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Clinical Investigation

CLINICAL INVESTIGATION

High-sensitivity cardiac troponin T in young, healthy adults undergoing non-cardiac surgery

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Abstract

Background: It is unclear if isolated postoperative cardiac-troponin elevation, often referred to as myocardial injury, represents a pathological event, as control studies in otherwise healthy adults are lacking.

Methods: In this single-centre prospective observational cohort study, serial high-sensitivity cardiac troponin T (hscTnT) plasma concentrations were obtained from young, healthy adults undergoing elective orthopaedic surgery at three time points: before operation, 2–6 h, and 18–30 h after surgery. End points were hscTnT increases after surgery: ≥20% (exceeding analytical variability), ≥50% (exceeding short-term biological variability), and ≥85% (exceeding long-term biological variability). The secondary end point was myocardial injury, defined as new postoperative hscTnT elevation >99th % upper reference limit (URL) (women >10 ng litre^{-1}; men >15 ng litre^{-1}).

Results: Amongst the study population (n=95), no hscTnT increase ≥20% was detected in 68 patients (73%). A hscTnT increase between 20% and 49% was observed in 17 patients (18%), 50–84% in seven patients (7%), and ≥85% in three patients (3%). Twenty patients (21%) had an absolute ΔhscTnT between 0 and 2 ng litre^{-1}, 12 patients (13%) between 2 and 4 ng litre^{-1}, three patients between 4 and 6 ng litre^{-1}, and one patient (1%) between 6 and 8 ng litre^{-1}. Myocardial injury (new hscTnT elevation >99th%) was diagnosed in one patient (1%). The median hscTnT concentrations did not increase after operation, and were 4 (3.9–5, inter-quartile range) ng litre^{-1} at baseline, 4 (3.9–5) ng litre^{-1} at 2–6 h after surgery, and 4 (3.9–5) ng litre^{-1} on postoperative day 1.

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Conclusions: One in four young adult patients without known cardiovascular disease developed a postoperative hscTnT increase, but without exceeding the 99th% URL and without evidence of myocardial ischaemia. These results may have important ramifications for the concept of postoperative myocardial injury, as they suggest that, in some patients, postoperative cardiac-troponin increases may be the result of a normal physiological process in the surgical setting.
Clinical trial registration: NCT 02394288.

Keywords: Troponin; Heart; Surgery

Editor's key points

- Troponin I and T are regulatory proteins necessary for muscle contraction, and are sensitive and specific indicators of myocardial damage.
- There are many non-ischaemic causes of troponin elevation.
- High-sensitivity troponin assays have lower cut-off values to indicate 'abnormal'.
- This study suggests that some postoperative troponin elevations can be expected in young, healthy patients.

Myocardial injury after non-cardiac surgery, defined as an isolated postoperative cardiac troponin (cTn) elevation without evidence for myocardial ischaemia, is common, particularly amongst patients with or at risk for cardiovascular disease. Even minor postoperative cTn elevations, seen in 11–24%[1–3] of patients with increased cardiovascular risk, are prognostically important, and are associated with increased morbidity and mortality in these patients.[1–6] However, elevated cTn is not by itself evidence of an acute ischaemic event, and there are multiple cardiac-related mechanisms for cTn elevations, including myocardial ischaemia, infarction, pulmonary embolism, heart failure, myocarditis, or—in a trauma population—chest and cardiac trauma. There are also non-cardiac causes for elevated cTn, the most prominent of which is renal failure.[7]

It is also clear that cTn may be released during normal physiological stress. For example, a recent study in healthy triathletes found a >300% increase of cTn concentrations after 1 h of high-intensity exercise.[8] A study involving healthy volunteers showed that a brief dobutamine infusion causes an increase in high-sensitivity cardiac troponin T (hscTnT).[9] Likewise, rapid atrial pacing leads to a significant increase in hscTnT, both in patients with or without significant coronary-artery disease.[10] It is, therefore, conceivable that postoperative cTn elevation may occur in patients without cardiovascular risk factors.

The aim of this study, therefore, was to determine if young, healthy patients devoid of known cardiac disease would develop postoperative increases in hscTnT after non-cardiac surgery. High-sensitivity cTn assays have a substantially increased sensitivity and are able to measure small changes in cTn values.[7,11–13] Our expectation was that we would not observe a hscTnT increase after surgery.

Methods

Design and setting

We conducted a prospective cohort study of patients who underwent elective orthopaedic surgery on the upper or lower extremity under general or regional anaesthesia. Perioperative treatment was at the discretion of the clinical team and was not influenced by study participation. The study was approved by the Institutional Review Board of the Medical University of Vienna and registered at ClinicalTrials.gov (NCT02394288). Informed consent was obtained from each patient. Recruitment was done from patients scheduled for elective orthopaedic surgery at the Vienna General Hospital, Vienna, Austria, from March 2015 to March 2016. Reporting followed the recommendations from the STROBE initiative.[14]

Study population

Eligible patients were 18–35 yr old, scheduled for elective orthopaedic surgery and had ASA physical status I or II. Patients were excluded from participation if they had a history or symptoms of cardiac disease, kidney disease, pulmonary embolism, thrombosis, stroke, diabetes, and head or chest trauma, or were pregnant.

Measurements

Patient characteristics, medical history, home medication, and type of surgery were recorded. Vital parameters, type and duration of anaesthesia, tourniquet use, and fluid balance were captured through the electronic anaesthesia record. Serial blood samples and 12-lead ECGs were obtained at three time points for each patient: before operation on the day of surgery, 2–6 h [postoperative day (POD) 0], and 18–30 h (POD 1) after surgery.

For the assessment of hscTnT plasma concentrations, 3 ml of whole blood was drawn into K_3EDTA-coated polyethylene terephthalate tubes (Greiner Bio-One, Kremsmünster, Austria) at each reported time point, and transported within 30 min to the Biobank (www.biobank.at), a centralized sample processing and storage facility at the Department of Laboratory Medicine, Medical University of Vienna. The samples were transferred to an automated pre-analytical system (Roche Diagnostics, Rotkreuz, Switzerland) for further centrifugation (1884 × g, 10 min, ambient temperature) and aliquotation into 2D barcoded polypropylene tubes. Aliquots were then stored until analysis at −70°C. After thawing, hscTnT was quantified by means of electro-chemiluminescence immunoassays using CE-labelled Troponin T hs STAT kits (Roche Diagnostics) on a cobas e 602 integrated into a cobas 8000 modular analyser series (Roche Diagnostics). All samples were analysed in the same batch/run to minimize analytical variability. For this kit/test system combination, the manufacturer reports an intra-assay precision of 2.5–3.7% coefficient of variability for concentrations between 10 and 17 ng litre^{-1}. ECGs were checked for signs of myocardial ischaemia according to the criteria of the Third Universal Definition of Myocardial Infarction[15] by a blinded expert investigator. At each sampling time point, the