

# Chest computed tomography-derived muscle mass and quality indicators, in-hospital outcomes, and costs in older inpatients

Yanjiao Shen<sup>1</sup>, Li Luo<sup>2</sup>, Hongbo Fu<sup>2</sup>, Lingling Xie<sup>3</sup>, Wenyi Zhang<sup>2</sup>, Jing Lu<sup>4\*</sup> & Ming Yang<sup>5\*</sup>

<sup>1</sup>Department of Guideline and Rapid Recommendation, Cochrane China Centre, MAGIC China Centre, Chinese Evidence-Based Medicine Centre, West China Hospital, Sichuan University, Chengdu, China; <sup>2</sup>Center of Gerontology and Geriatrics, West China Hospital, Sichuan University, Chengdu, China; <sup>3</sup>West China School of Nursing, West China Hospital, Sichuan University, Chengdu, China; <sup>4</sup>Medical Insurance Office, West China Hospital, Sichuan University, Chengdu, Sichuan, China; <sup>5</sup>National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University, Chengdu, Sichuan, China

## Abstract

**Background** Muscle mass and muscle quality assessed by computed tomography (CT) have been associated with poor prognosis in oncology and surgery patients, but the relevant evidence was limited in older patients. We hypothesized that muscle mass and muscle quality indicators derived from opportunistic chest CT images at the 12th thorax vertebra level (T12) could predict in-hospital death, length of hospital stay (hospital LOS), and hospital costs among older patients in acute care wards.

**Methods** We conducted a prospective cohort study. Older patients admitted to the acute geriatric wards of a teaching hospital were continuously recruited. Chest CT images were analysed using SliceOmatic software. The skeletal muscle area, skeletal muscle radiodensity, and intermuscular adipose tissue (IMAT) at the T12 level were measured. Skeletal muscle index (SMI) was calculated using skeletal muscle area divided by body height squared.

**Results** We included 1135 older patients with a median age of 80 years (interquartile range, 73 to 85 years), 498 (44%) were women, 148 (13%) patients died during hospitalization. The SMI and SMD were negatively correlated to age ( $\rho = -0.11$ ,  $P < 0.001$ ,  $\rho = -0.30$ ,  $P < 0.001$ , respectively), whereas the IMAT was positively correlated to age ( $\rho = 0.27$ ,  $P < 0.001$ ). Compared with survivors, dead patients had significantly lower SMI in men ( $P < 0.001$ ) but not in women ( $P = 0.760$ ). After adjusting for sex and other potential confounders, the SMI [increased per 1 cm<sup>2</sup>/m<sup>2</sup>, odds ratio (OR) 0.96, 95% confidence interval (CI) 0.93 to 0.99] and SMD (increased per 1 Hounsfield unit, OR 0.93, 95% CI 0.90 to 0.96) were negatively and independently associated with in-hospital death, whereas the IMAT (increased per 1 cm<sup>2</sup>, OR 1.09, 95% CI 1.05 to 1.14) was independently and positively associated with in-hospital death. None of the SMI, SMD, or IMAT was significantly related to long hospital LOS or increased hospital costs.

**Conclusions** Chest CT-derived muscle mass indicator (T12 SMI) and muscle quality indicators (T12 SMD and T12 IMAT) may serve as prognostic factors for predicting in-hospital death among older inpatients. Opportunistic chest CT images might be an overlooked resource for measuring muscle mass and muscle quality and for predicting short-term prognosis in older inpatients.

**Keywords** Muscle wasting; Muscle depletion; Sarcopenia; Myosteatosis; Geriatrics

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\*Ming Yang, National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University, No. 37 Guoxue Lane, Chengdu 610041, Sichuan, China. Email: yangmier@gmail.com, yangmier@scu.edu.cn;

Jing Lu, Medical Insurance Office, West China Hospital, Sichuan University, No. 37 Guoxue Lane, Chengdu 610041, Sichuan, China. Email: lujing1209@gmail.com; lujing1209@126.com

Yanjiao Shen and Li Luo contribute equally to this work.

## Introduction

Researchers are getting increasingly interested in sarcopenia, the age-related loss of muscle mass and function, across multiple disciplines.<sup>1</sup> Notably, there is emerging evidence that not only muscle mass but also muscle quality substantially decreased with ageing.<sup>2</sup> The relationships between low muscle mass and adverse health-related outcomes (e.g. functional disability, poor quality of life, and mortality) among different populations have been well-established.<sup>3–6</sup> Recent studies indicated that muscle quality might also be associated with some adverse outcomes, including mortality in mechanically ventilated patients<sup>7</sup> or colorectal cancer patients,<sup>8</sup> post-operative complications in gynaecologic cancer patients,<sup>9</sup> and falls in octogenarians.<sup>10</sup> Thus, the updated European Working Group on Sarcopenia in Older People (EWGSOP2) emphasizes that muscle quality is as important as muscle mass for diagnosing sarcopenia.<sup>11</sup>

Muscle quality can be defined either by changes in the architecture and composition of muscles<sup>11</sup> or by muscle strength (or power) delivered per unit of muscle mass.<sup>12</sup> Our study defined muscle quality based on muscle composition rather than muscle strength per unit of muscle mass. Highly sensitive imaging tools, such as computed tomography (CT) and magnetic resonance imaging (MRI), have been recommended to assess muscle quality.<sup>11</sup> Due to accessibility and costs, CT is far more frequently used than MRI for assessing muscle quality. Using specific software, muscle quality can be assessed by measuring skeletal muscle density (SMD), indicating intramuscular adipose tissue (IntraMAT) and intramyocellular lipid (IMCL),<sup>13</sup> and the amount of adipose tissue between muscles (also known as intermuscular adipose tissue or IMAT) via CT images.<sup>7,14</sup> Meanwhile, CT can be used to determine muscle mass by measuring skeletal muscle area (SMA).

However, CT is expensive and increases the risk of radiation exposure. Therefore, previous studies mainly utilized opportunistic CT scans (CT scans taken for other purposes, predominantly to screen or diagnose cancer) to measure muscle mass and/or muscle quality. As a result, most previous studies focused on muscle quality and prognosis in cancer patients.<sup>15–17</sup> Acute care unit residents, especially older patients, are thought to be at high risk of deteriorating muscle quality; but the relationship between muscle quality and prognosis in this population was rarely reported in the literature. Furthermore, according to a recent systematic review, the majority of previous studies (66 out of 70 studies) measured muscle quality by abdominal CT, and only one study used chest CT.<sup>18</sup> Nevertheless, chest CT is more commonly utilized in clinical practice than abdominal CT,<sup>19</sup> especially among patients with respiratory diseases.<sup>20</sup> Here, we hypothesized that muscle mass and muscle quality indicators derived from opportunistic chest CT images could predict in-hospital death, length of stay (hospital LOS) in hospital, and hospital costs among older patients in acute care wards.

## Methods

### *Study design and participants*

We conducted a prospective cohort study. From March 2017 to March 2020, we continuously recruited older patients admitted to the acute geriatric wards of West China Hospital, Sichuan University. Patients were included if they were aged 65 years or older and had a chest CT scan within 48 h after admission. The exclusion criteria were as follows: (1) acute stroke; (2) severe respiratory failure that needs mechanical ventilation; (3) haemodialysis; (4) terminal diseases; (5) trauma, surgery, or bone fracture within 3 months before enrolment; (6) low-quality CT images or any anatomical distortion (e.g. chest wall oedema or pleural effusion) or loss of any muscle mass area on CT images; (7) any type of cancer; (8) delirium; (9) medical history of dementia, depression, anxiety, or schizophrenia; (10) refusal to sign the consent. The Biomedical Ethics Committee of West China Hospital, Sichuan University approved the study protocol. All participants signed written informed consent.

### *Measurements of muscle mass and muscle quality indicators*

A chest CT scan was obtained within 48 h of each participant's admission for acute respiratory infection, chest pain, or other reasons. The 16-slice spiral CT scanners from Philips Healthcare (Brilliance, Ohio, USA) were used with a 5 mm slice thickness to perform the CT scans. An unenhanced cross-sectional CT image at the 12th thorax (T12) vertebral level for each patient was analysed using SliceOmatic software (Tomovision, Version 5.0, Montreal, QC, Canada).

Using a single CT image, the SMA of all skeletal muscle visible at the T12 vertebral level was segmented according to the most widely used muscle tissue thresholds [–29 to 150 Hounsfield unit (HU)].<sup>19</sup> An HU scale of a CT scan indicates the density of the tissue.<sup>21</sup> As reported in past studies,<sup>22,23</sup> the skeletal muscle index (SMI), a muscle mass indicator, was calculated using the following formula:  $SMI = SMA (cm^2) / \text{body height squared } (m^2)$  to account for the influence of body size. A higher SMI indicates more skeletal muscle.<sup>19</sup> For muscle quality analysis, SMD and IMAT were measured. SliceOmatic software automatically calculated the mean SMD of all SMAs at the T12 vertebral level. Skeletal muscle with a lower SMD shows higher IntraMAT and/or IMCL, which indicate poorer muscle quality. A quantitative assessment of IMAT was performed by using fat tissue thresholds (–30 to –190 HU)<sup>24,25</sup> to identify visible fat within muscle fascia at the T12 vertebral level. Higher IMAT indicates poorer muscle quality. Supporting information, Figure S1 presents a representative CT image after segmentation.

## Measurements of covariates

Using the Hospital Information System, we obtained the following details: age, sex, height, and weight, along with the top five comorbidities in our study population (hypertension, cardiovascular disease, diabetes, chronic obstructive pulmonary disease, and acute infection). Nurses took blood within 48 h of admission after patients had fasted for over 8 h. To determine cystatin C (CysC) concentration in serum, a simple immunoturbidimetric assay was used (Sichuan Mike Biotechnology Co., Ltd., Chengdu, China). Standard methods were also used to measure serum creatinine, albumin, and haemoglobin levels. Furthermore, to assess all participants' nutrition status, the Mini Nutrition Assessment Short Form (MNA-SF)<sup>26</sup> questionnaire was used. The MNA-SF test has a range of scores from 0 points (*worse*) to 14 points (*best*). A score of 8 to 11 indicates 'malnutrition risk', whereas a score of 0 to 7 indicates malnutrition.

## In-hospital outcomes and hospital costs

We prospectively collected the information about the in-hospital outcomes (in-hospital death and hospital LOS) and hospital costs from the Hospital Information System. Hospital LOS and hospital costs were treated as continuous data and dichotomized according to the corresponding median. Hospital LOS and hospital costs exceeding the median were labelled as 'long hospital LOS' and 'increased costs', respectively.

## Statistical analyses

All statistical analyses were performed using R version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria). Statistical significance is determined by a two-sided *P* value of 0.05. Using the Shapiro–Wilk test, we determined the distribution of continuous data. We described the study population by using mean and standard deviation (SD) for normally distributed continuous variables or median and interquartile range (IQR) for non-normally distributed continuous variables. The categorical data were presented as absolute numbers and percentages (%). We used the Wilcoxon rank-sum test, one-way ANOVA, or Pearson's  $\chi^2$  test, as appropriate, to assess the statistical difference between groups with or without 'in-hospital death', 'long hospital LOS', or 'increased costs', respectively. Boxplots with jitter points were used to show the absolute differences of SMI, SMD, and IMAT between groups.

We performed the Spearman's rank correlation analysis ( $\rho$ ) to explore the correlations between the continuous variables. Univariable logistic regression models were performed to explore the associations of in-hospital outcomes

(in-hospital death, long hospital LOS, or increased costs) with SMI, SMD, IMAT, and other potential confounders. When necessary, subgroup analyses were conducted according to sex. We also performed multivariable logistic regression models to explore the associations of in-hospital outcomes with SMI, SMD, and IMAT. Based on previous studies<sup>19</sup> and the results of the univariable logistic analyses ( $P < 0.1$ ), we adjusted for some confounders. Model 1 adjusted for age (per 1 year) and sex (men or women). Model 2 adjusted for age (per 1 year), sex (men or women), nutrition status (normal, malnutrition risk, or malnutrition), cardiovascular disease (yes or no), diabetes (yes or no), acute infection (yes or no), creatinine (per 10  $\mu\text{mol/L}$ ), and serum albumin (per 10 g/L). Odds ratios (ORs) were calculated, as well as corresponding 95% confidence intervals (CIs).

## Results

### Baseline characteristics

We included a total of 1135 patients including 498 (44%) women. The median age of the study population was 80 years (IQR: 73 to 85 years). Table 1 shows the baseline characteristics of the study population according to in-hospital death status. Age, nutrition status, and serum albumin at baseline were significantly associated with in-hospital death (Table 1).

### Correlations of muscle mass and quality indicators with age, body mass index, hospital length of stay, and costs

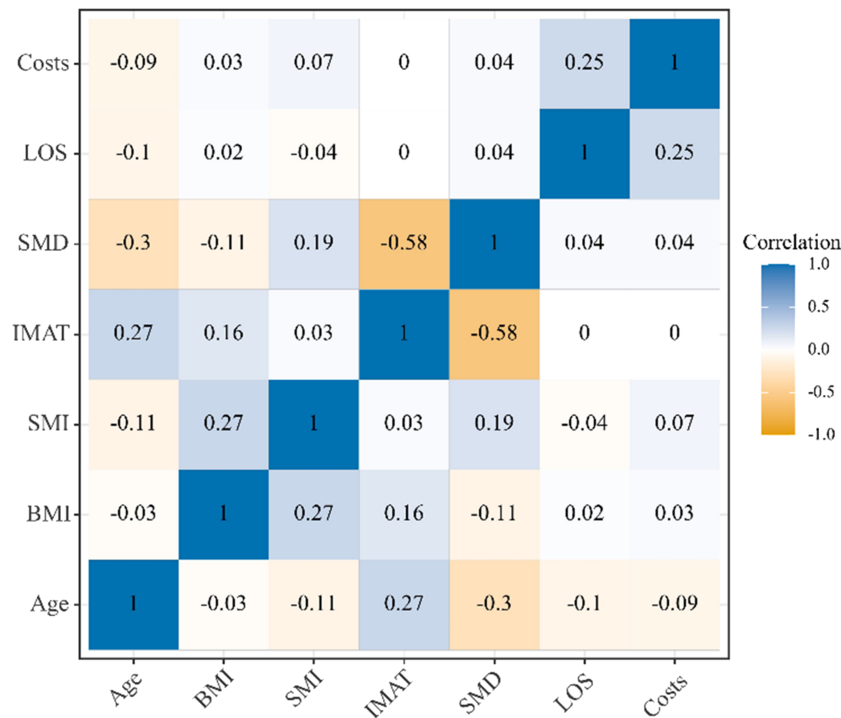
Figure 1 shows the correlation coefficients of muscle mass and muscle quality indicators with age, BMI, hospital LOS, and hospital costs. The SMI was negatively correlated to age ( $\rho = -0.11$ ,  $P < 0.001$ ), positively correlated to the BMI ( $\rho = 0.27$ ,  $P < 0.001$ ) and the hospital costs ( $\rho = 0.07$ ,  $P = 0.001$ ) but not significantly correlated to the hospital LOS ( $\rho = -0.04$ ,  $P = 0.935$ ) and the IMAT ( $\rho = 0.03$ ,  $P = 0.259$ ). The SMD was also negatively correlated to age ( $\rho = -0.30$ ,  $P < 0.001$ ), positively correlated to the BMI ( $\rho = 0.16$ ,  $P < 0.001$ ), but not significantly correlated to the hospital LOS ( $\rho = 0.04$ ,  $P = 0.051$ ) and hospital costs ( $\rho = 0.04$ ,  $P = 0.082$ ). Furthermore, the IMAT was positively correlated to age ( $\rho = 0.27$ ,  $P < 0.001$ ), negatively correlated to the BMI ( $\rho = -0.11$ ,  $P < 0.001$ ), but not significantly correlated to the hospital LOS ( $\rho = 0$ ,  $P = 0.523$ ) and hospital costs ( $\rho = 0$ ,  $P = 0.399$ ).

**Table 1** Baseline characteristics of the study population

| Characteristic                     | Overall, N = 1135    | In-hospital death    |                     | P value <sup>a</sup> |
|------------------------------------|----------------------|----------------------|---------------------|----------------------|
|                                    |                      | No, N = 987          | Yes, N = 148        |                      |
| Age, year, Median (IQR)            | 80 (73, 85)          | 80 (72, 85)          | 82 (74.75, 87)      | 0.001                |
| Women, n (%)                       | 498 (44%)            | 432 (44%)            | 66 (45%)            | 0.850                |
| Nutrition status, n (%)            |                      |                      |                     | 0.005                |
| Malnutrition                       | 459 (40%)            | 383 (39%)            | 76 (51%)            |                      |
| Malnutrition risk                  | 303 (27%)            | 264 (27%)            | 39 (26%)            |                      |
| Normal                             | 373 (33%)            | 340 (34%)            | 33 (22%)            |                      |
| Hypertension, n (%)                | 573 (50%)            | 503 (51%)            | 70 (47%)            | 0.406                |
| Cardiovascular disease, n (%)      | 286 (25%)            | 251 (25%)            | 35 (24%)            | 0.641                |
| Diabetes, n (%)                    | 352 (31%)            | 303 (31%)            | 49 (33%)            | 0.555                |
| COPD, n (%)                        | 239 (21%)            | 215 (22%)            | 24 (16%)            | 0.121                |
| Acute infection, n (%)             | 295 (26%)            | 255 (26%)            | 40 (27%)            | 0.758                |
| BMI, kg/m <sup>2</sup> , mean (SD) | 22.85 (3.25)         | 22.86 (3.23)         | 22.76 (3.36)        | 0.767                |
| Creatinine, μmol/L, median (IQR)   | 72 (62, 85)          | 73 (62, 85)          | 71 (60.75, 81)      | 0.275                |
| Cystatin C, mg/L, median (IQR)     | 0.97 (0.83, 1.11)    | 0.97 (0.83, 1.11)    | 0.97 (0.82, 1.11)   | 0.677                |
| Serum albumin, g/L, Mean (SD)      | 36.99 (6.20)         | 37.35 (6.06)         | 34.64 (6.60)        | <0.001               |
| Haemoglobin, g/dL, Median (IQR)    | 11.20 (10.20, 12.40) | 11.20 (10.20, 12.45) | 11.15 (9.98, 12.30) | 0.377                |

<sup>a</sup>Wilcoxon rank-sum test; one-way ANOVA; or Pearson's  $\chi^2$  test.

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; IQR, interquartile range.



**Figure 1** The correlation coefficients of SMI, SMD, and IMAT with age, BMI, hospital LOS, and hospital costs. BMI, body mass index; IMAT, intermuscular adipose tissue; LOS, length of stay; SMD, skeletal muscle radiodensity; SMI, skeletal muscle index.

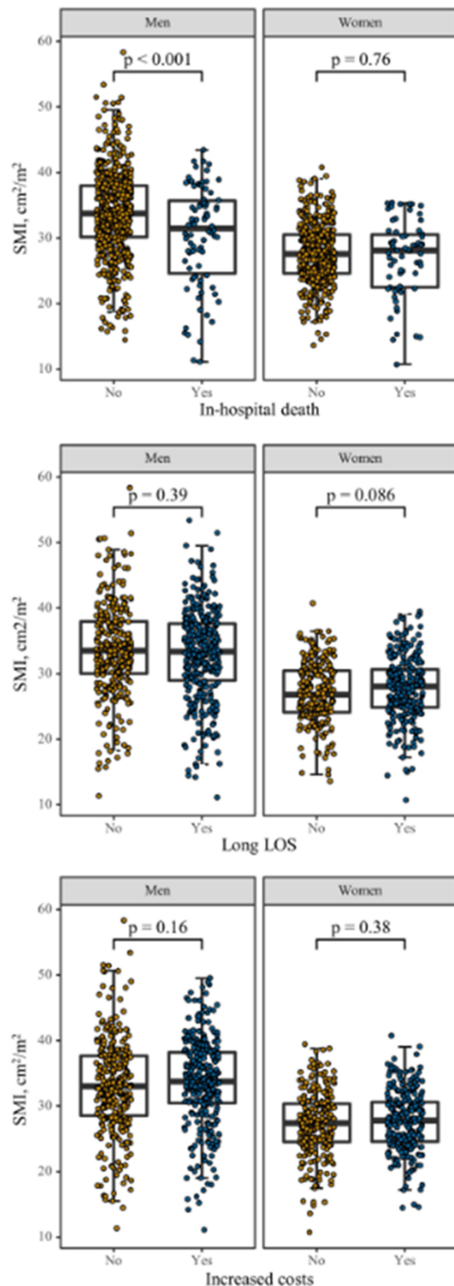
**Associations of muscle mass with in-hospital outcomes and hospital costs**

A total of 148 (13%) patients died in the hospital. As shown in Figure 2, compared with survivors, dead patients had significantly lower SMI in men ( $P < 0.001$ ) but not in women ( $P = 0.760$ ). The median hospital LOS was 17 days. Compared with their counterparts, patients with long hospital LOS had

similar SMI in both men and women (Figure 2). The median hospital cost of the whole population was 26 128 RMB. In both men and women, there was no significant difference in SMI between patients with and without increased hospital costs (Figure 2).

Table 2 shows the univariable logistic regression models to explore the associations of in-hospital death, hospital LOS, and hospital costs with different variables. Among men, the





**Figure 2** Boxplots with jitter points of SMI in different groups according to in-hospital death, long hospital LOS, or increased costs. BMI, body mass index; HU, Hounsfield unit; LOS, length of stay; SMI, skeletal muscle index.

SMI was negatively associated with in-hospital death (OR 0.93, 95% CI 0.90 to 0.96) but not associated with either long hospital LOS (OR 1.01, 95% CI 0.98 to 1.03) or increased costs (OR 1.01, 95% CI 0.99 to 1.04). Among women, the SMI was not associated with in-hospital death (OR 0.97, 95% CI 0.92 to 1.02), long hospital LOS (OR 1.03, 95% CI 0.99 to 1.07), or increased costs (OR 1.03, 95% CI 0.99 to 1.07). Additionally, malnutrition was associated with in-hospital death,

whereas serum albumin was associated with in-hospital death and long hospital LOS (Table 2).

Table 3 shows the multivariable logistic regression models to explore the associations of in-hospital death, hospital LOS, and hospital costs with muscle mass and muscle quality indicators. After full adjustment for sex and other potential confounders, the SMI was negatively and independently associated with in-hospital death (OR 0.96, 95% CI 0.93 to 0.99) but not associated with either long hospital LOS (OR 1.01, 95% CI 0.99 to 1.04) or increased costs (OR 1.01, 95% CI 0.99 to 1.04).

### Associations of muscle quality with in-hospital outcomes and hospital costs

As shown in Figure 3, compared with survivors, dead patients had significantly lower SMD and higher IMAT in both men (SMD:  $P < 0.001$ ; IMAT:  $P < 0.001$ ) and women (SMD:  $P < 0.001$ ; IMAT:  $P = 0.003$ ). Additionally, men with long hospital LOS had significantly more IMAT than men without long hospital LOS ( $P = 0.032$ ).

Univariable logistic regression models indicated that SMD was significantly and negatively associated with in-hospital death among men (OR 0.90, 95% CI 0.86 to 0.94) and women (OR 0.92, 95% CI 0.89 to 0.96). IMAT was also significantly and positively associated with in-hospital death among men (OR 1.12, 95% CI 1.06 to 1.18) and women (OR 1.11, 95% CI 0.92 to 1.17). However, neither SMD nor IMAT was significantly associated with long hospital LOS or increased costs (Table 2).

As shown in Table 3, after full adjustment, the SMD was independently and negatively associated with in-hospital death (OR 0.93, 95% CI 0.90 to 0.96), and IMAT was independently and positively associated with in-hospital death (OR 1.09, 95% CI 1.05 to 1.14). Neither SMD nor IMAT was independently associated with long hospital LOS or increased costs (Table 3).

## Discussion

This prospective study showed that among older patients in acute care wards, the T12 SMI and T12 SMD derived from chest CT images were negatively associated with in-hospital death; whereas the T12 IMAT was positively associated with in-hospital death. However, none of the SMI, SMD, or IMAT was independently associated with long hospital LOS or increased hospital costs. These findings imply that opportunistic chest CT images are valuable for assessing muscle mass and muscle quality and for predicting short-term prognosis in hospitalized older patients.

**Table 2** Univariable logistic models to explore the associations of short-term outcomes with muscle mass and quality

| Characteristic                             | In-hospital death |            |         | Long hospital LOS |            |         | Increased costs |            |         |
|--|-------------------|------------|---------|-------------------|------------|---------|-----------------|------------|---------|
|  | OR                | 95% CI     | P value | OR                | 95% CI     | P value | OR              | 95% CI     | P value |
| Age, per 1 year                            | 1.03              | 1.01, 1.06 | 0.002   | 1.03              | 1.01, 1.04 | <0.001  | 0.99            | 0.97, 1.00 | 0.096   |
| Women                                      | 1.03              | 0.73, 1.46 | 0.850   | 1.04              | 0.82, 1.32 | 0.730   | 0.94            | 0.74, 1.19 | 0.614   |
| Nutrition status                           |                   |            |         |                   |            |         |                 |            |         |
| Normal                                     | 1 (Ref)           | 1 (Ref)    |         | 1 (Ref)           | 1 (Ref)    |         | 1 (Ref)         | 1 (Ref)    |         |
| Malnutrition risk                          | 1.52              | 0.93, 2.50 | 0.093   | 1.40              | 1.03, 1.90 | 0.030   | 0.90            | 0.66, 1.21 | 0.476   |
| Malnutrition                               | 2.04              | 1.34, 3.19 | 0.001   | 1.03              | 0.79, 1.36 | 0.812   | 0.98            | 0.75, 1.29 | 0.910   |
| Hypertension                               | 0.86              | 0.61, 1.22 | 0.406   | 1.17              | 0.93, 1.48 | 0.185   | 0.85            | 0.67, 1.07 | 0.163   |
| Cardiovascular disease                     | 0.91              | 0.60, 1.35 | 0.642   | 1.71              | 1.31, 2.26 | <0.001  | 1.08            | 0.82, 1.41 | 0.596   |
| Diabetes                                   | 1.12              | 0.77, 1.61 | 0.555   | 1.40              | 1.09, 1.80 | 0.009   | 0.93            | 0.73, 1.20 | 0.594   |
| COPD                                       | 0.69              | 0.43, 1.08 | 0.123   | 1.03              | 0.78, 1.38 | 0.815   | 0.80            | 0.60, 1.06 | 0.123   |
| Acute infection, n (%)                     | 1.06              | 0.71, 1.56 | 0.758   | 1.44              | 1.10, 1.88 | 0.008   | 1.12            | 0.86, 1.47 | 0.389   |
| Creatinine, per 10 µmol/L                  | 0.99              | 0.94, 1.03 | 0.657   | 1.05              | 1.02, 1.10 | 0.009   | 1.02            | 1.00, 1.05 | 0.112   |
| Cystatin C, per 1 mg/L                     | 0.68              | 0.33, 1.37 | 0.297   | 0.98              | 0.62, 1.56 | 0.929   | 1.20            | 0.76, 1.92 | 0.435   |
| Serum albumin, per 10 g/L                  | 0.50              | 0.37, 0.66 | <0.001  | 0.67              | 0.55, 0.81 | <0.001  | 0.97            | 0.81, 1.17 | 0.766   |
| Haemoglobin, per 1 g/dL                    | 0.78              | 0.29, 2.10 | 0.622   | 0.61              | 0.31, 1.19 | 0.147   | 1.07            | 0.55, 2.10 | 0.833   |
| Men  |                   |            |         |                   |            |         |                 |            |         |
| BMI, per 1 kg/m <sup>2</sup>               | 0.98              | 0.91, 1.06 | 0.647   | 1.05              | 1.00, 1.10 | 0.067   | 1.04            | 0.99, 1.09 | 0.150   |
| SMI, per 1 cm <sup>2</sup> /m <sup>2</sup> | 0.93              | 0.90, 0.96 | <0.001  | 1.01              | 0.98, 1.03 | 0.651   | 1.01            | 0.99, 1.04 | 0.286   |
| IMAT, per 1 cm <sup>2</sup>                | 1.12              | 1.06, 1.18 | <0.001  | 1.01              | 0.97, 1.05 | 0.724   | 1.02            | 0.98, 1.06 | 0.341   |
| SMD, per 1 HU                              | 0.90              | 0.86, 0.94 | <0.001  | 0.99              | 0.97, 1.02 | 0.651   | 1.00            | 0.97, 1.03 | 0.957   |
| Women                                      |                   |            |         |                   |            |         |                 |            |         |
| BMI, per 1 kg/m <sup>2</sup>               | 1.00              | 0.92, 1.08 | 0.990   | 0.97              | 0.92, 1.03 | 0.345   | 0.99            | 0.93, 1.04 | 0.582   |
| SMI, per 1 cm <sup>2</sup> /m <sup>2</sup> | 0.97              | 0.92, 1.02 | 0.266   | 1.03              | 0.99, 1.07 | 0.134   | 1.03            | 0.99, 1.07 | 0.145   |
| IMAT, per 1 cm <sup>2</sup>                | 1.11              | 1.04, 1.17 | <0.001  | 0.99              | 0.97, 1.02 | 0.615   | 0.97            | 0.93, 1.02 | 0.242   |
| SMD, per 1 HU                              | 0.92              | 0.89, 0.96 | <0.001  | 1.02              | 1.00, 1.05 | 0.069   | 1.02            | 0.99, 1.04 | 0.186   |

Abbreviations: BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HU, Hounsfield unit; IMAT, intermuscular adipose tissue; LOS, length of stay; OR, odds ratio; SMD, skeletal muscle radiodensity; SMI, skeletal muscle index.

**Table 3** Multivariable logistic models to explore the associations of short-term outcomes with muscle quantity and quality

| Characteristic                             | In-hospital death |                     |         | Long hospital LOS |                     |         | Increased costs |                     |         |
|--|-------------------|---------------------|---------|-------------------|---------------------|---------|-----------------|---------------------|---------|
|  | OR <sup>a</sup>   | 95% CI <sup>a</sup> | P value | OR <sup>a</sup>   | 95% CI <sup>a</sup> | P value | OR <sup>a</sup> | 95% CI <sup>a</sup> | P value |
| Model 1                                    |                   |                     |         |                   |                     |         |                 |                     |         |
| SMI, per 1 cm <sup>2</sup> /m <sup>2</sup> | 0.95              | 0.92, 0.98          | <0.001  | 1.00              | 0.98, 1.02          | 0.706   | 1.01            | 0.99, 1.03          | 0.269   |
| IMAT, per 1 cm <sup>2</sup>                | 1.10              | 1.06, 1.15          | <0.001  | 1.00              | 0.97, 1.03          | 0.898   | 1.01            | 0.98, 1.04          | 0.711   |
| SMD, per 1 HU                              | 0.92              | 0.89, 0.95          | <0.001  | 1.01              | 0.99, 1.03          | 0.453   | 1.00            | 0.98, 1.02          | 0.934   |
| Model 2                                    |                   |                     |         |                   |                     |         |                 |                     |         |
| SMI, per 1 cm <sup>2</sup> /m <sup>2</sup> | 0.96              | 0.93, 0.99          | 0.016   | 1.01              | 0.99, 1.04          | 0.175   | 1.01            | 0.99, 1.04          | 0.177   |
| IMAT, per 1 cm <sup>2</sup>                | 1.09              | 1.05, 1.14          | <0.001  | 0.99              | 0.96, 1.02          | 0.420   | 1.00            | 0.97, 1.04          | 0.803   |
| SMD, per 1 HU                              | 0.93              | 0.90, 0.96          | <0.001  | 1.02              | 1.00, 1.04          | 0.066   | 1.00            | 0.97, 1.04          | 0.803   |

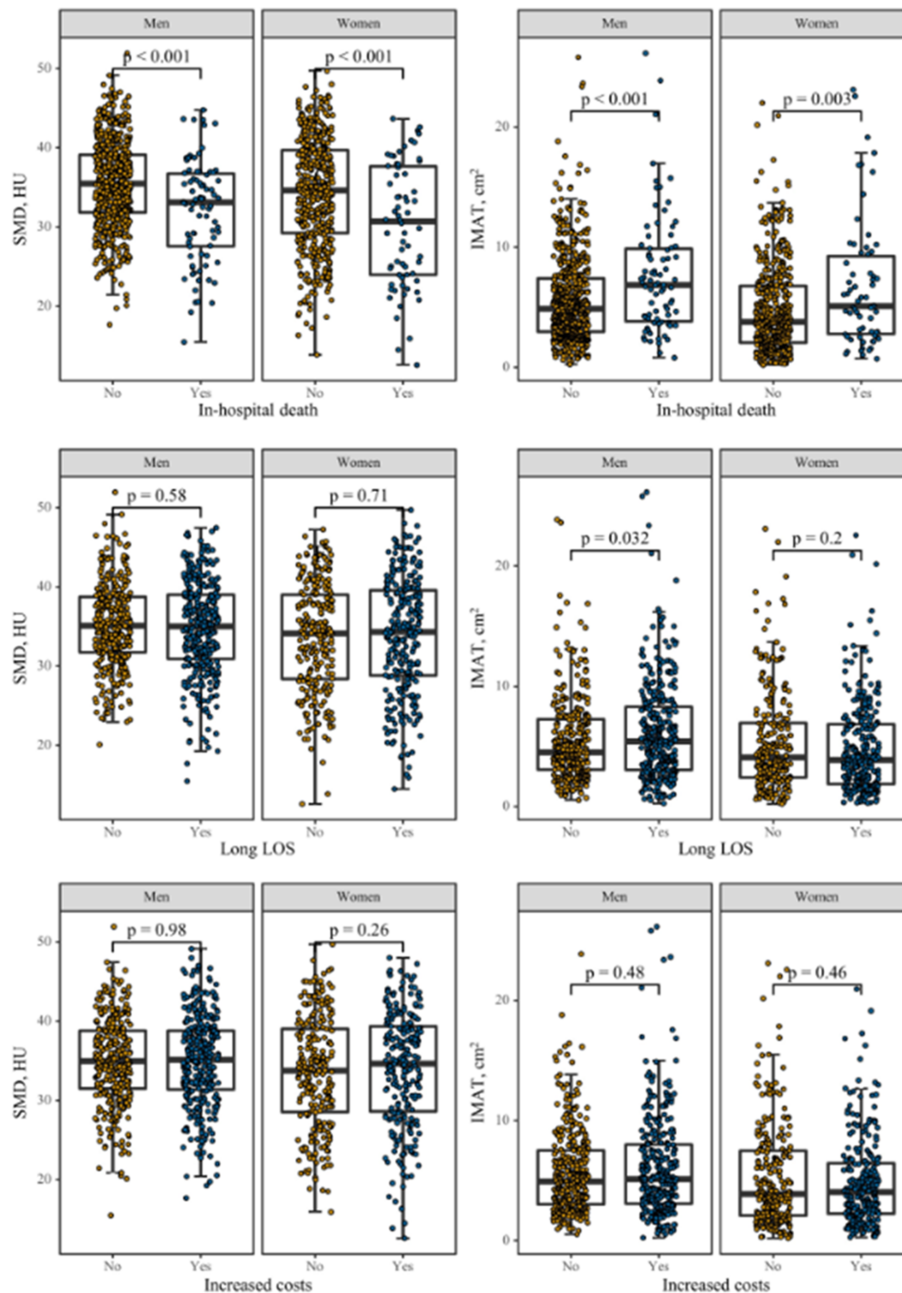
Abbreviations: BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HU, Hounsfield unit; IMAT, intermuscular adipose tissue; LOS, length of stay; OR, odds ratio; SMD, skeletal muscle radiodensity; SMI, skeletal muscle index.

<sup>a</sup>Model 1: adjusted for age (per 1 year) and sex (men or women); Model 2: adjusted for age (per 1 year), sex (men or women), nutrition status (normal, malnutrition risk of malnutrition), cardiovascular disease (yes or no), diabetes (yes or no), acute infection (yes or no), creatinine (per 10 µmol/L), and serum albumin (per 10 g/L).

### Computed tomography-derived muscle mass and mortality

The association between CT-derived low muscle mass and mortality has been widely reported in patients with cancer,<sup>27</sup> including lung cancer<sup>28</sup> and pancreatic cancer.<sup>29</sup> Although the association between low muscle mass and mortality in older adults has also been well-established in previous studies,<sup>30–32</sup> most of these studies measured muscle mass

with bioimpedance analysis or dual-energy X-ray absorptiometry instead of CT scan. Most recently, the National Lung Screening Trial (NLST) included 11 361 community-dwelling older adults, measured paraspinal muscle mass via chest CT images at the T12 vertebral level, and followed up 6.4 years.<sup>33</sup> The NLST reported that low muscle mass was associated with a higher risk of all-cause mortality in older men but not in older women.<sup>33</sup> In a retrospective cohort study published in *JAMA Surgery*, Kaplan *et al.* reported that



**Figure 3** Boxplots with jitter points of SMD, and IMAT in different groups according to in-hospital death, long hospital LOS, or increased costs. BMI, body mass index; HU, Hounsfield unit; IMAT, intermuscular adipose tissue; LOS, length of stay; SMD, skeletal muscle radiodensity.

CT-derived T12 SMI was negatively associated with 1 year mortality in 460 older trauma patients.<sup>34</sup> Our study observed similar results that CT-derived T12 SMI was negatively related to in-hospital death even after adjustment for sex and other confounders. The possible mechanism linking CT-derived SMI and mortality remains unclear. However, decreased T12 SMI indicates low muscle mass, which is a key component of sarcopenia,<sup>35</sup> malnutrition,<sup>36</sup> and cachexia.<sup>37</sup> All these conditions are associated with an increased risk of mortality.

### Computed tomography-derived muscle quality and mortality

The evidence regarding the association between CT-derived muscle quality and mortality was mainly conducted in oncology patients as well.<sup>8,38</sup> Nevertheless, the NLST study recently revealed that T12 SMD was negatively associated with long-term mortality in community-dwelling older men but not in older women.<sup>33</sup> Our study applied both SMD and IMAT as muscle quality indicators. We found that SMD was nega-

tively associated with in-hospital death, whereas IMAT was positively associated with in-hospital death. In addition, a recent study conducted in mechanically ventilated patients showed that lower SMD was associated with 6 month mortality, but higher IMAT was not significantly associated with 6 month mortality.<sup>7</sup> One explanation for these differences may be the heterogeneity of the study population. For example, the NLST study population was U.S. community adults aged 55–74 years, whereas our participants were Chinese older inpatients aged 60–101 years.

Both low SMD and high IMAT indicate myosteatosis (i.e. over-infiltration of fat in the muscles).<sup>19</sup> The mechanism linking myosteatosis to mortality is not fully understood, but it is known that myosteatosis induces metabolic and mechanical dysfunction of skeletal muscles.<sup>39</sup> These conditions have been linked to systemic inflammation and oxidative stress, which could impair protein synthesis, muscle protein turnover, and function of internal organs, and may ultimately increase the risk of death.<sup>18,40</sup>

### *Associations of muscle mass and muscle quality with hospital length of stay*

A previous study reported that patients with low SMI or low SMD were more likely to have prolonged hospital LOS after colon cancer surgery.<sup>51</sup> Another study found that higher SMD was associated with shorter hospital LOS, whereas IMAT was not associated with hospital LOS in mechanically ventilated patients.<sup>7</sup> Additionally, Lee *et al.* reported that a lower SMI was related to prolonged hospital LOS in community-dwelling older adults during an 8 year follow-up.<sup>52</sup> However, after retrieving PubMed and Web of Science, we were unable to locate a previous study that addressed muscle quality and hospital LOS in hospitalized older patients. We found that neither SMI, SMD, nor IMAT contributed to hospital LOS among older inpatients in acute care wards. More prospective studies are needed to address this issue.

### *Associations of muscle mass and muscle quality with costs*

We did not find evidence regarding muscle quality and hospital costs among older patients in the literature. However, a previous study revealed that low muscle mass was related to increased medical costs in community-dwelling older adults.<sup>52</sup> In addition, according to a recent review, six retrospective studies found low muscle mass was in relation to perioperative medical costs related in primarily older surgery patients.<sup>53</sup> Our study excluded surgery patients and found no significant association of increased hospital costs with SMI, SMD, or IMAT. It is difficult to compare our results with previous studies due to the significant differences in study pop-

ulations, study design, clinical settings, and measuring skeletal muscle methods.

### *Clinical and research implications*

In recent years, chest CT images have been increasingly used to opportunistically diagnose other diseases, such as osteoporosis.<sup>54</sup> Our study suggests that chest CT images can be opportunistically applied to evaluate muscle mass (SMI) and muscle quality (SMD and IMAT) and to predict the prognosis of hospitalized older patients. As aforementioned, CT-derived SMI can be used to determine low muscle mass (a key component of sarcopenia,<sup>35</sup> malnutrition,<sup>36</sup> and cachexia<sup>37</sup>), whereas low SMD and high IMAT indicate myosteatosis.<sup>19</sup> All these conditions are highly prevalent in older adults, especially in older inpatients and nursing home residents, and have been associated with a range of poor health outcomes, such as falls, functional disability, and mortality.<sup>19,35–37</sup> Assessment and management of these conditions are therefore critical for older adults. If our results are validated in future studies, the opportunistic use of chest CT images for assessing muscle mass and quality would facilitate relevant research on sarcopenia, malnutrition, cachexia, and myosteatosis. However, there is still a long way to go before it can be implemented in clinical practice. Priority should be given to establishing the SMI cutoff for low muscle mass and SMD and IMAT cutoffs for myosteatosis.

### *Limitations*

First, our study sample was recruited from a teaching hospital. In general, patients in teaching hospitals are more likely to have severe diseases than those in other clinical settings. Therefore, our results may not be generalized to non-teaching hospital patients, nursing home residents, or community-dwelling populations. It will be necessary to validate our findings among various ethnic groups and in different clinical settings. Second, we did not assess and adjust for some important confounders, such as physical activities, polypharmacy, and inflammatory factors. Third, we used the chest CT images at the T12 vertebral level instead of the most widely used abdominal CT images at the 3rd lumbar (L3) vertebral level to assess muscle mass and muscle quality.<sup>18</sup> Several recent studies have validated the high correlation between T12 SMA and L3 SMA.<sup>55–57</sup> However, the correlation and consistency between T12 and L3 muscle quality indicators need to be further investigated in the future. Fourth, because we tried to provide more details about comorbidities, we did not use a standard comorbidity scale, such as the Charlson comorbidity index. On the other hand, we did not report the admission diagnoses because older inpatients usually have multiple diagnoses (generally over 10 diagnoses per

patient). In our study population, over 50 diagnoses have been determined by using the International Classification of Diseases, 10th Revision, codes even for primary admission diagnoses. Therefore, we summarized and reported the top five comorbidities in our participants. Consequently, we may not be able to fully adjust for the impact of comorbidities on our results. However, because of this, our results could be more generalizable because our sample comprised a diverse group of participants with different diagnoses.

## Conclusions

Chest CT-derived muscle mass indicator (T12 SMI) and muscle quality indicators (T12 SMD and T12 IMAT) may serve as prognostic factors for predicting in-hospital death among older inpatients. However, none of these indicators was associated with hospital LOS and hospital costs in our study population.

Considering chest CT is widely used in clinical practice and even for screening lung cancer and other diseases among middle-aged and older adults in health check-ups, the opportunistic use of chest CT images would be an overlooked resource for measuring muscle mass and muscle quality at the same time without increasing radiation risk or costs. In the future, researchers may opportunistically use chest CT images in sarcopenia and/or myosteatosis research among older adults, similar to how abdominal CT has been used in relevant research among oncology and surgery patients.

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The authors certify that they comply with the ethical guidelines for publishing in the *Journal of Cachexia, Sarcopenia, and Muscle*.<sup>58</sup>

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## Conflict of interest

Yanjiao Shen, Li Luo, Hongbo Fu, Lingling Xie, Wenyi Zhang, Jing Lu, and Ming Yang declare that they have no conflict of interest.

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## Ethical Guidelines

The study protocol was approved by the Biomedical Ethics Committee of West China Hospital, Sichuan University, and the study has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Written informed consent was obtained from all participants prior to their inclusion in the study.

## Online supplementary material

Additional supporting information may be found online in the Supporting Information section at the end of the article.



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