Are beta-blockers effective in patients who develop heart failure soon after myocardial infarction: a meta-regression analysis of randomised trials

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Authors' objectives
To investigate the extent to which heart failure or evidence of major cardiac dysfunction influenced the outcome, in previous trials of beta-blockers in heart failure after myocardial infarction (MI).

Searching
MEDLINE, EMBASE, BIOSIS Previews, HealthSTAR, SIGLE, IHTA, Conference Papers Index, Derwent Drug File, Dissertation Abstracts, Pascal, International Pharmaceutical Abstracts and the Science Citation Index were searched. The reference lists from each identified study, existing bibliographies and reviews were examined for relevant studies, including data from the Beta-Blocker Pooling Project (see Other Publications of Related Interest no.1).

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), without crossover, with 50 or more patients per group were eligible for inclusion. Of the included studies, all but two were double-blind. The follow-up ranged from 3 to 48 months.

Specific interventions included in the review
Studies of beta-blockers versus placebo or control, with treatment that lasted more than one month (long-term use), were eligible for inclusion. Treatment may have begun at any stage after MI and may have been commenced intravenously. The beta-blockers used in the included studies were practolol, oxprenolol, timolol, metoprolol, propranolol, sotalol, carvedilol, acebutolol and pindolol. The treatment initiation ranged from less than 6 hours to more than 2 months.

Participants included in the review
Studies in patients who had experienced a MI were eligible for inclusion. The proportion of patients with heart failure varied substantially between the included studies.

Outcomes assessed in the review
Studies that provided information on the proportion of patients with heart failure or major cardiac dysfunction, either in the original or subsequent articles, were included. The primary analysis was to examine the extent to which the proportion of patients included in each trial with heart failure influenced the relative odds of all-cause mortality in the trials.

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
Study quality was appraised on the basis of concealment of allocation, level of blinding, and loss to follow-up. 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.
The data extracted from each study included: the number of patients randomised to treatment and control, the beta-blocker used, route and dose, specific study inclusion and exclusion criteria, the duration of follow-up, and deaths from all causes.

Methods of synthesis
How were the studies combined?
A meta-analysis was conducted using a full random-effects approach, based on the Markov chain Monte Carlo simulation suited to meta-regression analysis (see Other Publications of Related Interest no.2).

How were differences between studies investigated?
A meta-regression analysis was used to investigate to what extent heart failure or evidence of major cardiac dysfunction influenced the outcomes. In the analysis, the logit transformation of the probability of death in the intervention group was attributed to a constant, the effects of treatment, the inclusion of heart failure patients and its effect on outcome. A subgroup analysis was also conducted for mortality among patients with and without heart failure or major ventricular dysfunction, using subgroup data reported in the included studies.

Results of the review
Seventeen trials (n=20,333) were included.

Overall, the effect of beta-blockade on all-cause mortality was a 22.6% (95% confidence interval, CI: 11.0, 32.3) reduction in the odds of death.

A meta-regression analysis, which investigated the influence of the proportion of patients with heart failure included, showed treatment with a beta-blocker to be associated with a non significant interaction with the presence of heart failure (odds ratio for the interaction 0.60, 95% CI: 0.32, 1.13). Therefore, the proportion of patients included with heart failure had no clear effect on the benefits of beta-blockers.

A subgroup analysis of patients with heart failure or ventricular dysfunction after MI showed similar relative benefits with beta-blockers, compared with placebo, in patients with and without heart failure or ventricular dysfunction (based on data available from eight of the included trials). Patients with heart failure were, however, at greater absolute risk and the benefits of treatment appeared to be greater in this group.

Authors' conclusions
The relative benefit of beta-blockers on mortality after a MI was similar in the presence or absence of heart failure, but the absolute benefit might be greater in patients with heart failure.

CRD commentary
The review addressed a clear question in terms of the participants, intervention, outcome and study design. The search for studies included several appropriate sources, but the dates and the search terms used were not reported. Details of the included studies were adequately presented in tables which showed the clinical heterogeneity between the trials. The methodological quality of the included studies was appraised, although only double-blinding (yes/no) and loss to follow-up were reported. The allocation concealment data were not shown, and trial quality was not mentioned in the interpretation of the review's findings. The actual conduct of the review was not described, therefore, it is not possible to assess the potential for bias and error in the paper selection, quality assessment and data extraction processes. The analysis was conducted using appropriate methods, and some of the limitations of the available data were discussed.

The conclusions appear to be consistent with the evidence presented.

Implications of the review for practice and research
Practice: The authors state that current clinical practice has changed rapidly since the majority of the included studies
were conducted. They discuss several reasons why care is needed in extrapolating their findings to current practice.

Research: The authors state that further trial evidence is desirable to confirm that beta-blockers are effective for patients with post-infarction left ventricular systolic dysfunction and/or heart failure in contemporary clinical practice. Also, that there are few direct comparisons of beta-blockers post-infarction.

**Bibliographic details**


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**Other publications of related interest**


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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.