quality was assessed (independence of the outcome assessment) and the findings were not considered in the context of study quality.

Relevant details of the participants in the individual studies were provided. It appeared appropriate to pool the studies. Statistical heterogeneity was assessed and investigated in a sensitivity analysis. While the authors’ conclusions follow from the evidence presented, it is unclear whether the quality of the included studies can be relied upon.

**Implications of the review for practice and research**

Practice: The authors concluded that patients undergoing lower limb bypass surgery should be considered for antithrombotic therapy to improve graft patency.

Research: The authors stated that the use of antithrombotic therapy to reduce lower limb amputation deserves further study. They also stated that further research is required to determine which antithrombotic agent is of most benefit, and what the role of antiplatelet agents is, either alone or in combination with anticoagulant drugs.

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