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Association Between High-Sensitivity Troponin T on Admission and Organ Dysfunction During Hospitalization in Patients Aged 80 Years and Older with Hip Fracture: A Single-Centered Prospective Cohort Study

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Background: Prognostic evaluation of elderly patients with hip fracture is an issue that has been highly concerned by clinicians. Only a few studies have focused on organ dysfunction after hip fracture in the elderly. This study aimed to investigate the association between high-sensitivity troponin T (hs-TnT) at admission and organ dysfunction during hospitalization in elderly patients with hip fracture.

Methods: We enrolled 168 patients with hip fracture who were aged 80 years and older at Geriatric Orthopaedic Center of Sichuan Provincial Orthopedic Hospital between January 2020 and August 2020. Baseline characteristics, perioperative information, and short-term clinical outcomes were analyzed.

Results: Of the 208 patients admitted during the study period, 168 met the inclusion criteria; of these, 91 (54.2%) had higher hs-TnT than the 99th percentile in the normal population. After adjustment for confounders, elevated hs-TnT was independently associated with multiple organ dysfunction syndrome in the elderly (MODSE) (adjusted OR, 5.76; 95% CI, 1.74–19.10; P = 0.004), heart dysfunction (adjusted OR, 7.48; 95% CI, 2.17–25.82; P = 0.001), MODS severity score > 3 (adjusted OR, 5.22; 95% CI, 1.32–20.60; P = 0.018), and length of hospital stay > 14 days (adjusted OR, 2.38; 95% CI, 1.05–5.36; P = 0.037).

Conclusion: Increased hs-TnT on admission is an independent risk factor for MODSE after hip fracture in patients aged 80 years and older. Effective measures should be applied to avoid progression of MODSE from pre-failure stage to failure stage.

Keywords: high-sensitivity troponin T, hip fracture, multiple organ dysfunction syndrome in the elderly, short-term outcomes

Introduction

As the aging process accelerated, hip fracture in the elderly has become a global issue where prevalence in China is increasing fourfold per decade and nearly 30% of these are 80 years and older. Surgical intervention should be performed within 48 hours after fracture to reduce complications and mortality in these patients, and a large number of clinical practices have also confirmed the significant benefit of early surgery.[1–3] However, the preoperative pathophysiological changes in the elderly are a critical part that has to be carefully considered. Inadequate

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preoperative assessment or optimization inevitably increases perioperative complications, while "overassessment" often leads to delayed or lost timing of surgery.

Many evaluation systems have now been applied for the prediction for postoperative complications and mortality risk in hip fracture, and some studies also use clinical laboratory findings at admission (such as hemoglobin concentration, peripheral blood lymphocyte count, etc.) as predictors for postoperative adverse events.[4–7] hs-TnT, as a marker of myocardial injury, has been widely used in the diagnosis and prognostic evaluation of acute coronary syndrome(ACS) and has been confirmed to be associated with the prognosis of many non-coronary diseases such as sepsis, chronic obstructive pulmonary disease, and acute ischemic stroke.[8–12] However, there are little studies on the effect of hs-TnT on the short-term prognosis of elderly patients with hip fracture. The purpose of this study was to investigate the association between hs-TnT and organ dysfunction and provide early warning to patients aged 80 years and older with hip fracture.

Methods

Study Design and Population

This is a single-centered prospective observational cohort study that included consecutive elderly patients with femoral neck or intertrochanteric fracture admitted to the Geriatric Orthopaedic Center of Sichuan Provincial Orthopedic Hospital, Chengdu, China between January 2020 and August 2020. The inclusion criteria were: patients diagnosed with femoral neck or intertrochanteric fracture and aged ≥ 80 years; history of definite trauma. The exclusion criteria were: pathological fracture caused by bone tumor, osteoma-like lesion; periprosthetic fracture, old fracture; previous ipsilateral hip fracture or surgery history; polytrauma and multiple fractures; the interval from fracture to surgery (time-to-surgery) exceeded 14 days; conservative intervention (non-surgical treatment); discharge against medical advice or transfer to another hospital during hospitalization; lack of follow-up data on the 28th day after surgery. Plasma hs-TnT was measured using the Elecsys Troponin T hs STAT assay (Roche, Germany, Lot 48,625,201) on a Cobas instrument. The manufacturer's recommended 99th percentile level of hs-TnT is 14 pg/mL. Based on the hs-TnT values at admission, patients were divided into low-risk group (hs-TnT ≤ 14 pg/mL, group L) and high-risk group (hs-TnT > 14 pg/mL, group H).

The study was approved by the Ethics Commission of Sichuan Orthopaedic Hospital (approval number, KY2020-032-01) and the requirement for informed consent was exempted since this was an observational study where no attempt was made to change the standard of care.

Data Collection

The Geriatric Orthopaedic Center of Sichuan Provincial Orthopedic Hospital contains 108 beds and consists of three medical units (general ward, High Dependency Unit, and Intensive Care Unit), where the co-management model is implemented by orthopedic surgeons, physicians, and intensivists. Patients aged 80 years and older with hip fracture are routinely admitted to the Intensive Care Unit for postoperative monitoring and treatment on the day of surgery. On the first postoperative day, patients are downgraded to High Dependency Unit or general ward unless the occurrence of conditions requiring organ function support.

All data were prospectively measured and recorded in electronic medical records. Admission baseline status contained demographic data, type of fracture, comorbidities, function grading of vital organs, and vital signs. In addition, red cell distribution width (RDW), as an indicator of a patient's physiologic reserve, was included in the evaluation of baseline status.[13] Perioperative information included time-to-surgery, duration of operation, non-surgical intervention on the day of surgery and laboratory findings on the first day after surgery. We identified organ dysfunction during hospitalization as the primary clinical outcome, including the occurrence of single organ dysfunction and MODSE. In addition, MODS severity score, length of hospital stay (LOS) and 28-day mortality were collected.

Organ Function Assessment

It is part of preoperative management for all elderly patients with hip fracture to receive basal organ function assessment on admission, which is performed by two experienced physicians. Information on basal organ function was obtained from either the patients or their main caregivers. Stages of Heart Failure, modified British Medical Research Council dyspnoea scale (mMRC), Water Swallow Test (WST), Mini-Mental State Examination (MMSE) and Barthel Index were used to evaluate cardiac, respiratory, swallowing, cognitive function and self-care ability of patients, respectively.[14–16] The diagnostic criteria for single organ dysfunction or MODSE during hospitalization and MODS severity score were based on the Diagnostic Criteria for Multiple Organ

Dysfunction Syndrome in the Elderly (MODSE) (draft, 2003) and Replacing "Lushan conference in 1995" guideline of the staging diagnosis and severity score standard of multiple organ dysfunction syndrome (2015) (Table 1).[17,18] As pulmonary artery wedge pressure (PAWP) was not readily available in daily clinical practice, we used lung ultrasound findings as an alternative to PAWP referring to the previous study.[19]

Statistical Analysis

Patient characteristics were reported as means with standard deviations (normal distribution) or medians with interquartile ranges (skewed data), and we used the Student's *t*-test or Mann–Whitney *U*-test to compare differences between group L and group H, as appropriate. Categorical variables were expressed as percentages and compared using the Chi-squared test. The associations between hs-TnT and clinical outcomes were estimated with univariate and multivariate logistic regression models and reported as odds ratios (ORs) with 95% confidence intervals (CIs). Considering the collinearity between Stages of Heart Failure, and chronic heart disease and hs-TnT, as well as between mMRC and chronic lung disease, the multivariate regression model included the following covariates: age, sex, type of fracture, time-to-surgery, hypertension, diabetes, chronic central nervous system disease, chronic kidney disease, mMRC, WST, MMSE, Barthel index, RDW, vital signs. Statistical analyses were performed using SPSS24.0 software and significance was assumed at $P < 0.05$.

Table 1 Diagnostic Criteria for MODSE[a]

	Pre-Failure Stage	Failure Stage
Heart[b]	i. Emerging arrhythmia, normal cardiac enzymes ii. Exertional dyspnea, no definite signs of heart failure iii. Increased PAWP (13 ~ 19mmHg)[c]	i. Reduced stroke volume (EF ≤ 40%) ii. PAWP ≥ 20mmHg[d] iii. Definite signs and symptoms of heart failure
Lung	i. $PaCO_2$ 45 ~ 49mmHg ii. SaO_2 < 90% iii. pH 7.30 ~ 7.35 or 7.45 ~ 7.50 iv. 200mmHg < PaO_2/FiO_2 ≤ 300mmHg v. No MV requirement	i. $PaCO_2$ > 50mmHg ii. SaO_2 < 80% iii. pH < 7.30 iv. PaO_2/FiO_2 ≤ 200mmHg v. MV requirement
Kidney	i. Decreased UOP (20 ~ 40mL/h), good response to diuretics ii. Scr 177.0 ~ 265.2μmol/L (or > 20% increase from baseline) iii. No dialysis requirement	i. Decreased UOP (< 20mL/h) and poor response to diuretics ii. Scr > 265.2μmol/L (or > 20% increase from baseline) iii. Dialysis requirement
PC	i. Decreased UOP (20–40mL/h) ii. MAP 50 ~ 60mmHg or > 20% decrease from baseline, good response to vasopressors iii. Exclude hypovolemia	i. Decreased UOP (< 20mL/h) complicated with cold limbs and cyanosis ii. MAP < 50mmHg, multiple vasopressors and inotropic agents dependence iii. Exclude hypovolemia
Liver	i. TBIL 35 ~ 102μmol/L ii. ALT elevated < 2 × normal value iii. Markedly increased bilirubin with normal or decreased transaminases	i. TBIL ≥ 102μmol/L ii. ALT elevated > 2 × normal value iii. Hepatic encephalopathy
GT	i. Abdominal distension ii. Hypoactive bowel sounds iii. Acalculous cholecystitis	i. Severe abdominal distension, disappeared bowel sounds ii. Stress ulceration complicated bleeding or perforation iii. Necrotizing enteritis iv. Spontaneous gallbladder perforation
CNS	i. Obtundation ii. Disorientation iii. GCS 9 ~ 12	i. Diffuse neurologic injury ii. No response to speech or voice iii. No response to pain iv. GCS ≤ 8
CS	i. PLT 51 ~ 99 × 10^9/L ii. FIB ≥ 2 ~ 4g/L iii. PT and TT prolonged < 3s iv. D-dimer increased < 2 × normal value v. No obvious signs of bleeding	i. PLT ≤ 50 × 10^9/L with decreasing trend ii. FIB < 2g/L iii. PT and TT prolonged > 3s iv. D-dimer increased > 2 × normal value v. Obvious bleeding

Notes: [a]If two or more organ functions meet the criteria for pre-failure stage while other organ functions are normal, a diagnosis of MODSE pre-failure stage is made. If two or more organ functions meet the criteria for failure stage while other organ functions are normal or in the pre-failure stage, a diagnosis of MODSE failure stage is made. Two or more abnormal values are required for the diagnosis of each criterion. [b]The criterion of PAWP is replaced by LUS findings, [c]replaced by ≤ 30 B-lines on 28 zone LUS, [d]replaced by > 30 B-lines on 28 zone LUS.

Abbreviations: PAWP, pulmonary artery wedge pressure; EF, ejection fraction; $PaCO_2$, partial pressure of carbon dioxide; SaO_2, arterial oxygen saturation; PaO_2, arterial partial pressure of oxygen; FiO_2, inspired oxygen concentration; MV, mechanical ventilation; UOP, urine output; Scr, serum creatinine; PC, peripheral circulation; MAP, mean arterial pressure; TBIL, total bilirubin; ALT, alanine aminotransferase; GT, gastrointestinal tract; CNS, central nervous system; GCS, Glasgow score; CS, coagulation system; PLT, platelet; FIB, fibrinogen; PT, prothrombin time; TT, thrombin time; LUS, lung ultrasound.

Results

01-JAN-2020 to 31-AUG-2020, 208 patients aged 80 years and older with hip fracture were hospitalized in the Geriatric Orthopaedic Center of Sichuan Orthopaedic Hospital, among which 6 patients did not undergo surgical treatment, 9 patients had fracture at other sites, 8 patients had periprosthetic fracture, 13 patients had time-to-surgery exceeded 14 days, and 4 patients were discharged against medical advice. Forty patients were excluded, and a total of 168 patients were finally included in the statistical analysis. Among the included patients, 46 (27.4%) were male and 122 (72.6%) were female, aged 80–99 years, with a mean age of (86.0 ± 4.4) years, and all patients were admitted for hip fractures due to falls. The value of 168 patients at admission was 16.0 (11.0, 14.0) pg/mL, the minimum and maximum values were 5 pg/mL and 294 pg/mL, respectively, and 91 cases (54.2%) were higher than the reference value. None of the patients had definite evidence of acute coronary syndrome (ACS) during hospitalization. According to the hs-TnT level at admission, 168 patients were divided into group L (n = 77) and group H (n = 91).

Compared with group L, group H had older age (P = 0.001), more males (P < 0.001), more chronic kidney disease (P = 0.016), higher proportion in stages B and C of heart failure (P < 0.001), and worse swallowing and cognitive function on admission (P = 0.014, 0.004, respectively) (Table 2).

Table 2 Baseline Characteristics and Differences Between Low-Risk Group and High-Risk Group

		Total (n =168)	Group L (n = 77)	Group H (n = 91)	*P*
Age (years), mean (SD)		86.0 (4.4)	84.8 (4.0)	87.1 (4.5)	0.001
Gender (male), n (%)		46 (27.4)	11 (14.3)	35 (38.5)	< 0.001
Type of fracture (femoral neck), n (%)		70 (41.7)	28 (36.4)	42 (46.2)	0.213
Comorbidities, n (%)	Hypertension	78 (46.4)	33 (42.9)	45 (49.5)	0.439
	Diabetes	38 (22.6)	17 (22.1)	21 (23.1)	1.000
	Heart disease	30 (17.9)	11 (14.3)	19 (20.9)	0.315
	Lung disease	20 (11.9)	9 (11.7)	11 (12.1)	1.000
	CKD	7 (4.2)	0	7 (7.7)	0.016
	CNS disease	35 (20.8)	14 (18.2)	21 (23.1)	0.454
Stages of Heart Failure, n (%)	A	60 (35.7)	40 (51.9)	20 (22.0)	< 0.001
	B	97 (57.7)	37 (48.1)	60 (65.9)	
	C	11 (6.5)	0	11 (12.1)	
	D	0	0	0	
mMRC, n (%)	0	1 (0.6)	1 (1.3)	0	0.828
	1	82 (48.8)	39 (50.6)	43 (47.3)	
	2	76 (45.2)	33 (42.9)	43 (47.3)	
	3	9 (5.4)	4 (5.2)	5 (5.5)	
	4	0	0	0	
WST (abnormal), n (%)		17 (10.1)	3 (3.9)	14 (15.4)	0.014
MMSE, median (range)		26.0 (24.0–28.0)	26.0 (25.5–28.0)	26.0 (22.8–28.0)	0.004
Barthel index, median (range)		35.0 (28.5–45.0)	35.0 (30.0–45.0)	35.0 (20.0–45.0)	0.158
RDW (%), mean (SD)		13.9 (1.7)	13.8 (1.5)	14.0 (1.9)	0.483
Vital signs, mean (SD)	SBP (mmHg)	134.4 (19.9)	134.7 (20.6)	134.1 (19.5)	0.857
	DBP (mmHg)	73.2 (10.9)	72.0 (10.6)	74.3 (11.1)	0.169
	HR (beats/min)	84.5 (15.1)	83.5 (15.2)	85.3 (15.1)	0.437
	RR (breaths/min)	19.9 (0.8)	19.9 (0.6)	20.0 (0.9)	0.787

Abbreviations: SD, standard deviation; CKD, chronic kidney disease; CNS, central nervous system; mMRC, modified British Medical Research Council dyspnoea scale; WST, Water Swallow Test; MMSE, Mini-Mental State Examination; RDW, red cell distribution width; SBP, systemic blood pressure; DBP, diastolic blood pressure; HR, heart rate; RR, respiratory rate.

The following parameters were significantly higher/longer on the first postoperative day in group H: time-to-surgery (P = 0.029), neutrophil-to-lymphocyte ratio (NLR) (P < 0.001), prothrombin time (P = 0.024), international normalized ratio (P = 0.024), pro-brain natriuretic peptide (pro-BNP) (P < 0.001), hs-TnT (P < 0.001), procalcitonin (P = 0.027), interleukin-6 (P = 0.022), creatinine (P = 0.001), cystatin C (P < 0.001), and blood uric acid (P = 0.008); the following parameters were significantly lower: peripheral blood lymphocyte count (P = 0.003), and standard bicarbonate (P = 0.007) (Table 3).

The lung, central nervous system (CNS), and heart were the most commonly involved organs (Figure 1). Respiratory dysfunction was mainly induced by infection, delirium was the main manifestation of CNS dysfunction, and cardiac dysfunction was almost an acute exacerbation of chronic heart disease. The incidences of MODSE and heart dysfunction in group H were significantly higher than those in group L (P = 0.002, 0.006, respectively). Thirty-nine patients (23.2%) met the diagnostic criteria for MODSE, 35 remained in the pre-failure stage and 4 eventually progressed to the failure stage. Three of the 4 patients in the failure stage died within 28 days, including 2 cases of respiratory failure with cardiogenic shock and 1 case of massive cerebral infarction with respiratory failure.

Patients with MODSE, single organ dysfunction (except lung, peripheral circulation, gastrointestinal tract, coagulation system), MODS severity score > 3 and LOS > 14 days had significantly higher mean hs-TnT values on admission (Table 4). After adjustment for confounders (age, sex, type of fracture, time-to-surgery, hypertension, diabetes, chronic CNS disease, chronic kidney disease, mMRC, WST, MMSE, Barthel index, RDW, vital signs), elevated hs-TnT was independently associated with MODSE (adjusted OR, 5.76; 95% CI, 1.74–19.10; P = 0.004), heart dysfunction (adjusted OR, 7.48; 95% CI, 2.17–25.82; P = 0.001), MODS severity score > 3 (adjusted OR, 5.22; 95% CI, 1.32–20.60; P = 0.018), and length of hospital stay > 14 days (adjusted OR, 2.38; 95% CI, 1.05–5.36; P = 0.037) (Table 4).

Discussion

In elderly patients with hip fracture, the functional status of vital organs is the important prerequisite of surgical treatment, the basis of enhanced recovery after surgery, and the goal and guidance of restoring lower limb function. These patients are inevitably associated with chronic organ dysfunction prior to injury, and MODSE after injury and/or surgery is mostly a continuation or exacerbation on a chronic basis. Unlike adult MODS, MODSE has its particularities including organ aging, comorbidities, decreased physiological reserves of many organs, insidious symptoms and signs, and protracted course, etc.[20] Wang et al proposed diagnostic criteria for MODSE according to the characteristics of elderly patients, in which MODSE was divided into pre-failure and failure stages.[17] The criteria for MODSE were met in 23.2% of the cases in this study, and although most of them (89.7%) were in the pre-failure stage, a high 28-day mortality (75%) occurred once MODSE progressed to the failure stage. It is therefore to be certain that effective early warning system/indicator on MODSE would be important components in preoperative assessment and management. At present, there are many studies of the prediction on short- or long-term mortality in elderly patients with hip fracture, and the early warning system/indicator on perioperative MODSE has rarely been reported.[4–7] In addition, the conceptualization of “adverse events” or “complications” in the aforementioned study was difficult to define and standardize. As a classical marker of myocardial injury, hs-TnT has been widely used in the diagnosis, stratification and prognostic evaluation of ACS. Moreover, a variety of pathological factors can lead to myocardial injury and hs-TnT should be considered an organ-specific rather than disease-specific biomarker.[21] Low-level elevated hs-TnT is prevalent in elderly non-ACS patients.[22] Previous studies showed that hs-TnT was higher than 14 pg/mL in 40–50% of elderly hospitalized non-ACS patients and 79% of elderly residents in a nursing home.[23,24] This study found that hs-TnT values of 168 patients at admission ranged from 5 to 294 pg/mL with a median of 16.0 pg/mL, and 54.2% of the cases exceeded 14 pg/mL. In addition to poor baseline conditions, factors such as acute trauma, blood loss, and pain caused by hip fracture may be associated with hs-TnT abnormalities at admission.

In this study, patients were divided into two groups based on the 99th percentile in the normal population of hs-TnT and only low-level increased hs-TnT was found in group H. However, there were significant differences in baseline status of admission, perioperative conditions and short-term clinical outcomes between two groups. It was noteworthy that these differences showed a strong inherent relationship and exhibited the continuity of disease development. Differences in baseline status can be explained as follows: although the symptoms were insidious, cardiac

Table 3 Perioperative Information and Differences Between Low-Risk Group and High-Risk Group

	Total (n = 168)	Group L (n = 77)	Group H (n = 91)	*P*
Basic information on operation day				
Time-to-surgery (days), median (range)	6.0 (4.0–9.0)	5.0 (4.0–8.0)	6.0 (5.0–9.0)	0.029
Operation time (min), median (range)	50.0 (40.0–60.0)	50.0 (40.0–67.5)	50.0 (40.0–60.0)	0.165
Total venous input (mL), mean (SD)	3126.0 (569.3)	3117.1 (609.8)	3133.5 (535.9)	0.853
Average hourly UOP (mL), median (range)	57.5 (42.0–80.0)	57.5 (42.2–77.9)	57.2 (41.0–82.0)	0.880
APACHEII score, median (range)	10.0 (8.0–12.0)	9.0 (8.0–12.0)	10.0 (8.0–12.0)	0.315
Blood transfusion, n (%)	75 (44.6)	37 (48.1)	38 (41.8)	0.439
Human albumins infusion, n (%)	65 (38.7)	25 (32.5)	40 (44.0)	0.153
Diuretic use, n (%)	31 (18.5)	11 (14.3)	20 (22.0)	0.234
Laboratory findings on the first day after surgery				
WBC ($\times 10^9$/L), mean (SD)	8.6 (2.8)	8.4 (3.1)	8.7 (2.5)	0.393
NEUT ($\times 10^9$/L), mean (SD)	6.7 (2.5)	6.5 (2.9)	6.9 (2.2)	0.269
LYMPH ($\times 10^9$/L), median (range)	0.8 (0.6–1.2)	0.9 (0.7–1.3)	0.8 (0.6–1.0)	0.003
NLR, median (range)	7.6 (5.1–10.2)	6.1 (4.4–8.6)	8.9 (6.2 −11.3)	< 0.001
RBC ($\times 10^9$/L), mean (SD)	3.4 (0.6)	3.3 (0.5)	3.4 (0.5)	0.218
RDW (%), mean (SD)	14.3 (2.1)	14.3 (1.8)	14.4 (2.2)	0.715
HGB (g/L), mean (SD)	101.2 (12.7)	99.4 (12.1)	102.8 (13.6)	0.081
PLT ($\times 10^9$/L), mean (SD)	166.9 (63.3)	164.4 (61.8)	169.0 (64.7)	0.641
PT (s), median (range)	14.4 (13.9–15.1)	14.2 (13.6–15.0)	14.4 (14.1–15.2)	0.024
APTT (s), mean (SD)	41.5 (6.4)	41.0 (6.4)	41.9 (6.5)	0.388
INR, median (range)	1.2 (1.2–1.3)	1.2 (1.1–1.3)	1.2 (1.2–1.3)	0.024
TT (s), median (range)	16.1 (15.1–17.8)	15.9 (15.1–17.8)	16.4 (15.6–17.9)	0.315
FIB (g/L), mean (SD)	4.1 (0.9)	4.0 (0.9)	4.1 (0.9)	0.254
D-D (μg/mL), median (range)	2.7 (1.7–5.6)	2.8 (1.7–6.4)	2.7 (1.8–5.4)	0.707
FDP (μg/mL), median (range)	9.7 (5.3–20.6)	10.3 (5.1–23.4)	9.6 (5.4–20.2)	0.658
pro-BNP (pg/mL), median (range)	700.0 (352.8–1315.8)	475.1 (304.7–897.3)	989.3 (539.4–1734.0)	< 0.001
hs-TnT (pg/mL), median (range)	17.0 (11.0–28.0)	10.0 (10.0–15.0)	26.0 (17.0–39.0)	< 0.001
PCT (ng/mL), median (range)	0.2 (0.1–0.2)	0.1 (0.1–0.2)	0.2 (0.1–0.2)	0.027
IL-6 (pg/mL), median (range)	151.1 (95.2–223.2)	141.6 (87.5–199.5)	161.6 (111.8–233.7)	0.022
ALT (U/L), median (range)	17.0 (11.0–25.0)	17.0 (11.0–28.0)	17.0 (12.0–24.0)	0.966
TBIL (μmol/L), median (range)	12.1 (8.8–17.4)	12.0 (8.8–17.2)	12.6 (8.8–18.1)	0.825
PA (mg/L), mean (SD)	117.3 (35.6)	118.7 (35.4)	110.2 (34.9)	0.540
ALB (g/L), mean (SD)	29.6 (3.3)	29.8 (3.1)	30.1 (3.5)	0.332
Scr (μmol/L), median (range)	61.0 (48.0–81.8)	55.0 (47.0–73.5)	69.0 (52.0–90.0)	0.001
CysC (mg/L), median (range)	1.2 (1.0–1.6)	1.1 (1.0–1.4)	1.3 (1.1–1.8)	< 0.001
UA (μmol/L), median (range)	220.0 (168.3–296.3)	202.0 (159.5–255.5)	247.0 (183.0 −312.0)	0.008
Glucose (mmol/L), median (range)	5.9 (5.2–6.9)	5.8 (5.2–6.8)	6.0 (5.2–6.9)	0.596
Potassium (mmol/L), mean (SD)	4.1 (0.4)	4.1 (0.4)	4.2 (0.4)	0.160
Sodium (mmol/L), median (range)	138.5 (137.0–140.8)	139.0 (137.5 −140.0)	138.0 (136.0 −141.0)	0.460
Chloride (mmol/L), mean (SD)	102.3 (3.8)	102.3 (3.1)	102.3 (4.3)	0.982
Calcium (mmol/L), mean (SD)	2.0 (0.1)	2.0 (0.1)	2.0 (0.1)	0.325
Phosphorus (mmol/L), mean (SD)	1.1 (0.2)	1.1 (0.2)	1.1 (0.2)	0.983
Arterial pH, mean (SD)	7.39 (0.04)	7.39 (0.04)	7.39 (0.04)	0.919
PaO_2/FiO_2 (mmHg), median (range)	283.0 (242.1–333.0)	278.0 (242.0–313.6)	290.0 (245.0–354.6)	0.322
$PaCO_2$ (mmHg), mean (SD)	42.0 (6.6)	43.1 (5.7)	41.4 (7.1)	0.053
SB (mmol/L), mean (SD)	24.8 (3.0)	25.7 (1.9)	24.7 (2.7)	0.007
Lactate (mmol/L), median (range)	1.0 (0.9–1.3)	1.0 (0.9–1.2)	1.1 (0.9–1.3)	0.234

Abbreviations: SD, standard deviation; UOP, urine output; APACHE, acute physiology and chronic health evaluation; WBC, white blood cell count; NEUT, neutrophil count; LYMPH, lymphocyte count; NLR, neutrophil-to-lymphocyte ratio; RBC, red blood cell count; RDW, red cell distribution width; HGB, haemoglobin; PLT, platelet count; PT, prothrombin time; APTT, activated partial thromboplastin time; INR, international normalized ratio; TT, thrombin time; FIB, fibrinogen; D-D, D-dimer; FDP, fibrin (ogen) degradation products; pro-BNP, pro-brain natriuretic peptide; hs-TnT, high-sensitivity cardiac troponin T; PCT, procalcitonin; IL-6, interleukin-6; ALT, alanine aminotransferase; TBIL, total bilirubin; PA, prealbumin; ALB, albumin; Scr, serum creatinine; CysC, cystatin C; UA, uric acid; GLU, glucose; PaO_2, arterial partial pressure of oxygen; FiO_2, inspired oxygen concentration; $PaCO_2$, partial pressure of carbon dioxide; SB, standard bicarbonate.

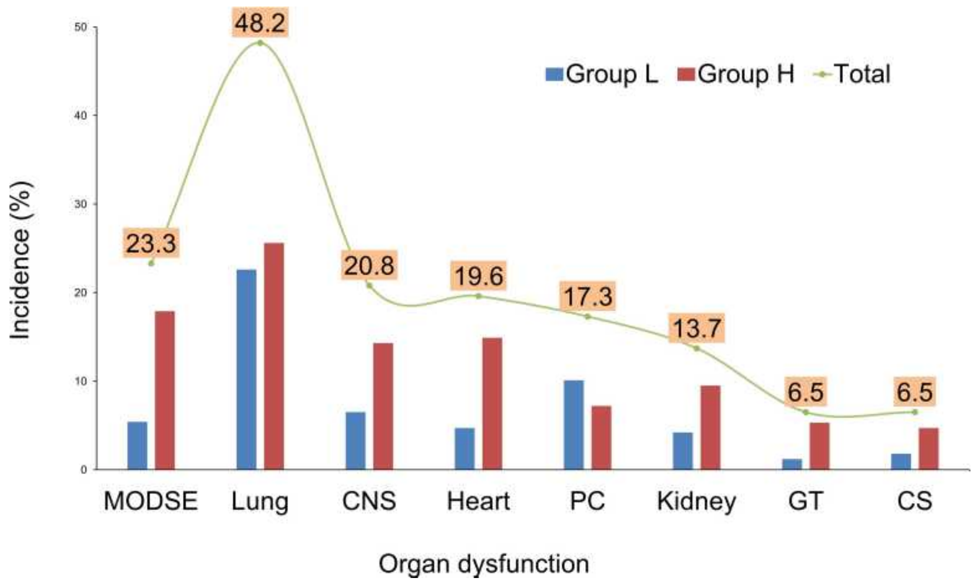

Figure 1 Incidence of MODSE and single organ dysfunction in 168 patients. Figure shows the overall incidence of organ dysfunction and its distribution between the two groups.
Abbreviations: MODSE, multiple organ dysfunction syndrome in the elderly; CNS, central nervous system; PC, peripheral circulation; GT gastrointestinal tract; CS coagulation system.

failure with preserved ejection fraction was extremely common with increasing age, which often resulted in marked hemodynamic disturbance and was more likely to adversely affect renal function and cognitive competence.[25,26] Definitions such as "cardiorenal syndrome" and "cardiogenic dementia" indicated the

Table 4 Admission High-Sensitivity Troponin T and Perioperative Outcomes

Outcome	Admission hs-TnT			Univariable OR (95% CI)	*P*	Multivariable OR (95% CI)	*P*
	Outcome Present	Outcome Absent	*P*				
MODSE (n=39)	22.0 (15.0–34.0)	14.0 (10.0–22.0)	< 0.001	3.72 (1.64–8.45)	0.002	5.76 (1.74–19.10)	0.004
Single organ dysfunction							
Lung (n = 81)	15.0 (11.0–22.0)	17.0 (10.0–27.0)	0.652	0.92 (0.50 −1.69)	0.786	–	–
CNS (n = 35)	21.0 (11.0–30.0)	15.0 (10.0–22.5)	< 0.001	2.15 (0.98–4.74)	0.058	–	–
Heart (n = 33)	22.0 (14.5–43.5)	14.0 (10.0–22.0)	0.002	3.27 (1.38–7.58)	0.007	7.48 (2.17–25.82)	0.001
PC (n = 29)	13.0 (10.0–22.0)	17.0 (11.0–25.0)	0.426	0.54 (0.24–1.21)	0.132	–	–
Kidney (n = 23)	26.0 (13.0–41.0)	15.0 (10.0–22.0)	0.001	2.13 (0.83–5.49)	0.116	–	–
GT (n = 11)	21.0 (15.0–71.0)	15.0 (10.0–24.0)	0.057	4.12 (0.86–19.66)	0.076	–	–
CS (n = 11)	24.0 (10.0–32.0)	16.0 (11.0–23.0)	0.179	2.38 (0.61–9.30)	0.213	–	—
Liver (n = 6)	15.0 (10.0–24.0)	24.0 (21.0–31.0)	0.024	4.42 (0.51–38.66)	0.179	–	–
MODS severity score > 3 (n = 28)	23.0 (15.8–36.3)	14.0 (10.0–22.0)	0.009	4.87 (1.75–13.54)	0.002	5.22 (1.32–20.60)	0.018
LOS > 14 (n = 88)	18.0 (11.0–30.0)	13.5 (10.0–20.0)	0.010	2.04 (1.10–3.77)	0.024	2.38 (1.05–5.36)	0.037

Note: Adjustments: age, sex, type of fracture, time-to-surgery, hypertension, diabetes, chronic CNS disease, chronic kidney disease, modified British Medical Research Council dyspnoea scale, Water Swallow Test, Mini-Mental State Examination, Barthel index, RDW, vital signs.
Abbreviations: OR, odds ratio; CI, confidence interval; MODSE, multiple organ dysfunction syndrome in the elderly; CNS, central nervous system; PC, peripheral circulation; GT, gastrointestinal tract; CS, coagulation system; LOS, length of hospital stay.

interconnection between various organ functions.[27] Swallowing disorder was similarly associated with advanced age, cognitive impairment and poor cardiac and pulmonary function, and might be aggravated by prolonged bed rest, malnutrition, and debilitation after fracture.[28–30] Secondly, higher pro-BNP, hs-TnT, creatinine, cystatin C, serum uric acid and lower standard bicarbonate on the first postoperative day indicated poorer cardiac and renal function in group H. These laboratory findings might be either continuation of chronic organ dysfunction before fracture or signs of subsequent MODSE. Notably, the NLR on the first postoperative day was at a high level in all patients[7.6 (5.1, 10.2)], the rise of NLR was more significant [8.9 (6.2, 11.3)] in group H, accompanied by increased inflammation indicators and decreased peripheral blood lymphocyte count. NLR is considered to be a comprehensive variable reflecting systemic inflammation-immune status and has been demonstrated to be associated with various pathological factors including chronic heart failure, chronic kidney disease, dementia, osteoporosis and even fracture itself. With the increase of NLR, the incidence of postoperative myocardial injury and infection increased exponentially.[31] Abnormalities in NLR might clarify that patients in group H had worse baseline status and clinical prognosis from the perspective of systemic inflammation-immunity. Finally, the incidence of MODSE in group H rose significantly with a higher MODS severity score and longer hospital stay. Meanwhile, the incidence of heart dysfunction also increased significantly in group H, which became one of the main components of MODSE. MODSE initiated either in the period between fracture and surgery or within several days after hip fracture surgery. Patients in the pre-failure stage generally had a good prognosis if early and appropriate management was implemented, but a very high 28-day mortality occurred once they progressed to the failure stage. Therefore, effective preoperative assessment and management are important means to block or delay the MODSE process. As an independent factor for MODSE, heart dysfunction, MODS severity score > 3 and LOS > 14 days, increased hs-TnT may be regarded as an early warning indicator of short-term poor prognosis in hip fracture patients aged 80 years and older.

There are several limitations that deserve consideration: First, the 28-day mortality was not powered to assess and the association between 28-day mortality and hs-TnT was not evaluated because of the small sample size. Second, some patients were excluded from the study due to factors such as conservative treatment and prolonged time-to-surgery, and the clinical characteristics and short-term prognosis of such patients may require further study. Finally, despite statistical adjustments, there remained a possibility of residual confounding in all observational studies.

Conclusion

In summary, a low-level increase of hs-TnT at admission was not uncommon, which could be used as an early warning indicator for perioperative MODSE in patients aged 80 years and older with hip fracture. Patients with elevated hs-TnT had worse vital organ functions at baseline and were more likely to be induced to MODSE by acute stress factors such as trauma, surgery and blood loss. Effective measures should be applied to avoid the occurrence of MODSE failure stage.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Commission of Sichuan Orthopaedic Hospital (approval number, KY2020-032-01) and the requirement for informed consent was exempted. We confirmed that all procedures followed were in accordance with the Helsinki Declaration and patient data was maintained with confidentiality.

Disclosure

The authors report no conflicts of interest in this work.

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