CLINICAL UPDATE

Perioperative β-blocker therapy in vascular surgery: Clinical update

Daniel G. Hackam, MD, FRCPC,[a,b,c,d] *Toronto, Ontario, Canada*

Patients undergoing vascular surgery comprise a group at elevated risk of fatal and nonfatal perioperative cardiovascular events. In four recent longitudinal studies, the 30-day incidence of death in such patients was 3% to 6%, and the incidence of myocardial infarction was 5% to 14%. Growing evidence suggests that β-adrenergic receptor antagonists prevent cardiovascular morbidity and mortality in high-risk patients undergoing noncardiac surgery, including those undergoing vascular surgery. This article reviews the available evidence concerning β-blockers and provides guidance for their use in the perioperative setting. (J Vasc Surg 2006;43:632-4.)

Peripheral arterial disease and aortic aneurysms account for 272,000 hospitalizations and 38,748 deaths in the United States each year.[1] Many patients with these conditions undergo vascular surgery, and a substantial proportion of them are at increased risk of perioperative cardiovascular events. For instance, four recent cohorts of patients undergoing major vascular surgery or infrainguinal revascularization had a 30-day mortality rate of 3% to 6% and a 30-day myocardial infarction rate of 5% to 14%.[2-5]

From the Division of Clinical Pharmacology & Toxicology, Sunnybrook & Women's College Health Sciences Center[a]; Institute for Clinical Evaluative Sciences, University of Toronto[b]; Cardiac Rehabilitation and Secondary Prevention Program, Toronto Rehabilitation Institute[c]; and Clinical Epidemiology and Health Care Research Program, Department of Health Policy, Management, and Evaluation, Faculty of Medicine, University of Toronto.[d]

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Reprint requests: Dr Daniel Hackam, Room G157, Sunnybrook & Women's College Hospital, 2075 Bayview Avenue, Toronto, Ontario M4N 3M5, Canada (e-mail: daniel.hackam@ices.on.ca).

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This situation has prompted the investigation of a diverse array of therapies for preventing ischemic events in patients scheduled for peripheral arterial or aortic reconstructive surgeries. Approaches studied have included antiplatelets, statins, β-blockers, calcium-channel blockers, α-agonists, preoperative coronary revascularization, and postoperative intensive monitoring. Of these approaches, β-blockers have received the lion's share of recent attention. This article reviews the evidence concerning β-blockers and provides recommendations for their use in patients undergoing vascular surgery.

CLINICAL EVIDENCE

Randomized trials outside the operative setting demonstrate that β-blockers prevent coronary events and death in patients with chronic heart failure, myocardial infarction, or ventricular arrhythmias.[6] Moreover, they reduce morbidity in patients with angina or atrial fibrillation and prevent arrhythmias following cardiac or thoracic surgery.[7] Systematic reviews of randomized trials suggest β-blockers may also prevent ischemic events in patients undergoing

Table I. Randomized trials of β-blockers in vascular surgery with cardiovascular outcomes

Trial	*Sample and procedures*	*Intervention*	*Findings*
Poldermans[12]	112 patients; aortic or infrainguinal surgery	Oral bisoprolol*	91% reduction in cardiac death or MI; findings maintained at 2 years
Powell[13]	103 patients; infrarenal vascular surgery	Oral metoprolol*	No difference in cardiac events; hospital stay 3 days shorter in the metoprolol arm
Raby[14]	26 patients; aortic, infrainguinal or carotid surgery	Esmolol infusion	Only 2 cardiac events occurred (1 per arm); postoperative ischemia on Holter reduced by 54% ($P < .05$)
Yang[15]	496 patients; aortic, infrainguinal or extra-anatomic revascularization	Oral metoprolol*	Nonsignificant 16% reduction in cardiac events at 30 days ($P = .40$); longer-term outcomes not yet reported

MI, Myocardial infarction.
*Supplemented with intravenous metoprolol as needed.

Table II. Lindenauer's modification of the revised cardiac risk index (RCRI)[12]

*Criteria**	*Definition*
High-risk surgery	Intrathoracic, intraperitoneal, and suprainguinal vascular procedures
Ischemic heart disease	By history
Cerebrovascular disease	By history
Renal insufficiency	By history
Diabetes mellitus	History of diabetes mellitus or treatment with hypoglycemic therapy

*Each criterion counts as one point towards the total RCRI score.

noncardiac surgery.[8-11] The largest and most comprehensive of these reviews was recently published by Devereaux et al.[8]

Devereaux et al pooled data from 22 trials of β-blocker treatment for noncardiac surgery, including six studies that exclusively enrolled patients undergoing vascular surgery. Overall, a statistically significant, sizeable reduction was noted in the composite outcome of cardiovascular mortality, myocardial infarction, or cardiac arrest, with a relative risk (RR) of 0.44 (95% confidence interval [CI], 0.20 to 0.97).[8] Significance was not reached for the individual components of this outcome, although favorable trends were seen (eg, myocardial infarction had a RR of 0.40; 95% CI, 0.14 to 1.15). On the other hand, β-blockers were associated with increases in certain adverse events, namely, hypotension (RR, 1.27; 95% CI, 1.04 to 1.56) and bradycardia (RR, 2.27; 95% CI, 1.53 to 3.36). Consistent findings have been noted in other systematic reviews.[9-11] The β-blocker trials in vascular surgery that reported cardiac outcomes are described in Table I.

The relative efficacy of perioperative β-blockade may be tied to baseline risk. In a very large propensity-matched cohort study of 663,635 perioperative patients that included 51,095 who underwent vascular surgery, β-blocker therapy was associated with benefit only in patients at moderate-to-high perioperative risk, which was defined as a revised cardiac risk index (RCRI) ≥2.[16] Patients in the lowest tiers of risk (RCRI <2) did not accrue any treatment-related benefit (Table II). Although the study was nonrandomized, these data do concur with the pooled results from randomized trials in suggesting a benefit of perioperative β-blocker therapy in high-risk patients. Additional perioperative β-blocker trials are ongoing. Another interesting but unresolved question is whether β-blockers decrease the severity of perioperative myocardial infarction as assessed by the magnitude of elevated cardiac biomarkers.

RECOMMENDATIONS

The available evidence supports the use of β-blockers in at-risk patients scheduled for noncardiac surgery, including vascular surgery. Given their usual risk factor burdens, comorbidity, and underlying atherosclerosis, many patients undergoing major vascular surgery would be candidates for β-blocker therapy. Some evidence suggests that clinical practice may be catching up to the evidence. In three recent studies of patients undergoing vascular surgery, for instance, the rates of perioperative β-blocker use were 68%,[3] 85%,[5] and 69%,[17] respectively.

The β-blocker regimens used in clinical trials vary widely. It is likely that two variables are most important: the consistent attainment of a β-blocked heart rate and the use of a long-acting agent.[18] In elective cases, treatment should be started at least 1 to 2 weeks before surgery and titrated to achieve a heart rate of ≤60 beats/min. The β-blocker should ideally be continued for at least 30 days after surgery, given the continued high risk throughout this interval. In urgently admitted patients without contraindications, an alternative would be an intravenous β-blocker. Several effective regimens are summarized in Table III.

Table III. Perioperative β-blocker therapy

Contraindications[6]:
Reactive airways disease, hypotension, bradycardia (heart rate <50), second- or third-degree heart block (without a pacemaker), allergy or intolerance, decompensated heart failure

Oral regimen:
Oral agents studied in vascular surgery patients are atenolol, bisoprolol, and metoprolol. Other oral agents studied in noncardiac surgery settings are labetalol, oxprenolol, timolol, and propranolol.

Start low-dose β-blocker, such as atenolol (50 mg once daily), at least 1 to 2 weeks before surgery. Titrate to achieve a heart rate of 50 to 60 beats/min. In postoperative patients unable to take β-blocker orally, administer an intravenous β-blocker. Hold the β-blocker if blood pressure is <100 mm Hg or heart rate is <55 beats/min before a scheduled dose. Continue therapy for at least 30 days postoperatively. Some evidence suggests that therapy continued >30 days is even more advantageous.[14,19]

Intravenous regimen:
Intravenous agents studied in vascular surgery patients are esmolol and metoprolol. Other intravenous agents studied in noncardiac surgery settings are labetalol and atenolol.

A successfully trialed atenolol regimen with evidence of long-term benefit follows.[20] Thirty minutes before surgery, administer atenolol as two 5-mg aliquots over 5 minutes each (total of 10 mg). Immediately after surgery, repeat the same dose. Starting the morning after surgery and each day thereafter until discharge, administer atenolol (10 mg, intravenously) every 12 hours or (preferably) atenolol (50 to 100 mg, orally) once daily. Titrate dose to achieve a heart rate <65. If heart rate is <55 or the systolic blood pressure is <100 mm Hg before a scheduled dose, hold the β-blocker.

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