BJA

British Journal Of Anaesthesia, 117 (5): 559–68 (2016)

doi: 10.1093/bja/aew321
Review Article

REVIEW ARTICLE

Troponin elevations after non-cardiac, non-vascular surgery are predictive of major adverse cardiac events and mortality: a systematic review and meta-analysis

S. Ekeloef[1,*], M. Alamili[1], P. J. Devereaux[2,3] and I. Gögenur[1]

[1]Department of Surgery, Center for Surgical Science, Zealand University Hospital, Koege and Roskilde, Denmark, [2]Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada and [3]Department of Medicine, McMaster University, Hamilton, Ontario, Canada

*Corresponding author. E-mail: savb@regionsjaelland.dk

Abstract

Background: Patients undergoing non-cardiac, non-vascular surgery are at risk of major cardiovascular complications. In non-cardiac surgery, troponin elevation has previously been shown to be an independent predictor of major adverse cardiac events and postoperative mortality; however, a majority of studies have focused on vascular surgery patients. The aim of this meta-analysis was to determine whether troponin elevation is a predictor of major adverse cardiac events and mortality within 30 days and 1 yr after non-cardiac, non-vascular surgery.
Methods: A systematic review and meta-analysis was conducted in January 2016 according to the Meta-analysis Of Observational Studies in Epidemiology guidelines. Both interventional and observational studies measuring troponin within the first 4 days after surgery were eligible. A systematic search was performed in PubMed, EMBASE, Scopus, and the Cochrane Central Register of Controlled Trials.
Results: Eleven eligible clinical studies (n=2193) were identified. A postoperative troponin elevation was a predictor of 30 day mortality, odds ratio (OR) 3.52 [95% confidence interval (CI) 2.21–5.62; I^2=0%], and an independent predictor of 1 yr mortality, adjusted OR 2.53 (95% CI 1.20–5.36; I^2=26%). A postoperative troponin elevation was associated with major adverse cardiac events at 30 days, OR 5.92 (95% CI 1.67–20.96; I^2=86%), and 1 yr after surgery, adjusted OR 3.00 (95% CI 1.43–6.29; I^2=21%).
Conclusions: Postoperative myocardial injury is an independent predictor of major adverse cardiac events and mortality within 30 days and 1 yr after non-cardiac, non-vascular surgery. The meta-analysis provides evidence that supports troponin monitoring as a cardiovascular risk stratification tool.

Key words: cardiovascular diseases; mortality; myocardial ischaemia; perioperative period; postoperative complications; troponin

Accepted: August 25, 2016

Editor's key points

- This pooled analysis has focused on patients having mostly orthopaedic and abdominal surgery.
- Postoperative troponin elevations have prognostic importance.
- Although evidence is lacking, basic cardiac medications for secondary prevention should be considered in this setting.
- Randomized trials of treatments for patients with postoperative troponin elevations are needed.

Worldwide, millions of patients annually undergo major non-cardiac surgery.[1 2] A significant proportion of the patients suffer from major cardiovascular complications (e.g. non-fatal myocardial infarction, cardiac arrest, cardiovascular death) during the perioperative period and the first years after surgery.[3–5] Perioperative myocardial infarction is the most common cardiovascular complication and is associated with poor outcomes. Moreover, even myocardial injury after non-cardiac surgery that does not fulfil the universal definition of myocardial infarction is independently associated with 30 day mortality.[5]

A recent meta-analysis including 3318 surgical patients concluded that an elevation of postoperative troponin is an independent predictor of mortality, particularly within the first year after non-cardiac surgery.[6] A majority of the studies in the meta-analysis restricted enrolment to patients undergoing vascular surgery. Hence, >60% of the patients in the meta-analysis underwent major vascular surgery. Likewise, major randomized clinical trials and the VISION cohort study pooled vascular and non-vascular surgery when addressing perioperative cardiovascular risk estimation and cardiovascular optimization.[4 5 7] Major vascular surgery is, in comparison with other types of non-cardiac surgery, a procedure with a high risk of major cardiovascular complications and is commonly executed in a high-risk population with cardiovascular co-morbidities and manifest systemic atherosclerosis resulting in an increased risk of perioperative myocardial injury.[3 8 9] Hence, the cardiovascular risk profile of patients undergoing vascular surgery differs from the often more moderate risk profiles of patients undergoing other types of non-cardiac surgery.[10] Moreover, major vascular surgery independently increased the risk of perioperative myocardial infarction in a cohort study enrolling 8351 patients undergoing non-cardiac surgery.[3] Major studies have ignored the likelihood that differences between non-cardiac surgical procedures affect the pathogenesis of postoperative cardiovascular morbidity in different degrees and directions.[11]

In recent years, a substantial number of studies have evaluated the prognostic impact of troponin elevation after non-cardiac, non-vascular surgery.[12–15] The aim of this meta-analysis was to determine whether postoperative troponin elevation is an independent predictor of mortality or major adverse cardiac events after non-cardiac, non-vascular surgery.

Methods

Eligibility criteria and information source

A systematic review and meta-analysis was executed according to the Meta-analysis Of Observational Studies in Epidemiology guidelines.[16] Study eligibility criteria included the following: a population limited to adults undergoing non-cardiac, non-vascular surgery; patients had to have at least one troponin measurement within the first 4 days after surgery; one or more patients had to suffer a major cardiac event or die after surgery; and the study had to assess the prognostic impact of postoperative troponin elevation in terms of major adverse cardiac events or mortality within 30 days or 1 yr after surgery or, alternatively, provided data that could be included in the quantitative analyses. Studies on non-cardiac surgery that separately reported the results for non-vascular surgery could be included. Major adverse cardiac events were defined as non-fatal cardiac arrest, emergent coronary revascularization, acute coronary syndrome, stroke, congestive heart failure, atrial fibrillation (new onset or destabilization of pre-existing atrial fibrillation), major arrhythmia, cardiovascular death, and rehospitalization for cardiovascular reasons. Atrial fibrillation and major arrhythmia were determined by documentation in the medical records by the treating unit. We excluded non-English publications, retracted studies, and unpublished studies, including proceedings abstracts.

A literature search was conducted in January 2016 in PubMed, EMBASE, Scopus, and the Cochrane Central Register of Controlled Trials. Reference lists were reviewed manually, and the 'related citations' and 'cited by' features were used for studies fulfilling our eligibility criteria. Duplicates were removed manually. The following search terms were used in the systematic search strategy: nonvascular surgery, non-vascular surgery, non-cardiac surgery, noncardiac surgery, surgical procedures, operative, surgery, operation, cardiovascular events, cardiovascular event, postoperative complication, postoperative complications, perioperative complications, perioperative complication, death, mortality, prognosis, morbidity, cardiac event, cardiac events, human, humans, and troponin. The search terms were fitted to each database individually (MeSH terms, subject heading).

Study selection and data collection

Two reviewers (S.E. and M.A.) independently screened the manuscripts' titles and abstracts for potential eligibility and resolved disagreement through discussion or by consulting a third reviewer (I.G.). All articles selected as potentially eligible during the screening process underwent full-text review by two independent reviewers (S.E. and M.A.) to determine eligibility. Disagreements were resolved using the same procedure as for the screening process. Two independent reviewers (S.E. and M.A.) extracted data from all studies that fulfilled eligibility criteria. Disagreements were resolved using an identical process as for eligibility and screening. Data were extracted on author, year of publication, study design, number of participants, age, type of surgery, priority of surgery, lengths of follow-up, troponin type, troponin assay and manufacturer, cut-off value of myocardial injury in non-cardiac surgery, timing of postoperative measurements of troponin, number of patients with elevated troponin after surgery, definition of major adverse cardiac events, and number of deaths and major adverse cardiac events within 30 days and 1 yr after surgery.

Study quality and risk of bias

Risk of bias within the studies was evaluated according to the following predefined terms: the degree to which the study cohort represented the average patients undergoing non-cardiac, non-vascular surgery in the population;[17] blinding of troponin measurement; preoperative troponin measurement; completeness of follow-up; method of patient follow-up; and