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**None declared.**

# Prevalence and mortality risk of low skeletal muscle mass in critically ill patients: an updated systematic review and meta-analysis

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**Review question / Objective:** **The PICOS principle was adopted when we confirmed the study eligibility. The inclusion criteria were as follows: (1) patients were critically ill, which was defined as adult patients who were from the ICU department; (2) exposure: patients had a clear definition of LSMM based on CT scans, anthropometric methods and ultrasound; (3) presented the prevalence of LSMM or could be calculated by the available data from the article; and (4) study design: observational study (cohort study or cross-sectional study). Articles that were reviews, case reports, comments, correspondences, letters or only abstracts were excluded.**
**Condition being studied:** **Critical illness often results in low skeletal muscle mass for multiple reasons. Multiple studies have explored the association between low skeletal muscle mass and mortality. The prevalence of low skeletal muscle mass and its association with mortality are unclear. This systematic review and meta-analysis aim to identify the prevalence and mortality risk of low skeletal muscle mass among critically ill patients.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 November 2022 and was last updated on 25 November 2022 (registration number INPLASY2022110132).

## INTRODUCTION

**Review question / Objective:** **The PICOS principle was adopted when we confirmed the study eligibility. The inclusion criteria were as follows: (1) patients were critically ill, which was defined as adult patients who were from the ICU department; (2) exposure: patients had a clear definition of LSMM based on CT scans, anthropometric methods and ultrasound; (3) presented the prevalence of LSMM or could be calculated**

by the available data from the article; and (4) study design: observational study (cohort study or cross-sectional study). Articles that were reviews, case reports, comments, correspondences, letters or only abstracts were excluded.

**Rationale:** Two authors independently formulated the search strategy and screened the articles. First, the results of the relevant studies from three databases were imported into EndnotX9 software, and duplicates were deleprinciple, with the full text after checking the abstract for potential relevance. The final studies were confirmed after careful review by full text. During the process, disagreements were resolved following discussion by the third reviewer. Two authors also independently extracted the data based on the standardized forms, consisting of author, years, country, reason for intensive care, age, sample size, prevalence of sarcopenia, number of females/males, prevalence of sarcopenia by gender, definition of sarcopenia, and the effect size between LSMM and mortality.

Assessment of study quality

We used the Newcastle-Ottawa Scale to assess the quality and methodology of the included studies. The total score of the included studies ranged from 0 to 9 points, and the quality of the study was defined as three classifications consisting of poor, moderate and high, with corresponding scores of 0-4, 5-6 and 7-9 points

Outcome measures

The main outcomes of this systematic review were the prevalence of LSMM and all-cause mortality.

Statistical analysis

All statistical analyses were performed with STATA (Version 14. StataCrop, TX, USA). Metaprop, a Stata command, was used to pool the prevalence of sarcopenia from each included study, and the metan command was used to combine the results of all the studies about the association between LSMM and mortality risk. Based on the high heterogeneity across studies, a random-effects model was used because of the different countries, definitions and various sample sizes and various reasons for ICU admission. In addition, we used different subgroup analyses based on county, sex, sample size, various reasons for ICU admission and mechanical ventilation. Sensitivity analysis and the test of publication bias ted. Then, the authors screened the title and abstract based on the PICOS were also used.

**Condition being studied:** Critical illness often results in low skeletal muscle mass for multiple reasons. Multiple studies have explored the association between low skeletal muscle mass and mortality. The prevalence of low skeletal muscle mass and its association with mortality are unclear. This systematic review and meta-analysis aim to identify the prevalence and mortality risk of low skeletal muscle mass among critically ill patients.

## METHODS

**Search strategy:** Study selection and data extraction. Two authors independently formulated the search strategy and screened the articles. First, the results of the relevant studies from three databases were imported into EndnotX9 software, and duplicates were deleted. Then, the authors screened the title and abstract based on the PICOS principle, with the full text after checking the abstract for potential relevance. The final studies were confirmed after careful review by full text. During the process, disagreements were resolved following discussion by the third reviewer. Two authors also independently extracted the data based on the standardized forms, consisting of author, years, country, reason for intensive care, age, sample size, prevalence of sarcopenia, number of females/males, prevalence of sarcopenia by gender, definition of sarcopenia, and the effect size between LSMM and mortality.

**Participant or population:** In recent decades, LSMM has become a focus of research in critical care. Critically ill patients can easily be subjected to LSMM attributed to malnutrition, inactivity, and inflammatory reactions13. A large number of studies have explored the association between LSMM and adverse outcomes among critically ill patients14-16. Studies

found that LSMM based on CT scans was associated with a high risk of all-cause death among critically ill patients14,17, and total psoas muscle area can improve the performance for predicting mortality18. In addition, a great number of studies have reported that the prevalence of LSMM among critically ill people is higher than that among older people19,20. Recently, a systematic review reported a prevalence of LSMM of 50.9. However, this review only consisted of 9 studies of 1563, and they only included studies that used CT scans to assess muscle mass. Some studies have detected LSMM by new technologies, such as ultrasound22,23. Most importantly, the systematic review did not perform subgroup analysis, which was very important. Moreover, many new articles have explored the impact on mortality14,15,17,22,24-32. Therefore, it was very important to update this systematic review to summarize the prevalence and mortality risk of LSMM in critically ill patients. The aim of our study was to systematically summarize the prevalence of sarcopenia among critically ill patients and identify whether critical illness with LSMM could increase the risk of mortality.

**Intervention:** None.

**Comparator:** Exposure: patients had a clear definition of LSMM based on CT scans, anthropometric methods and ultrasound;.

**Study designs to be included:** Observational study (cohort study or cross-sectional study). Articles that were reviews, case reports, comments, correspondences, letters or only abstracts were excluded.

**Eligibility criteria:** Two authors independently formulated the search strategy and screened the articles. First, the results of the relevant studies from three databases were imported into EndnotX9 software, and duplicates were deleted. Then, the authors screened the title and abstract based on the PICOS principle, with the full text after checking the abstract for potential relevance. The final studies were confirmed after careful review by full text. During the process, disagreements were resolved following discussion by the third reviewer. Two authors also independently extracted the data based on the standardized forms, consisting of author, years, country, reason for intensive care, age, sample size, prevalence of sarcopenia, number of females/males, prevalence of sarcopenia by gender, definition of sarcopenia, and the effect size between LSMM and mortality.

**Information sources:** This systematic review followed the PRISMA principles and was preregistered in the PROSPERO database. Two authors searched the relevant articles via three internet databases: PubMed, Embase, and Web of Science. The time of study was defined as from the inception of these three databases to September 1, 2022. We used keywords and MeSH to search the studies consisting of muscle mass or sarcopenia and (mortality or death or survival).

**Main outcome(s):** The initial record identified in our search was 1582, and 38 studies consisted of 6891 patients for the final quantitative analysis. The pooled prevalence of low skeletal muscle mass (LSMM) was 51.0% (44.5%, 57.5%). Subgroup analysis found that the prevalence of LSMM was slightly higher in mechanical ventilated patients than those without mechanical ventilation (53.4%, 95% CI: 43.2, 63.6; versus 48.9%, 95% CI: 39.7%, 58.1%).

**Additional outcome(s):** The pooled results found that critically ill patients with LSMM had a higher risk of mortality than those patients without LSMM, with a pooled OR of 2.29 (95% CI: 1.87, 2.81). The subgroup analysis based on the assessment tool of muscle mass found that critically ill patients with LSMM had similar results when using both CT-scan and anthropometric methods. However, this association between LSMM and risk of mortality based on muscle ultrasound did not reach statistical significance, partially due to the limited number of studies.

**Data management:** Three internet databases were searched by two independent investigators to check the relevant studies. A random-effect model was used to pool the prevalence of low skeletal muscle mass and its association with mortality.

**Quality assessment / Risk of bias analysis:** We used the Newcastle-Ottawa Scale to assess the quality and methodology of the included studies. The total score of the included studies ranged from 0 to 9 points, and the quality of the study was defined as three classifications consisting of poor, moderate and high, with corresponding scores of 0-4, 5-6 and 7-9 points.

**Strategy of data synthesis:** All statistical analyses were performed with STATA (Version 14. StataCrop, TX, USA). Metaprop, a Stata command, was used to pool the prevalence of sarcopenia from each included study, and the metan command was used to combine the results of all the studies about the association between LSMM and mortality risk. Based on the high heterogeneity across studies, a random-effects model was used because of the different countries, definitions and various sample sizes and various reasons for ICU admission. In addition, we used different subgroup analyses based on county, sex, sample size, various reasons for ICU admission and mechanical ventilation. Sensitivity analysis and the test of publication bias were also used.

**Subgroup analysis:** Subgroup analysis for the pooled prevalence by different variables

Based on region

The results of the subgroup analysis for pooling the prevalence of LSMM based on region found that the prevalence of LSMM was 51.1% (40.6,61.6%) for Asians, followed by 46.9% (33.9%,60.0%) for Europe, 51.7% (43.2%,60.2%) for Americans and 65.8% (60.6%,70.9%) for Oceania (Table 2).

Subgroup analysis by sex

There were 25 studies providing the prevalence of LSMM by sex. The results found that there was no statistically significant difference between gender regarding the prevalence of LSMM. Notably, the prevalence of LSMM was 48.8% (40.0%, 57.6%) for males and 45.5% (37.9%, 53.2%) for females (Table 2).

Subgroup analysis by mechanical ventilation

There were 17 studies of critical illness with mechanical ventilation during the period of hospitalization. The results of this subgroup analysis found that the prevalence of LSMM was slightly higher in mechanical ventilated patients than that in patients without mechanical ventilation, with a prevalence of 53.4% (43.2, 63.6) for critically ill patients with mechanical ventilation(MV) and 48.9% (39.7%, 58.1%) for critically ill patients without MV. However, there was no significant difference between these two groups (Table 2).

Subgroup analysis by diagnosis

We categorized these studies into four classifications based on the main diagnosis. There were 14 studies focusing on sepsis, and the prevalence of LSMM among these participants was 55.1% (44.6%, 65.6%). In addition, 7 studies consisted of critically ill patients with trauma, and the prevalence of LSMM was 47.6% (33.8%,61.3%). Only three studies of critical illness were mainly for surgery, and the prevalence in these groups was 43.0% (24.4-61.6%). The remaining 13 studies had mixed diagnoses, and the pooled prevalence of LSMM was 50.2% (38.4%-62.0%) (Table 2).

Other subgroup analysis for the prevalence of LSMM

We split the sample size into two groups (=100), and the results showed that the prevalence of LSMM was close, with the figure of 49.3% (41.4, 57.2%) among the sample sizes less than 100 and 51.8% (43.5, 60.2%) in sample size more than or equal to 100. Additionally, the subgroup analysis between age groups split by mean age found a prevalence of LSMM (Table 2).

**Sensitivity analysis:** The sensitivity analysis was performed by omitting one study and pooling the remaining studies, which was used to test whether the pooled results had major changes. The results of the

sensitivity analysis regarding prevalence or mortality did not show a significant change (SFigure 2a and SFigure2b).

**Language restriction:** No limits.

**Country(ies) involved:** China.

**Keywords:** Prevalence, mortality, low skeletal muscle mass（LSMM）, critically ill patients, systematic review and meta-analysis.

**Contributions of each author:**

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