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Association of Acute Perioperative Myocardial Injury With All-Cause Mortality Within 90 Days After Hip Fracture Repair in the Elderly: A Prospective Study

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Abstract

Introduction: It remains unclear whether acute perioperative myocardial injury (APMI) increases mortality in the elderly. This study aimed to investigate APMI's association with mortality within 90 days after hip fracture repair in elderly patients.
Materials and Methods: This prospective study enrolled elderly patients admitted to the department of Traumatology and Orthopaedics in XXX Hospital, who underwent surgery in 2018–2019 with a 90-day follow-up. According to survival status within 90 days, survival and death groups were constituted. Clinical, demographic, and laboratory indicators and 90-day mortality post-surgery were recorded. APMI's association with 90-day mortality post-surgery was analyzed by logistic regression.
Results: Totally 248 participants were enrolled, including 224 and 24 in the survival and death groups, respectively, for a mortality rate of 9.7%. Compared with surviving individuals, the death group was older [81 (75–86) vs 87 (82–89) years], and had higher incidence rates of APMI (24.6% vs 58.3%), intertrochanteric fractures (41.1% vs 62.5%), preoperative atrial fibrillation (8.9% vs 29.2%), and dementia (73.7% vs 95.8%) (all P<.05). They also showed higher pre-injury frail scale scores [1 (0–2) vs 3 (1–4)] and Nottingham hip fracture scores (NHFSs) [4 (4–5) vs 6.5 (5–7)], lower Glomerular filtration [62 (46.1–78.6) vs 44.37 (35–61.92) ml/min], and reduced odds of glomerular filtration rate <60 mL/min (75.0% vs 46.9%) (all P < .05). APMI (OR = 3.294, 95% CI: 1.217–8.913) and NHFS (OR = 2.089, 95% CI: 1.353–3.225) independently predicted 90-day mortality post-surgery (all P<.05).
Conclusions: APMI is associated with increased mortality risk within 90 days after hip fracture repair in elderly patients.

Keywords

acute perioperative myocardial injury, elderly population, hip fracture, 90-day all-cause mortality, myocardial injury and mortality

Introduction

More than 200 million non-cardiac surgeries are performed every year worldwide, and addressing perioperative cardiovascular accidents remains a challenge facing both physicians and patients.[1,2] Perioperative myocardial injury (PMI) is an important factor resulting in cardiovascular accidents.[3] According to the *Fourth Universal*

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Definition of Myocardial Infarction 2018,[4,5] acute myocardial infarction is characterized by elevated myocardial enzymes (cTn value above the 99th percentile upper limit of normal (ULN)) combined with newly discovered evidence of myocardial necrosis, such as new abnormal ventricular wall stage movement in echocardiography, alteration of ST-T in electrocardiography, or evidence of a vascular blockage in coronary CTA, while myocardial damage is characterized by abnormal myocardial enzymology in the absence of evidence of necrosis at echocardiography, electrocardiogram, or coronary CTA.[4,5] The Perioperative Ischemic Evaluation Study (POISE) reported a 30-day mortality of 11–25% for PMI patients in non-cardiac surgery, that is, 5 times higher than that of non-PMI patients.[6] Acute myocardial injury (AMI) that occurs between preoperative and postoperative 30 days is defined as acute perioperative myocardial injury (APMI).[5]

Hip fracture is a common fracture in the elderly, with significant morbidity and mortality.[7,8] Hip fracture repair significantly improves the quality of life and reduces mortality in elderly individuals.[9] In such patients, PMI significantly increases mortality within 30 days and even 1 year after surgery in the elderly following hip fractures,[10–14] but some studies suggest that cTn increase is not related to perioperative hospital mortality in patients with hip fractures.[15,16] The above studies used cTn levels to assess the degree of PMI, and few considered electrocardiography and imaging findings. In addition, elevated cTn during the perioperative period can be due to perioperative myocardial infarction,[17] and not using electrocardiography and/or imaging might bias the results. Whether APMI is associated with postoperative all-cause mortality in elderly patients with hip fractures remains unknown, as well as the effect of APMI on mortality at 90 days after surgery.

Therefore, this study aimed to investigate the association of APMI with 90-day all-cause mortality after hip fracture repair in elderly patients.

Materials and Methods

Study Design

This study was a prospective study that was carried out at the emergency department of Traumatology and Orthopaedics of XXX Hospital from September 2018 to February 2019.

Sample Size Estimation

The PASS software (NCSS, LLC, Kaysville, UT, USA) was used to calculate the minimum sample size. According to the literature,[6] the 90-day mortality rate of the group with AMJ was about 18%, and the mortality rate of the group without AMJ was about 4%. Considering $\alpha = .05$, $\beta = .20$, and $1\text{-}\beta = .80$, the minimum sample size was calculated to be 196 participants, or 216 participants when considering 10% of loss to follow-up.

Sampling Technique

This prospective study enrolled elderly patients aged ≥65 years with hip fractures admitted to the emergency department of Traumatology and Orthopaedics in XXX Hospital from September 2018 to February 2019.

Participants

The participants were all diagnosed with femoral neck or intertrochanteric fracture by X-ray and underwent artificial femoral head/total hip replacement or closed/limited open reduction combined with internal fixation with an intramedullary nail on admission. The inclusion criteria were that cardiac troponin I (cTnI) measured preoperatively and at 24 and 72 h after surgery was higher than normal value and fluctuated more than 20% in any 1 of the 3 times.[18] The exclusion criteria were 1) perioperative acute myocardial infarction through comprehensive assessments of cTnI, electrocardiography (ECG), and echocardiography and 2) perioperative cTnI elevation due to pulmonary embolism, sepsis, or severe tachyarrhythmia. The perioperative period referred to 30 days before and after surgery.

Outcomes

The outcome of this study was 90-day all-cause mortality.

Intervention

At the study center, patients >65 years of age presenting with hip fracture in the emergency department are routinely examined for troponin, myocardial enzymes, echocardiography, and electrocardiogram. Classic procedures were performed as confined operations during daytime for artificial femoral head/total hip replacement or limited open reduction and internal fixation with intramedullary nail.[18]

Comparison

The participants were assigned to the survival and death groups according to survival status during the follow-up period. Grouping was done at the end of the study when all participants were enrolled and according to their 90-day outcome.

The data were all collected from the paper-based medical records of the emergency department of Traumatology and Orthopaedics of XXX Hospital. Demographic and clinical data were recorded on admission, including gender, height, body weight, fracture type, preoperative waiting time, preoperative and pre-discharge hemoglobin, glomerular filtration rate, cTnI, N-terminal pro-brain natriuretic peptide (NT-proBNP), creatine kinase MB (CK-MB), underlying diseases, oral medications, age-adjusted Charlson Comorbidity Index (aCCI), hospital stay, and length of stay in the ICU. Body mass index (BMI), frail scale (FS), nutritional risk scale score (NRS), and Nottingham hip fracture score (NHFS) were determined based on a questionnaire and examination results. In this study, cTnI, CK-MB, and NT-pro-BNP amounts were examined at 4 time points: before admission to the emergency department, before surgery, and at 24 and 72 h after surgery. In the case of normal CK-MB and at least one CTnI elevation with a variation greater than 20%, ECG and echocardiography were performed again postoperatively. ECG and echocardiography data were evaluated in a blinded manner by two cardiologists with 11 and 4 years of experience, respectively. In addition, 12-lead ECG and echocardiography data were recorded to exclude the possibility of cTnI elevation caused by perioperative myocardial infarction. According to the changes of myocardial enzymes during the perioperative period, combined with ECG and echocardiography data, a comprehensive diagnosis of APMI was made.[4,5]

The family members of all patients were contacted by telephone at 30, 60, and 90 days after surgery, respectively, to collect data such as survival, re-hospitalization after surgery, and activities of daily living after discharge. Telephone follow-up was conducted by 5 medical professionals after 2 weeks of training, including 1, 3, and 1 with 19, 17, and 5 years of experience, respectively.

The missing data generally involved that troponin was not checked within 72 h after the operation; these patients did not meet the inclusion criteria, and they were not included in the study. In addition, all baseline data are routinely taken after admission as surgery is not performed without complete preoperative data.

Ethics

This work has been carried out in accordance with the Declaration of Helsinki (2000) of the World Medical Association. This study was approved by the Ethics Committee of XXX (approval number: XXX). All participants or their relatives signed the informed consent form.

Statistical Analysis

Normally and non-normally distributed measurement data were presented as mean ± standard deviation and median (25 and 75 percentiles), respectively, and compared by the *t*-test and analysis of variance, respectively. Count data were presented as frequency (%) and assessed by the chi-square test. Logistic regression (the enter method) was used to analyze factors associated with 90-day all-cause mortality. Statistically significant ($P<.05$) factors in the univariable analyses were included in a logistic multivariable regression analysis to adjust the possible association between APMI and mortality for confounding factors. $P<.05$ was considered statistically significant. Statistical analyses were performed with the SPSS 25.0 software package (IBM Corp, Armonk, NY, USA).

Results

Patient Characteristics

This study enrolled 263 participants and excluded 15 according to the exclusion criteria, including acute myocardial infarction (n=5), chronic myocardial injury (n = 9), and severe tachyarrhythmia (n = 1). Finally, 248 participants were assessed. Among them, 73.4% were female. The median age was 82 (interquartile range, 76–86) years. Surgery was performed 3 (interquartile range, 2–4) days after fracture. Table 1 presents the clinical and laboratory characteristics of the participants. No participant was lost to follow-up. The mean follow-up time was 88.4 days, and the longest was 96 days.

90-day Survival (Primary Outcome)

Among the 248 participants, 24 died within 90 days after surgery, accounting for 9.7%. As shown in Table 1, compared with the survival group, the death group was older [81 (75,86) vs 87 (82,89) years, $P < .001$], and had higher incidence rates of APMI (24.6% vs 58.3%, $P < .001$), intertrochanteric fractures (41.1% vs 62.5%, $P = .044$), preoperative atrial fibrillation (8.9% vs 29.2%, $P = .002$), and dementia (73.7% vs 95.8%, $P = .016$). In addition, the death group showed elevated pre-injury FS scores [1 (0–2) vs 3 (1–4), $P < .001$] and NHFSs [4 (4–5) vs 6.5 (5–7), $P < .001$], lower serum creatinine levels [62 (46.1–78.6) vs 44.37 (35–61.92) ml/min, $P = .008$], and reduced odds of glomerular filtration rate <60 mL/min (75.0% vs 46.9%, $P = .032$). There were no significant differences between the survival and death groups in gender, preoperative waiting time, BMI, left ventricular ejection fraction, preoperative and pre-discharge hemoglobin amounts, blood transfusion rate, drug therapy, aCCI, and hospital stay, and coronary heart disease, hypertension, diabetes, chronic obstructive pulmonary disease, and cerebral infarction rates (all $P > .05$).

Association of APMI With 90-day All-Cause Mortality After Surgery

As shown in Table 2, after adjusting for age, fracture type, FS, renal function, a history of preoperative atrial fibrillation and dementia, APMI (OR = 3.294, 95% CI: 1.217–8.913; $P = .019$) and NHFS (OR = 2.089, 95% CI: 1.353–3.225;

Table 1. Patient Characteristics.

Characteristic	Total (n = 248)	Survival Group (n = 224)	Death Group (n = 24)	P
Gender, n (%)				.204
Male	66 (26.6)	57 (25.4)	9 (37.5)	
Female	182 (73.4)	167 (74.6)	15 (62.5)	
Age, years, median (IQR)	82 (76,86)	81 (75,86)	87 (82,89)	<.001
BMI, kg/m,[2] median (IQR)	21.48 (19.26,24.57)	21.48 (19.53, 24.65)	20.45 (17.82, 23.29)	.510
Fracture type, n (%)				.044
Femoral neck fracture	141 (56.9)	132 (58.9)	9 (37.5)	
Intertrochanteric fracture	107 (43.1)	92 (41.1)	15 (62.5)	
Preoperative waiting time, d, median (IQR)	3 (2,4)	3 (2, 4)	3 (2, 5.75)	.202
Preoperative status assessment, median (IQR)				
FS	1 (0,3)	1 (0, 2)	3 (1, 4)	<.001
FS>3	62 (25)	44 (9.8)	18 (37.5)	<.001
NHFS	5 (4,6)	4 (4, 5)	6.5 (5, 7)	<.001
Left ventricular ejection fraction, %, median (IQR)	75 (61,69)	65 (61, 70)	62.5 (60, 68)	.526
Preoperative hemoglobin, g/L, median (IQR)	117 (105,129)	119 (106, 131)	111 (95, 124)	.227
Blood transfusion, ml, median (IQR)	400 (0,800)	397 (0, 400)	500 (100, 800)	.280
Hemoglobin before discharge, g/L, median (IQR)	109 (101,118)	112 (105,126)	106 (94,114)	.493
Underlying diseases, n (%)				
Coronary heart disease	53 (21.4)	45 (20.1)	8 (33.3)	.133
Pre-injury atrial fibrillation	27 (10.9)	20 (8.9)	7 (29.2)	.002
Hypertension	130 (52.4)	116 (51.8)	14 (58.3)	.542
Diabetes	57 (23.0)	53 (23.7)	4 (16.7)	.439
Chronic obstructive pulmonary disease	21 (8.5)	20 (8.9)	1 (4.2)	.426
Cerebral infarction	41 (16.5)	35 (15.6)	6 (25.0)	.240
Dementia	188 (75.8)	165 (73.7)	23 (95.8)	.016
Laboratory test				
Glomerular filtration, ml/min, median (IQR)	60 (45,78)	62 (46.1, 78.6)	44.37 (35, 61.92)	.008
Glomerular filtration rate <60 mL/min, n (%)	123 (49.6)	105 (46.9)	18 (75.0)	.032
Drug therapy, n (%)				
Insulin	25 (10.1)	24 (10.7)	1 (4.2)	.311
Statins	39 (15.7)	37 (16.5)	2 (8.3)	.295
Antiplatelet drugs	48 (19.4)	45 (20.1)	3 (12.5)	.371
β blockers	35 (14.1)	31 (13.8)	4 (16.7)	.705
Nitrate	20 (8.1)	17 (7.6)	3 (12.5)	.401
Calcium channel blockers	77 (31.0)	79 (35.3)	8 (33.3)	.850
ACEI/ARB	42 (16.9)	38 (17.0)	4 (16.7)	.971
Diuretics	14 (5.6)	11 (4.9)	3 (12.5)	.126
aCCI	5 (4,6)	5 (4, 6)	6 (5, 7)	.021
APMI, n (%)	69 (27.8)	55 (24.6)	14 (58.3)	<.001
ICU Stay, d, median (IQR)	0 (0,0)	.3 (0, 0)	.88 (0, 1)	.002
Hospital stay, d, median (IQR)	4 (3,5)	4.36 (3, 5)	4.62 (4, 5)	.551

ACEI, angiotensin-converting enzyme inhibitor; APMI, acute perioperative myocardial injury; ARB, angiotensin II receptor blocker; BMI, body mass index; FS, Frail Scale; ICU, intensive care unit; IQR, interquartile range; NHFS, Nottingham hip fracture score; aCCI, age-adjusted Charlson Comorbidity Index.

P = .001) were independent risk factors for mortality within 90 days after surgery.

Discussion

This study showed that after hip fracture repair in the elderly, the death group showed remarkable differences compared with surviving individuals, including higher APMI incidence. In addition, APMI was found to be an independent risk factor for mortality within 90 days after surgery in this patient population. These findings suggest that special care should be given to individuals with APMI when undergoing hip fracture repair. The NHFS was also independently associated with mortality, as supported by previous studies,[19–22]

Table 2. Associations of Various Factors with 90-Day All-Cause Mortality After Surgery.

	Univariate Analysis		Multivariable Analysis	
Variables	OR (95% CI)	P	Or (95% CI)	P
Age	1.123 (1.050–1.200)	.001	1.025 (.938-1.120)	.583
FS	1.764 (1.294–2.405)	<.001	1.307 (.866-1.973)	.202
NHFS	2.414 (1.700–3.427)	<.001	2.089 (1.353-3.225)	.001
Dementia	8.224 (1.087–62.25)	.041	3.373 (.389-29.234)	.270
APMI	4.302 (1.808–10.234)	.001	3.294 (1.217-8.913)	.019
aCCI	1.364 (1.042–1.784)	.024	.701 (.457-1.076)	.104

APMI, acute perioperative myocardial injury; CI, confidence interval; FS, Frail Scale; NHFS, Nottingham hip fracture score; OR, odds ratio; aCCI, age-adjusted Charlson Comorbidity Index.

indicating that patients with APMI and detrimental NHFS should receive special attention and monitoring.

Different from other reports,[15,16] patients with elevated cTnI before or after surgery in this study were reassessed by ECG and echocardiography post-surgically to exclude the possibility of cTnI elevation due to perioperative myocardial infarction in addition to routine examinations before surgery. Patients with acute elevation of cTnI and no changes in ECG and echocardiography data were diagnosed with APMI. As shown above, APMI was an independent risk factor for 90-day all-cause mortality after surgery. Differently, a study by Huddleston *et al.* in 2012 assigned elderly patients with hip fractures to the perioperative myocardial infarction, perioperative subclinical myocardial ischemia (only elevated cTn or CK-MB), and non-myocardial ischemia groups based on perioperative cTn, CK-MB, and ECG ischemic changes.[23] They reported significantly higher 1-year mortality after surgery in the perioperative myocardial infarction group compared with the other 2 groups, with no difference between the subclinical myocardial ischemia and non-myocardial ischemia groups. It may be because their patient data were obtained from 1988 to 2002 when CK-MB was used to diagnose myocardial ischemia, which is somewhat different from the current definition of myocardial injury. In addition, Vallet et al.[16] assessed 312 elderly hip fracture patients over 70 years of age from 2009 to 2013 and used cTnT as an indicator for evaluating myocardial injury. Combining with ECG analysis, their results showed that elevation of cTnT alone was not associated with increased all-cause mortality and re-hospitalization rates at 6 months after surgery in elderly patients with hip fractures.

The findings reported by the above studies are different from the present conclusions probably because the myocardial injury is a multifactorial event involving myocardial ischemia and non-myocardial ischemia factors. The clinical conditions of the patients are complicated, and it is often inaccurate to determine the presence or absence of myocardial ischemia simply by ECG. In addition, unlike the above reports, this study was based on the European universal definition of myocardial infarction of 2018, [4] using cTn elevation above the 99 percentile to indicate myocardial injury and cTn value variation to define acute or chronic myocardial injury. AMJ suggests new myocardial injury during the perioperative period or aggravated previous chronic myocardial injury by surgery.[5,24] Meanwhile, chronic myocardial injury can be persistent, with no overt relationship with the current surgery. For example, in myocardial injury associated with structural heart disease or chronic kidney disease, cTn can be steadily elevated without dynamic changes.

Supporting the present study, the POISE research team and Beattie et al.[25,26] published findings in 2017 demonstrating that even when non-cardiac surgery patients aged over 45 years do not meet the diagnostic criteria for myocardial infarction, postoperative cTn elevation alone is associated with 30-day and 1-year mortality rates after surgery. The VISION study showed that hsTnT levels during the first 3 days after non-cardiac surgery were associated with 30-day mortality.[25] Vasireddi et al[27] showed that PMI in patients at low cardiac risk preoperatively was associated with long-term mortality. Two meta-analyses of 11 and 10 studies, published in 2016 and 2018, showed that PMI (indicated by troponins) was associated with major adverse cardiovascular events and mortality at 30 days and 1 year after non-cardiac, non-vascular surgery.[28,29] Still, the exact definition of PMI in relation to mortality should be investigated since Park et al[30] reported that patients with cTnI above the limit of detection but below the 99th percentile had an increased mortality risk after non-cardiac surgery. Different cutoff points should be investigated in future studies.

Hence, patients with APMI should be more closely monitored after discharge and possibly referred to a cardiologist for evaluation. In addition, it is speculated that enhanced monitoring and appropriate drug intervention such as aspirin, betalox, statins, and other drugs might benefit the patients,[24,31] but further large-scale clinical trials are needed for confirmation.

The main strength of the present study was to exclude the cases of acute myocardial infarction keeping only those with APMI. Still, this study had several limitations. First, the present study had a single-center design with a small sample size, which indicates the low generalizability of the findings. Second, patients with renal failure were not excluded, which might constitute an additional bias since renal failure can induce cTnI elevations. In general, the elevation of troponins caused by CKD is low and persistent, with no significant fluctuation at multiple reviews. This low elevation has been excluded in the present study, which focused on APMI. Third, many included patients who had a definite history of coronary artery disease, but we did not assess the rate of cardiovascular death. In China, the exact cause of death is often unclear, and elderly individuals generally suffer from multiple underlying diseases, making it difficult to define the ultimate cause of death. Fourth, high-sensitivity cTnI detection was not used for the diagnosis of APMI; instead, cTnI was used because of a more widespread application in real-world hospitals. Thus, the current results may be more suitable for promotion; however, this method reduces the diagnostic rate of patients with PMJ, which may have a certain impact on statistical analysis. Fifth, all enrolled patients after admission were transferred to the elderly orthopedics unit, which adopts a multidisciplinary cooperation model. Indeed, physicians from the geriatrics, rehabilitation, and anesthesiology departments participate in patient treatment, and surgery could be completed within 24 h. This significantly reduces perioperative complications and mortality and increases the proportion of patients with normal functional recovery after surgery.[32] Meanwhile, not all teams in previous studies had access to this hospitalization and surgery model, which may lead to incomparable results.

Conclusion

This study suggests that APMI is an independent risk factor for mortality within 90 days after surgery in elderly patients with hip fractures.

Author contributions

All authors made substantial contributions to study conception and design, and data acquisition, analysis and interpretation. In addition, all took part in drafting the manuscript or revising it critically for important intellectual content, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Statement

This work has been carried out in accordance with the Declaration of Helsinki (2000) of the World Medical Association. This study was approved by the Ethics Committee of Beijing Jishuitan Hospital (approval number: 201807-201811). All participants or their relatives signed the informed consent form.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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