Postoperative Troponin Elevation: Increased Risk or Inevitable Fact?

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Learning objectives:
1 Recognize the association of postoperative troponin elevation with adverse outcome after surgery.
2 Understand the universal definition of myocardial infarction
3 Discuss therapeutic options in patients with postoperative troponin elevation.

Troponins are structural proteins of the contractile apparatus of skeletal and myocardial myocytes. The troponin complex consists of three subunits: T (TnT), I (TnI), and C (TnC). The corresponding isoforms of TnI and TnT are different enough to allow for high specificity in the measurement of the cardiac forms (the cardiac troponins, cTn). Troponins are released into circulation as intact proteins or degradation products upon the occurrence of myocardial cell death. Tests measuring the cTnT and cTnI are in widespread clinical use. Every test has its specific cut-off value (defined as the upper 99\textsuperscript{th} percentile of the values measured in a reference population).\textsuperscript{1} Recently, “high sensitivity” tests have been introduced into clinical practice.\textsuperscript{3} Analysis of cTn is a cornerstone in the assessment of patients presenting with acute coronary syndromes (ACS),\textsuperscript{3, 4} and contains strong diagnostic and prognostic information. In patients with non-ST-segment elevation myocardial infarction, elevated cTn levels identify a group of patients who are at high risk for adverse outcome and who profit from early invasive treatment.\textsuperscript{3, 5}

Not surprisingly, cTn analyses are the basis of the "universal definition of myocardial infarction", jointly published by American and European cardiological societies.\textsuperscript{6, 7} The guidelines distinguish five main groups of myocardial infarction (MI):

- Type 1: Spontaneous myocardial infarction
- Type 2: Myocardial infarction secondary to an ischaemic imbalance
- Type 3: Myocardial infarction resulting in death when biomarker values are unavailable
- Type 4a: Myocardial infarction related to percutaneous coronary intervention (PCI)
- Type 4b: Myocardial infarction related to stent thrombosis
- Type 5: Myocardial infarction related to coronary artery bypass grafting (CABG)

It is important to realize that cTn levels can be increased also in other than MI situations,\textsuperscript{8, 9} e.g., in acute congestive heart failure\textsuperscript{10} or in pulmonary embolism.\textsuperscript{11} Accordingly, additional diagnostic criteria (e.g., new Q-waves or new left bundle branch block, or new regional wall motion abnormalities) have to be fulfilled for diagnosis of MI. According to the “Universal definition”, the MI in patients undergoing non-cardiac will mainly be characterized as type 1 or 2 (or less often 4b), and MI after CABG surgery as type 5.\textsuperscript{6, 7}

In surgical patients, the significance of troponin measurements is not as well established as in non-surgical patients. However, there is growing evidence demonstrating the association between elevated postoperative cTn levels and adverse short- and midterm outcomes after major non-cardiac,\textsuperscript{12} and cardiac surgery.\textsuperscript{13} During cardiac surgery, some leakage of cTn seems inevitable. Nevertheless, elevated postoperative cTn levels were shown to be associated with mortality after adult cardiac surgery. A meta-analysis included seventeen studies with a total of 296 short-term deaths in 9703 patients (3.1\%) and 237 mid-term deaths (≥12 months) in 5189 patients (4.6\%) after adult cardiac surgery.\textsuperscript{13} The odds ratio of increased cTn concentrations was 6.57 (95%
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confidence interval (CI): 4.3 - 10.1) for short-term mortality and 5.46 (95% CI: 2.0 - 14.6) for mid-term mortality. Unfortunately, high between-study variability, differences in populations, timing of cTn testing, cTn subunits and cTn essays made definitive conclusions about effect size and cut-off values difficult. In a cohort study of 741 adult patients undergoing cardiac surgery a cut-off value for cTnT > 0.9 µg/l was determined using ROC analysis. Adjusted for EuroSCORE, a cTnT elevation on the first or second postoperative day above 0.9 µg/l had an OR 3.83 (95% CI 2.10 - 7.12) for 12-month all-cause mortality. A study by Fellahi and colleagues in 905 patients undergoing cardiac surgery reported similar results. A recent study in more than 1500 adult patients analysed the impact on cTn levels for outcome after adjustment not only for preoperative and operative findings (EuroSCORE) but also for postoperative complications and found an adjusted hazard ratio (aHR) of peak cTnT >0.8 µg/L of 2.13 (95%CI 1.47 - 3.15) for major adverse cardiac events within 12 months after cardiac surgery. One half of the events occurred later than 30 days after surgery (93/176), highlighting that cTn measurements have the potential to flag high-risk patients early, i.e. at a time point when management optimization holds promise for outcome improvement. However, so far no data are available to prove that the incorporation of perioperative troponin measurements in perioperative clinical practice will guide therapeutic decisions resulting in outcome optimization.

An association between postoperative cTn elevation and outcome up to one year after surgery was also shown after non-cardiac surgery. In a very recent study, myocardial injury, evident as an elevation of cTnI, was found in 315 of 1627 patients (19%); a cTnI level above >0.06 µg/L was associated with a 4.2 (95% CI 2.1 to 8.6) fold increase in the risk of death within 30 days after surgery. An even larger study with over 15’000 patients found a stepwise increase in the risk of 30-day mortality compared with the reference group (peak TnT ≤ 0.01 µg/L ); peak TnT of 0.02 µg/L (aHR: 2.41; 95% CI 1.33 - 3.77); 0.03 to 0.29 µg/L (aHR: 5.00; 95% CI 3.72 - 6.76); and 0.30 ng/mL or greater (aHR: 10.48; 95% CI 6.25-16.62). So far, data and guidelines for the management of patients with perioperative ACS are lacking. In our institution, we use similar strategies as in non-surgical patients, but adapt the application of antiplatelet drugs to the perioperative situation. For decision making concerning early invasive vs. conservative treatment of patients suffering from perioperative ACS, cTn levels are crucial.

In conclusion, perioperative cTn analyses help to identify high risk patients after cardiac and non-cardiac surgery and may be useful in improving prognosis.

References

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