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Review Article

REVIEW ARTICLE

Effect of beta-blockers on perioperative outcomes in vascular and endovascular surgery: a systematic review and meta-analysis

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Abstract

Background. To investigate the role of perioperative beta-blocker use in vascular and endovascular surgery.
Methods. We performed a systematic review in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement standards. The review protocol was registered with International Prospective Register of Systematic Reviews (registration number:CRD42016038111). We searched electronic databases to identify all randomized controlled trials and observational studies investigating outcomes of patients undergoing vascular and endovascular surgery with or without perioperative beta blockade. We used the Cochrane tool and the Newcastle-Ottawa scale to assess the risk of bias of trials and observational studies, respectively. Random-effects models were applied to calculate pooled outcome data.
Results. We identified three randomized trials, five retrospective cohort studies, and three prospective cohort studies, enrolling a total of 32,602 patients. Our analyses indicated that perioperative use of beta-blockers did not reduce the risk of all-cause mortality [odds ratio (OR) 1.10, 95% confidence interval (CI) 0.59-2.04, $P = 0.77$], cardiac mortality (OR 2.62, 95% CI 0.86-8.05, $P = 0.09$), myocardial infarction (OR 0.89, 95% CI 0.59-1.35, $P = 0.58$), unstable angina (OR 1.34, 95% CI 0.41- 4.38, $P = 0.63$), stroke (OR 2.45, 95% CI 0.89-6.75, $P = 0.08$), arrhythmias (OR 0.76, 95% CI 0.41-1.43, $P = 0.40$), congestive heart failure (OR 1.12, 95% CI 0.77-1.63, $P = 0.56$), renal failure (OR 1.48, 95% CI 0.90-2.45, $P = 0.13$), composite cardiovascular events (OR 0.88, 95% CI 0.55-1.40, $P = 0.58$), rehospitalisation (OR 0.86, 95% CI 0.48-1.52, $P = 0.60$), and reoperation (OR 1.17, 95% CI 0.42-3.27, $P = 0.77$) in vascular surgery.
Conclusions. Beta-blockers do not improve perioperative outcomes in vascular and endovascular surgery.

Key words: beta blocker; perioperative; vascular

Perioperative cardiac mortality and morbidity are the most frequent adverse events in vascular surgery.[1] There is a strong relationship between perioperative cardiac and noncardiac complications and subsequent mortality; nearly half of the patients experiencing cardiac morbidity will develop other types of noncardiac complications and mortality.[2]

Beta-adrenoceptor blocking agents are traditionally used to treat hypertension and are the primary treatment choice after

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Editor's Key Points

- Vascular surgical patients are at particular risk of adverse cardiac events
- The effects of perioperative beta-blocker therapy may be different in vascular surgery
- This pooled analysis could not identify any beneficial or harmful effects of beta-blockers in vascular surgery

myocardial infarction or for chronic angina.[3 4] In addition, beta-blockers have been shown to reduce morbidity and mortality in patients with mild, moderate and severe chronic heart failure.[5–7] It has been proposed that beta- blockers reduce the risk of perioperative cardiac complications by slowing heart rate, decreasing blood pressure, and moderating haemodynamic stress responses.[8] The effectiveness and safety of perioperative beta-blockers for patients undergoing noncardiac surgery remains controversial. Some authors have reported that perioperative beta-blockers started within one day or less of noncardiac surgery prevent nonfatal myocardial infarction but increase the risk of stroke, death, hypotension, and bradycardia.[9] Others have found no clear evidence for the effect of perioperative beta-blockers on all-cause mortality, cerebrovascular events, myocardial infarction, or arrhythmias.[10 11]

We thus conducted a comprehensive systematic review and meta-analysis to investigate the role of perioperative beta-blockers in noncardiac vascular and endovascular surgery.

Methods

This systematic review was performed according to an agreed predefined protocol which was registered with the International Prospective Register of Systematic Reviews (registration number: CRD42016038111). The review was conducted and presented according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement standards.[12]

Eligibility criteria

We included all observational studies and randomized controlled trials (RCTs) investigating outcomes of patients undergoing vascular and endovascular surgery with or without perioperative beta blockade. Perioperative beta-blockers of any dose, titration, duration and mode of administration were considered as intervention of interest, and placebo or no treatment was considered as comparator. Adults more than 18 yr of age undergoing noncardiac vascular and endovascular surgery were considered as participants of interest. We defined noncardiac vascular and endovascular surgery as any surgical or endovascular intervention for treatment of vascular disease in carotid or vertebral arteries, other supra-aortic arteries, aortoiliac arteries, renal and visceral arteries, upper or lower extremity arteries, and for vascular access for haemodialysis.

Outcome measures

All-cause mortality was considered the primary outcome measure. The secondary outcome measures included cardiac mortality, myocardial infarction (MI), unstable angina, stroke, arrhythmias, congestive heart failure (CHF), renal failure, composite cardiovascular events (MI, unstable angina, stroke, dysrhythmia or cardiac death), rehospitalization, and reoperation.

Literature search strategy

Two authors (S.H., S.H.) independently searched the following electronic databases: MEDLINE, EMBASE, CINAHL, and the Cochrane Central Register of Controlled Trials (CENTRAL). The last search was run on 30 April 2016. Thesaurus headings, search operators and limits in each of the above databases were adapted accordingly. The literature search strategy is outlined in Appendix I. In addition, World Health Organization International Clinical Trials Registry (http://apps.who.int/trialsearch/), ClinicalTrials.gov (http://clinicaltrials.gov/), and ISRCTN Register (http://www.isrctn.com/) were searched for details of ongoing and unpublished studies. The bibliographic lists of relevant articles and reviews were searched for further potentially eligible studies. Moreover, leading journals in vascular and endovascular surgery were hand-searched. No language restrictions were applied in our search strategies.

Study selection

The title and abstract of articles identified from the literature searches were assessed independently by two authors (S.H., S.H.). The full-texts of relevant reports were retrieved and those articles that met the eligibility criteria of our review were selected. Any discrepancies in study selection were resolved by discussion between the authors. An independent third author (S.A.A.) was consulted in the event of disagreement.

Data collection

We created an electronic data extraction spreadsheet which was pilot-tested in randomly selected articles and was adjusted accordingly. Our data extraction spreadsheet included: study-related data (first author, yr of publication, country of origin of the corresponding author, journal in which the study was published, study design, study size, clinical condition of the study participants); baseline patient characteristic and clinical information of the study populations (age, gender, diabetes mellitus, coronary heart disease, hypertension, cerebrovascular disease, and smoking status); and primary and secondary outcome data. Data collection was performed independently by two authors (S.H., S.H.), and disagreements were resolved by discussion. If no agreement could be reached, a third author (SAA) was consulted.

Methodological quality and risk of bias assessment

Two authors (S.H. and S.H.) independently assessed the methodological quality and risk of bias of the included articles, using the Cochrane tool and the Newcastle-Ottawa scale (NOS)[13] for assessing the risk of bias of randomized trials and observational studies, respectively. The Cochrane's tool assesses domains including selection bias, performance bias, detection bias, attrition bias, reporting bias, and other sources of bias and, for each individual domain, classifies studies into low, unclear, and high risk of bias. The NOS uses a star system with a maximum of nine stars to evaluate a study in three domains (8 items): the selection of the study groups, the comparability of the groups, and the ascertainment of outcome of interest. For each item of the scale, we judged each study as low risk (one star awarded) or high risk (no star awarded). We determined studies that received a score of nine stars to be of low risk of bias, studies that scored seven or eight stars to be of moderate risk, and those that scored six or less to be of high risk of bias. Disagreements were resolved by discussion between the reviewers. If no