Long-term effect of chronic oral anticoagulation with warfarin after acute myocardial infarction

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CRD summary
This review concluded that long-term oral anticoagulation with warfarin did not reduce mortality or reinfarction after myocardial infarction, although there was a significantly higher rate of bleeding balanced by a reduction in the rate of stroke. These conclusions follow from the presented evidence but, given limitations in the conduct and reporting of the review, they may not be reliable.

Authors' objectives
To evaluate the risk and benefit of long-term oral anticoagulation with warfarin after myocardial infarction.

Searching
PubMed and Ovid SR were searched for relevant evidence published in any language. Search terms were reported, but search dates were not.

Study selection
Randomised controlled trials (RCTs) that evaluated chronic oral anticoagulation with warfarin post-infarction were eligible for inclusion in the review. Eligible trials were required to have at least 30 days follow-up and measure death as an outcome. Trials evaluating oral anticoagulation for conditions other than myocardial infarction were excluded.

Included trials compared oral anticoagulation, with or without aspirin, versus placebo or aspirin alone. Most of the included patients were male; their mean age ranging from 57 to 66 years among treatment arms. Prevalence of diabetes mellitus ranged from 6 to 38% and arterial hypertension ranged from 22 to 55% (where reported). Use of other interventions (e.g. beta-blockers, statins, coronary artery bypass grafting) were not reported by all included trials.

The authors did not state how many reviewers selected studies for the review.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Data were extracted on rates of death, stroke, new infarctions, major and minor bleeding. For each trial outcome, odds ratios (ORs) and related 95% confidence intervals (CIs) were calculated.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Odds ratios and 95% confidence intervals were pooled using fixed-effect and random-effects models, although after confirming similarity between the analyses, only fixed-effect results were presented. Statistical heterogeneity was assessed using the $\chi^2$ test.

Analyses were first performed for all patients and then only for patients randomised to aspirin versus aspirin plus oral anticoagulation.

Publication bias was assessed using funnel plots and Egger's test.

Results of the review
Ten RCTs were included in the review (n=24,542 patients). Length of follow-up ranged from three to 63 months.
There was no significant difference between oral anticoagulation patients and non-oral anticoagulation patients for the incidence of death (p=0.43) or recurrent infarction (p=0.18). There were significantly fewer strokes in patients treated with oral anticoagulation (OR 0.75, 95% CI 0.63 to 0.89; seven RCTs), but significantly more major bleeding events (OR 1.83, 95% CI 1.50 to 2.23; ten RCTs) and minor bleeding events (OR 3.46, 95% CI 2.95 to 4.05; eight RCTs).

Statistically significant heterogeneity was observed for the outcomes of new infarctions, stroke and minor bleeding events. There was no evidence of publication bias (p=0.73).

Similar results were reported for the analysis that compared only patients randomised to aspirin versus aspirin plus oral anticoagulation.

**Authors' conclusions**
Chronic oral anticoagulation with warfarin did not reduce mortality or reinfarction after myocardial infarction, regardless of concomitant aspirin use. There was a significantly higher risk of bleeding in patients receiving oral anticoagulation, which was balanced by a reduction in the risk of stroke.

**CRD commentary**
The review question was clearly defined in terms of the participant, interventions, outcomes and study designs of interest. It appeared that only one electronic database was searched for published studies, so relevant evidence could have potentially been overlooked. The authors did not report using methods designed to minimise the potential for reviewer error and bias at any stage of the review process.

The quality of the included trials was not assessed, so the impact of trial quality on the findings of the review could not be determined. Established statistical techniques were used to combine trials and investigate heterogeneity and publication bias. Although some aspects of the review were well reported (e.g. exclusion of specific studies, participant details), other aspects of the review were inconsistently reported or missing (e.g. details of the minor bleeding meta-analysis).

The authors' conclusions appeared to follow from the presented evidence, but given limitations in the conduct and reporting of the review, these conclusions may not be reliable.

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

**Practice:** The authors stated that the current American College of Cardiology/American Heart Association guidelines on oral anticoagulation for post-infarction care be revised in light of the findings of this review.

**Research:** The authors stated that dedicated clinical trials may be conducted to identify selected subsets of patients who would benefit from long-term oral anticoagulation.

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