Critical Care

REVIEW

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Exploring the association between computed tomography (CT)-derived skeletal muscle mass and short- and long-term mortality in critically ill patients: a systematic review and meta-analysis

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Abstract

Background Low skeletal mass, often present at hospital admission, has been associated with poor prognoses.

Aim To explore the association between computed tomography (CT)-derived skeletal muscle mass at the lumbar level and short- and long-term mortality in critically ill patients.

Methods Following PRISMA 2020 guidelines, we included studies on critically ill adults (≥ 18 years) hospitalized in intensive care units (ICU) that measured CT-derived skeletal muscle mass at the lumbar vertebral level within ± 7 days of ICU admission. The primary outcome was mortality, categorized as short-term (including ICU, hospital, 28- and 30-day mortality) and long-term (> 30 days) mortality. MEDLINE and Embase databases were searched without date restrictions. Study screening was performed using Rayyan, data extraction was guided by a custom-designed tool, and quality assessment was performed using the JBI Cohort Study Checklist. A meta-analysis was conducted, focusing on studies that reported short- and long-term mortality among patients with preserved and reduced skeletal muscle. A prevalence meta-analysis was also performed for studies that reported the size of subgroups with low muscle mass.

Results Out of 1248 unique records, 35 studies met the inclusion criteria, involving 9366 participants. The majority were retrospective, single-centre studies conducted on four continents and included heterogeneous populations such as patients with sepsis, COVID-19 and trauma. Sample sizes ranged from 36 to 939, with a wide age range, from 40 to 70 s, and a predominance of male patients (62%). Skeletal mass was most commonly reported as skeletal muscle index at the third lumbar vertebra. Studies reported mainly short-term mortality on day 28 or 30. Long-term mortality, measured at 90 days, 6 months, and 1 year, was evaluated in 11 studies. Meta-analyses revealed that low skeletal muscle mass area and index were significantly associated with increased risks of both short (OR = 2.33, CI 1.90–2.87, I^2 = 41.39%)—and long-term mortality (OR = 2.67, CI 1.45–4.92, I^2 = 62.24%). The overall prevalence of low muscle mass was 42% (CI 34–49%, I^2 = 98.2%).

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Conclusions CT-assessed skeletal muscle mass at the lumbar level on admission to ICU is associated with both short- and long-term mortality. It may serve as a prognostic marker in critically ill patients. Standardized protocols for measuring and defining low skeletal muscle mass in this population are essential to improve comparability across studies.

Keywords Muscle mass, Skeletal muscle mass, Intensive care, Critical illness, Computed tomography, Mortality

Introduction

Around 40% of patients admitted to hospital have a low skeletal muscle mass [1], a condition associated with an increased risk of disability, accidental falls, longer hospital stays and higher mortality [2]. In addition, skeletal mass decreases rapidly during hospitalization, particularly in critically ill patients, where loss can be as much as 2% per day during the first week of ICU admission [3]. Thus, muscle mass is a determinant of clinical outcomes in hospitalized patients.

Body composition can be assessed by mid-arm circumference, bioelectrical impedance analysis (BIA), ultrasound (US), dual-energy X-ray absorptiometry (DXA), and computed tomography (CT) [4]. However, in critically ill patients, mid-arm muscle circumference and BIA are often unreliable due to fluid overload [5], and US lacks standardized measurement protocols [6]. DXA, while precise, is limited by high costs, radiation exposure, and the need for specialized equipment and trained personnel [4]. CT, often used for diagnostic purposes in critically ill patients [6], provides a detailed analysis of skeletal muscle mass and muscle quality using imaging attenuation to determine muscle fat infiltration (IMAT or myosteatosis) [6–10]. Skeletal muscle mass is typically measured at the third lumbar (L3) vertebra level, as this correlates well with total skeletal muscle mass in healthy individuals [11], though measurements at the level of other vertebral levels or thighs are also used. The L3 measurement includes the psoas, abdominal wall muscles (rectus abdominis, internal and external obliques, transversus abdominis) and paraspinal muscles (quadratus lumborum, erector spinae). Skeletal muscle mass has been expressed mostly as cross-sectional skeletal muscle area (SMA, cm^2) [11], SMA adjusted for height squared resulting in skeletal muscle index (SMI, cm^2/m^2) [12], but other parameters as psoas cross-sectional area (PMA) or psoas muscle index (PMI) have also been used.

Existing systematic reviews have examined the relationship between skeletal muscle mass and outcomes in critically ill patients, but they differ in their approach. Variations include the methods used to measure skeletal muscle mass [3, 13], timing of assessments [13, 14] and reported outcomes [13].

This systematic review aims to specifically evaluate CT-derived skeletal muscle mass at the lumbar level, measured within ± 7 days of ICU admission, and its association with short- and long-term mortality in critically ill patients.

Materials and methods

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [15]. The inclusion criteria for articles were as follows: critically ill adults (≥ 18 years) hospitalized in ICU and receiving either invasive or non-invasive mechanical ventilation; at least one CT-derived measurement of skeletal mass at ICU admission ± 7 days, at the lumbar vertebral level; the outcome was short- and long-term mortality. Exclusion criteria were: non-English language publications; low skeletal muscle mass detected by modalities other than CT; studies in children and adolescents; and reviews, meta-analyses, case reports and abstracts.

Search strategy

The electronic MEDLINE database (Pubmed) and Embase were searched electronically without restriction to publication dates. The full search strategy was developed jointly by the first and last authors, in collaboration with a professional documentalist, and is listed in Supporting information Table 1. The last search by the authors was carried out on 28 October 2024.

Selection process

Using the search strategy, all citations identified were imported into Zotero [16], a reference management software, and duplicates were systematically identified and removed. The refined set of references was imported into Rayyan [17], a web-based systematic review tool, where any remaining duplicates were identified and removed. The screening of titles and abstracts was carried out independently by two of the authors (VABM and LG) in Rayyan, using the pre-defined inclusion and exclusion criteria. When necessary, discrepancies in judgment between reviewers were resolved through discussion and consensus.

A full-text review was performed by VABM and LG on articles that were considered potentially relevant after title and abstract screening. For this stage, an Excel file was used to document the decision to include or exclude each item, and the reason for exclusion, if applicable. Any discrepancies were resolved by discussion.

Data collection process

Data extraction was performed by VABM and included details on study populations and methods, CT-derived skeletal muscle mass measurements, sample size of patients with low muscle mass, and cut-off values used to classify low vs. preserved muscle mass patients. Additionally, data on short-term mortality (ICU, hospital, 28-day, 30-day) and long-term mortality (> 30 days), and overall mortality, along with their corresponding statistical measures (n, %, *p*-values, OR, and 95% CI), were collected. LG and FRH reviewed and validated the extracted data to ensure accuracy and consistency, making any necessary corrections or adjustments to discrepancies.

Study risk of bias assessment

Eligible studies were critically evaluated by 2 independent reviewers (VABM and LG) for methodological quality using critical appraisal checklist for cohort studies from JBI [18]. Any disagreements that arose were discussed and resolved. The outcome considered in the assessment was mortality. Question 6 "Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?" was not considered as all patients were alive at the time of CT scan. A study was considered to have a low risk of bias if it received 6 or more "low" responses, an unclear risk if it received 4–5 "low" responses and a high risk if it received only 0–3 "low" responses. This classification method was arbitrarily chosen by the review group.

Data synthesis and analysis

A narrative synthesis was performed for all included studies, categorizing data into ICU, hospital, 28- and 30-day, 90-day, 6-month and 1-year mortality according to the original authors' definitions and based on area and index muscle mass.

For the meta-analysis, data were extracted in studies where odd ratios (OR) were available and categorized into short-term (ICU, hospital, 28- and 30-days) and long-term (90-days, 6-months, 1-year) mortality. Patients with low muscle mass were compared to those with preserved muscle mass, using study-specific cut-off values.

To address heterogeneity, separate analyses were performed for studies using SMA and SMI. Units were standardized where possible, converting measurements to cm^2 for SMA and cm^2/m^2 for SMI. In Ji et al. 2018, patients with normal SMI and visceral adiposity were grouped as having preserved muscle mass, while those with low SMI, with or without visceral obesity, were classified as low muscle mass [19]. Similarly, in Kaplan et al. 2016, patients with low SMI and osteopenia were grouped under low muscle mass, and those with osteopenia only were categorized as having preserved muscle mass to ensure consistent comparison [20].

A random-effects model was used for the meta-analysis to estimate pooled effect sizes, accounting for both within-study and between-study variability. Heterogeneity was assessed using the I^2 statistic. The number of deaths (n) in both low and preserved muscle mass groups was used to calculate log-transformed OR. Forest plots were generated to display OR and 95% confidence intervals (CI), indicating whether the results favored low or preserved muscle mass. Regarding studies that did not report the number of deaths (n), we used the published OR and included these 4 additional studies for short-term mortality and 1 additional study for long-term mortality in distinct meta-analysis performed on OR instead of exact mortality counts. We performed a funnel plot to assess potential publication bias for the analysis of short- and long-term mortality.

For studies that indicated the size of subgroups with low muscle mass, we performed a prevalence meta-analysis.

All analyses and visualizations were performed using Stata version 18.0 software (Statcorp, 2023, College Station, USA), with forest plots created via the meta forestplot command.

Results

Study selection

After removing duplicates and excluding studies that did not met the inclusion criteria, 35 studies remained for the systematic review (Fig. 1). Reasons for the exclusion of studies after full-text screening are presented in Supporting Information Table 2.

Characteristics of the studies and participants

A summary of the characteristics of the 35 included studies is detailed in Table 1. All studies were single-center, and most (31 out of 35) were retrospective, with patient inclusion years ranging from 2003 to 2022. Most studies were conducted in the United States (n = 8 studies) [20–27], followed by Turkey [28–31], Korea [32–35], and other countries, as shown in Supporting information Fig. 2, which illustrates the distribution by country and continent. The year of publication ranged from 2003 to 2024, with most studies published in 2021 (n = 7) [21, 31, 36–40]. The study populations varied, with sepsis/septic shock (n = 10 studies) [19, 21, 22, 32–35, 37, 41, 42],

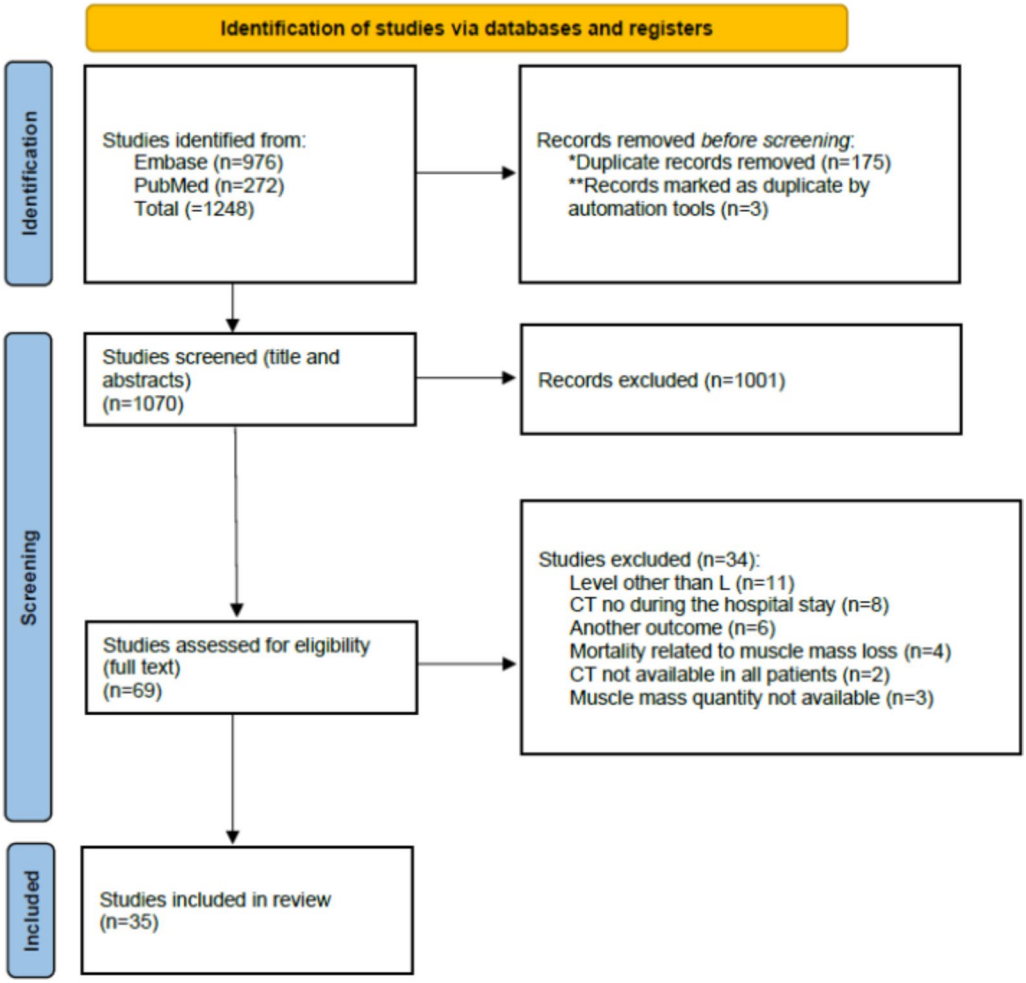

Fig. 1 PRISMA flow diagram study selection and inclusion process

COVID-19 [28, 31, 39, 43, 44] and trauma [20, 26, 38, 40, 45] (n = 5 each), surgical patients (n = 3) [23, 24, 27], general intensive care populations (n = 4) [29, 46–48], and mechanical ventilation (n = 2) [49, 50] being the most common. Sample sizes ranged from 36 to 939 patients, with a total of 9366 participants across all studies. The age range was wide, with medians and means reported in the 40 s and 70 s. The average proportion of female participants was 37.9%, revealing a predominance of male participants within the study populations.

Skeletal muscle mass was primarily assessed using SMI (n = 27) [4, 19–26, 28, 29, 31, 32, 34–36, 38, 41, 43–45, 47–49, 51–53] compared to SMA, which was reported 5 times [42, 43, 46, 49, 50]. The cut-off values used to classify low SMI ranged from 34.8 to 55.4 cm^2/m^2 for men and from 27.7 to 41.0 cm^2/m^2 for women. Other systems of measurement, such as the PMI (n = 6) [26, 30, 31, 33, 37, 40] or PMA (n = 2) [27, 39], were also utilized, though cut-off values varied or were not consistently defined. Cut-offs for low skeletal muscle mass are presented in Supporting information Table 3. The L3 vertebra level was the most frequently used anatomical reference point, with 29 out of 35 studies using this level. Among these, 17 studies measured total muscle mass including the psoas, paraspinal muscles and abdominal wall muscles. Several studies employed other levels, including L1, L2, L3–L4, L4, and L4–L5, focusing either on the psoas, abdominal wall, and paraspinal muscles or specifically on the psoas muscle [26, 27, 30, 33, 37, 39, 40]. Slice thickness was reported in only a few studies and ranged from 1 to 5 mm. The most used software for CT analysis were sliceOmatic (n = 10) [20, 21, 25, 36, 39, 41, 43, 44, 49–51], ImageJ [19, 22, 32, 45] and Osirix [23, 29, 37, 46] (n = 4 each) and three reported manual outlining [24, 30, 40].

Table 1 Characteristics of included studies (n = 35 studies; n = 9366 patients)

Study Reference	Study Design	Sample, ICU population, country	Age	Female n (%)	CT methodology	CT timing	Outcome
L1 (n = 1)							
Emekli et al. 2023 [28]	Retrospective Single-center 11.03.2020–31.08.2022	498, COVID-19, Turkey	65.98 ± 14.84	224 (45.0%)	Device: Alexion Toshiba Level: between L1 and the vein entry, without contrast material Muscles: NA Slice thickness: NA Software: MATLAB	5 days before to 24 h after ICU admission	Hospital mortality
L1-L2 or L3 (n = 1)							
Damanti et al. 2022 [43]	Retrospective Single-center 02.2020–05.2020	81, COVID-19, Italy	59.3 ± 11.91	10 (12.3%)	Device: NA Level: L1, 2 or 3 Muscles: NA Slice thickness: NA Software: sliceOmatic	Routine CT during hospitalization	ICU & hospital mortality
L3 (n = 29)							
Akan et al. 2024 [29]	Retrospective Single-center 05.2017–04.2018	93, ICU, Turkey	NA	37 (39.8%)	Device: Aquilion, Toshiba Level: L3 Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: 2 mm Software: Osirix	At admission	30-day mortality
Akkoc et al. 2020 [30]	Retrospective Single-center Date NA	89, Pulmonary embolism, Turkey	In-hospital mortality 70.7 ± 12.7 No in-hospital mortality 66.5 ± 16.2	38 (42.7%)	Device: NA Level: L3 Muscles: right and left psoas Slice thickness: NA Manual outlining	Admission CT available	In-hospital mortality
Baggerman et al. 2020 [41]	Retrospective Single-center 07.2013–08.2017	155, Abdominal sepsis, Netherlands	66.0 ± 13.6	62 (40.0%)	Device: NA Level: L3, with contrast material Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: NA Software: sliceOmatic	6 days before to 2 days after ICU admission	Hospital mortality
Bear et al. 2021 [36]	Retrospective Single-center 09.2010–06.2017	215, VV-ECMO, United Kingdom	Mdn 46 IQR 35.0–57.0	92 (42.8%)	Device: NA Level: L3 Muscles: NA Slice thickness: NA Software: sliceOmatic	Within 24 h of VV-ECMO	ICU & 6-month survival

Table 1 (continued)

Study Reference	Study Design	Sample, ICU population, country	Age	Female n (%)	CT methodology	CT timing	Outcome
Beypinar et al. 2021 [31]	Retrospective Single-center 11.05.2020–15.06.2020	36, COVID-19, Turkey	Mdn 68 IQR NA	8 (22.2%)	Device: NA Level: L3 Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: NA Software: NA	Emergency room or patient's clinic	Survival
Cox et al. 2021 [21]	Prospective Single-center 04.2016–06.2018	47, Intra-abdominal sepsis, United States	53 ± 14	33 (70.2%)	Device: NA Level: L3 Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: NA Software: sliceOmatic	1st: within 48 h of sepsis diagnosis (only these results were used in our analyses), 2nd: at 3-month follow-up, 3rd: at 12-month follow-up	Inpatient mortality One year survival
Darden et al. 2023 [22]	Retrospective Single-center 09.2014–12.2020	150, Sepsis, United States	↓ SMM Mdn 75 IQR 63.83 Normal SMM Mdn 63 IQR 52.69	63 (42.0%)	Device: NA Level: L3, without intravenous contrast Muscles: psoas, paraspinal, extracostal abdominal wall, intercostal, and diaphragm Slice thickness: 3 mm Software: ImageJ	Within 7 days of hospitalization	In-hospital & one year mortality
Fuchs et al. 2018 [23]	Prospective Single-center 01.12.2012–31.01.2014	231, Surgical, United States	56.25 ± 18.92	79 (34.2%)	Device: NA Level: L3 Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: NA Software: Osirix	Within 5 days of extubation in ICU	30-day mortality
Hwang et al. 2019 [24]	Retrospective Single-center 2012–2014	230, Surgical, United States	NA	101 (43.7%)	Device: NA Level: L3 Muscle: NA Slice thickness: NA Manual outlining	Day of admission	In-hospital mortality

Table 1 (continued)

Study Reference	Study Design	Sample, ICU population, country	Age	Female n (%)	CT methodology	CT timing	Outcome
Ji et al. 2018 [19]	Retrospective Single-center 01.08.2012–31.07.2016	236, Intra-abdominal sepsis underwent urgent surgical intervention, China	Normal SMM & no visceral obesity Mdn 58 IQR 44–69 Visceral obesity Mdn 66 IQR 53–74 ↓ SMM Mdn 76 IQR 65–81 ↓ SMM & obesity Mdn 75 IQR 69–83	97 (41.1%)	Device: NA Level: L3 Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: NA Software: ImageJ	Before surgical intervention	30-day mortality
Joyce et al. 2020 [46]	Retrospective Single-center 03.02.2018–03.02.2019	279, UCI, Australia	63.7 ± 16.4	116 (41.6%)	Device: NA Level: L3 Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: NA Software: Osirix	7 days prior to 1 day after ICU admission	ICU & 30-day mortality
Kaplan et al. 2016 [20]	Retrospective Single-center 01.2011–05.2014	450, Older trauma, United States	↓ SMM & Osteopenia Mdn 83 IQR 75–89 ↓ SMM Mdn 75 IQR 69–83 Osteopenia Mdn 78.5 IQR 72–83 Normal SMM & no osteopenia Mdn 72 IQR 68–78	181 (40.2%)	Device: NA Level: L3 Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: NA Software: sliceOmatic	Within 48 h of admission	In-hospital death, 30-day & One-year all-cause mortality
Kim et al. 2024 [32]	Retrospective Single-center 2013–2022	618, Sepsis-induced acute kidney injury undergoing continuous renal replacement therapy, Korea	Survivor Mdn 69 IQR 58–77 Non-survivor Mdn 72 IQR 62–80	250 (40.5%)	Device: NA Level: L3 Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: NA Software: ImageJ	Within 3 days preceding ICU admission	28-day mortality
Lee et al. 2018 [33]	Retrospective Single-center 03.2007–02.2016	274, Sepsis, Korea	70.9 ± 14.9	148 (54.0%)	Device: NA Level: L3 Muscles: psoas Slice thickness: NA Software: NA	At emergency department admission	28-day & 6-month mortality

Table 1 (continued)

Study Reference	Study Design	Sample, ICU population, country	Age	Female n (%)	CT methodology	CT timing	Outcome
Lin et al. 2024 [52]	Retrospective Single-center 01.2021–06.2022	224, Severe acute pancreatitis China	Range 45–82	86 (38.4%)	Device: NA Level: L3, with contrast material Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: 5 mm Software: NA	Within 48 h of admission	30-day mortality
Looijaard et al. 2016 [49]	Retrospective Single-center 09.2003–04.2013	491, Mechanically ventilated, Netherlands	58 ± 18	186 (37.9%)	Device: NA Level: L3 Muscles: NA Slice thickness: NA Software: sliceOmatic	Day -1 to + 4 after ICU admission	6-month mortality
Loosen et al. 2020 [47]	Prospective Single-center 2006–2015	155, Medical ICU, Germany	60, Range 21–88	61 (39.4%)	Device: NA Level: L3 Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: 5 mm Software: 3D Slicer ®	At ICU admission	ICU & 30-day & 180-day & one-year mortality
Mangana del Rio et al. 2023 [53]	Retrospective Single-center 01.12.2010–31.12.2019	192, Acute-on-chronic liver failure, Switzerland	Mdn 62.0 IQR 53.2–70.0	51 (26.6%)	Device: NA Level: L3 Muscles: NA Slice thickness: NA Software: NA	At admission ± 7 days	28-day mortality
Meyer et al. 2024 [45]	Retrospective Single-center 2008–2019	472, Mechanically ventilated trauma patients, Germany	Mdn 49 IQR 31–63.25	118 (25.0%)	Device: Ingenuity, Philips Level: L3, with contrast material Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: 1 mm Software: ImageJ	At admission	30-day mortality
Moisey et al. 2013 [25]	Retrospective Single-center 2009–2010	149, Severely injured elderly patients, United States	79 IQR 72–85	64 (43.0%)	Device: NA Level: L3 Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: NA Software: sliceOmatic	On the day of admission	Mortality

Table 1 (continued)

Study Reference	Study Design	Sample, ICU population, country	Age	Female n (%)	CT methodology	CT timing	Outcome
Ng et al. 2019 [48]	Retrospective Single-center 01.2016–12.2016	228, UCI, Malaysia	54.4 ± 17.8	80 (35.1%)	Device: SOMATOM, Siemens Level: L3, with contrast material, in portovenous phase Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: NA Software: NA	Within 72 hours of UCI admission	Hospital mortality
Oh et al. 2022 [34]	Retrospective Single-center 07.2008–03.2019	905, Septic shock, Korea	65.7 ± 15.1	475 (52.5%)	Device: NA Level: L3 Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: NA Software: AquariusNET	Within 24 h of admission	28-day & 1-year mortality
Okada et al. 2021 [37]	Retrospective Single-center 01.2012–12.218	255, Sepsis, Japan	Mdn 76 IQR 64–84	102 (40.0%)	Device: NA Level: L3 (L2 or L4 if abnormal anatomy of L3) Muscle: right and left psoas Slice thickness: NA Software: Osirix	Within 24 h of ICU admission	90-day mortality
Osuna-Padilla et al. 2022 [44]	Prospective Single-center 11.2020–03.2021	86, COVID-19, Mexico	48.6 ± 12.9	23 (26.7%)	Device: Somaton Sensations®, Siemens Level: L3 Muscles: NA Slice thickness: 1 mm Software: sliceOmatic	With 24 to 48 h of ICU admission	In-hospital mortality
Seo et al. 2019 [35]	Retrospective Single-center 01.2013–12.2015	175, Septic shock, Korea	Mdn 65.0 IQR 58.0–72.0	65 (37.1%)	Device: NA Level: L3 Muscles: psoas, paraspinal and abdominal wall muscles Slice thickness: NA Software: AsanJ-MorphometryTM	1st, 3–6 months before ICU admission, 2nd, at ICU admission (only these results were used in our analyses)	28-day mortality

Table 1 (continued)

Study Reference	Study Design	Sample, ICU population, country	Age	Female n (%)	CT methodology	CT timing	Outcome
Shibahashi et al. 2017 [42]	Retrospective Single-center 01.2012–02.2016	150, Elderly patients with sepsis, Japan	Mdn 75 IQR 68–82	47 (31.0%)	Device: NA Level: L3 Muscles: psoas and paraspinal Slice thickness: NA Software: Synapse	Day of ICU admission	In-hospital mortality
Toledo et al. 2018 [51]	Retrospective Single-center 07.2010–07.2014	99, Critically ill cancer patients, Brazil	61.6 ± 13.5	43 (43.4%)	Device: NA Level: L3 Muscles: psoas, paraspinal and abdominal wall Slice thickness: NA Software: sliceOmatic	Within 72 h of ICU admission	Hospital mortality
Weijs et al. 2014 [50]	Retrospective Single-center 12.2003–09.2012	240, Mechanically ventilated, Netherlands	52.3 ± 19.0	96 (40.0%)	Device: NA Level: L3 Muscles: psoas, paraspinal and abdominal wall Slice thickness: NA Software: sliceOmatic	Day -1 to +4 after ICU admission	ICU-, 28-day & hospital -mortality
Xi et al. 2021 [38]	Retrospective Single-center 01.2010–04.2020	451, Abdominal trauma, China	Low SMM 41.39 ± 15.94 Normal SMM 40.49 ± 14.65	78 (17.3%)	Device: NA Level: L3 Muscles: NA Slice thickness: NA Software: Image J2	Within 1 week of onset of trauma	Death at 28 & 90 day
L3-L4 (n = 1)							
Rossi et al. 2021 [39]	Retrospective Single-center 08.03.2020–31.01.2021	153, COVID-19, Italy	64.19 ± 9.98	32 (20.9%)	Device: NA Level: L3-L4 Muscle: psoas Slice thickness: NA Software: sliceOmatic	CT available (no more information)	28-day survival
L4 (n = 2)							
Ebbeling et al. 2013 [26]	Retrospective Single-center 2005–2010	180, Elderly trauma, United States	Mdn 74 IQR 63–82	77 (42.8%)	Device: NA Level: L4 Muscles: right and left psoas Slice thickness: NA Software: NA	Admission CT	In hospital mortality
Tee et al. 2021 [40]	Retrospective Single-center 05.2008–12.2016	939, Trauma, Taiwan	42.2 ± 17.6	245 (26.1%)	Device: NA Level: L4 Muscles: psoas Slice thickness: NA Manual outlining	CT performed primarily for trauma indications	Overall mortality

Table 1 (continued)

Study Reference	Study Design	Sample, ICU population, country	Age	Female n (%)	CT methodology	CT timing	Outcome
L4-L5 (n = 1)							
Yeh et al. 2018 [27]	Retrospective Single-center Date NA	140, Surgical, United States	60.1 ± 17.4	72 (51.4%)	Device: 64-MDCT Level: L4-L5 Muscles: psoas Slice thickness: 5 mm Software: standard image viewing	Within 72 h of ICU admission	In-hospital mortality

CT, computed tomography scan; ICU, intensive care unit; ICU-AW, intensive care unit-acquired weakness; IQR, interquartile range; L3, third lumbar vertebra; Mdn, median; NA, not available; SMM, skeletal muscle mass; T4, fourth thoracic vertebral; VV-ECMO, venovenous extracorporeal membrane oxygenation

Abdominal wall muscles: transverse abdominus, external and internal obliques, rectus abdominus; Paraspinal muscles: erector spinae, quadratus lumborum

Risk of bias in studies

We used the robvis (Risk-Of-Bias Visualization) tool [54] to present the results of the critical appraisal of risk of bias for each included study (Supporting information Fig. 1). Among the 35 included studies, only one had an unclear overall risk of bias [31]. The most frequently identified sources of bias were related to reliability (14/35 studies) and potential confounders (5/35 studies).

Mortality outcomes

Supporting information Table 4 shows the mortality rate of the studies to highlight differences between study centres or studies. The included studies reported the mortality in ICU, in hospital, at days 28, 30 & 90, at 6-months, at 1-year. ICU mortality rate varied from 6.5 [46] to 38.7% [29], and hospital mortality from 8.5 [21] to 44.8% [28]. Long-term follow-ups revealed mortality rates of up to 45.3% at 1-year [22].

The association between mortality and muscle mass was evaluated by (1) comparison of mortality rates at defined time-points between patients categorized with low or preserved muscle mass according to cut-offs that may differ, (2) comparison of muscle mass size at defined time-points between deceased patients and survivors, and (3) mortality risk predicted by muscle mass as continuous or categorical values.

ICU mortality

ICU mortality related to skeletal muscle mass was investigated in six studies [29, 36, 43, 46–48] (Supporting information Table 5).

Two studies reported significant higher ICU mortality in patients with low L3 SMI [29, 48]. In contrast, one study found no statistically significant association between low L3 SMI and ICU mortality [36] while another did not find any statistically significant difference in ICU mortality based on L3 SMA [46].

One study did not find a significant difference in L3 SMI size between deceased patients and survivors [47].

Damanti et al. 2022 found a significant association between lower L1-L2 or L3 SMI and higher ICU mortality risk when adjusted for age, sex, and frailty index, but not when adjusted for BMI, and no association between SMA and ICU mortality [43]. Bear et al. 2021 did not show any significant increase in ICU mortality risk with low L3 SMI [36].

Hospital mortality

Hospital mortality was assessed in 16 out of 35 studies [20–22, 24–28, 30, 41, 43, 44, 48, 50, 51, 55] (Supporting information Table 6).

Six studies reported significant higher hospital mortality in patients with low L3 SMI [21, 25, 41, 48], low L1 SMI [28] or low L3 SMA [50]. In one study, a significant difference was only found for women, but not for men [51]. Several studies [20, 22, 24, 26, 27, 44] did not find significant differences in hospital mortality between patients with low vs. preserved muscle mass. They used different SMI cut-off values [20, 22, 24], or BMI-adjusted SMI cut-offs [44]. One study used the L4 PMI [26], while another categorised patients according to L4-L5 PMA tertiles [27].

Four studies found significantly smaller size of L3 PMI [30], L3 SMA [42], L3 SMI [51] or L1 SMI [28] in deceased patients compared to survivors.

Five studies have reported significantly higher hospital mortality risk in patients with low SMI [25, 28, 30, 48], and low SMA [42]. One study found that L1-L2 or L3 SMI and SMA were positively associated with a reduction in the risk of hospital mortality when analyzed individually, but not after adjusting for age, sex and body mass index (BMI) or frailty index [43]. Another study found an increased, though not statistically significant, risk of adverse outcomes in patients with a low L4 SMI in univariate analysis, remained non-significant after adjusting for age, comorbidities and Abbreviated Injury Scale [26].

28-day & 30-day mortality

Seventeen studies analysed 28-day and 30-day mortality [19–21, 23, 32–35, 38, 39, 45–47, 50–53] (Supporting information Table 7).

Six studies reported significantly higher 28 & 30-day mortality rates in patients with low L3 SMI [21, 32, 34, 45], low L3 PMI [33], or low L3 SMA [50] compared to those with preserved values. One study reported a higher 30-day mortality rate in patients with low L3 SMI and visceral obesity [19]. Six of these studies based their results on muscle index [19, 21, 32–34, 45], but only two used the same cut-offs [21, 45]. In contrast, three studies did not observe a significant difference in mortality rates between patients with low and normal L3 SMI [35, 38] or L3 SMA [46]. Kaplan et al. 2016 compared patients with low L3 SMI and osteopenia with those without low L3 SMI and/or low bone density and also found no significant difference in mortality rates [20].

Four studies observed that patients who died at 28 or 30-day had a significant smaller muscle mass size in SMI [23, 32, 52] or PMI [33] than the survivors. In contrast, several studies reported no statistically significant differences in muscle mass size for L3 SMI [45, 47] or L3-L4 PMA [39] between deceased and surviving patients at 28–30 days.

Nine studies reported a significant higher mortality risk at day 28 or 30, with depleted L3 SMI [19, 23, 32, 34,

45, 51, 53] or L3 PMI [33] or L3 SMA [46]. Ji et al. 2018 found a significant association particularly in patients with visceral obesity and low L3 SMI [19].

90-day & 100-day mortality

Three studies looked at 90-day and 100-day mortality in relation to CT-derived skeletal mass [37, 38, 42] (Supporting information Table 8).

Two studies reported 90-day mortality rates: one assessed L3 SMI and found no significant differences [38] while the other analyzed L3-L4 PMI in tertiles but did not compare mortality rates as percentages [37].

Shibahashi et al. 2017 found that patients who did not survive up to 100 days after admission had significantly lower size of L3 SMA compared to survivors [42].

Okada et al. 2021 found a significantly higher 90-day mortality risk in patients with an L3-L4 PMI in the highest tertile compared to the lowest [37]. Shibahashi et al. 2017 reported significantly lower 100-day survival rates in patients with low L3 SMA compared to those with higher SMA [42].

6-month mortality

Four studies analysed 6-month mortality [33, 36, 47, 49] all at the L3 level (Supporting information Table 9).

Two studies found a significantly higher mortality rate in patients with low PMI [33] or low SMA [49] compared with preserved muscle mass, while one study found no significant difference using SMI [36].

Two studies report a significantly smaller size of SMI or SMA [47, 49] in deceased patients compared with SMA and SMI in surviving patients.

The 6-month mortality risk was significantly higher in patients with low PMI compared to those with normal PMI [33]. However, Bear et al. 2021 found no significant association between SMI and 6-months mortality [36].

1-year mortality

Five studies consistently found an association between low skeletal mass at the L3 level and increased 1-year mortality [20–22, 34, 47] (Supporting information Table 10).

Three studies reported significantly higher 1-year mortality rates in patients with low SMI compared to those with normal SMI [21, 22, 34]. Kaplan et al. 2016 also found that low SMI was significantly associated with higher 1-year mortality, particularly when combined with osteopenia [20].

One study showed a significantly smaller size of SMI in patients who had died at 1 year as compared to those who survived [47].

Four studies showed that a low SMI significantly predicted 1-year mortality [20–22, 34]. One study did not perform regressions [47].

Other mortality

Death has also been studied in terms of overall mortality [34, 40], and overall survival [31, 47] (Supporting information Table 11). The follow-up of these studies ranged from admission to 4000 days (e.g., Oh et al. 2022 [34]).

The overall mortality rate was significantly higher in patients with low L3 SMI [34], but did not differ significantly between patients with low and preserved L4 PMI [40].

Oh et al. 2022 showed that patients with low L3 SMI had a significantly higher risk of overall mortality than those with normal SMI [34]. Beypinar et al. 2021 reported an association between L3 PMI and survival days [31]. Furthermore, Loosen et al. 2020 found that an L3 SMI of less than 75.0 mm^2/cm was associated with a significantly increased risk of reduced overall survival [47].

Meta-analysis

Twenty-two studies evaluated the association between short or long-term mortality and lumbar muscle mass [19–22, 24, 26–30, 32, 33, 36, 38, 41, 44–46, 48, 50, 53, 56].

Risk of short-term mortality

A total of 18 studies were included in the meta-analysis to assess the risk of death in the short term based on muscle mass [19–22, 24, 26, 27, 29, 32–34, 38, 41, 44–46, 48, 50]. Three studies considered muscle mass area [27, 46, 50], while the remaining used the muscle mass index [19–22, 24, 26, 29, 32–34, 38, 41, 44, 45, 48].

Patients with low muscle mass had a significantly higher risk of short-term mortality, with an OR of 2.28 (CI 1.79–2.91, $P<0.001$). This increased risk remained even when SMA and SMI were analysed separately. Figure 2A shows the OR for mortality based on the sample sizes (n) reported in the primary studies, and Fig. 2B shows additionally the OR for SMI reported in the primary studies [28, 30, 36, 53]. The risk of short-term mortality remained elevated and showed minimal variation, with an OR of 2.33 (CI 1.90–2.87, $P=0.01$).

Supporting information Fig. 3 presents the meta-analysis ranked by the cut-offs used to define low muscle mass. Studies applying lower cut-offs (e.g., <38 cm^2/m^2 for women and <50 cm^2/m^2 for men) consistently

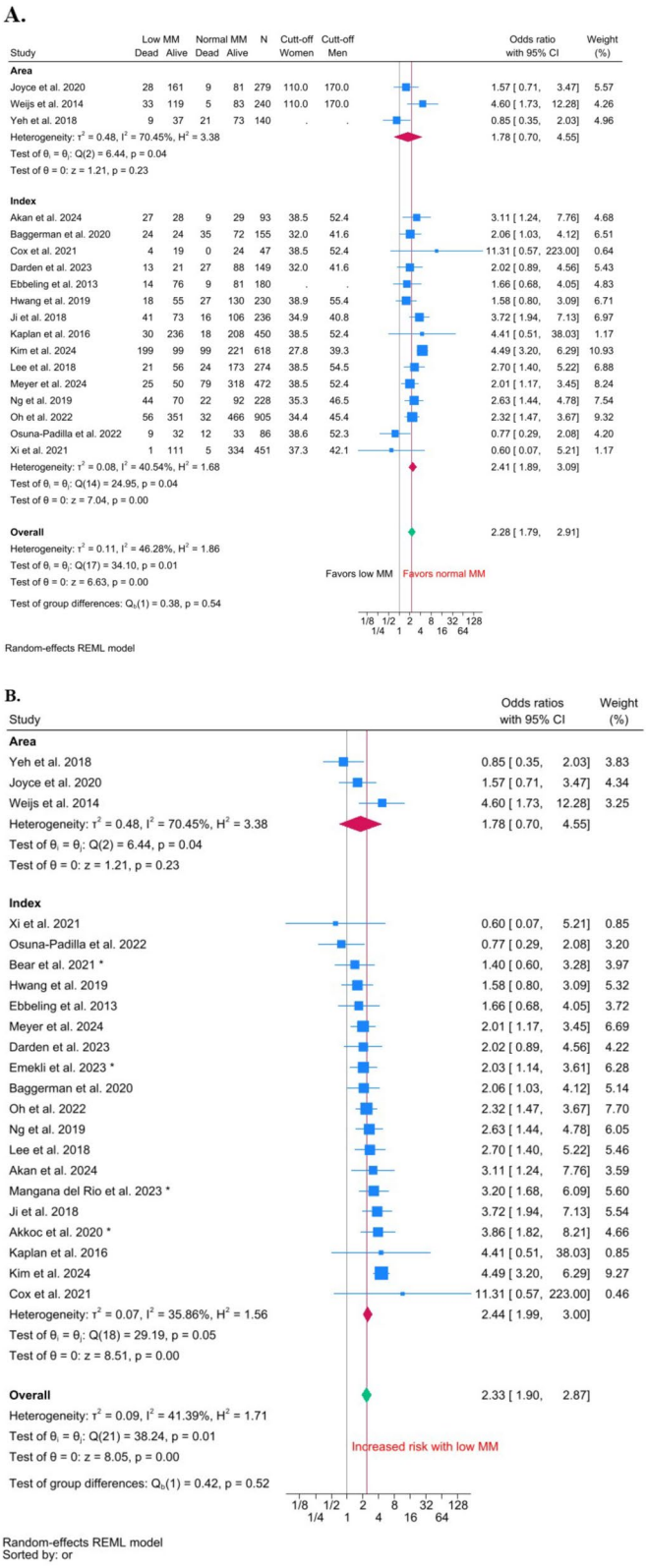

Fig. 2 Meta-analysis of low muscle mass (MM) and short-term (ICU, hospital, 28- and 30-day) mortality in critically ill patients. Figure **A** shows the OR mortality calculated according to the number of deaths (n), when reported in the primary studies. Figure **B** adds 4 additional studies where the sample size of the number of deaths was not reported

found significantly higher odds of short-term mortality among patients with low muscle mass, with ORs ranging from 2.02 to 4.49 except for Xi et al. 2021 (OR 0.60) [38]. In contrast, studies using higher cut-offs reported a slightly lower pooled OR (2.07 vs. 2.82), with reduced heterogeneity.

The funnel plot for studies investigating the association between low muscle mass and short-term mortality is presented in Supporting information Fig. 4.

Risk of long-term mortality

All the articles that looked at long-term mortality also reported results for short-term mortality, and none examined only long-term mortality. In the included studies, long-term mortality was assessed at 90 days, 6 months, and 1 year. A total of five studies were included in the meta-analysis [20–22, 33, 38]. Patients with low muscle mass had a threefold higher risk of long-term mortality (OR 3.02, CI 1.40–6.51, $P<0.001$) (Fig. 3). When one additional study reporting the OR was included [36], the risk of long-term mortality remained significantly higher for patients with low muscle mass (OR 2.67, CI 1.45–4.92, $P<0.001$).

The studies were ranked according to the sex-specific cut-offs used to define low muscle mass in Supporting information Fig. 5. The association between low muscle mass and long-term mortality is stronger and more consistent when higher cut-offs are used to define low muscle mass.

The funnel plot for studies investigating the association between low muscle mass and long-term mortality is presented in Supporting information Fig. 6.

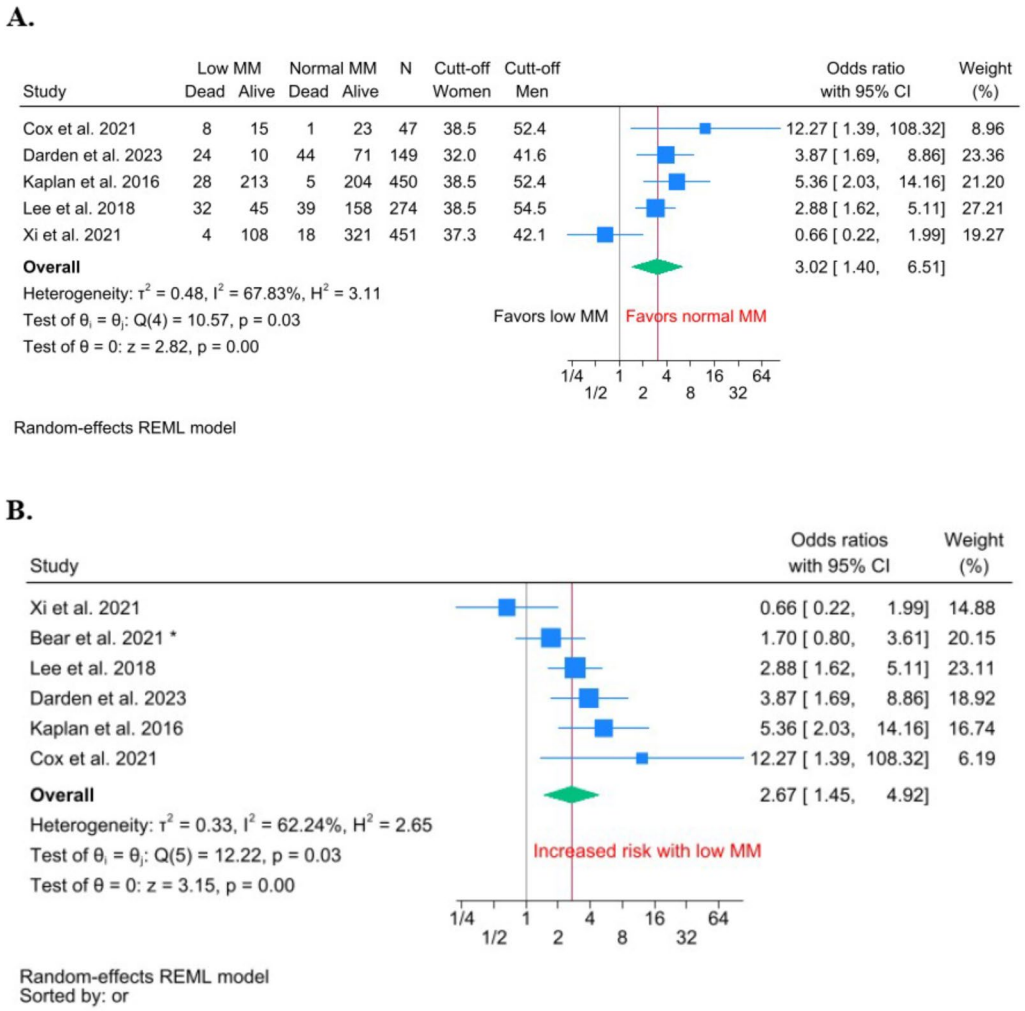

Fig. 3 Meta-analysis of low muscle mass (MM) and long-term (90-days, 6-months, 1-year) mortality in critically ill patients. Figure **A** shows the OR mortality calculated according to the number of deaths (n), when available, or provided in the primary studies. Figure **B** adds 1 additional study where the sample size of the number of deaths was not reported

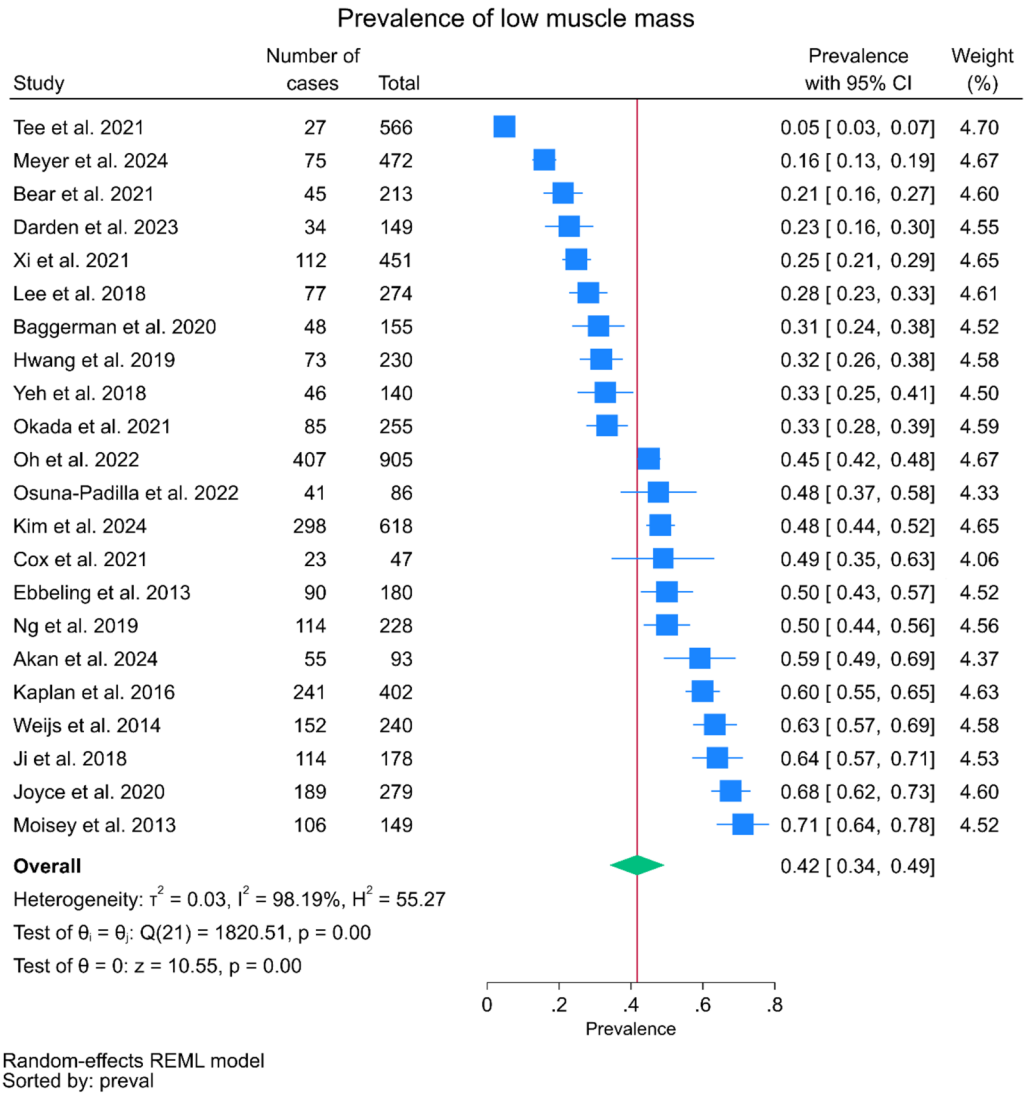

Fig. 4 Meta-analysis of the prevalence of low muscle mass among 22 Studies reporting subgroup sample sizes

Prevalence of low muscle mass

Figure 4 shows considerable heterogeneity ($I^2 = 98.2\%$) in the prevalence of low muscle mass among the 22 studies that provided sample sizes for the subgroups [19–22, 24–27, 29, 32–34, 36–38, 40, 41, 44–46, 48, 50]. The overall prevalence amounted to 42% (CI 34–49%), ranging from 5 to 71%. Forest plot resulting from the meta-analysis of the single, untransformed prevalence of low muscle mass. When a study prevalence is close to 0 or 1, its estimated variance is very small, and thus the study is assigned an artificially large weight in the meta-analysis.

Discussion

Our study focuses solely on baseline skeletal muscle mass as assessed by CT scans at admission. Key findings of the narrative synthesis include: (a) SMI was predominantly used to assess skeletal mass across studies, with widely varying cut-off values for defining low skeletal mass; (b) hospital and 28- to 30-day mortality were the main time points reported; (c) the studies compared mortality rates between patients with low and preserved muscle mass, analyzed the differences in the size of the muscle mass between the deceased and the surviving patients, or assessed the risk of death in patients with reduced muscle mass, but the results were heterogeneous. The meta-analyses show that low muscle mass more than doubles the risk of short- and long-term mortality. Furthermore, the pooled prevalence of low skeletal muscle mass was substantial, but with high variability and heterogeneity between studies.

Previous systematic reviews have highlighted differences in assessment methods, time of muscle mass measurement and time of outcome evaluation. Fazzini et al. 2023 focused on studies measuring the association between muscle mass loss during critical illness, measured by various methods, and ICU, in-hospital, or 60-day mortality [3]. They found that ultrasound was used in 85% of studies (n = 28), while CT was used in only 15% (n = 5), and that muscle mass loss was inconsistently associated with mortality. They did not perform any meta-analysis because of the different time-points of mortality assessment [3]. Yang et al. 2023 included studies that measured muscle mass by CT (n = 33), anthropometry (n = 2), and ultrasound (n = 2) in critically ill patients, not especially at ICU admission [13]. They reported a 51% prevalence of low skeletal muscle mass, and a 2- to 3-times higher hospital, 30-day and 1-year mortality in patients with low muscle mass [13]. Finally, Meyer et al. 2021 reported a high prevalence of low skeletal muscle mass assessed exclusively by CT scan, again associated with a 2–3 times higher short-term mortality [14]. Long-term mortality was not assessed, and the time frame for CT acquisition varied, ranging from days around ICU admission to 28–30 days after major ICU events [14]. Our results confirm that low muscle mass at admission more than doubles the risk of short-term mortality and additionally highlight its association with increased long-term mortality. The high prevalence of low muscle mass in our study (42%, ranging from 5 to 71%) was similar to the 50.9% found by Meyer et al. 2021, ranging from 26.3 to 71.1%, though they did not provide information on heterogeneity [14].

Since there are no universally accepted cut-off values to define low skeletal muscle mass, studies often rely on cut-offs that have been validated in other populations of different sex, ethnicity, age, and health status. In our systematic review, the cut-offs used to define low SMI in critically-ill patients were sex-specific and established in healthy adults [22, 32, 34, 36, 41, 43], patients with cancer [19–21, 24, 25, 29, 35, 44, 45], and patients with liver disease [53]. While these approaches are pragmatic, they introduce variability in the definition of low muscle mass, which may affect comparability and the consistency of findings across studies. Our additional analysis explored whether the choice of cut-off values influences the observed association between muscle mass and mortality. For short-term mortality, studies using lower cut-offs (e.g., < 38 cm^2/m^2 for women and < 50 cm^2/m^2 for men) tended to report higher ORs, although results were more heterogeneous. In contrast, studies using higher cut-offs (≥ 38/50) showed a slightly lower OR but lower heterogeneity. For long-term mortality, the pattern was reversed: higher cut-offs (≥ 38/50) exhibited a stronger and more consistent association with mortality. However, cut-off variability alone does not fully explain the inconsistencies across studies. For example, Osuna-Padilla et al. 2022 [44] reported no association with short-term mortality despite using cut-offs similar to other positive studies [21, 45]. These findings suggest that the prognostic value of muscle mass may depend not only on the presence of low mass, but also on how it is defined, as well as on larger factors such as population characteristics, ethnic origin, illness severity, or underlying muscle quality.

The psoas, paraspinal, and abdominal wall muscles were included in the CT scans in most studies. Nonetheless, some studies used the SMA of the psoas and paraspinal muscles, excluding the abdominal muscles [42] and others used only the PMA [27, 39] or PMI [26, 27, 30, 31, 33, 37, 39, 40]. Pigneur et al. 2023 showed that PMI correlated weakly with SMI, making it an unreliable measurement for detecting low muscle mass in cancer patients [57]. To improve standardization and comparability of results, we propose the consistent use of L3 SMI, including the psoas, paraspinal, and abdominal wall muscles, as the preferred measurement. In addition, assessment of muscle quality using CT-derived attenuation values (e.g., normal vs. low attenuation or poor quality muscle) could provide further valuable insight into muscle composition and improve interpretation of results, allowing a more comprehensive assessment of its prognostic significance.

This systematic review has several strengths. First, it includes only studies focusing on critically ill patients admitted to the ICU, regardless of specific pathologies, making it representative of the overall ICU population. Second, it relies exclusively on muscle mass assessment using CT scans at the lumbar level, which is considered the gold standard for muscle mass assessment. Third, by reinforcing the evidence that low skeletal muscle mass significantly increases short-term mortality risk, but also extending this analysis to long-term mortality and showing the considerable variability in reported prevalence. Fourth, despite the heterogeneity of the study populations, our review systematically examined key variables that may influence muscle mass assessment, including differences in measurement techniques (muscle area vs. index; muscle included in the measurement), cut-off values, and patient ethnicity. However, it has several limitations. The lack of standardized adjustment models, particularly for important confounders such as the severity of acute illness and the burden of comorbidities, limits the comparability of results and highlights the need for future research to establish consistent multivariate approaches. Moreover, most of the included studies were retrospective and single center, which may limit the external validity of the results and preclude conclusions

about causality. Differences in patient characteristics such as ethnicity, age and comorbidities (as cancer, chronic obstructive pulmonary disease, and advanced liver disease), as well as differences in the reasons for ICU admission (e.g. elderly patients with sepsis vs. trauma in young adult's patients), may influence both skeletal muscle mass and mortality outcomes. Although the focus of this review was on CT-derived measurements at the lumbar level, variations in anatomical landmarks, measurement protocols and software used between studies may have contributed to inconsistencies in reported values. In addition, the retrospective use of diagnostic CT scans, which were not primarily performed to assess muscle mass, may have introduced bias into the data collection. Finally, the timing of CT measurements varied across studies, ranging from 7 days before to 7 days after ICU admission. In some cases, CT scans were performed at specific times, such as before surgery or at the onset of sepsis, while some studies did not specify the exact day of CT acquisition (e.g. on admission). Given the rapid and significant muscle loss in critically ill patients, this variability in timing may have influenced the results across studies.

Conclusions

This systematic review and meta-analysis highlight that CT-assessed skeletal muscle mass at ICU-admission is associated with short- and long-term mortality and may serve as a prognostic marker in critically ill patients. The high prevalence of low muscle mass on admission, together with the considerable heterogeneity between studies, highlights the need for standardization of both measurement methods and definitions. Future research should focus on the development and validation of standardized assessment protocols. In addition, integrating indicators of muscle quality may contribute to a more comprehensive understanding.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13054-025-05427-2.

Supplementary Material 1.

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Author contributions
VABM and LG designed the study and performed the systematic review. LG contributed to quality assessment, data extraction and analysis. VABM and LG drafted the manuscript. FRH and VABM performed the statistics for the meta-analysis. AP, AM, FRH, YMD, ADW, and CPH critically revised the manuscript for important intellectual content.

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Data availability
The datasets used and analyzed during the current study will be available from the corresponding author upon reasonable request.

Declarations

Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interest
The authors declare that they have no competing interests.

Declaration of generative AI and AI-assisted technologies in the writing process
During the preparation of this work the authors used DeepL Write and ChatGPT to improve language and readability. After using these tools, the authors reviewed and edited the content as needed and takes full responsibility for the content of the publication. This systematic review was conducted in parallel with a retrospective observational study, for which a protocol was submitted to the Ethics Committee of the Canton of Geneva and registered on ClinicalTrials.gov (NCT05834894). While the overarching study protocol was registered, a separate protocol specific to this systematic review was not published.

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