

Perioperative Cardiac Outcome and its Predictors in Patients Undergoing Non-Cardiac Surgery in a Tertiary Care Hospital in South India - A Prospective Study

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Abstract: ***Background:** Perioperative cardiovascular complications are commonly encountered challenges for the clinician. As an ever increasing number of elderly patients with coronary artery disease (CAD) are undergoing major and minor surgeries, cardiovascular complications remain a major clinical problem and the numbers will increase in the future. **Objective:** The objective of this study was 1) to study the incidence of myocardial damage and perioperative cardiac events 2) to find the risk factors of poor outcome. **Materials and Methods:** The correlation between perioperative myocardial damage and short- and long-term outcome was studied in 186 patients, aged 70 years above, undergoing non-cardiac surgery for a minimum duration of 30 minutes. **Results:** This study showed a strong relation between postoperative myocardial damage and poor short term and long term prognosis. Elevated Troponin T was a strong predictor of mortality during and after surgery. In 33% of the 186 patients with ASA physical status classification III or IV undergoing non-elective surgery, myocardial damage was detected. Preoperative cardiac damage was found to be a predictor of major adverse cardiac events (MACE) in the postoperative period. **Conclusion:** In conclusion, this study stresses on the importance of detecting elevated cardiac markers in patients undergoing elective or emergency surgery. It also has identified predictors of poor outcome in the perioperative period that could be used as criteria for screening patients at risk.*

Keywords: Myocardial damage, major adverse cardiac event, NT-proBNP

1. Introduction

Myocardial damage and cardiovascular complications in the perioperative period continues to be a major challenge for patients undergoing surgery and the treating clinician. Approximately 100 million adults undergo non-cardiac surgery worldwide yearly (1) and up to 40% of these patients are at risk of coronary artery disease (CAD) (2). Four million patients every year suffer from a major perioperative cardiovascular complication, including cardiac death, myocardial infarction or cardiac arrest (1). In high-risk patients, the incidence of major perioperative cardiac complications ranges from 4 to 25% (3-5). Many studies prove that perioperative myocardial infarction (PMI) is associated with in-hospital mortality of 15 to 25% (6-9). These high mortality could be due to the difficulty in detecting PMI devoid of its classical symptoms in the perioperative period (10). It has been found that only 14% of patients with a PMI have typical chest pain and so most PMI will be missed by clinical methods alone (11). Hence cardiac markers are important for detecting perioperative myocardial damage. The exact cut-off levels of cardiac markers for detecting myocardial in the perioperative period is still a controversy. However, elevated cardiac markers with or without clinical or ECG signs of ischaemia are usually associated with poor outcome in both patients undergoing cardiac and non cardiac surgeries.

Despite improvements in preoperative testing, perioperative monitoring and management of myocardial ischemia in high

cardiac risk patients, cardiovascular disorders remain the leading causes of death in surgical patients (2, 12). Perioperative cardiovascular complications are associated with high resource utilization and, hence result in a major burden to the health care system (12, 13). The World Health Organization estimates that a growing number of patients with coronary artery disease (CAD) or with risk factors for CAD are undergoing non-cardiac surgery and hence cardiovascular complications will be a main clinical problem in the future.

2. Aims of the Study

- 1) To assess the prognostic importance of myocardial damage in elderly patients undergoing non-cardiac surgery.
- 2) To estimate the incidence of myocardial damage and major adverse cardiac events in high-risk patients undergoing emergency surgery and to determine the predictors of poor outcome.
- 3) To study the incidence of elevated NT-proBNP in high-risk patients

3. Material and Methods

Study population and design

All patients included in the present study underwent non-cardiac surgery. 211 patients in ASA physical status classification 3 or 4, undergoing emergent or urgent noncardiac surgery at our institute, a tertiary referral centre

in South India, were included in the study. This prospective observational study was conducted over a period of one year from April 15th 2014 to April 14th 2015. Fifteen patients were excluded due to incomplete data and 10 patients were lost to follow-up. 186 patients completed the study.

Data collection

The patients included after informed consent were examined and enquired about the following :

Age, gender, BMI (body mass index) ASA classification, history of ischaemic heart disease, previous myocardial infarction, CABG, PCI, congestive cardiac failure, renal failure (S-Creatinine > 170 $\mu\text{mol}\cdot\text{l}^{-1}$), stroke, insulin-dependent diabetes mellitus, and chronic medication. New York Heart Association (NYHA) functional classification, the Revised Cardiac Risk Index (RCRI), as well as the priority classification for non-elective surgery were also documented.

The perioperative characteristics included were: Type of surgery, type of anaesthesia, duration of surgery, blood loss, as well as preoperative complications.

Peroperative complications were defined as:
 tachycardia (heart rate >30/min from baseline for > 5 min)
 bradycardia (heart rate <30/min from baseline or < 50 beats per minute for > 5 min)
 haemodynamic instability (systolic blood pressure \pm 30 % of baseline)
 hypoxaemia (SpO₂ < 90% for > 5 min).

These complications were also documented in the postoperative period.

Troponin I was the assay used. Troponin T was determined by Elecsys 2010® immunoassays (Roche Diagnostics, Mannheim, Germany) and troponin I was analyzed using the Stratus® CS Acute Care™ Diagnostic System.

Troponin T was measured one hour before surgery and on 24 and 48 hours after surgery and on the 5th to 7th postoperative days. In case of a high troponin preoperatively, surgery was delayed if necessary.

NT-proBNP

NT-proBNP was measured one hour prior to surgery in high risk patients.

Electrocardiogram

ECG data were analyzed by a cardiologist blinded to clinical symptoms, the laboratory reports and treatment. ECG signs of myocardial ischaemia were defined as follows:

ST segment elevation or depression \geq 1-mm or presence of new Q waves lasting \geq 0.04s and \geq 1-mm deep in at least two adjacent leads.

ECG was obtained preoperatively and on the 5th to 7th days after surgery.

In the postoperative period, 12-lead ECG was done in case of an elevated TnI.

The primary endpoint was myocardial damage (defined as an increase in TnI above 0.06 $\mu\text{g}\cdot\text{l}^{-1}$). The secondary endpoints were postoperative major adverse cardiac events (MACE), death, and preoperatively elevated NT-proBNP. The definition of a major adverse cardiac event (MACE) was acute myocardial infarction, and/or cardiovascular death. In this study, MACEs were limited to within 1 and 3 months following surgery. Follow-up was conducted by telephone interviews undertaken 1 and 3 months after surgery. If the patient expired during the follow-up, death certificates, medical records, and autopsy reports were examined to determine the cause of death

Statistical Methods

The association between baseline and perioperative characteristics were analysed using un-paired t -test or Mann-Whitney U test for continuous variables, and χ^2 test or Fisher's Exact test for dichotomous data. Multivariate logistic regression analysis was used to detect variables predictive of myocardial damage and major adverse cardiac events. Odds ratios (OR) and their corresponding 95% confidence interval (CI) were calculated.

Ethical considerations

The Institute Ethics Committees approved the protocols for the study which was conducted in accordance to the Declaration of Helsinki. All the patients included in the study gave written informed consent.

4. Results

Table 1: Per- and postoperative characteristics

Duration of surgery	73 \pm 93	
Blood loss	414 \pm 1010	
	Perop complications	Postop complications
Tachycardia	5(3%)	20(11%)
Bradycardia	4(2%)	2(1%)
Hypertension	7(4%)	15(8%)
Hypotension	59(32%)	17(9%)
Hypoxaemia	9(5%)	13(7%)

Perioperative myocardial damage and long-term outcome in elderly undergoing non-cardiac surgery

Myocardial Damage

Fifty-three patients (9.7%) had a myocardial ischemia (defined as TnT >0.02 $\mu\text{g}\cdot\text{l}^{-1}$) on day 5 to 7 after surgery. The patients with a Troponin T elevation were significantly older, with lower BMI, high ASA risk classification category, a previous history of ischaemic heart disease, congestive heart failure, or peripheral vascular disease more frequently. Patients with elevated TnT were significantly more often treated with diuretics and anticoagulants.

Table 2: Perioperative characteristics of patients with myocardial damage:

	Troponin T > 0, 02 µg/l	%	Troponin T ≤ 0, 02 µg/l	%	p value
Perioperative bleeding	975±1984		268±609		p=0.01
Perioperative complications-Tachycardia	4	7.5%	0 0,	0%	p=0.004
Bradycardia	4	7.5%	11	10.1%	p=0.59
Hypotension	19	35.8%	22	20.4%	p=0.03
Hypertension	1	1.9%	6	5.6%	p=0.28
Hypoxaemia	3	5.7%	0	0%	p=0.01

Table 3: Causes of death during the first postoperative year

	Troponin T > 0, 02 µg/l (n=53)	Controls (n=108)	p value
Cardiovascular	10	2	0.02
Malignancy	6	2	<0.001
others	1	1	0.33
total	17	5	<0.001

Elevated TnT, peroperative episodes of tachycardia were independent predictors of death within one-year of surgery. Using Cox regression analysis, the only independent predictor for cardiovascular cause of death was found to be TnT > 0.02 µg.

Major adverse cardiac events- high-risk patients undergoing emergency surgery:

In high-risk group of patients (ASA classification 3 or 4), 62 patients (33%) had high Troponin I levels (TnI > 0.06 µg·l-1) 12 hours after surgery. 40 of these patients (64%) had history of a myocardial damage before surgery. Sixteen patients with high TnI (26% were diagnosed to have a perioperative myocardial infarction). Patients with postoperative myocardial ischemia had postoperative episodes of tachycardia more frequently than patients without myocardial damage (19% versus 6%, p=0.007).

Table 4: Outcome in high risk patients undergoing Emergency surgery:

	TnI > 0.06µg·l-1	TnI ≤ 0.06µg·l-1	p
Major Adverse Cardiac Events	22(35%)	4(3%)	<0.001
30 days mortality	14(23%)	9(7%)	0.003
3 months mortality	23(37%)	20(16%)	0.001

Mortality

30 days post surgery, 23 patients (12%) did not survive. 14 patients (23%) who had Troponin I levels > 0.06 µg·l-1, 12 hours postoperatively, did not survive compared to 9 patients (7%) with normal TnI levels postoperatively (p=0.003)

5. Discussion

In the present study, among patients undergoing elective surgery, the incidence of TnT elevation was about 10%. Among high-risk patients undergoing non-elective surgery, a significantly higher incidence of Troponin elevation (33%) at 12 hours after surgery was observed. Important predictors of myocardial damage in the postoperative period were

ProBNP > 1800 ng·l-1 prior to surgery, medication with organic nitrates, tachycardia at recovery, and intraoperative hypertension.

Among patients undergoing emergency surgery we find a high incidence of myocardial damage in case of a major emergency non-cardiac surgery (38%) as detected by troponin elevation in the perioperative period. Intermittent ECGs and clinical signs were found to be poor instruments for the identification of myocardial damage in the perioperative period. The detection of perioperative myocardial damage is thus mainly dependent on surveillance using sensitive cardiac markers. We found perioperative clinical events that were associated with elevated troponin and myocardial damage- high-risk surgery, tachycardia, hypoxaemia, hypotension, as well as large perioperative bleeding.

Hence these clinical events including tachycardia, hypotension/hypertension, and hypoxaemia in the perioperative period should be aggressively treated in order to reduce the risk of myocardial damage.

Previous studies have shown that myocardial damage usually occurs towards the end of surgery or within the first 24-48 hours postoperatively (14). In the present study, among patients > 70 years old undergoing elective surgery in 90% of the cases, we found preoperatively elevated TnT in 26% of the patients with TnT elevation in the postoperative period. Among patients who underwent emergency or urgent surgery, 64% of the patients with TnI elevation 12 hours after surgery already had a TnI elevation prior to surgery. This is clinically significant. Hence, cardiac monitoring including analyses of trop and NT-proBNP in high-risk patients should start before the surgery. In this way, we can better identify patients with pathological TnI levels preoperatively.

Predictors of outcome in non-cardiac surgery

During the last decades, several risk indices have been developed for prediction of cardiac complications in patients undergoing non-cardiac surgery. The one most commonly used is the Revised Cardiac Risk Index (RCRI), (15). This study has established a close relation between perioperative myocardial damage and poor short- and long-term outcome in patients undergoing non-cardiac surgery.

The focus has shifted towards interventions and treatments to reduce the risk of myocardial damage in the perioperative period. Many therapeutic interventions are already available for this purpose, which essentially optimize the myocardial oxygen supply/demand equation including statins and beta-blockers (16). Treatment with beta-blocker can reduce episodes of tachycardia and hypertension. However, the risk/benefit of perioperative beta-blocker treatment remains to be established (17). Acetylsalicylic acid treatment could be continued in perioperative period to reduce the risk of coronary thrombosis without any increased risk of bleeding. Our results have to be verified by larger randomized controlled trials in patients with ischemic heart disease. In addition, evidence about other medical treatments, such as ACE inhibitors, calcium channel blockers, or α2-adrenergic

agonists in reducing myocardial damage and improving postoperative outcome is unclear.

6. Conclusions

- Postoperative myocardial damage is an independent risk factor for death within one year of surgery in elderly patients undergoing non-cardiac surgery. Perioperative TnT values provide prognostic information and regular TnT surveillance in the postoperative period is useful to identify patients with increased risk of adverse cardiac events.
- Perioperative myocardial damage is common in high-risk patients undergoing emergency surgery. An asymptomatic preoperative increase in TnI is an independent predictor of perioperative major adverse cardiac events. An elevated NT-proBNP prior to surgery is also an independent predictor of perioperative myocardial damage.
- Elevated NT-proBNP prior to surgery is frequent in elderly high-risk patients

Undergoing surgery. NT-proBNP was found to be an independent predictor of perioperative adverse cardiac outcome in this group of patients. The use of NT-proBNP as a routine test in high-risk patients undergoing emergency surgery could be a useful tool in assessing perioperative risk and help in making clinical decisions on pre-, per-, and postoperative treatment and monitoring.

References

- [1] Mangano D. Peri-operative cardiovascular morbidity: new developments. In: Baillière's Clin Anaesthesiol; 1999:335-48.
- [2] Mangano DT. Perioperative cardiac morbidity. Anesthesiology 1990;72:153-84.
- [3] Devereaux PJ, Goldman L, Cook DJ, Gilbert K, Leslie K, Guyatt GH. Perioperative cardiac events in patients undergoing noncardiac surgery: a review of the magnitude of the problem, the pathophysiology of the events and methods to estimate and communicate risk. CMAJ 2005;173:627-34.
- [4] Le Manach Y, Godet G, Coriat P, et al. The impact of postoperative discontinuation or continuation of chronic statin therapy on cardiac outcome after major vascular surgery. Anesth Analg 2007;104:1326-33, table of contents.
- [5] Abraham N, Lemech L, Sandroussi C, Sullivan D, May J. A prospective study of subclinical myocardial damage in endovascular versus open repair of infrarenal abdominal aortic aneurysms. J Vasc Surg 2005;41:377-80; discussion 80-1.
- [6] Kumar R, McKinney WP, Raj G, et al. Adverse cardiac events after surgery: assessing risk in a veteran population. J Gen Intern Med 2001;16:507-18.
- [7] Badner NH, Knill RL, Brown JE, Novick TV, Gelb AW. Myocardial infarction after noncardiac surgery. Anesthesiology 1998;88:572-8.
- [8] Shah KB, Kleinman BS, Rao TL, Jacobs HK, Mestan K, Schaafsma M. Angina and other risk factors in patients with cardiac diseases undergoing noncardiac operations. Anesth Analg 1990;70:240-7.
- [9] Ashton CM, Petersen NJ, Wray NP, et al. The incidence of perioperative myocardial infarction in men undergoing noncardiac surgery. Ann Intern Med 1993;118:504-10.
- [10] Mangano DT, Hollenberg M, Fegert G, et al. Perioperative myocardial ischemia in patients undergoing noncardiac surgery--I: Incidence and severity during the 4 day perioperative period. The Study of Perioperative Ischemia (SPI) Research Group. J Am Coll Cardiol 1991;17:843-50.
- [11] Devereaux PJ, Goldman L, Yusuf S, Gilbert K, Leslie K, Guyatt GH. Surveillance and prevention of major perioperative ischemic cardiac events in patients undergoing noncardiac surgery: a review. CMAJ 2005;173:777-88.
- [12] Mackey WC, Fleisher LA, Haider S, et al. Perioperative myocardial ischemic injury in high-risk vascular surgery patients: incidence and clinical significance in a prospective clinical trial. J Vasc Surg 2006;43:533-8.
- [13] Fleischmann KE, Goldman L, Young B, Lee TH. Association between cardiac and noncardiac complications in patients undergoing noncardiac surgery: outcomes and effects on length of stay. Am J Med 2003;115:515-20.
- [14] Landesberg G, Luria MH, Cotev S, et al. Importance of long-duration postoperative ST-segment depression in cardiac morbidity after vascular surgery. Lancet 1993;341:715-9.
- [15] Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation 1999;100:1043-9.
- [16] Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery): Developed in Collaboration With the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. Circulation 2007;116:1971-96.
- [17] Poldermans D, Schouten O, Vidakovic R, et al. A clinical randomized trial to evaluate the safety of a noninvasive approach in high-risk patients undergoing major vascular surgery: the DECREASE-V Pilot Study. J Am Coll Cardiol 2007;49:1763-9.