



# Troponin T as a predictive marker of morbidity in patients with fractured neck of femur

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## KEYWORDS

Hip fractures;  
Troponin;  
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## Summary

**Introduction:** This study aims prospectively to assess perioperative measurement of Troponin T, a marker of myocardial injury, as a predictor of morbidity and mortality in patients undergoing surgery for fractured neck of femur.

**Method:** All patients aged 65 years and over presenting with a fractured neck of femur over a 4-month period were initially included. Exclusion criteria were renal failure, polymyositis and conservative fracture management. Troponin T levels were measured on admission, day 1 and 2 post-surgery. According to local protocol, a level of  $>0.03$  ng/mL was considered to be raised. Adverse outcome measures were cardiorespiratory events (myocardial infarction, congestive cardiac failure, unstable angina, major arrhythmias requiring treatment and pulmonary embolism), death and length of inpatient stay.

**Results:** One hundred and twenty-nine patients presented with femoral neck fractures. 108 patients were included after application of the exclusion criteria. 42 (39%) showed a Troponin rise. Of these, 25 sustained one or more outcome complications versus seven with no rise ( $p < 0.001$ ). The mean hospital stay was 25.7 days for patients with elevated Troponin, 18.3 days in the normal group ( $p < 0.012$ ). There were nine deaths in the raised Troponin group, and five with no rise ( $p < 0.05$ ).

**Discussion:** The principle causes of early death after hip fracture surgery are cardiac failure and myocardial infarction. Troponin T is a sensitive enzymatic marker of myocardial injury. The association between raised Troponin and hip fractures has not

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previously been made. In our series, 39% showed a perioperative Troponin rise. This was significantly associated with increased morbidity, mortality and longer hospitalisation. Many patients appear to be having silent events, causing significant morbidity. We recommend Troponin measurement in all patients to identify this risk and allow appropriate optimisation measures.

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## Introduction

Fractured neck of femur is a common cause of morbidity, use of hospital care, and death in the elderly population.<sup>10</sup> Age specific incidence rates have increased substantially in most Western populations in recent decades.<sup>19</sup> The 90-day mortality rate for these patients is reported as 18.9%.<sup>19</sup> Previous studies indicated that the principle causes of death after hip fracture surgery were cardiac failure and myocardial infarction, peaking at 2 days; bronchopneumonia, which accounted for the majority of late deaths and pulmonary embolism, which peaked in the second week after injury.<sup>4,16,18,22</sup> The medical profile of patients with fractured neck of femur is such that there is a high prevalence of cardiovascular disease.<sup>6</sup> Previous studies have shown overall incidence of perioperative myocardial ischaemia in patients undergoing hip fracture surgery is 35–42%.<sup>15,20,22</sup>

There are a number of methods available for the detection of perioperative myocardial damage which include electrocardiogram, cardiac scanning and the measurement of blood concentrations of cardiac specific enzymes. Cardiac enzymes such as Troponins and CK-MB have been shown to be effective at detecting perioperative myocardial damage.<sup>12</sup> Troponins are heteromeric proteins playing an important role in the regulation of skeletal and cardiac muscle contraction. They include Troponins I, T and C.

Most intramuscular Troponin is part of the muscle contractile apparatus. After damage to cardiac muscle cells, Troponins are released into the circulation and may be measured in the peripheral blood.<sup>1</sup> They can be detected in patient's blood 3–6 h after onset of an acute coronary event and remain raised for 4–10 days.<sup>6</sup> Troponin I and T, highly sensitive markers of myocardial injury, are widely used in patients who present with acute coronary syndromes and can help identify risks of future coronary events. Troponin T has been found to have a higher positive and negative predictive value, sensitivity and specificity than either Troponin I or CK-MB.<sup>11</sup> A rise in Troponin T is not normally associated with musculoskeletal trauma.

Perioperative Troponin T has been shown to be a useful marker of long-term adverse cardiac out-

comes in elective orthopaedic patients,<sup>11,17</sup> but has not been routinely used in emergency orthopaedic admissions. The aim of this study is to assess prospectively whether Troponin T may potentially be used as a predictor of morbidity and mortality in emergency admissions with fractured neck of femur.

## Materials and methods

A pilot study comprising 20 patients was carried out, after which a proposal was successfully submitted to the Local Research Ethics Committee. Any patient aged 65 years and over presenting through the emergency department with fractured neck of femur was initially included in the study. Data were collected over four calendar months. All were patients whose presenting diagnosis was a fractured hip, as opposed to chest pain or other medical symptoms. Patients already admitted with medical diagnoses who subsequently fell and fractured their femoral neck were not included.

At the time of presentation, background data were collected on each patient. In addition to simple demographic information, a record was made of the following cardiac risk factors; hypertension, previous myocardial infarction or angina, congestive cardiac failure, diabetes mellitus (DM), atrial fibrillation and presence of a pacemaker. Additionally, a note was made of whether the patient was taking any of the following 'cardiac' drugs; aspirin, calcium-channel blockers, angiotensin-converting enzyme (ACE) inhibitors,  $\beta$ -blockers or nitrates. Exclusion criteria were applied such that patients with polymyositis, renal failure, and conservatively treated fracture were not included. Troponins are excreted via the kidneys, so any impairment in renal function may lead to increased plasma levels even in the absence of other pathologies. Renal failure was defined according to local biochemical guidelines such that creatinine of over 200  $\mu\text{mol/l}$  was considered diagnostic.

All patients had serial venous blood samples taken for measurement of Troponin T levels. Following discussion with a consultant cardiologist, the timing of the samples was based on previous studies investigating post-operative rises in cardiac enzymes.<sup>12,17</sup> This was established as follows—at

**Table 1** Interpretation of Troponin levels

Troponin T level (ng/mL)	Significance
<0.03	No significant myocardial damage
0.03–0.1	Probable myocardial damage
>0.1	Definite myocardial damage

the time of patient admission, and on days 1 and 2 post-operatively. According to local pathology guidelines the Troponin T levels were interpreted as shown in Table 1.

For the purpose of this study any Troponin T concentration >0.03 ng/mL was interpreted as a significant result. Patients with a significant rise in Troponin T (i.e. implying probable or definite myocardial damage) were discussed with the on-call medical team, and appropriate investigative or treatment measures taken where required. For the purpose of analysing the data, patients with a rise in any one or more of the serial samples were included in the raised Troponin cohort.

The outcome measures recorded for this study were the following adverse cardiovascular events<sup>14</sup> – myocardial ischaemia, congestive cardiac failure, unstable angina, major arrhythmias requiring active treatment, pulmonary embolism – length of inpatient stay, and death from any cause whilst in hospital.

Data were collected using a proforma which recorded the following information on each patient; patient demographic data, the relevant medical and drug history outlined above, outcome measures listed, results of the serial blood tests, and total number of days spent in hospital on this particular admission.

## Results

The results are summarised in Tables 2 and 3, and Figs. 1–3.

Over the 4-month period studied, 129 patients presented with fractured neck of femur. After application of the exclusion criteria, 108 patients were included in the study (21 patients excluded). The associations between a significant Troponin T rise and length of inpatient stay or adverse cardiorespiratory outcomes were statistically examined using the chi-squared test.

A rise in Troponin T >0.03 ng/mL in at least one of the samples occurred in 42 patients (39%). Of those patients that exhibited a rise in Troponin T, 12 had elevated levels at presentation. The remaining 30 patients had a normal Troponin T level on admission but demonstrated a rise post-operatively. Of particular note, the patient groups with normal and abnormal ECG traces were equally likely to have perioperative Troponin T rise.

Of the 42 patients with an enzyme rise, 25 patients sustained at least one of the outcome complications including death. This compares to seven patients from the 66 patients who showed no Troponin T rise ( $p < 0.001$ ).

The mean length of stay was 25.7 days (range 5–86) for patients with elevated Troponin T levels, compared with 18.3 (6–67) days for those with a normal Troponin T ( $p < 0.012$ ). There were nine deaths in the raised Troponin group, and five in the group with no rise ( $p < 0.05$ ).

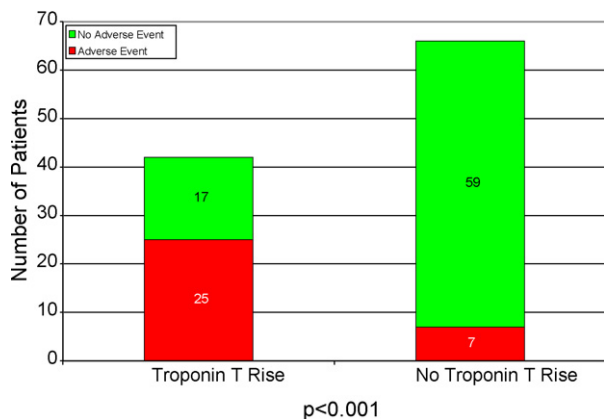
In 57 of the 108 patients at least one cardiac risk factor was reported from the list in the proforma. Of these 57 patients, 27 had a rise in one or more Troponin T assays, as opposed to only 15 patients

**Table 2** All outcome measures

	No. of Patients ( <i>n</i> = 108)	All adverse events	In-patient mortality	Mean days in hospital
Troponin T rise	42 (39%)	25	9	25.7 (5–86)
Normal Troponin T	66 (61%)	7	5	18.3 (6–67)
		$p < 0.001$	$p < 0.05$	$p < 0.012$

**Table 3** Morbidity and mortality

Outcome measure	Patients with NO Troponin T rise ( <i>n</i> = 66)	Patients with a Troponin T rise ( <i>n</i> = 42)	<i>p</i> value (NS, not significant)
Death, all causes ( <i>n</i> = 14)	5	9	<0.05
Arrhythmia ( <i>n</i> = 4)	1	3	>0.1 (NS)
MI ( <i>n</i> = 11)	0	11	<0.001
PE ( <i>n</i> = 1)	0	1	>0.05 (NS)



**Figure 1** All adverse events.

from the group with no reported risk factors (51 patients) ( $p < 0.05$ ). In 51 cases, the drug history included one or more of the cardiac medications recorded. Of these 51 patients, 27 patients had a Troponin T rise, as opposed to 15 patients of the group of 57 who were not using these drugs ( $p < 0.01$ ). The specific factors found to be associated with an increased likelihood of a Troponin T rise were; a previous history of myocardial infarction ( $p < 0.01$ ), and inclusion of aspirin ( $p < 0.05$ ), a nitrate ( $p < 0.01$ ) or an ACE-inhibitor ( $p < 0.02$ ) in the drug history.

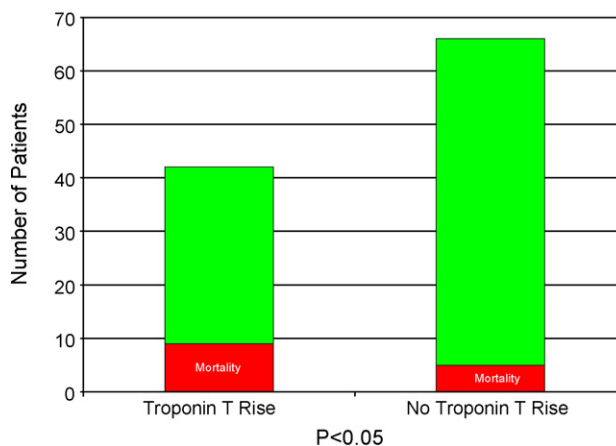
## Discussion

Over recent decades there has been a rise in the incidence of fractured neck of femur.<sup>3,9</sup> Whilst associated mortality rates fell significantly between the late 1960s and early 1980s, there has been little further improvement over the past 20 years.<sup>19</sup> Some authors still quote 1-year mortality as high as

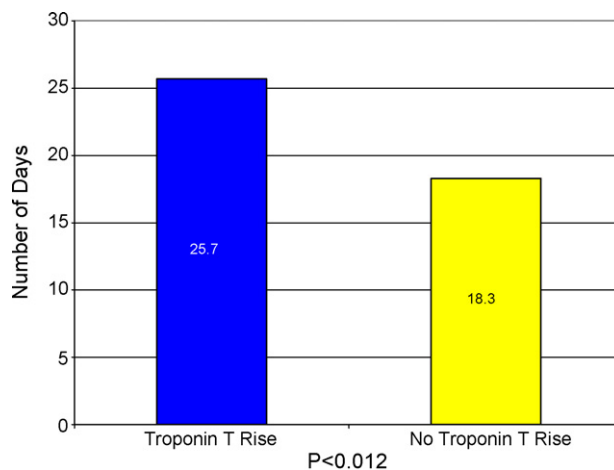
38%,<sup>5,7,8,13,21,23</sup> 90-day mortality rates of 18.9%,<sup>19</sup> with a sharp rise also being seen with increase in age. It is not clear whether this current mortality rate represents an irreducible minimum level, or whether there remains scope for further improvement. On this premise, any measures that may help to reduce medical complication rates in the perioperative period should be considered. Mangano identified that in the post-operative setting MI and clinically important ischaemia are often silent as a result of altered pain perception, caused by residual anaesthetics, by analgesia or by competing incisional pain, and that they may occur without haemodynamic changes.<sup>14</sup>

The association between raised Troponins and neck of femur fractures has not previously been made. Studies carried out by Higham et al.,<sup>11</sup> and Neill et al.,<sup>17</sup> enrolled 157 and 80 elective patients, respectively, undergoing either vascular or major joint arthroplasty surgery. They investigated measurements of Troponin I and T as markers of long-term post-operative adverse events. Both of the studies showed a significant association between a raised Troponin and an adverse cardiac outcome.

More recent discussion in the literature suggests that, whilst Troponins are certainly highly sensitive markers of cardiac ischaemia, they may not be as specific as previously thought. Ammann et al.<sup>2</sup> list 14 other cardiac and 10 non-cardiac causes of raised Troponin in addition to ischaemia of the myocardium. For example, this group suggest that up to 85% of patients with generalised sepsis in the absence of myocardial ischaemia show elevated Troponin levels. Nevertheless, they still draw the conclusion from a number of previous clinical studies that elevated Troponin levels are predictors for increased mortality or worse clinical outcome, independently of acute coronary syndromes and myocardial infarction.



**Figure 2** Mortality in all patients.



**Figure 3** Length of stay in hospital.

In our series, 39% of all patients undergoing surgery for neck of femur fracture had elevated Troponin T levels in the perioperative period. There was a statistically significant association between a rise in Troponin and increased morbidity and mortality whilst in hospital. The majority of these adverse outcomes were demonstrably related to cardiac events (on the basis of clinical, ECG, echocardiographic or radiological parameters). Troponin measurement is a simple assay costing approximately £6, and may allow the early assessment of preoperative ischaemia that may otherwise be initially undetected in this group, allowing the clinician to minimise its effects with prompt medical consultation and treatment. Equally, however, in those patients whose co-morbidity is not found to be cardiac in origin, identification of this sub-group may nevertheless allow them to be monitored more carefully in the perioperative period, enabling optimal preoperative work-up as well as rapid and aggressive treatment of post-operative complications.

The aim of this study has not been to demonstrate that perioperative measurement of Troponin levels leads to an improved outcome in patients undergoing surgery for fractured neck of femur. However, on the basis of our findings an association is proposed between neck of femur fractures and elevated Troponin T concentrations. The results suggest that hip fracture patients with elevated Troponin T have poorer clinical outcomes and longer stay in hospital than those whose levels are normal. This is an area that requires further investigation, and it is proposed that, ultimately, measurement of Troponin levels should be used in conjunction with the other standard perioperative screening tests to identify those patients at greatest risk, with a view to providing early optimum medical intervention.

### Conflict of interest

None.

### References

1. Ammann P, Fehr T, Minder E, et al. Elevation of Troponin I in sepsis and septic shock. *Intensive Care Med* 2001;27:965–9.
2. Ammann P, Pfisterer M, Fehr T, Rickli H. Raised cardiac troponins—causes extend beyond acute coronary syndromes. *Br Med J* 2004;328:1028–9.
3. Balasegaram S, Majeed A, Fitz-Clarence H. Trends in hospital admissions for fractures of the hip and femur in England: 1989–1990 to 1997–1998. *J Public Health* 2001;23:11–7.
4. Beals R. Survival following hip fracture. Long follow-up of 607 patients. *J Chronic Dis* 1972;25:235–44.
5. Beringer T, Gilmore D. Outcome following proximal femoral fracture in the elderly female. *Ulster Med J* 1991;60:28–34.
6. Bertinchant J, Laruee C, Pernel I, et al. Release kinetics of serum cardiac Troponin I in ischaemic myocardial injury. *Clin Biochem* 1996;29:587–94.
7. Boereboom F, Raymakers J, Duursma S. Mortality and causes of death after hip fractures in Netherlands. *Neth J Med* 1992;41:4–10.
8. Center J, Nguyen T, Schneider D, et al. Mortality after all major types of osteoporotic fracture in men and women; an observational study. *Lancet* 1999;353:878–82.
9. Evans J, Seagrott V, Goldacre M. Secular trends in proximal femur fracture: Oxford record linkage study area and England 1968–86. *J Epidemiol Community Health* 1997;51:424–9.
10. Goldacre M, Roberts S, Yeates D. Mortality after admission to Hospital with fractured neck of femur: database study. *Br Med J* 2002;325:868–9.
11. Higham H, Sear J, Sear Y, et al. Perioperative troponin I concentration as a marker of long-term postoperative adverse cardiac outcomes—a study in high-risk surgical patients. *Anaesthesia* 2004;59:318–23.
12. Jules-Elysee K, Urban M, Urquhart B, Milman S. Troponin I as a diagnostic marker of a perioperative myocardial infarction in the orthopedic population. *J Clin Anesth* 2001;13:556–60.
13. Keene G, Parker M, Pryor G. Mortality and morbidity after hip fractures. *Br Med J* 1993;307:1248–50.

14. Mangano D. Perioperative cardiac morbidity. *Anesthesiology* 1990;72:153–84.
15. Marsch S, Schaefer H, Skarvan K, et al. Perioperative myocardial ischemia in patients undergoing elective hip arthroplasty during lumbar regional anesthesia. *Anesthesiology* 1992;76:518–27.
16. Myers A, Robinson E, Van Natta M, et al. Hip fractures among the elderly: factors associated with in-hospital mortality. *Am J Epidemiol* 1991;134:1128–37.
17. Neill F, Sear J, French G, et al. Increases in serum concentrations of cardiac proteins and the prediction of early postoperative cardiovascular complications in noncardiac surgery patients. *Anaesthesia* 2000;55:641–7.
18. Perez J, Warwick D, Case C, Bannister G. Death after proximal femoral fracture—an autopsy study. *Injury* 1995;26:237–40.
19. Roberts S, Goldacre M. Time trends and demography of mortality after fractured neck of femur in an English population, 1968–98: database study. *Br Med J* 2003;327:771–5.
20. Scheini H, Virtanen T, Kentala E, et al. Epidural infusion of bupivacaine and fentanyl reduces perioperative myocardial ischaemia in elderly patients with hip fracture—a randomized controlled trial. *Acta Anaesthesiol Scand* 2000;44:1061–70.
21. Walker N, Norton R, Vander Hoorn S, et al. Mortality after hip fracture; regional variations in New Zealand. *N Z Med J* 1999;112:269–71.
22. Weatherall M. Case mix and outcome for patients with fracture of the proximal femur. *N Z Med J* 1993;106:451–2.
23. Weatherall M. One year follow up of patients with fracture of the proximal femur. *N Z Med J* 1994;107:308–9.