Ejection fraction improvement by beta-blocker treatment in patients with heart failure: an analysis of studies published in the literature

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Authors’ objectives
To evaluate the effect of treatment with different beta-blockers on the left ventricular ejection fraction (LVEF) at rest, in patients with congestive heart failure.

Searching
MEDLINE was searched from January 1975 through June 1997 using the following keywords: ‘heart failure’, ‘beta-blockers’ or ‘beta-adrenergic receptor blockers’, and ‘left ventricular ejection fraction’. A search was also conducted using the keyword combination of ‘heart failure’ and ‘ejection fraction’, with specific beta-blockers (metopropol, carvedilol, bucindolol, atenolol, nebivolol, bisoprolol, propranolol). The reference lists of the identified articles were also examined for additional articles that may have been missed. Only articles reported in the English language were considered. Reviews or abstracts were discarded.

Study selection
Study designs of evaluations included in the review
There was no restriction as to the type of study design included. Probable duplicates of patient findings by the same research group were excluded.

Specific interventions included in the review
Beta-blockers. The following beta-blockers (dosages not stated) were included: metopropol, carvedilol, bucindolol, atenolol, nebivolol, bisoprolol, propranolol and placebo.

Participants included in the review
Patients with congestive heart failure were included.

Outcomes assessed in the review
The outcomes assessed were the duration of follow-up and the LVEF. The LVEF was measured at rest using echocardiography, radionuclide ventriculography, or angiography. The etiology of left ventricular failure (LVF) was scored as idiopathic dilated cardiomyopathy and/or coronary artery disease.

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

Methods of synthesis
How were the studies combined?
The weighted mean difference between the LVEF at baseline and after beta-blocker therapy, and the weighted mean
follow-up, were calculated. The degree of improvement, and the statistical significance of this improvement, were noted. In studies comparing beta-blockers with placebo, the change in LVEF in the placebo group (from baseline to after treatment) was subtracted from the increase in the beta-blocker group. Therefore, in these studies, the delta LVEF presented may differ from the difference between the LVEF at baseline and after beta-blocker treatment. This approach was published previously (see Other Publications of Related Interest).

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.

Results of the review
Forty-one studies (1,785 patients), encompassing 29 studies that were placebo-controlled, were included. This included 2 of the authors’ studies using carvedilol in patients with left ventricular dysfunction and hypertension. Four hundred and fifty-eight patients were treated with metoprolol (16 studies), 1,030 with carvedilol (13 studies), 199 with bucindolol (7 studies), 10 with atenolol (1 study), 44 with nebivolol (2 studies) and 44 with propranolol (2 studies). Eleven studies examined 361 patients with idiopathic dilated cardiomyopathy, and 11 studies looked at 269 patients with ischaemic cardiomyopathy.

For patients treated with metoprolol, there was a weighted mean follow-up of 9.5 months and a mean increase in LVEF units of 7.4% (range: 3 to 16).

For patients treated with carvedilol, there was a weighted mean follow-up of 7 months and a mean increase in LVEF units of 5.7% (range: 3 to 11).

For patients treated with bucindolol, there was a weighted mean follow-up of 4 months and a mean increase in LVEF units of 4.6% (range: 0 to 8).

For patients treated with nebivolol, atenolol and propranolol combined, there was a weighted mean follow-up of 13 months and a mean increase in LVEF units of 8.6% (range: 4 to 15).

When patients with idiopathic and ischaemic cardiomyopathies were compared, the average increases in LVEF units were 8.5% (range: 3 to 16) and 6.0% (range: 3 to 11), respectively.

Information about the etiology of LVF was available for 630 patients.

Authors’ conclusions
The current analysis showed the following:

in almost all studies, significant increase in the LVEF occurred after treatment with beta-blockers; differences among the various beta-blockers were small and probably clinically insignificant; and the data suggested that there was only a small difference between patients with idiopathic and ischaemic cardiomyopathy, which is also probably clinically insignificant.

However, this type of analysis did not allow an accurate statistical comparison of the various beta-blockers, for which a meta-analysis with data for individual patients is needed. Nevertheless, the differences in improvement were small and, importantly, mean the baseline LVEF values for the different beta-blocker studies were almost identical.

CRD commentary
The authors presented a clearly stated objective and used specific inclusion and exclusion criteria. However, the literature search was limited to only English language publications and only one database (MEDLINE) was searched. This may have resulted in some important information being missed. In addition, there was no information presented on the methodological issues of conducting the review, and the validity of the included studies was not assessed. The
authors did not state which method was used to weight the studies. Also, the possible heterogeneity of the included studies was not investigated, which means that the reader is unable to assess the appropriateness of pooling the results. The combining of the placebo and non-placebo studies may lead to erroneous results because two different methods were used to calculate the LVEF.

The authors’ conclusions seem to follow on from the results.

**Implications of the review for practice and research**
The authors did not state any further implications for research, but report that there is an ongoing, large scale, placebo-controlled multicentre mortality study on metoprolol.

**Bibliographic details**

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**Other publications of related interest**

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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.