Perioperative beta blockers in patients having non-cardiac surgery: a meta-analysis
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CRD summary
This review assessed the use of β blockers for the prevention of perioperative outcomes in patients undergoing non-cardiac surgery. The authors concluded that the evidence did not support this intervention. Their conclusions are likely to be reliable.

Authors' objectives
To assess the evidence for the use of perioperative β blockers in patients having non-cardiac surgery.

Searching
PubMed, EmBASE and the Cochrane Library were searched without language restriction from January 1966 to May 2008. Search terms were reported. References of identified articles and meta-analyses were also checked.

Study selection
Randomised controlled trials (RCTs) which compared intravenous or oral β blockers with active control, placebo or no intervention, in patients with or without cardiovascular morbidities undergoing non-cardiac surgery were eligible for inclusion. Trials were required to initiate treatment in the perioperative period and to assess perioperative efficacy and safety outcomes within 30 days of the surgery. Primary outcomes were all-cause mortality, cardiovascular mortality, non-fatal myocardial infarction, non-fatal stroke, heart failure, and adverse effects including bradycardia, hypotension, and bronchospasm.

Almost all included trials were placebo-controlled and the majority included patients in the intermediate surgical risk category. Mean ages ranged from 32.9 to 74.5 years. The following β blockers were used: atenolol, bisoprolol, esmolol, labetalol, metoprolol, nadolol, oxprenolol, propanolol and timolol.

The authors did not state how the papers were selected for the review or how many reviewers performed the selection.

Assessment of study quality
Two reviewers independently assessed the studies for validity using the following criteria: allocation concealment, randomisation, blinding, attrition, and selective reporting of outcomes. Studies with a high or unclear risk of bias from the first three of these criteria were considered to be low quality. Disagreements were resolved through consensus.

Data extraction
Two reviewers independently performed the data extraction. Authors were contacted for clarification where necessary. Intention-to-treat (ITT) data were extracted where possible.

Methods of synthesis
Studies were combined in a meta-analysis and Peto odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Numbers needed to treat (NNT) or harm (NNH) were calculated. Statistical heterogeneity was assessed using the I² statistic. Sensitivity analyses were employed to assess the appropriateness of the Peto method. Subgroup analyses were carried out for the following variables: trial quality, incidence of medical risk (defined as known coronary artery disease), surgical risk category, age (mean age ≤ 60 years), duration of β blockers, use of titrated dose of blocker, adequacy of β blocker blockage, proportion of patients with perioperative bradycardia and proportion with perioperative hypotension. Where significant results were found in subgroup analyses the interaction was examined to assess the differential treatment effect. Publication bias was assessed using funnel plots or by Begg's and Egger's tests.

Results of the review
Thirty-three RCTs (N = 12,306) were included in the review. Of these 13 were considered to be at low risk of bias with 20 considered high risk.
In patients treated with beta-blockers no significant reductions were found in mortality (OR 1.20, 95% CI: 0.95, 1.51), cardiovascular mortality (OR 1.15, 95% CI: 0.85, 1.56) or heart failure (OR 1.20, 95% CI: 0.95, 1.52). There was a significantly lower risk of non-fatal myocardial infarction (OR 0.65, 95% CI: 0.54, 0.79, NNT 63) and myocardial ischaemia (OR 0.36, 95% CI: 0.26, 0.50, NNT 16) associated with treatment. However there was also a significantly increased rate of non-fatal stroke (OR 2.16, 95% CI: 1.27, 3.68, NNH 275). In addition there was a higher risk of perioperative bradycardia (OR 2.74, 95% CI: 2.29, 3.29, NNH 22) and hypotension requiring treatment (OR 1.62, 95% CI: 1.44, 1.82, NNH 17) but no difference in rates of bronchospasm. Statistical heterogeneity was low or moderate in the majority of analyses.

Detailed results of subgroup analyses were reported, indicating that a number of the findings were driven by trials with a high risk of bias.

There was no evidence of publication bias.

**Authors' conclusions**
The evidence did not support the use of blocker therapy for the prevention of perioperative clinical outcomes in patients having non-cardiac surgery.

**CRD commentary**
The review question and the inclusion criteria were clear. The lack of language restriction reduced the chance of language bias, while publication bias was assessed appropriately. The authors reported using methods designed to reduce reviewer bias and error for the data extraction and validity assessment but not for the selection of studies. An appropriate validity assessment was conducted, the results of which were used to inform the synthesis. The use of meta-analyses was appropriate and appropriate investigations of heterogeneity were carried out. Although a large number of subgroup analyses were undertaken, the authors noted the possible impact of multiple comparisons and employed appropriate caution in their interpretation. The authors' conclusions accurately reflected the results of the review and are likely to be reliable.

**Implications of the review for practice and research**
Practice: The authors stated that β blockers should not be routinely used for perioperative treatment of patients undergoing non-cardiac surgery unless patients are already taking them for clinically indicated reasons. They also stated that the ACC/AHA guidelines committee should reduce their support for the use of blockers in patients having non-cardiac surgery until conclusive evidence becomes available.

Research: The authors did not state any implications for further research.

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