

## Incidence of Troponin Elevation Myocardial Infarction After Hip Fracture Intramedullary Nailing in Early Postoperative Period

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### Abstract

**Background:** The purpose of the study was to evaluate the trends of Troponin I (cTnI) levels and to determine whether the increased levels of this marker are associated with the presence of perioperative myocardial infarction (MI), in patients following hip intramedullary nailing, for hip fracture treatment.

**Methods:** One hundred thirty-two patients with risk factors for coronary artery disease, who underwent hip intramedullary nailing for intertrochanteric hip fracture, were participated in this prospective study. Troponin trends observed after hip nailing were recorded in association with demographic and clinical data. Besides, the cases of MI developed in the operated patients were also recorded and analyzed.

**Results:** Sixty-two (46.96%) patients, who underwent hip surgery, had raised Troponin levels during the postoperative period. However, only 5 (8.06%) patients of them with elevated Troponin levels experienced MI. Significant increase of Troponin levels, more than 300 folds was reported in all patients sustained MI after hip surgery. It was noteworthy that all the patients sustained MI had cTnI levels more than 230 pg/ml on the first postoperative day. Elevated Troponin levels was significantly associated with older age ( $p=0.02$ ), history of angina ( $p=0.028$ ) and heart failure stage C ( $p=0.05$ ).

**Discussion:** Elevated cTnI levels are common in the early post-operative period after hip intramedullary nailing, in patients with risk factors for MI. So, the routine use of cardiac Troponin assays should be encouraged, especially in older patients with risk factors especially angina or heart failure, in order to detect clinical silent MI and improve the mortality rates postoperatively.

**Keywords:** Troponin; Myocardial infarction; Hip; Intramedullary nailing

### Introduction

Cardiac incidents are the main cause of death following anaesthesia and surgery [1]. Many patients with coronary artery disease predisposition, who are subjected to non-cardiac surgical procedures including hip surgery, have a high incidence of perioperative myocardial ischemia [2]. The pathophysiological mechanism of perioperative myocardial injury is subject to debate. Hypotension and increased heart rate due to intraoperative blood loss are major risk factors in the perioperative period, leading to mismatch between oxygen demands and supply, predisposing to myocardial infarction (MI) type II [3]. Rupture

of atheromatic plaque is another mechanism of perioperative myocardial injury, leading to myocardial infarction (MI) type I according to 4th Universal Definition of MI [1,3].

The incidence of myocardial ischaemia ranges from 14% to 31% in high-risk patients undergoing total hip arthroplasty and up to 43% in patients with hip fracture surgery [4-7].

Most of the cases (almost 80%) with peri-operative myocardial infarctions may be undetected when the diagnosis is only based on clinical signs and symptoms [6]. Postoperative analgesia, diabetes, impaired patient communication due to post-surgical

delirium and nonspecific electrocardiographic changes can make the detection of myocardial infarction difficult [2, 3].

Cardiac Troponin is considered as a specific marker for detection of myocardial infarction in the postoperative period [3,7]. However, increased Troponin levels have also been reported in pulmonary embolism, sepsis, pneumonia, renal failure and stroke [5,8]. As a matter of fact, all these conditions are common comorbidities in the elderly. So, is Troponin a reliable marker to detect myocardial infarction after hip surgery? The answer to such a question is not quite clear. Fisher et al reported increased Troponin levels in 29% of patients who underwent hip surgery, but only 33% of them showed evidence of myocardial infarction [8]. Although many studies report elevated levels of Troponin after hip surgery, it is not known if the increased levels are attributed to myocardial infarction or due to other conditions [9-13]. The basic limitation of these studies is that Troponin levels before surgery were not estimated or there was no confirmation in the diagnosis of myocardial infarction according to the most reliable criteria. In addition, the patients who participated in these trials underwent different types of hip surgery, making the sample of these studies heterogenous.

We hypothesized that the increased levels of cTnI seen after hip nailing are not associated always with MI. So, the purpose of our study was to evaluate the trends of Troponin I (cTnI) levels and to determine whether the increased levels of this marker are associated with the presence of perioperative MI, in patients following hip intramedullary nailing.

**Materials and Methods**

This is a prospectively conducted study that took place in a regional general hospital, from February 2018 to January 2020. The study protocol was approved by the ethical committee of the hospital (REF NUMBER: 1185) and was in accordance with the ethical principles set out in the Declaration of Helsinki. Patients who were included in our study were informed about the study protocol and were voluntarily recruited after their consent.

Criteria for inclusion in the study were those with clinical risk factors for coronary artery disease (CAD) according to the revised cardiac risk index, included: angina and / or previous myocardial infarction, heart failure, stroke or transient ischaemic attack, serum creatinine > 2mg/dl, diabetes mellitus requiring insulin therapy, undergoing hip intramedullary nailing for intertrochanteric hip fracture (a minimal invasive surgery with intermediate surgical risk), performed under spinal anaesthesia, regardless of their gender [13].

Lumbar puncture for spinal anaesthesia was performed in sitting position using a 25-gauge needle. Then 1.5 ml lidocaine 5% (75 mg lidocaine) with 0.1 mg epinephrine was injected. Also, all patients received supplemental oxygen via a facemask at a rate of 6 L per minute during the procedure. Post-operative analgesia included intravenously administrated paracetamol every 8 hours. Besides in case of extremely pain, tramadol was administrated.

Patients without risk factors for coronary artery disease were excluded as it has been proposed that routine use of cTnI should be discouraged in non-cardiac patients undergoing non cardiac surgery [13]. Similarly, patients with increased cTnI

levels before surgery were also excluded, in order to determine the direct effect of surgery on Troponin measurements.

The 4th criteria of 4th Universal Definition of Myocardial Infarction for type I and II MI were used in this study [3]. These criteria include: detection of a rise and/or fall of cTn and evidence at least one of the following:

1. Symptoms of acute myocardial ischemia
2. New ischemic ECG changes
3. Development of pathological Q waves
4. Imaging evidence of new loss of viable myocardium, or new regional wall motion abnormality in a pattern consistent with an ischemic etiology.
5. Angiography or autopsy for identification of coronary thrombus (only for type I MI).

In order to report the trends of cTnI levels and to identify operated patients with perioperative MI (as a consequence of atheromatic plaque rupture – type I of myocardial infarction or as a consequence of mismatch between oxygen demand and supply – type II of myocardial infarction, according to 4th Universal Definition of Myocardial Infarction), as outcome measurements after hip fracture intramedullary nailing, the following procedures were carried out [3]:

- a) Venous blood samples were obtained from all patients, prior to surgery, immediately after, six hours later and at 24, 48, 72, 96 and 120 hours for the estimation of cTnI levels. Cardiac Troponin was measured by a Baxter Stratus II analyzer (high sensitivity assay), which utilized two monoclonal antibodies. According to our laboratory standards, any values of cTnI levels greater than 15pg/ml are considered positive.
- b) Symptoms or clinical signs that indicated MI such as chest

Figure 1: Flow chart diagram of patients enrolled in the study.

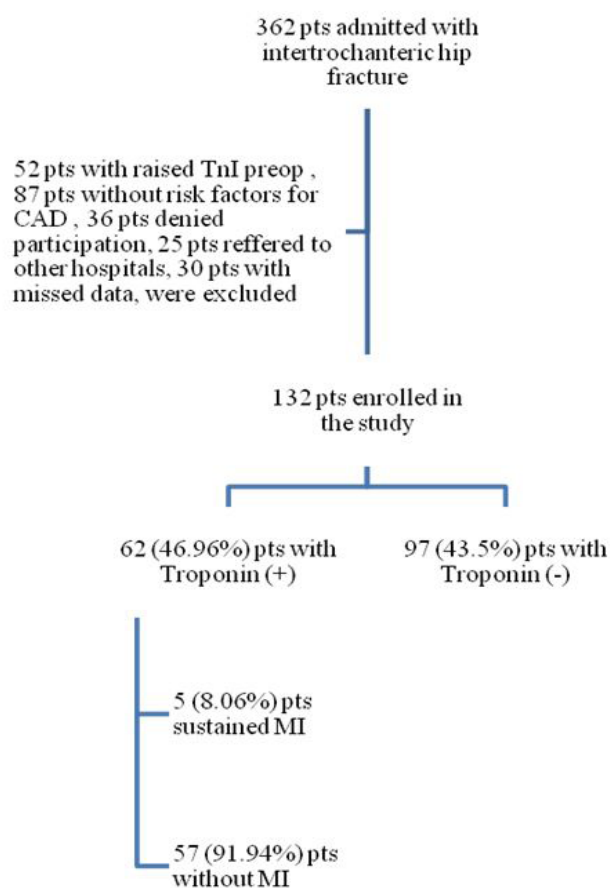


Table 1: Demographic and clinical data of patients underwent hip intramedullary nailing in association with Troponin levels.

	Troponin (+)	Troponin (-)	p-value
Age (ys)	83.2±4.1	78.4±3.6	0.02*
Female Gender (%)	71.8	73.6	0.71
Functional capacity before fracture (METs < 4)	45	51	0.37
Time from fracture to surgery (>48h)	51	43	0.46
Duration of surgery (>45min)	38	43	0.98
History of angina (n pts)	38	16	0.028*
History of previous myocardial infraction (n pts)	6	8	0.93
History of heart failure (n pts)			
Stage A	13	11	0.43
Stage B	5	7	0.37
Stage C	7	2	0.05*
Stage D	2	1	0.48
History of stroke or transient ischemia (n pts)	12	9	0.52
History of diabetes mellitus requiring insoulin therapy (n pts)	18	13	0.3
Preoperative creatinine levels > 2mg/dl	15	17	0.85

ys= years old, n pts = number of patients \*statistical significance

Table 2: Patients with MI development, after hip intramedullary nailing.

Patient	History of risk factor for MI	Clinical symptoms	ECG findings	Two dimensional echo post-operatively	Stress echo postoperatively (myocardium wall)
1	Stroke (before 6 years)	None	ST-T changes	Abnormal wall movement	Dyskinesia
2	MI (before 10 years)	Chest pain	ST-T changes	Abnormal wall movement	Dyskinesia
3	Insulin therapy	None	None	Abnormal wall movement	Dyskinesia
4	MI (before 14 years)	None	None	Abnormal wall movement	Dyskinesia
5	Angina	Chest pain	ST-T changes	Abnormal wall movement	Dyskinesia

Table 3: Mean cTnI levels in study population, after intramedullary hip nailing.

Troponin levels (pg/ml)	0h	6h	24h	48h	72h	96h	120h
Patients without sustained MI	11±1.6	15±2.3	22±4.6	42±3.1	38±4.1	25±2.8	14±3.4
Patients sustained MI	43±3.1	62±2.7	258±6.6	1035±34	9842±56	3446±42	1232±22

pain, dyspnoea or signs of hemodynamic unstable patient were recorded

c) A resting 12-lead electrocardiogram was performed on all patients undergoing hip intramedullary nailing surgery preoperatively, 6 hours postoperatively, and at 1, 2, 3 and 5 days postoperatively, in order to exclude any signs of MI (prolonged new convex ST-segment elevation, particularly when associated with reciprocal ST-segment depression, T wave inversions, presence of new Q-waves, new LBBB etc)

d) All patients were submitted to a two-dimensional echocardiogram preoperatively and on the 4th to 5th day postoperatively. Any abnormality in segmental-wall motion observed postoperatively by the two-dimensional echocardiogram was considered as indicative of perioperative infarction. Experienced cardiologists performed the echocardiograms and they were blind to troponin measurements.

e) Patients experienced sudden death after hip fracture intramedullary nailing underwent autopsy for identification possible MI.

Descriptive statistics were used to present the results for continuous and discrete variables. Comparisons between groups were performed using the Student’s t-test (unpaired) for continuous normally distributed variables. For discrete categorical variables, chi-square with Fisher’s exact test was also carried out. Logistic regression analysis using a statistical model adjusted for confounding parameters was performed to test the association between post-operative raise of cTnI levels and various demographic and clinical parameters. Statistical significance was set at p<0.05. Statistical analysis was performed with statistical packet STATA 7.0 (Stata Corp., College Station, TX).

**Results**

The flowchart for the enrollment of patients in the study is shown at Fig.1. The demographic and clinical data of the 132 patients who underwent hip intramedullary nailing surgery and were participated in our study are summarized in Table I. Elevated Troponin levels were significantly associated with older age (p=0.02), history of angina (p=0.028) and cardiac failure stage C (p=0.05).

Sixty-two (46.96%) from the total of 132 patients, had raised Troponin levels during the postoperative period. However only 5 (8.06%) patients of them, experienced myocardial infarction which was confirmed by clinical examination, ECG changes, positive two-dimensional echo or echo stress. Three of these patients developed a clinical silent MI and one of them died during hospitalization. ECG changes reported in 3 patients with MI and two-dimensional echo and stress echo were positive in all cases with MI. The characteristics of patients sustained MI are presented at Table II. Also, all four MI were confirmed with angiography and the other one (the patient who died) with autopsy. The mean postoperative values of Troponin levels in hip surgery patients are shown at Table III. The rest 57 patients with elevated Troponin levels did not develop clinical symptoms. Also, they had not ECG changes, two-dimensional echo or echo stress findings.

The increase of Troponin levels in 41 (66.12%) of the patients was less than 3 folds. Twelve (19.35%) patients in the hip surgery group had a 3-to-6-fold increase of Troponin levels. Among these patients, one suffered from pulmonary embolism, 2 from pneumonia, 3 from renal failure and one from cardiac failure. These seven patients did not develop MI according to 4th Universal Definition of MI. Nine patients (14.5 %) presented with more than 6 folds increase in Troponin levels. More than 300 folds increase of Troponin levels in hip surgery patients was observed in 5 cases post-operatively, whereas a myocardial infarction was evidenced. All 5 patients had cTnI levels more than 230 pg/ml on the first postoperative day. One of these patients had Troponin levels more than 1200 pg/ml and died during hospitalization.

The maximal increase of Troponin levels was detected on the second postoperative day ( $p < 0.0001$ ). These levels remained at high levels until the third postoperative day and returned to preoperative values on the fifth postoperative day.

## Discussion

The present study systematically evaluated the estimation of cTnI levels in patients with risk factors for MI, in the postoperative period after hip intramedullary nailing. To the best of our knowledge, this is the first study to evaluate systematically the measurement of cTnI in older patients operated exclusively with hip intramedullary nailing for hip intertrochanteric fracture.

According to this research, almost half of the patients with risk factors for MI were found with elevated cTnI levels in the early postoperative period. Our results are in accordance with the study of Chong et al who reported raised cTnI levels in 53% of emergency orthopaedic patients over 60 years of age post-operatively [2]. Other studies have shown elevated cTnI levels in 12–42% of patients after hip fracture surgery [3,7-11,14-19]. However, the percentage of patients with elevated cTnI (46.96%) after hip nailing reported in the present study is one of the highest reported in the literature. The main explanation of this finding is that in our study participated patients with risk factors for MI exclusively and not healthy subjects. A previous study has shown that patients with a history of coronary artery disease had a greater chance to develop myocardial injury [3,8].

Although the elevation of cTnI is common during the periop-

erative period after hip surgery, only a few patients develop MI. It has been postulated that elevated cTnI levels after surgery reflect myocardial injury but not coronary artery disease necessarily [12]. A broad variety of other factors such as perioperative stress, anaemia, acidosis, sepsis, excessive sympathetic activity, anaesthetic drugs, renal failure, congestive heart failure, pulmonary embolism and chronic obstructive pulmonary disease, which cause an imbalance between myocardial oxygen supply and demand, can lead to myocardial injury and the subsequent cTnI elevation [8]. This is consistent with the results of the present study, since 70 patients out of the 132 showed elevated cTnI levels after hip surgery but did not fulfil the criteria of 4th Universal definition of MI. In these cases, the slight elevation of cTnI was attributed to other factors besides MI. On the other hand, five patients were presented with elevated cTnI levels of more than 230pg/ml on first day after hip surgery and these patients experienced MI which was confirmed with a positive echo stress and angiography or autopsy. Three of these patients developed a clinical silent MI, which was detected by the elevated levels of cTnI and 1 of them died during hospitalization. Gupta et al reported an incidence of MI up to 13.8% in a cohort study of 1,212 elderly patients with mean age of 85 years old who underwent hip fracture surgery [18]. Also, Fisher et al diagnosed clinical myocardial infarction in 23 out of 69 (33 %) patients with raised cTnI levels [8].

The maximal increase of cTnI levels after hip nailing was detected on the second postoperative day. These levels remained high until the third postoperative day and returned to preoperative values on the fifth postoperative day in most of the patients.

The majority of the MI incidents (92%) occurred within the first 48 hours of surgery and the 75% of them were asymptomatic.

Another remarkable finding of this study was that significant association between increased levels of Troponin and older age, history of angina and heart failure stage C. Similarly, Chong et al reported significant association between increased Troponin levels and older age and history of CAD, heart failure or renal failure, in patients underwent different types of emergency orthopaedic procedure [2]. Also, Fisher et al mentioned significant association between elevated Troponin levels and older age, ASA score  $>3$ , history of CAD or stroke and smoke habits, in operated patients for hip fracture [8]. On the other hand, Mortazavi et al found no significant relationship between age, gender, BMI, daily activity, underlying illness and cTnI levels after arthroplasty [20]. Also, Jules-Elysee did not mention any correlation between elevated Troponin levels and age, gender or risk factors for CAD in patients underwent hip and knee arthroplasty or spine surgery [21].

The main strength of this study was that the trends of cTnI levels were reported on 132 patients with risk factors for MI who sustained intertrochanteric hip fracture and underwent hip intramedullary nailing. So the results are referred exclusively to this particular type of hip surgery. The entrance of patients with risk factors for MI development and not healthy subjects in the study, in addition to the specific type of hip surgery increases the homogeneity of this study. However, there are several limitations of the present study such as the single hospital used and the small number of participants which probably limit the power analysis of data. A multicentre study with a greater



number of participants would have allowed the extraction of safer conclusions. Furthermore, the patients with elevated Troponin levels (except the four with MI) did not undergo angiography postoperatively, a useful examination to rule out MI type I. However, pharmaceutical echo stress was performed, which is characterized by high negative predictive value.

## Conclusion

In conclusion, the results of the current study suggest that elevated cTnI levels are common in the early post-operative period after hip intramedullary nailing in patients with risk factors for MI. The routine use of cardiac Troponin assays should be encouraged, especially in older patients in order to detect clinical silent MI and improve the mortality rates postoperatively of patients with elevated cTnI levels.

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