

β blockers for elective surgery in elderly patients: population based, retrospective cohort study

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Abstract

Objective To test whether atenolol (a long acting β blocker) and metoprolol (a short acting β blocker) are associated with equivalent reductions in risk for elderly patients undergoing elective surgery.

Design Population based, retrospective cohort analysis.

Setting Acute care hospitals in Ontario, Canada, over one decade.

Participants Consecutive patients older than 65 who were admitted for elective surgery, without symptomatic coronary disease.

Main outcome measure Death or myocardial infarction.

Results 37 151 patients were receiving atenolol or metoprolol before surgery, of which the most common operations were orthopaedic or abdominal procedures. As expected, the two groups were similar in demographic characteristics, medical therapy, and type of surgery. 1038 patients experienced a myocardial infarction or died, a rate that was significantly lower for patients receiving atenolol than for those receiving metoprolol (2.5% *v* 3.2%, $P < 0.001$). The decreased risk with atenolol persisted after adjustment for measured demographic, medical, and surgical factors; extended to comparisons of other long acting and short acting β blockers; was accentuated in analyses that focused on patients with the clearest evidence of β blocker treatment; and reflected the immediate postoperative interval.

Conclusions Patients receiving metoprolol do not have as low a perioperative cardiac risk as patients receiving atenolol, in accord with possible acute withdrawal after missed doses.

Introduction

Myocardial infarction and death are common perioperative complications after elective surgery.¹⁻³ β blockers are a medical treatment that may reduce the perioperative cardiac risk associated with surgery.⁴⁻⁶ Comparisons of the relative effectiveness of different β blockers have rarely been conducted,⁷ and clinicians often assume a general class effect shared by all agents.^{8 9}

Sudden withdrawal of β blockers may result in tachycardia, hypertension, and cardiac ischaemia.¹⁰⁻¹³ Clinical manifestations tend to be accentuated in agents with rapid rather than extended elimination.¹⁴⁻¹⁸ The loss of β blockade around the time of surgery may predispose patients to a myocardial infarction.¹⁹⁻²³ We tested the hypothesis that short acting β blockers may differ from long acting β blockers in preventing perioperative myocardial infarction and death.

Methods

We identified elderly patients (older than 65) admitted to any hospital throughout Ontario, Canada for elective surgery between April 1992 and April 2002. To reduce confounding from differing amounts of pre-existing illness,²⁴ we excluded in advance patients with symptomatic coronary disease as evidenced by chronic use of nitrates.²⁵ (For more details of exclusion criteria see bmj.com.)

β blockers


For each patient we searched previously validated, population wide prescription records for the year before admission,^{26 27} reasoning that β blocker medications would probably be continued in the perioperative setting. We classified individual patients who received two or more prescriptions for atenolol using this medication on an ongoing basis. Similarly, two or more prescriptions for metoprolol identified patients with ongoing use of that β blocker. We analysed patients with mixed exposures or receiving other β blockers separately.


Outcome and characteristics

We obtained information on the nature of the surgical procedure and postoperative recovery from the Canadian Institutes of Health Information database. In addition, we classified operations according to type of surgery as either cardiac or non-cardiac, with non-cardiac surgery further distinguished as high risk non-cardiac, medium risk non-cardiac, and low risk non-cardiac (see bmj.com). We defined the primary outcome as death or myocardial infarction occurring during hospitalisation.²⁸ We also analysed non-cardiac complications after surgery to check for a lack of differences where no differences would be anticipated. For secondary analysis see bmj.com.

Results

A total of 454 336 elderly patients had a total of 634 925 admissions for elective surgery across 252 separate hospitals during the 10 year interval. A minority of patients had symptomatic coronary disease ($n = 48\ 128$), and most ($n = 345\ 253$) had not received a β blocker on an ongoing basis as an outpatient in the year before surgery. The most commonly used β blockers were atenolol ($n = 23\ 091$) and metoprolol ($n = 14\ 060$), forming a ratio of about 5:3 that was stable over the decade. The median dose of atenolol was 50 mg once daily and that of metoprolol 50 mg twice daily.

 Characteristics of patients not having cardiac surgery are on bmj.com

 This is the abridged version of an article that was posted on bmj.com on 6 October 2005: <http://bmj.com/cgi/doi/10.1136/bmj.38603.746944.3A>

As expected, the baseline characteristics for patients receiving atenolol or metoprolol overlapped substantially. The degree of similarity between the two groups was further accentuated after excluding patients who had cardiac surgery. We found no major differences between the two groups in other medications used to treat chronic medical and psychiatric conditions. We also found no clinically important differences in demographic characteristics between the two groups.

A total of 1038 patients experienced a myocardial infarction or died during their stay in hospital. The risk of this combined end point was one fifth lower for patients receiving atenolol rather than metoprolol (2.5% *v* 3.2%, $P < 0.001$). The difference in risk was also apparent for the solitary end points of myocardial infarction (1.6% *v* 2.0%, $P = 0.004$) and of death (1.2% *v* 1.6%, $P = 0.007$). The difference persisted in those patients not having cardiac surgery, both for the combined end point (2.0% *v* 2.6%, $P < 0.001$), and the solitary end points of myocardial infarction (1.1% *v* 1.4%, $P = 0.024$) and death (1.2% *v* 1.6%, $P = 0.003$; see [bmj.com](#)).

The important independent predictors of myocardial infarction or death were the patient's age and sex; four medications (furosemide, calcium channel blockers, angiotensin converting enzyme (ACE) inhibitors, and statins), and type of surgery (table). The overall goodness of fit of this model was moderate (area under the receiver operating characteristic curve 0.74, $P < 0.001$) and similar to past published perioperative prediction rules (area under the curve 0.60-0.65).²⁹ The difference between atenolol and metoprolol persisted after adjusting for these predictors (relative risk reduction 13%, 95% confidence interval 1% to 22%).

A comparison of any long acting β blocker (not just atenolol) to any short acting β blocker (not just metoprolol) showed a comparable reduction in risk of myocardial infarction or death. A comparison of patients with confirmed ongoing use of atenolol or metoprolol (both defined as two or more prescriptions for the corresponding medication in the year after surgery) yielded a larger reduction in risk. We observed no differences between atenolol and metoprolol when we

Independent predictors of myocardial infarction or death

Predictor variable	Odds ratio (95% CI)
Demographic characteristics:	
Age $\geq 70^*$	1.41 (1.22 to 1.63)
Male sex	1.37 (1.20 to 1.57)
Medications in preceding year:	
Furosemide	1.55 (1.30 to 1.85)
Calcium channel blocker	1.17 (1.03 to 1.34)
ACE inhibitor	1.17 (1.02 to 1.34)
Statin	0.82 (0.71 to 0.95)
Surgery type†:	
Cardiac	2.57 (2.17 to 3.04)
Thoracic	1.79 (1.24 to 2.60)
Vascular	1.99 (1.65 to 2.40)
Lower urological or gynaecological	0.21 (0.15 to 0.29)
Orthopaedic	0.62 (0.51 to 0.76)
Breast or skin	0.29 (0.17 to 0.50)
Ophthalmological	0.05 (0.01 to 0.19)

*Binary classification compared with younger age group.

†Comparison is abdominal, retroperitoneal, external head and neck, neurosurgical, unclassified.

examined non-cardiac outcomes and processes of care after surgery.

Most deaths occurred soon after admission, with postoperative day 3 as the most common. Differences between atenolol and metoprolol were primarily observed from postoperative days 2 through 14, in keeping with acute cardiac stress after surgery (figure). Analyses based on comparing any long acting β blocker to any short acting β blocker showed similar patterns.

Discussion

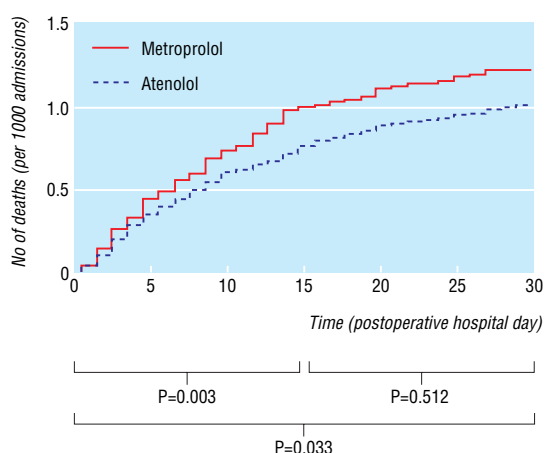
The risk of myocardial infarction and death for patients having non-cardiac surgery is lower for patients receiving atenolol than for those receiving metoprolol, with a number needed to treat equal to about 165 patients to prevent one adverse event. We found no postoperative complications that were significantly less common with metoprolol. In addition, we found that factors related to patient and surgical procedure were still the major determinants of whether a patient experienced a major cardiac complication after the operation.

Limitations

Our study is not a randomised trial and so the results might be exaggerated by hidden confounding,³⁰ but we think this is unlikely (see [bmj.com](#)). The second large limitation of our research relates to the absence of direct data on the exact timing of β blocker doses while in hospital (including recently started β blockers initiated preoperatively). We do not know how many patients had their β blocker deliberately withheld around the time of surgery, but this decision would not be expected to differ between atenolol and metoprolol. We also have no direct evidence that missed doses of β blockers indicate sloppy surgical care.

Conclusion

Our study shows that patients receiving atenolol should not switch to metoprolol at the time of elective non-cardiac surgery. Patients receiving metoprolol, in contrast, may wish to consider switching to a longer acting agent (sustained release metoprolol is available



Absolute risk of death in hospital within 30 days of elective surgery. Absolute risk of death comparing atenolol with metoprolol after surgery. Data expressed as cumulative number of deaths per 1000 admissions on corresponding day. P values compare death rate with atenolol relative to metoprolol for entire interval and for consecutive 14 day intervals, using log rank test

What is already known on this topic

β blocker medications can prevent perioperative myocardial infarction and death

Withdrawal of β blockers can cause haemodynamic instability and myocardial ischaemia

What this study adds

Short acting β blockers (such as metoprolol) are associated with less cardiac protection than long acting β blockers (such as atenolol) in the perioperative setting

Switching from short acting to long acting β blockers may prevent one myocardial infarction or death for every 165 patients with no increase in other common postoperative complications

but not widely marketed yet³¹). In addition, anaesthetists who initiate short acting β blockers during surgery may wish to provide explicit mention in the chart so that the risk of subsequent β blocker withdrawal is minimised on the ward by follow-up. To the extent that β blockers prevent ischaemia and β blocker withdrawal triggers ischaemia, errors in their application will lead to commensurate increases in the risk for patients. Given that lapses are inevitable, our data indicate that long acting β blockers provide a greater margin of safety for patients in the immediate postoperative period after elective non-cardiac surgery.

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