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Original Article

Perioperative Elevation of Troponin I Predicts Survival After Orthopaedic Surgery in Older Patients With Fracture

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SUMMARY

Background: To assess the relationship between perioperative elevation of Troponin I and one-year survival after orthopaedic surgery in older patients with fracture.
Methods: This prospective observational study was conducted from May 2014 to June 2015. 97 older patients (age>65 years) with orthopaedic surgery after fracture were included in the study. Troponin I was measured at the next day of admission, the first and the fifth day after surgery, respectively. Patients with elevated Troponin I in any of 3 time points were divided into the elevated group. All patients received at least one-year follow-up by telephone. All caused one-year mortality was recognized as the primary end-point.
Results: Perioperative elevated serum Troponin I (>0.03 mg/L) were found in 37.1% patients (36/97). In the one-year follow-up, 4 patients were lost with the follow-up rate 95.9%. Seventeen patients died during one-year follow-up, the cumulative all caused one-year mortality was 17.5%. The cumulative mortality rate was higher in the elevated Troponin I group, compared with the normal Troponin I group (27.8% Vs. 11.5%; Log Rank Chi-Square = 5.647, p = 0.015). The crude HR was 2.885, with 95% CI 1.105–7.627. Multivariate analyze by Cox proportional hazards model showed the adjusted HRs were 2.319 (95% CI 1.120–4.479) for perioperative elevated Troponin I and 2.375 (95% CI 1.131–4.488) for preoperative elevated Troponin I.
Conclusion: Elevated perioperative Troponin I level decreases one-year survival after orthopaedic surgery in older patients with fracture. We suggest routine surveillance and earlier diagnosis together with appropriate treatment of cardiac event should be given in older fracture patients at perioperative period and later follow-up.

1. Introduction

Population ageing is widespread across the world. It is most advanced in the most highly developed countries. According to United Nations, the proportion of the world's population aged 60 years or over increased from 8% in 1950 to 12% in 2013, and will increase more rapidly in the next four decades to reach 21% in 2050.[1] Older adults are closely related with bone loss and decreased bone mineral density, which increase fracture risks.[2,3] Fracture risk in older is also medicated by central nervous system.[4] Because the degradation of the nervous system functions, the elderly are easy to fall. Accordingly, the older fracture population increased annually.

Older patients with fracture are always related with high mortality. A population-based study showed overall one-year postoperative mortality in hip fracture patients aged 65 was 27.3% and mortality after hip fracture at the end of the follow-up was 79.0%, which was 3-fold higher than that of the general population.[5] Among older patients with orthopaedic surgery, the most common cause of death was circulatory diseases.[5] Urban et al. reported one year incidence of postoperative myocardial infarction in an orthopaedic population was 0.6%, and 6.5% of those patients were at risk of cardiac event.[6] Hietala P et al. found there were 35.5% asymptomatic myocardial infarctions in patients undergoing hip fracture surgery, and he believed perioperative myocardial infarctions were common and often unrecognized in these patients.[7]

Troponin I has emerged as the biomarker of choice for the detection of myocardial injury, being a more sensitive and specific marker compared to CK and CK-MB.[8,9] Chong C et al. have already found elevated post-operative troponin levels were predictive of one-year survival in older patients undergoing emergency orthopaedic surgery.[10,11]

The purpose of the present study was to assess the relationship between perioperative elevation of Troponin I and one-year survival after orthopaedic surgery in older patients with fracture.

2. Methods

2.1. Study design and inclusion criteria

This prospective observational study was conducted from May 2014 to June 2015. The enroll criteria included: ① patients who un-

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derwent orthopaedic surgery for fracture; ② older patients with age over 65 years. Patients complicated with active cancer and organ dysfunction (end stage renal disease, end stage heart failure, and end stage liver cirrhosis) were excluded. The study protocol was approved by the human research ethics committee of our hospital, and the included patients have signed an informed consent.

2.2. Patients

Our study recruited a total of 97 patients, which included 41 men (42.3%) and 56 women (57.7%) with a mean age of 72.6 years (range, 65–87 years). The clinical characteristics of the participants were listed in Table 1.

2.3. Laboratory test for Troponin I

Troponin I was tested at 3 time points perioperatively: the next day of admission, the first day after surgery, and the fifth day after surgery. It was measured immediately by the hospital laboratory using enhanced chemiluminescence (Johnson Vitros ECiQ) after samples collection. The cut-off level for an abnormal result is 0.03 mg/L. Patients with elevated Troponin I in any of 3 time points were divided into the elevated group, and patients without elevated Troponin I in all of 3 time points were divided into the normal group.

2.4. Follow-up and outcomes

All patients received at least one-year follow-up by telephone. Semi-structured interview with the patients or their immediate family member was conducted. The interview included fracture healing and major adverse cardiovascular events. The primary endpoint was all caused one-year mortality, and the secondly endpoint was cardiac caused one-year mortality. If the patients were died in the follow-up, their family members were asked to provide the date of death and the cause of death.

2.5. Statistical analysis

First, we compared the baseline clinical characteristics between the Troponin I elevated group and the normal group. Continuous variables were compared using the student t tests, and categorical variables using the chi-square test. Second, we assessed the prognostic significance of the Troponin I for one-year mortality by univariate and multivariate analyses. Kaplan–Meier method and log-rank test were used as univariate analyses; Cox proportional hazards model in a forward stepwise manner was used as multivariate analyses. Results were presented as hazard ratio (HR) with 95% confidence interval (95% CI). $P < 0.05$ was considered significant. All statistical analyses were performed using IBM SPSS statistics software (version 19.0, IBM, Armonk, NY).

3. Results

3.1. General characteristics

Among the 97 included patients, 36 patients (37.1%) were found with elevated serum Troponin I in the perioperative period. In these 36 patients, 30 were found elevated serum Troponin I preoperatively, and the other 6 were found elevated serum Troponin I postoperatively. There were no differ statistically in terms of age (p = 0.454), gender (p = 0.739), smoke (p = 0.260), alcoholism (p = 0.633), hypertension (p = 0.900), diabetes (p = 0.223), COPD (p = 0.180), stroke (p = 0.431), CKD (p = 0.633), fracture type (p = 0.539), surgery type (p = 0.805), length of surgery (p = 0.479), blood transfusion (p = 0.772) and postoperative pneumonia (p = 0.459), when compared the elevated group with the normal group. But between two groups, there was a statistically significant difference in CAD medications use

Table 1
Baseline clinical characteristics of the study population.

Variable	All Patients (n = 97)	Troponin I elevation		P Value
		Yes (n = 36)	No (n = 61)	
General characteristics				
Age (year)	72.6 ± 5.1	73.1 ± 5.0	72.3 ± 5.1	0.454
Gender (M/F)	41/56	16/20	25/36	0.739
Smoke (Y/N)	21/76	10/26	11/50	0.260
Alcoholism (Y/N)	9/88	4/32	5/56	0.633
Preoperative comorbidity				
Coronary heart disease (Y/N)	11/86	8/28	3/58	0.009
COPD (Y/N)	13/84	7/29	6/55	0.180
Stroke (Y/N)	8/89	4/32	4/57	0.431
CKD (Y/N)	9/88	4/32	5/56	0.633
Risk factor for CAD				
Hypertension (Y/N)	45/52	17/19	28/33	0.900
Hyperlipidemia (Y/N)	31/66	13/23	18/43	0.500
Diabetes (Y/N)	23/74	11/25	12/49	0.223
Family history (Y/N)	24/73	10/26	14/47	0.595
CAD medications (Y/N)	15/82	10/26	5/56	0.010
Orthopaedic surgery				
Fracture type (four limbs/hip/other)	38/42/17	12/16/8	26/26/9	0.539
Surgery Type (elective/emergency)	88/9	33/3	55/6	0.805
Length of surgery (min)	86 ± 27	88 ± 28	84 ± 26	0.479
Postoperative complication				
Cardiac event[a] (Y/N)	3/94	3/33	0/61	0.022
Blood transfusion (Y/N)	12/85	4/32	8/53	0.772
Pneumonia (Y/N)	8/89	2/34	6/55	0.459

[a] Cardiac event included readmission owing to worsening heart failure, or arrhythmia, or intervention.

(38.5% Vs. 8.9%, p = 0.010). 10 patients received CAD medications in Troponin I elevation group, and 5 patients received CAD medications in Troponin I normal group. They all used medications included ACEI, ARB, ASA, B-blocker, or statin. Significant difference were also found in preoperative comorbidity incidence of coronary heart disease (22.2% Vs. 4.9%, p = 0.009) and postoperative complication incidence of cardiac event (8.3% Vs. 0.0%, p = 0.020) between 2 groups. 3 patients suffered from postoperative cardiac event of frequent premature ventricular contractions. They received antiarrhythmic treatment, and all recovered on discharge. The baseline clinical characteristics of the study population were listed Table 1.

3.2. One-year survival

In the one-year follow-up, 4 patients were lost because of changing the address and the telephone number. The follow-up rate was 95.9%.

Seventeen patients died between one-year follow-up, the all caused one-year mortality of all included patients was 17.5%. In the elevated Troponin I group (n = 36), 10 patients died in 1-year follow-up. The cumulative mortality rate was 27.8%. In the normal Troponin I group (n = 61), 7 patients died, and the cumulative mortality rate was 11.5%. Kaplan–Meier curve was listed in Fig. 1A. Log-rank test showed patients in elevated Troponin I group had a worse all caused one-year mortality than in the normal Troponin I group (Log Rank Chi-Square = 5.647, p = 0.015). The crude HR was 2.885, with 95% CI 1.105–7.627.

Twelve patients died for cardiac cause between one-year follow-up, the cardiac caused one-year mortality of all included patients was 12.4%. Among these 12 patients, 9 patients died of myocardial infarction (4 STEMIs and 5 non-STEMIs), 3 patients died of heart failure. In the elevated Troponin I group (n = 36), 9 patients died for cardiac cause in 1-year follow-up. The cumulative mortality rate was 25.0%. Among these 9 patients, 7 patients died of myocardial infarction (3 STEMIs and 4 non-STEMIs), 2 patients died of heart failure. In the normal Troponin I group (n = 61), 3 patients died for cardiac cause, and the cumulative mortality rate was 4.9%. Among these 3 patients, 2 patients died of myocardial infarction (1 STEMI and 1 non-STEMI), 1 patient died of heart failure. Kaplan–Meier curve was listed in Fig. 1B. Log-rank test showed patients in elevated Troponin I group had a worse cardiac caused one-year mortality than in the normal Troponin I group (Log Rank Chi-Square = 6.445, p = 0.008). The crude HR was 2.956, with 95% CI 1.127–9.561.

Cox proportional hazards model for all caused one-year mortality showed elevated Troponin I, old age, perioperative comorbidity of coronary heart disease, and postoperative cardiac event were independent risk factors for one-year survival of older patients with fracture after orthopaedic surgery. After adjusted for these risk factors, the adjusted HR for perioperative elevated Troponin I was 2.319 (95% CI 1.120–4.479), and 2.375 (95% CI 1.131–4.488) for preoperative elevated Troponin I. The Cox proportional hazards model was listed in Table 2.

4. Discussion

In this study, we found patients with elevated perioperative

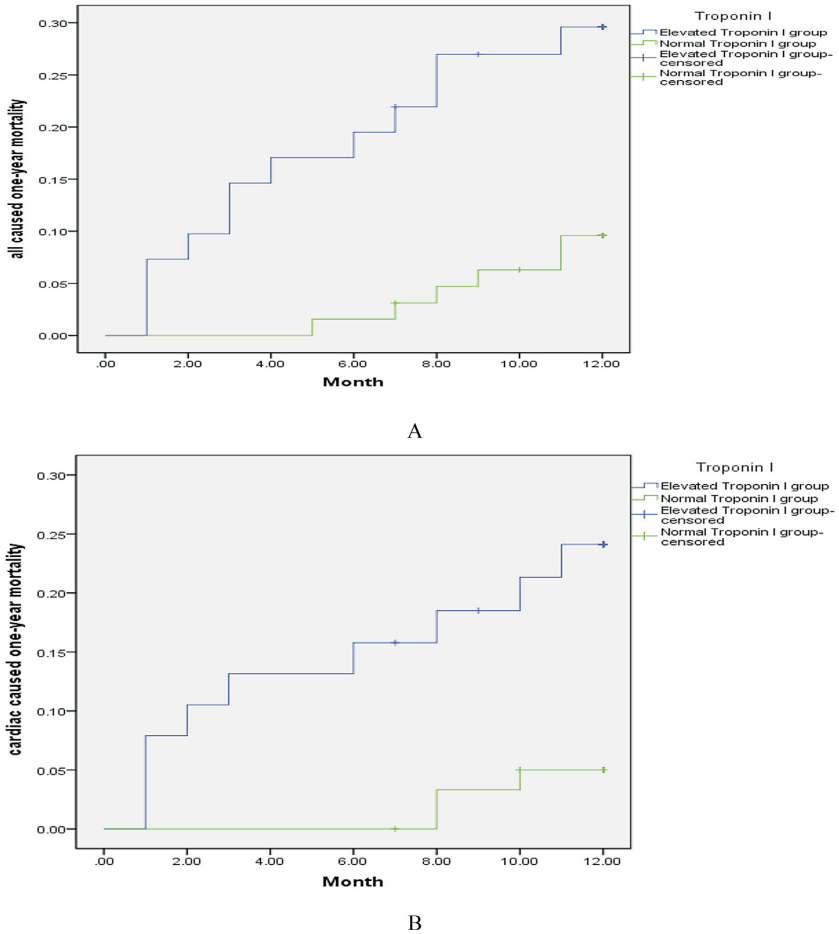

Fig. 1. Kaplane–Meier survival curve of patients divided into whether there was a Troponin I elevation perioperative. A, all caused one-year mortality, B, cardiac caused one-year mortality.

Table 2
Cox proportional hazards model for all caused one-year mortality of older patients with fracture after orthopaedic surgery. Model 1 (Perioperative elevation of Troponin I), Model 2 (Preoperative elevation of Troponin I).

Model 1					
Variable	B	SE	Wald	P Value	HR (95% CI)
Perioperative elevated Troponin I	0.841	0.423	5.259	0.015*	2.319 (1.120e4.479)
Age	0.035	0.020	4.455	0.015*	1.036 (1.014e1.102)
Preoperative CHD	0.543	0.384	4.672	0.008*	1.721 (1.156e4.699)
Postoperative cardiac event	0.675	0.336	4.924	0.028*	1.964 (1.134e4.239)
Model 2					
Variable	B	SE	Wald	P Value	HR (95% CI)
Preoperative elevated Troponin I	0.865	0.415	5.326	0.018*	2.375 (1.131e4.488)
Age	0.031	0.024	4.468	0.019*	1.031 (1.010e1.101)
Preoperative CHD	0.556	0.324	4.688	0.003*	1.744 (1.178e4.755)
Postoperative cardiac event	0.681	0.355	4.952	0.007*	1.976 (1.156e4.249)

*P<0.05.

Troponin I level had a worse one-year survival than patients with normal Troponin I. This result was confirmed by multivariate analyses, with the adjusted HR 2.342 (95% CI 1.122–4.464). The most common cause of death was circulatory diseases. In Chong et al.' study, they found all-cause mortality after emergency orthopaedic surgery in older patients was 20.6% at 1 year.[11] They also found post-operative troponin rise was associated with one-year all-cause mortality using multivariate analysis, with the OR 12.0 (37% mortality in troponin rise versus 2.1% without a rise, P < 0.0001).[11] Their results are same like us. But we think perioperative Troponin rise is a more sensitive indicator.

In our study, we divided patients with elevated Troponin I in any of 3 time points (the next day of admission, the first day after surgery, and the fifth day after surgery) were into the elevated group. Hietala reported Troponin T was elevated already at admission in 32.4% patients, and a later preoperative Troponin T rise was observed in 13 patients (18.3%).[7] Our study found 30 (30.9%) patients have elevated Troponin I in preoperative period, and another 6 (6.1%) patients have elevated Troponin I in postoperative period. Pre-operative and post-operative elevation of Troponin-I stand different meanings, and were affected by the inflammatory status (tissue injury, wound inflammation) or precipitating factors of cardiovascular events (blood loss; stress) by surgery. But they have same value in predicting prognosis.

In the perioperative period, antiplatelet drugs such as aspirin and clopidogrel cannot be used because of postoperative bleeding. In our study, all the patients complicated with CAD discontinued antithrombotic agents in the period between two days before surgery and discharge. It may be the confounding factor that influences risk of thromboembolic events and cardiac events. But no thromboembolic events were found in the perioperative period. Only 3 patients with postoperative frequent premature ventricular contractions was found.

The prognosis of perioperative myocardial infarction in noncardiac major surgery increased the mortality.[12–14] In the perioperative period, antiplatelet drugs such as aspirin and clopidogrel cannot be used because of postoperative bleeding, and invasive strategy with early revascularization also cannot be used. Strategies for perioperative myocardial infarction mainly included the use of perioperative β–blockers,[15] α-adrenoceptor agonists,[16] and statins.[17] After these strategies, the prognosis will be improved. However, perioperative myocardial infarctions are often asymptomatic and unrecognized in patients.[7,12] Therefore, it is important to routine measurements of troponin in older fracture patients at perioperative period. Symptomatic myocardial infarctions also can be diagnosed by cardiac enzyme and ECG. Our studies also found the survival between two groups were even poorer in very old age, hip fracture, and emergency surgery patients. The result indicated routine measurement of troponin is more important in these patients.

There are some limitations in our study. First, we only included 97 patients in one hospital. We found the calculated 95% CI of HRs were too wide because of small sample size. The wide 95% CI was imprecision, which decreased the level of evidence.[18] Second, the included patients were only follow-up with one year. We have no idea whether elevated perioperative Troponin I level still related with longer term survival. It seems studies with large sample and longer follow-up are needed. Third, we only used short-period perioperative Troponin I tests as a prediction of one year outcome. Maybe there were other offending factors after surgery associated with cardiovascular events. So, routine surveillance and earlier diagnosis together with appropriate treatment of cardiac event are needed for these patients during follow-up.

In conclusion, our study showed elevated perioperative Troponin I level decrease one-year survival after orthopaedic surgery in older patients with fracture. We suggest routine surveillance and earlier diagnosis together with appropriate treatment of cardiac event should be given in older fracture patients at perioperative period and later follow-up.

Author disclosure statement

No competing financial interests exist.

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