Effect of beta-blockade on mortality in patients with heart failure: a meta-analysis of randomized clinical trials
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Authors' objectives
To evaluate the current evidence for an effect of beta-blockade treatment on mortality in patients with congestive heart failure (CHF).

Searching
MEDLINE was searched from January 1995 to February 1997. The reference lists of all articles obtained were examined, and abstracts from presentations at national meetings were included if they met the study criteria.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) of greater than 3 months' duration, where no drug crossovers were planned before the reporting of mortality.

Specific interventions included in the review
Beta-blockers (metoprolol, bisoprolol, carvedilol, bucindolol, nebivolol) without any sympathomimetic, and placebo.

Participants included in the review
Participants with a history of CHF were included. The mean age ranged from 49 to 67 years, and the proportion of males ranged from 50 to 96%.

Outcomes assessed in the review
Total mortality, cardiac death and sudden death were assessed.

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 authors performed the selection.

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

Data extraction
Two reviewers extracted the data independently.

Methods of synthesis
How were the studies combined?
The data were combined using averages of effect, weighted by the inverse of variance. For studies with no deaths in the drug or control arms, the value of 0.5 was used instead of zero for the calculations. The summary odds ratio (OR) was calculated using both the Mantel-Haenszel fixed-effect model and the random-effects model of DerSimonian and Laird (see Other Publications of Related Interest).

How were differences between studies investigated?
A test for homogeneity was performed. Differences between the subgroups were evaluated using analysis of variance as described by Hedges and Olkin (see Other Publications of Related Interest).
Results of the review
Seventeen studies with a total of 3,039 participants (1,723 randomised to beta-blockers and 1,316 randomised to control) were included.

Total mortality.
Beta-blockade treatment was associated with a significant reduction in mortality with a summary OR of 0.69 (95% confidence interval, CI: 0.54, 0.88). The summary rate-difference between the control and treatment arms in the 17 studies was 2.9 deaths per 100 patients treated (95% CI: 22, 84). This suggests a number-needed-to-treat of 35 over 9 months to prevent one death. The chi-squared test for homogeneity was 0.9.

Cardiac and sudden death mortality.
Beta-blockade treatment was associated with a significant reduction in cardiac mortality with a summary OR of 0.68 (95% CI: 0.53, 0.89). The summary rate-difference between the control and treatment arms in the 14 studies was 3.0 deaths per 100 patients treated (95% CI: 1.0, 4.8). This corresponded to one cardiac death prevented for every 33 treated (95% CI: 21, 82). For sudden cardiac death, the summary OR was 0.84 (95% CI: 0.59, 1.2) (15 trials). For non-sudden cardiac death, the summary OR was 0.58 (95% CI: 0.40, 0.83).

Ischaemic versus non-ischaemic cardiomyopathy.
The combined OR for 7 trials of participants with ischaemic cardiomyopathy (n=1,387) was 0.69 (95% CI: 0.49, 0.98). This was not significantly different from the combined OR for 9 trials of participants with non-ischaemic cardiomyopathy (n=1,436) which was 0.69 (95% CI: 0.47, 0.99).

Carvedilol versus other beta-blockers.
The combined OR was 0.54 (95% CI: 0.36, 0.81) for trials of carvedilol and 0.82 (95% CI: 0.60, 1.12) for trials of other beta-blockers. This difference was not statistically significant (p=0.1).

Authors’ conclusions
The pooled evidence suggested that beta-blockers reduce all-cause mortality in patients with CHF. Additional trials are required to determine whether carvedilol differs from other agents in its effect.

CRD commentary
This was a well-written and clearly presented review. The inclusion criteria were clearly stated and details of the studies were provided. However, the search was quite limited, with the possibility of publication bias, and the validity of the studies was not assessed. The authors’ conclusions follow from the results presented.

Implications of the review for practice and research
The pooled evidence suggested that beta-blockers reduce all-cause mortality in patients with CHF. Additional trials are required to determine whether carvedilol differs from other agents in its effect.

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