

Original Article

Acute muscle wasting rate assessment and long-term mortality in critically ill trauma

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Background and Objectives: To evaluate the relationship between acute muscle wasting rate and long-term mortality in critically ill trauma. **Methods and Study Design:** A single-center, retrospective study was conducted in critically ill trauma. Patients with Computed Tomography scans including the L3 vertebra within 24 hours and at 1 week after trauma were recruited. Acute muscle wasting rate was defined as the mean percent variation per day of skeletal muscle index in the first week after trauma. Multivariate logistic regression analysis and receiver operating characteristic curve analysis were performed to determine whether acute muscle wasting rate could help predict hospital malnutrition and 1-year mortality. **Results:** Skeletal muscle index was $49.3 \pm 10.7 \text{ cm}^2/\text{m}^2$ at baseline and decreased to $45.1 \pm 9.6 \text{ cm}^2/\text{m}^2$ ($p < 0.001$) at 1 week and $39.8 \pm 10.8 \text{ cm}^2/\text{m}^2$ ($p < 0.001$) at 1 month after trauma. A sustained decrease of skeletal muscle index was observed from baseline up to 6 months ($33.7 \pm 8.4 \text{ cm}^2/\text{m}^2$, $p < 0.001$) post trauma, and lasted for 1 year ($37.7 \pm 5.6 \text{ cm}^2/\text{m}^2$, $p = 0.004$). Logistic regression analysis showed that acute muscle wasting rate was an independent risk factor for hospital malnutrition and 1-year mortality. Every 1% absolute increase of acute muscle wasting rate was associated with 1.82-fold higher odds of 1-year mortality in critically ill trauma. The area under curve of acute muscle wasting rate was 0.813 for hospital malnutrition prediction and 0.715 for 1-year mortality prediction. **Conclusions:** Acute muscle wasting rate was independently associated with higher 1-year mortality and hospital malnutrition in critically ill trauma.

Key Words: skeletal muscle, nutrition, mortality, trauma, critically ill

INTRODUCTION

Low skeletal muscle mass at admission was significantly associated with prolonged mechanical ventilation, increased ICU length of stay (LOS) and mortality in critically ill.^{1,2} Previously published studies reported that approximately 36-86% of critically ill patients suffered skeletal muscle atrophy.^{3,4,5} In trauma, the prevalence of skeletal muscle atrophy was about 30-50%.^{6,7} Decreased skeletal muscle index (SMI) assessed at the level of the 3rd lumbar (L3) vertebra derived from computed tomography (CT) scans was an independent risk factor for prolonged hospitalization and increased short-term mortality in trauma patients.^{8,9} However, skeletal muscle mass at baseline is an indicator of physiological reserve, but cannot reflect the severity of catabolism caused by diseases.

Intense catabolism occurring with critically ill patients results in acute skeletal muscle wasting,¹⁰ which is one of the typical symptoms and diagnostic criteria for malnutrition.¹¹ The longitudinal changes of acute muscle mass loss in critical illness have been demonstrated in several studies, which revealed that the cross-sectional area of the upper and lower limb muscles decreased significantly by 12.5-18.5% in the first week.^{12,13,14} A recent meta-analysis

which included 3251 patients concluded that critically ill patients lost approximately 2% of muscle mass per day during the first week of ICU admission, by different assessment methods such as ultrasound or CT.¹⁵ However, there was less evidence for acute muscle wasting to predict mortality in critically ill. In mechanically ventilated patients, every 1% loss of quadriceps muscle layer thickness over the first week was associated with 5% higher odds of 60-day mortality.¹⁶ A threshold of 1.84% decline per day of psoas muscle was identified for survival prediction in critically ill COVID-19 patients recently.¹⁷ Interestingly, our previous work suggested that the acute change rates of SMI were not associated with 90-day mortality in abdominal trauma patients, while the change rate of SMI over 3 weeks was a significant predictor of

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90-day mortality.¹⁸

However, no study has considered the relationship between acute skeletal muscle wasting and long term mortality in the critically ill. In addition, the cutoff value of acute skeletal muscle wasting for the diagnosis of malnutrition is still unclear. The present study explored whether acute muscle wasting rate was associated with new onset hospital malnutrition and long-term mortality in critically ill trauma.

METHODS

Study design

A single-center, retrospective, longitudinal observational study was conducted with critically ill trauma patients admitted to Intensive Care Unit (ICU) of Nanjing Drum Tower Hospital from January 1, 2018, to December 31, 2021. This cohort study was approved by the Hospital Ethics Review Board (Internal registration number: 2022-476-01).

Study population

Trauma patients who were admitted to ICU between January 2018 and December 2021 were recruited for this retrospective observational study. Critically ill trauma was defined according to the new Berlin criteria of poly-trauma.¹⁹ Eligibility criteria were: 1) 18 years old or over; 2) Injury Severity Score (ISS) was 16 points or greater; 3) Length of hospital stay was more than 7 days; 4) CT scans including the L3 vertebra were performed within 24 hours and 1 week (6-8 days) after trauma, respectively. Exclusion criteria were: 1) Cachexia before trauma; 2) Missing clinical data; 3) Unclear differentiation between muscle and surrounding tissue in CT image.

Data collection

Patient demographics and baseline clinical data were collected. Clinical outcomes involved new onset malnutrition in hospital, sepsis in hospital, requirement for mechanical ventilation, vasopressor, continuous renal replacement therapy, hospital LOS, ICU LOS, and 30-day, 60-day, 90-day, 1-year mortality. Hospital malnutrition was defined according to the Global Leadership Initiative on Malnutrition (GLIM) criteria,¹¹ excluding skeletal muscle measures. The Sepsis-3 definition was used to diagnose sepsis.²⁰

Muscle mass measurement

Skeletal muscle area (SMA) was assessed at the cross section of L3 vertebra derived from CT scans, including the psoas major, erector spinae, quadratus lumborum, transversus abdominis, external oblique and internal oblique muscles. Regions of Interest were demarcated using thresholds -29 to +150 Hounsfield units (HU) for muscle tissue, and the boundaries were corrected manually if necessary. The average SMA measured from three physicians was used as the result. SMI (cm^2/m^2) was equal to SMA in cm^2 divided by the square of height in metres. Acute muscle wasting rate ($\Delta\text{SMI}\%$) reflects the mean percent variation per day of SMI in the first week after trauma, and the formula is as follows:

$$\Delta\text{SMI}\% = (\text{Baseline SMI} - \text{SMI at 1 week}) / (\text{Baseline SMI} \times \text{days between 2 CT scans}) \times 100\%$$

Statistical analyses

Statistical analyses were performed using SPSS version 26 software (IBM, Inc., Armonk, NY, USA). *p*-values below 0.05 and 95% confidence intervals (CI) not containing 1 were considered statistically significant. Descriptive statistics for all numeric variables were presented as median and interquartile range (IQR) or mean and standard deviation ($\text{mean} \pm \text{SD}$). Data were compared using the *t*-test or Mann-Whitney *U* test, as appropriate. Proportions were compared using Chi square tests. Paired two-sample *t* tests were performed to compare SMI on baseline, 1 week, 1 month, 6 months and 1 year after trauma, respectively. Multivariate logistic regression models were created to evaluate the effects of independent variables on hospital malnutrition and 1-year mortality in critically ill trauma patients. The receiver operating characteristic (ROC) analysis was conducted to explore the sensitivity and specificity of $\Delta\text{SMI}\%$ for hospital malnutrition and 1-year mortality prediction. Youden index was calculated to determine a potential cut-off value for $\Delta\text{SMI}\%$.

RESULTS

Patient baseline data

From January 2018 to December 2021, a total of 742 patients with critically ill trauma were retrospectively enrolled, of whom 598 patients were excluded and 144 met the selection criteria for analysis (Figure 1). Overall, the median age was 51 (36, 58) years with 84.0% ($n=121$) male. The median scores of Acute Physiology and Chronic Health Evaluation II (APACHE II), Sequential Organ Failure Assessment (SOFA), Nutrition Risk in Critically Ill (NUTRIC), Injury Severity Score (ISS) were 14, 5, 4, and 30.5, respectively. The most frequently injured sites were the abdomen (87.5%), followed by the chest (61.8%), head and neck (31.9%). Causes of trauma were traffic accident (65.3%), fall (19.4%), industrial machine (9.7%), sports (4.2%) and assault (1.4%). More than half of the patients had surgery within 24 hours after trauma (Table 1).

Outcomes

During hospitalization, 63.2% of the patients suffered from hospital malnutrition, 79.9% were diagnosed with sepsis, and 70.8% underwent surgery under general anesthesia. The median duration of mechanical ventilation (56.9%), vasopressor (33.3%), CRRT (16.0%), hospital and ICU length of stay were 9 (4, 14), 3 (2, 6), 7 (4, 17), 31 (18, 46) and 17.5 (7, 30) days, respectively. The mortality rates at 30 days, 60 days, 90 days and 1 year after trauma were 4.2%, 10.4%, 18.1% and 22.9%, respectively (Table 2).

Changes of SMI in patients with critically ill trauma

Trauma patients exhibited acute and persistent muscle wasting. SMI at baseline was $49.3 \pm 10.7 \text{ cm}^2/\text{m}^2$ and decreased to $45.1 \pm 9.6 \text{ cm}^2/\text{m}^2$ at 1 week after trauma ($p < 0.001$), the acute muscle wasting rate ($\Delta\text{SMI}\%$) was $1.16 \pm 1.41\%$. In 101 patients with CT scans at 1 month after trauma, SMI was $39.8 \pm 10.8 \text{ cm}^2/\text{m}^2$ and decreased from baseline by 18.7% ($p < 0.001$) (Figure 2). CT scans were performed at 6 months and 1 year after trauma in few patients. With limited data, we observed a sustained

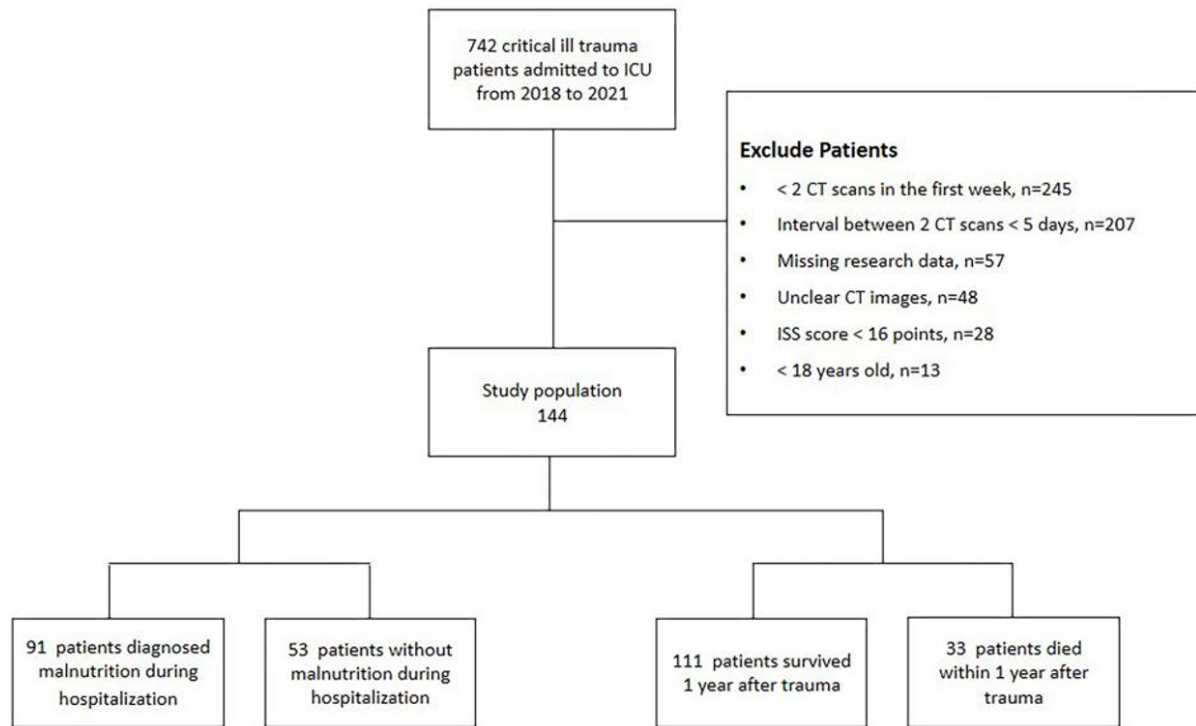


Figure 1. Study flowcharts

Table 1. Baseline clinical and demographic characteristics of the critically ill trauma patients

Characteristics	Value
n	144
Age, years [median (IQR)]	51 (36, 58)
Gender, n (%)	
Male	121 (84.0)
Female	23 (16.0)
BMI, kg/m ²	23.1±2.9
APACHE II, [median (IQR)]	14 (9, 19.75)
SOFA, [median (IQR)]	5 (3, 8)
NUTRIC, [median (IQR)]	4 (3, 5)
ISS, [median (IQR)]	30.5 (22, 40.3)
Operation within 24 hours, n (%)	82 (56.9)
Injured sites, n (%)	
Head and neck	46 (31.9)
Chest	89 (61.8)
Abdomen	126 (87.5)
Spine	40 (27.8)
Pelvis	30 (20.8)
Limbs	28 (19.4)
Cause, n (%)	
Traffic accident	94 (65.3)
Fall	28 (19.4)
Industrial machine	14 (9.7)
Sports	6 (4.2)
Assault	2 (1.4)
Laboratory results at admission	
WBC, ×10 ⁹ /L	13.8 ± 6.4
Lymphocyte, ×10 ⁹ /L	1.0 ± 0.8
Hemoglobin, g/L	109 ± 24.7
Platelet, ×10 ⁹ /L	155 ± 91.3
Total Bilirubin, μmol/L	30.5 ± 42.4
Albumin, g/L	31.7 ± 5.5
Creatinine, μmol/L	84.0 ± 44.9
Fibrinogen, g/L	3.6 ± 8.9
CRP, mg/L	98.3 ± 80.3
PCT, ng/mL	5.8 ± 14.2

BMI, body mass index; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; NUTRIC, Nutrition Risk in Critically Ill; ISS, Injury Severity Score; WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin

Table 2. Outcomes of the critically ill trauma patients

Outcomes	Value
MV, n (%)	82 (56.9)
MV days, median (IQR)	9 (4, 14)
VA, n (%)	48 (33.3)
VA days, median (IQR)	3 (2, 6)
CRRT, n (%)	23 (16.0)
CRRT days, median (IQR)	7 (4, 17)
Sepsis, n (%)	115 (79.9)
Surgical operation, n (%)	102 (70.8)
Malnutrition, n (%)	91 (63.2)
Hospital LOS, median (IQR)	31 (18, 46)
ICU LOS, median (IQR)	17.5 (7, 30)
30-day mortality, n (%)	6 (4.2)
60-day mortality, n (%)	15 (10.4)
90-day mortality, n (%)	26 (18.1)
1-year mortality, n (%)	33 (22.9)

MV, Mechanical ventilation; VA, Vasopressor; CRRT, Continuous Renal Replacement Therapy; LOS, Length of Stay.

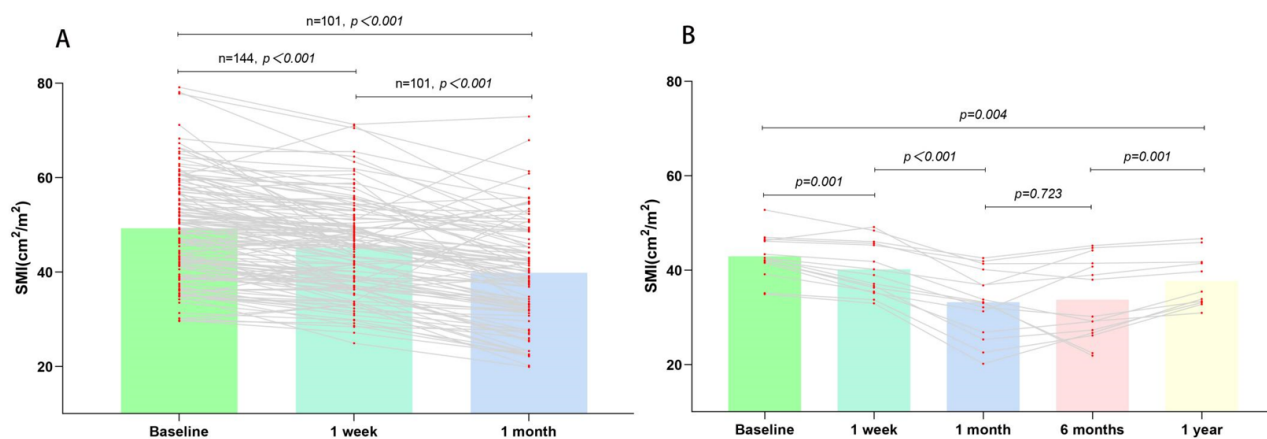


Figure 2. Short-term (A) and long-term (B) changes of SMI in the critically ill trauma patients. (A) SMI at baseline was $49.3 \pm 10.7 \text{ cm}^2/\text{m}^2$ and decreased to $45.1 \pm 9.6 \text{ cm}^2/\text{m}^2$ at 1 week after trauma ($p < 0.001$). In 101 patients with CT scans at 1 month after trauma, SMI descended to $39.8 \pm 10.8 \text{ cm}^2/\text{m}^2$ comparing to baseline ($p < 0.001$). (B) SMI decreased continuously from baseline up to 6 months ($42.9 \pm 4.6 \text{ cm}^2/\text{m}^2$ vs. $33.7 \pm 8.4 \text{ cm}^2/\text{m}^2$, $p < 0.001$) after trauma in 15 patients and lasted for at least 1 year ($42.9 \pm 5.3 \text{ cm}^2/\text{m}^2$ vs. $37.7 \pm 5.6 \text{ cm}^2/\text{m}^2$, $p = 0.004$) in 11 patients.

decrease in SMI from baseline up to 6 months ($42.9 \pm 4.6 \text{ cm}^2/\text{m}^2$ vs. $33.7 \pm 8.4 \text{ cm}^2/\text{m}^2$, $p < 0.001$) post trauma and a trough remaining for at least 1 year ($42.9 \pm 5.3 \text{ cm}^2/\text{m}^2$ vs. $37.7 \pm 5.6 \text{ cm}^2/\text{m}^2$, $p = 0.004$) (Figure 2).

Acute muscle wasting rate ($\Delta\text{SMI}\%$) and hospital malnutrition

Compared to well-nourished patients, critically ill trauma patients who developed malnutrition in hospital were characterized by higher BMI (23.5 ± 3.0 vs. 22.4 ± 2.7 , $p = 0.027$), APACHE II scores (16.1 ± 7.7 vs. 13.0 ± 8.7 , $p = 0.030$), lymphocyte counts (1.1 ± 1.0 vs. 0.8 ± 0.5 , $p = 0.028$) and $\Delta\text{SMI}\%$ (1.67 ± 1.32 vs. 0.28 ± 1.12 , $p = 0.000$), prolonged hospital stays (45.0 ± 29.5 vs. 25.1 ± 21.7 , $p = 0.000$) and ICU stays (26.6 ± 22.8 vs. 14.8 ± 16.8 , $p = 0.001$), increased 90-day (23.1% vs. 9.4%, $p = 0.040$) and 1-year (31.9% vs. 13.2%, $p = 0.034$) mortality (Table 3).

Binomial Logistic regression analysis showed that male (OR=5.111, 95%CI 1.468-17.800, $p = 0.010$) and $\Delta\text{SMI}\%$ (OR=2.892, 95%CI 1.895-4.416, $p < 0.001$) were independent risk factors for hospital malnutrition (Table 4). From ROC curve analysis, the area under curve (AUC) of

$\Delta\text{SMI}\%$ for hospital malnutrition prediction was 0.813 (95%CI 0.740-0.887, $p < 0.001$), and the optimal cut-off value was 0.687 with a sensitivity of 83.5% and a specificity of 71.7% (Table 5, Figure 3).

Acute muscle wasting rate ($\Delta\text{SMI}\%$) and mortality

ROC curve analysis showed that $\Delta\text{SMI}\%$ was a good predictor for 1-year mortality with AUC 0.715 (95% CI 0.581-0.849, $p = 0.001$), and the optimal cut-off point derived from the ROC curve for $\Delta\text{SMI}\%$ was 1.968 with a sensitivity of 62.5% and specificity of 83.3% (Figure 3). However, ROC curve analysis did not verify the predictive value of $\Delta\text{SMI}\%$ for 30-day, 60-day, 90-day mortality (Table 5).

Compared with patients who were alive at 1 year after trauma, those who died within 1 year had higher baseline SOFA scores (7.4 ± 4.0 vs. 5.1 ± 3.6 , $p = 0.006$) and $\Delta\text{SMI}\%$ (2.11 ± 1.86 vs. 0.97 ± 1.22 , $p = 0.007$) (Table 6). In multiple logistic regression, after adjustment for selected predictors of 1-year mortality, baseline SOFA score (OR=1.163, 95%CI 1.023-1.310, $p = 0.013$) and $\Delta\text{SMI}\%$ (OR=1.817, 95%CI 1.279-2.581, $p = 0.001$) were independent risk

Table 3. Characteristics of the critically ill trauma patients malnourished and well-nourished

Characteristics	Malnourished (n=91)	Well-nourished (n=53)	<i>p</i>
Age, years [median (IQR)]	51 (38, 58)	50 (36, 58)	0.720
Gender			0.076
Male, n (%)	72 (79.1)	48 (90.6)	
Female, (%)	19 (20.9)	5 (9.4)	
BMI, kg/m ²	23.5 ± 3.0	22.4 ± 2.7	0.027
APACHE II, [median (IQR)]	15 (10, 21)	10 (6, 18)	0.011
SOFA, [median (IQR)]	5 (3,8)	4 (2, 7)	0.118
NUTRIC, [median (IQR)]	4 (3, 5)	4 (2, 5)	0.283
ISS, [median (IQR)]	33 (24, 41)	27 (17, 34)	0.058
Laboratory tests at admission			
WBC, ×10 ⁹ /L	14.0 ± 6.6	13.4 ± 6.0	0.640
Lymphocyte, ×10 ⁹ /L	1.1 ± 1.0	0.8 ± 0.5	0.028
Hemoglobin, g/L	107 ± 25.5	112 ± 23.2	0.234
Platelet, ×10 ⁹ /L	152 ± 99.8	159 ± 75.1	0.666
Total bilirubin, μmol/L	32.5 ± 49.6	27.0 ± 25.9	0.454
Albumin, g/L	32.0 ± 5.6	31.1 ± 5.4	0.363
Creatinine, μmol/L	84.9 ± 42.4	82.6 ± 49.3	0.773
Fibrinogen, g/L	2.8 ± 1.7	4.9 ± 14.5	0.191
CRP, mg/L	107 ± 85.0	82.8 ± 69.5	0.076
PCT, ng/mL	6.6 ± 14.2	4.5 ± 14.2	0.407
Skeletal muscle index (cm ² /m ²)			
Baseline	50.1 ± 11.3	47.8 ± 9.4	0.198
1 Week	44.1 ± 10.2	46.8 ± 8.2	0.095
ΔSMI (%)	1.67 ± 1.32	0.28 ± 1.12	<0.001
Outcomes			
MV, n (%)	57 (62.6)	25 (47.2)	0.071
VA, n (%)	33 (36.3)	15 (28.3)	0.328
CRRT, n (%)	17 (18.7)	6 (11.3)	0.245
Hospital LOS, [median (IQR)]	36 (23, 52)	19 (13, 32)	<0.001
ICU LOS, [median (IQR)]	23 (9, 32)	10 (5.5, 20)	0.003
Mortality			
30-day, n (%)	3 (3.3)	3 (5.7)	0.801
60-day, n (%)	11 (12.1)	4 (7.5)	0.564
90-day, n (%)	21 (23.1)	5 (9.4)	0.040
1-year, n (%)	26 (31.9)	7 (13.2)	0.034

BMI, body mass index; APACHE II, acute physiology and chronic health evaluation II; SOFA, sequential organ failure assessment; NUTRIC, nutrition risk in critically ill; ISS, Injury Severity Score; WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin; ΔSMI(%), acute muscle wasting rate per day in the first week; MV, Mechanical ventilation; VA, Vasopressor; CRRT, Continuous Renal Replacement Therapy; LOS, Length of Stay

Table 4. Logistic regression analysis on risk factors of hospital malnutrition in the critically ill trauma patients

	β	S.E.	Wald	OR	95%CI	<i>p</i>
Age						0.905
Male	1.631	0.637	6.566	5.111	1.468-17.800	0.010
BMI						0.063
APACHE II						0.330
ISS						0.389
Lymphocyte	0.716	0.370	3.748	2.046	0.991-4.225	0.053
CRP						0.292
SMI						
Baseline						0.403
ΔSMI (%)	1.062	0.216	24.206	2.892	1.895-4.416	<0.001

BMI, body mass index; APACHE II, acute physiology and chronic health evaluation II; ISS, Injury Severity Score; CRP, C-reactive protein; SMI, Skeletal muscle index; ΔSMI (%), acute muscle wasting rate per day in the first week

factors. However, the baseline SMI was not significantly associated with 1-year mortality (Table 7).

DISCUSSION

The novel finding of this retrospective study is that acute skeletal muscle wasting quantified as ΔSMI%, was useful for prediction of 1-year mortality in critically ill trauma.

Every 1% absolute increase of ΔSMI% was associated with 1.82-fold higher odds of 1-year mortality. To our knowledge, this is the first study to investigate the relation between CT-derived markers for acute muscle wasting and long-term mortality in the critically ill.

Skeletal muscle mass is considered an important physiologic reserve in the critically ill.²¹ Sarcopenia at base-

Table 5. ROC analysis for Δ SMI (%) to predict hospital malnutrition and mortality

Predicted value	AUC	95% CI	<i>p</i>	Sensitivity	Specificity	Youden's index	Cut-off
Hospital malnutrition	0.813	0.740-0.887	<0.001	0.835	0.717	0.552	0.678
30-day mortality	0.495	0.186-0.805	0.967				
60-day mortality	0.606	0.396-0.816	0.225				
90-day mortality	0.623	0.462-0.785	0.091	0.500	0.794	0.294	1.968
1-year mortality	0.715	0.581-0.849	0.001	0.625	0.833	0.458	1.968

ROC, receiver operating characteristic curve; AUC, area under curve; CI, confidence interval

Table 6. Characteristics of the critically ill trauma patients survived or died over 1 year after trauma

Characteristics	Survived (n=111)	Died (n=33)	<i>p</i>
Age, years	51 (36, 58.8)	49 (36.5, 57.8)	0.582
Gender			
Male, n (%)	101 (84.2)	20 (83.3)	0.919
Female, (%)	19 (15.8)	4 (16.7)	
BMI, kg/m ²	22.9 ± 2.7	24.1 ± 3.5	0.118
APACHE II	14.4 ± 8.2	17.7 ± 7.9	0.075
SOFA	5.1 ± 3.6	7.4 ± 4.0	0.006
NUTRIC	3.8 ± 1.7	4.5 ± 1.5	0.104
ISS	30.1 ± 11.4	31.3 ± 9.5	0.686
Laboratory tests at admission			
WBC, ×10 ⁹ /L	13.5 ± 6.3	15.1 ± 6.6	0.268
Lymphocyte, ×10 ⁹ /L	1.0 ± 0.8	1.0 ± 0.9	0.906
Hemoglobin, g/L	109 ± 25.8	106 ± 18.8	0.583
Platelet, ×10 ⁹ /L	156 ± 95.3	148 ± 68.5	0.693
Total Bilirubin, μmol/L	28.6 ± 41.5	40.0 ± 46.6	0.231
Albumin, g/L	31.6 ± 5.4	32.3 ± 6.3	0.578
Creatinine, μmol/L	82.2 ± 45.0	93.3 ± 44.5	0.271
Fibrinogen, g/L	3.6 ± 9.7	3.5 ± 1.7	0.967
CRP, mg/L	92.7 ± 77.1	126 ± 91.8	0.060
PCT, ng/mL	5.7 ± 14.2	6.6 ± 14.5	0.773
Skeletal muscle index (cm ² /m ²)			
Baseline	48.6 ± 10.7	52.6 ± 10.3	0.095
1 Week	45.2 ± 9.9	44.4 ± 7.7	0.678
Δ SMI (%)	0.97 ± 1.22	2.11 ± 1.86	0.007

BMI, body mass index; APACHE II, acute physiology and chronic health evaluation II; SOFA, sequential organ failure assessment; NUTRIC, nutrition risk in critically ill; ISS, Injury Severity Score; WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin; Δ SMI (%), acute muscle wasting rate per day in the first week

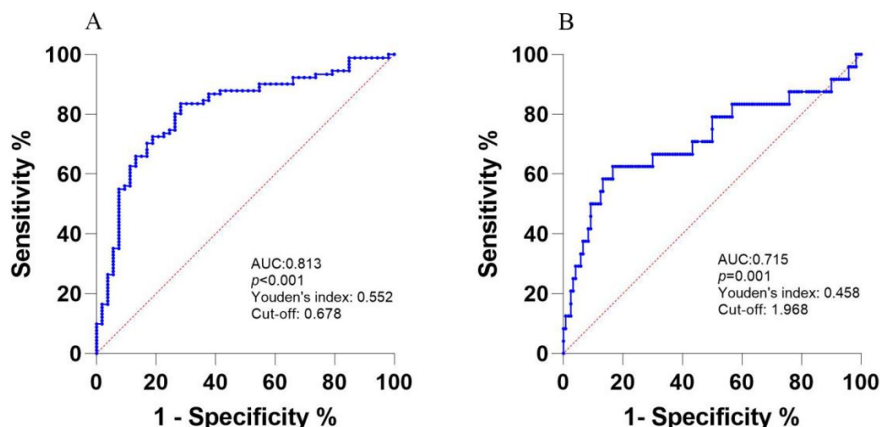


Figure 3. ROC analysis for Δ SMI (%) in predicting hospital malnutrition and 1-year mortality. (A) The area under curve of Δ SMI% for hospital malnutrition prediction was 0.813 (95% CI 0.740-0.887, *p*<0.001), and the optimal cut-off value was 0.687 with a sensitivity of 83.5% and a specificity of 71.7%. (B) The area under curve of Δ SMI% for 1-year mortality prediction was 0.715 (95% CI 0.581-0.849, *p*=0.001), and the optimal cut-off value was 1.968 with a sensitivity of 62.5% and a specificity of 83.3%.

line, as well as low muscle mass, was closely associated with poor prognosis and high disease related burden. Different cutoff levels for CT-derived SMI at the level of L3

vertebra were set according to age, gender and regions to define sarcopenia.^{22,23,24,25} Therefore, SMI less than the reference values means that there are insufficient energy

Table 7. Logistic regression analysis on risk factors of 1-year mortality in critically ill trauma

	β	S.E.	Wald	OR	95%CI	<i>p</i>
Age						0.368
Male						0.906
BMI						0.513
APACHE II						0.679
SOFA	0.151	0.061	6.178	1.163	1.023-1.310	0.013
NUTRIC						0.918
CRP						0.428
SMI (Baseline)						0.638
Δ SMI (%)	0.597	0.179	11.106	1.817	1.279-2.581	0.001

BMI, body mass index; APACHE II, acute physiology and chronic health evaluation II; SOFA, sequential organ failure assessment; NUTRIC, nutrition risk in critically ill; CRP, C-reactive protein; SMI, Skeletal muscle index; Δ SMI (%), acute muscle wasting rate per day in the first week

and protein reserves to negotiate critical illness, with resultant prolonged hospital stay and increased mortality.

However, SMI at baseline cannot reflect the severity of catabolism caused by diseases and adequately capture individual risk.²² It is well documented that muscle wasting occurs rapidly due to excessive catabolism in the critically ill, and is exacerbated thereafter during the ICU stay. Daily muscle wasting rate in the first week after trauma, abbreviated as Δ SMI%, is a good indicator of body composition change in response to metabolic stress, and reflects the severity of skeletal muscle atrophy in the acute phase. Our study showed that Δ SMI% was a good predictor for 1-year mortality with AUC 0.715 (95% CI 0.581-0.849), and that 1-year mortality increased by 1.82 times for every 1% absolute loss of SMI per day over the first week. However, the baseline SMI was not significantly associated with 1-year mortality.

The overall fatality rate of patients with severe trauma during hospitalization was 6.4%-27.2%.^{26,27} Malnutrition increased mortality chances 1.96 times in critically ill trauma patients.²⁸ In this study, the 90-day and 1-year mortality rate was significantly higher in severe trauma patients with hospital malnutrition than those without malnutrition. It was suggested that hospital malnutrition was strongly associated with long-term mortality in trauma. Additionally, our study showed that Δ SMI% was a good predictor for evaluating newly onset malnutrition during hospitalization, with an optimal cut-off value of 0.7%. It provided a novel insight into early recognition of potential malnutrition in acute and critical illness. Therefore, we propose that Δ SMI% can be used as an assessment tool for evaluating the nutritional status in the critically ill.

Our study also demonstrated the longitudinal changes of SMI over a year. In the first week after trauma, CT-derived SMI decreased by 8.5% compared with baseline. However, it has previously been reported that skeletal muscle area measured by ultrasound significantly reduced by up to 18.5% in critically ill patients during the first week of hospitalization.¹⁴ As is known, CT is a gold standard technique for assessment of skeletal muscle mass,²⁹ and that there is a good correlation between ultrasound and CT in assessing skeletal muscle mass and its rate of change, whereas the change rates for muscle mass measured by CT seem lower than those from ultrasound in general.^{13,15} Further research is needed to explore these differences and identify the reasons.

The decline of skeletal muscle mass in the critically ill occurs quickly and lasts for a long period of time.¹⁷ The short-term changes of muscle mass measured with CT or ultrasound have been described in several studies.¹⁵ However, the follow-up data for long-term changes of skeletal muscle mass among ICU survivors are rare. Sepsis patients exhibited persistent muscle wasting with an 8.4% decrease at 3 months and a 2.9% decrease at 1 year in SMI from baseline.³⁰ Critically ill trauma patients were worse off in the present study, with an 18.7% decrease in SMI at 1 month, 21.8% decrease at 6 months and a 11.7% decrease at 1 year from baseline. The trough of muscle mass was between 1 month and 6 months after trauma. Although the sample size was relatively small, these findings may provide insights into long-term skeletal muscle wasting in critical illness.

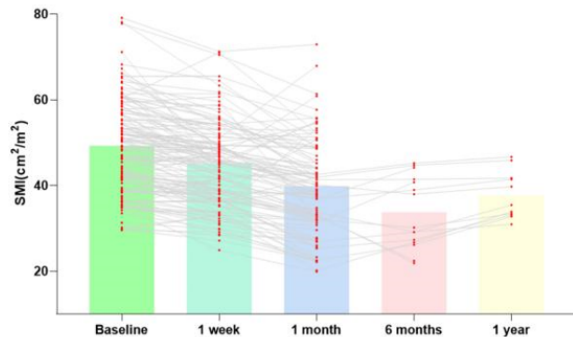
Limitations

Our study had several limitations. First, the single-center retrospective observational study design introduced the risk of bias and residual confounding. Second, the number of CT scans was limited due to the retrospective nature. Cases were deleted because they could not meet the eligibility criteria that 2 CT scans with an interval of more than 5 days in the first week were performed. The long-term variation in SMI is not convincing on account of data limitation. Third, nutrition intake and physical exercise during hospital stay and post-discharge were not considered in this study. Finally, although CT is considered a gold standard technique for assessment of skeletal muscle mass, ultrasound of skeletal muscle avoids the hazards of transportation and extra radiation exposure. It is not clear whether our findings would be supportable using ultrasound.

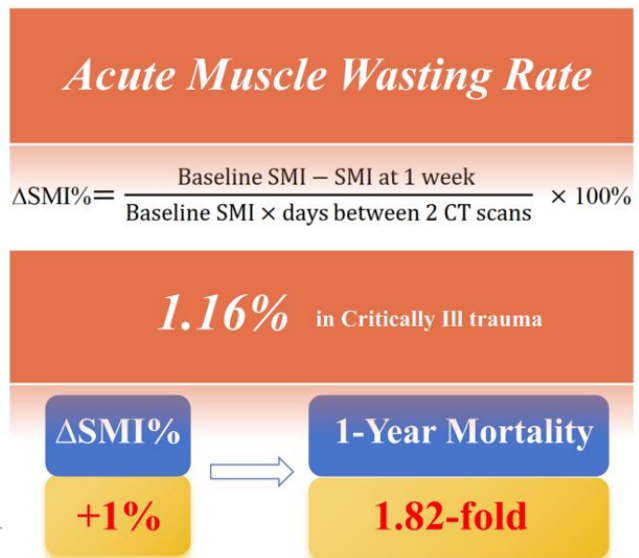
Conclusions

Skeletal muscle wasting occurred in the acute phase of trauma, and baseline muscle mass might not be fully restored a year after trauma. Acute skeletal muscle wasting rate, as assessed by Δ SMI%, was independently associated with a higher 1-year mortality and hospital malnutrition in critically ill trauma. Every 1% absolute increase of Δ SMI% was associated with 1.82-fold higher odds ratio for 1-year mortality in critically ill trauma. The area under the curve of Δ SMI% was 0.813 for the hospital malnutrition prediction and 0.715 for the 1-year mortality prediction. Future research should explore the relation-

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Graphical abstract



ship between acute muscle wasting rate and mortality in prospective studies with a larger sample size, in other populations, and with different methods for assessment of skeletal muscle mass. Furthermore, interventions to reduce acute skeletal muscle wasting, so reducing mortality in critically ill, await study.

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AUTHOR DISCLOSURES

We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

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REFERENCES

- Meyer HJ, Wienke A, Surov A. Computed tomography-defined low skeletal muscle mass as a prognostic marker for short-term mortality in critically ill patients: A systematic review and meta-analysis. *Nutrition*.2021;91-2:111417. doi: 10.1016/j.nut.21111417.
- Giani M, Rezoagli E, Grassi A, Porta M, Riva L, Famularo S et al. Low skeletal muscle index and myosteatosis as predictors of mortality in critically ill surgical patients. *Nutrition*.2022;101:111687. doi: 10.1016/j.nut.2022.111687.
- Seo DW, Kim KW, Sohn CH, Ryoo SM, Kim YJ, Shin A, Kim WY. Progressive loss of muscle mass could be an adverse prognostic factor of 28-day mortality in septic shock patients. *Sci Rep*. 2019;9:16471. doi: 10.1038/s41598-019-52819-w.
- Looijaard WGPM, Stapel SN, Dekker IM, Rusticus H, Remmelzwaal S, Girbes ARJ, Weijs PJM, Straaten HMO. Identifying critically ill patients with low muscle mass: agreement between bioelectrical impedance analysis and computed tomography. *Clin Nutr*. 2020;39:1809-17. doi: 10.1016/j.clnu.2019.07.020.
- Yanagi N, Koike T, Kamiya K, Hamazaki N, Nozaki K, Ichikawa T, Matsunaga A, Kuroiwa M, Arai M. Assessment of sarcopenia in the intensive care unit and 1-year mortality in survivors of critical illness. *Nutrients*. 2021;13:2726. doi: 10.3390/nu13082726.
- Proksch DM, Kelley KM, White S, Burgess JR. Identification of sarcopenia in elderly trauma patients: the value of clinical competency and experience. *Am Surg*. 2022;88:339-42. doi: 10.1177/0003134820982854.
- Akahoshi T, Yasuda M, Momii K, Kubota K, Shono Y, Kaku N et al. Sarcopenia is a predictive factor for prolonged intensive care unit stays in high-energy blunt trauma patients. *Acute Med Surg*. 2016;3:326-31. doi: 10.1002/ams2.195.
- Belger E, Truhn D, Weber CD, Neumann UP, Hildebrand F, Horst K. The Impact of Body Mass Composition on Outcome in Multiple Traumatized Patients-Results from the Fourth Thoracic and Third Lumbar Vertebrae: A Single-Center Retrospective Observational Study. *J Clin Med*. 2023;12:2520. doi: 10.3390/jcm12072520.
- Xi FC, Tan SJ, Gao T, Ding WW, Sun JF, Wei CY, Li WQ, Yu WK. Low skeletal muscle mass predicts poor clinical outcomes in patients with abdominal trauma. *Nutrition*. 2021;89:111229. doi: 10.1016/j.nut.2021.111229.
- Batt J, Herridge M, Dos Santos C. Mechanism of ICU-acquired weakness: skeletal muscle loss in critical illness. *Intensive Care Med*. 2017;43:1844-6. doi: 10.1007/s00134-017-4758-4.
- Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T et al; GLIM Core Leadership Committee; GLIM Working Group. GLIM criteria for the diagnosis of malnutrition - A consensus report from the global clinical nutrition community. *Clin Nutr*. 2019;38:1-9. doi: 10.1016/j.clnu.2018.08.002.
- Puthuchery ZA, Rawal J, McPhail M, Connolly B, Ratnayake G, Chan P et al. Acute skeletal muscle wasting in critical illness. *JAMA*. 2013;310:1591-600. doi: 10.1001/jama.2013.278481.
- Nakanishi N, Tsutsumi R, Okayama Y, Takashima T, Ueno Y, Itagaki T, Tsutsumi Y, Sakaue H, Oto J. Monitoring of muscle mass in critically ill patients: comparison of ultrasound and two bioelectrical impedance analysis devices. *J Intensive Care*. 2019;7:61. doi: 10.1186/s40560-019-0416-y.
- Mayer KP, Bastin MLT, Montgomery-Yates AA, Pastva AM, Dupont-Versteegden EE, Parry SM, Morris PE. Acute skeletal muscle wasting and dysfunction predict physical

- disability at hospital discharge in patients with critical illness. *Crit Care*. 2020;24:637. doi: 10.1186/s13054-020-03355-x.
15. Fazzini B, Märkl T, Costas C, Blobner M, Schaller SJ, Prowle J, Puthuchery Z, Wackerhage H. The rate and assessment of muscle wasting during critical illness: a systematic review and meta-analysis. *Crit Care*. 2023;27:2. doi: 10.1186/s13054-022-04253-0.
 16. Lee ZY, Ong SP, Ng CC, Yap CSL, Engkasan JP, Barakatun-Nisak MY, Heyland DK, Hasan MS. Association between ultrasound quadriceps muscle status with pre-morbid functional status and 60-day mortality in mechanically ventilated critically ill patient: A single-center prospective observational study. *Clin Nutr*. 2021;40:1338-47. doi: 10.1016/j.clnu.2020.08.022.
 17. Kolck J, Rako ZA, Beetz NL, Auer TA, Segger LK, Pille C, Penzkofer T, Fehrenbach U, Geisel D. Intermittent body composition analysis as monitoring tool for muscle wasting in critically ill COVID-19 patients. *Ann Intensive Care*. 2023;13:61. doi: 10.1186/s13613-023-01162-5.
 18. Xi FC, You Y, Ding WW, Gao T, Cao Y, Tan SJ, Yu WK. Association of longitudinal changes in skeletal muscle mass with prognosis and nutritional intake in acutely hospitalized patients with abdominal trauma: a retrospective observational study. *Front Nutr*. 2023;10:1085124. doi: 10.3389/fnut.2023.1085124.
 19. Pape HC, Lefering R, Butcher N, Peitzman A, Leenen L, Marzi I et al. The definition of polytrauma revisited: An international consensus process and proposal of the new 'Berlin definition'. *J Trauma Acute Care Surg*. 2014;77:780-6. doi: 10.1097/TA.0000000000000453.
 20. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315:801-10. doi: 10.1001/jama.2016.0287.
 21. Oh HJ, Kim JH, Kim HR, Ahn JY, Jeong SJ, Ku NS, Choi JY, Yeom JS, Song YG. The impact of sarcopenia on short-term and long-term mortality in patients with septic shock. *J Cachexia Sarcopenia Muscle*. 2022;13:2054-63. doi: 10.1002/jcsm.12995.
 22. Derstine BA, Holcombe SA, Ross BE, Wang NC, Su GL, Wang SC. Skeletal muscle cutoff values for sarcopenia diagnosis using T10 to L5 measurements in a healthy US population. *Sci Rep*. 2018;8:11369. doi: 10.1038/s41598-018-29825-5.
 23. Van der Werf A, Langius JAE, De van der Schueren MAE, Nurmohamed SA, Van der Pant KAMI, Blauwhoff-Buskermolten S, Wierdsma NJ. Percentiles for skeletal muscle index, area and radiation attenuation based on computed tomography imaging in a healthy Caucasian population. *Eur J Clin Nutr*. 2018;72:288-96. doi: 10.1038/s41430-017-0034-5.
 24. Bahat G, Turkmen BO, Aliyev S, Catikkas NM, Bakir B, Karan MA. Cut-off values of skeletal muscle index and psoas muscle index at L3 vertebra level by computerized tomography to assess low muscle mass. *Clin Nutr*. 2021;40:4360-65. doi: 10.1016/j.clnu.2021.01.010.
 25. Kong M, Geng N, Zhou Y, Lin N, Song W, Xu M et al. Defining reference values for low skeletal muscle index at the L3 vertebra level based on computed tomography in healthy adults: A multicentre study. *Clin Nutr*. 2022;41:396-404. doi: 10.1016/j.clnu.2021.12.003.
 26. Torabi M, Abadi FMS, Baneshi MR. Blood sugar changes and hospital mortality in multiple trauma. *Am J Emerg Med*. 2018;36:816-19. doi: 10.1016/j.ajem.2017.10.029.
 27. Driessen MLS, Sturms LM, van Zwet EW, Bloemers FW, Duis HJT, Edwards MJR et al. Evaluation of the Berlin polytrauma definition: A Dutch nationwide observational study. *J Trauma Acute Care Surg*. 2021;90:694-9. doi: 10.1097/TA.00000000000003071.
 28. Ceniccola GD, Okamura AB, Neta JSS, Lima FC, De Deus ACS, De Oliveira JA, Dos Santos SSM, De Sousa RB, De Brito-Ashurst I. Association Between AND-ASPEN Malnutrition Criteria and Hospital Mortality in Critically Ill Trauma Patients: A Prospective Cohort Study. *JPEN J Parenter Enteral Nutr*. 2020;44:1347-54. doi: 10.1002/jpen.1795.
 29. Viertel M, Bock C, Reich M, Löser S, Plauth M. Performance of CT-based low skeletal muscle index, low mean muscle attenuation, and bioelectric impedance derived low phase angle in the detection of an increased risk of nutrition related mortality. *Clin Nutr*. 2019;38:2375-80. doi: 10.1016/j.clnu.2018.10.018.
 30. Cox MC, Booth M, Ghita G, Gardner A, Hawkins RB, Darden DB et al. The impact of sarcopenia and acute muscle mass loss on long-term outcomes in critically ill patients with intra-abdominal sepsis. *J Cachexia Sarcopenia Muscle*. 2021;12:1203-13. doi: 10.1002/jcsm.12752.