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Posted Date: 26 September 2025

doi: 10.20944/preprints202509.2233.v1

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Article

Skeletal Muscle Quality Evaluation for Prognostic Stratification in the Emergency Department of Patients ≥ 65 Years with Major Trauma

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Abstract

Background: In patients over 65 years who experience severe trauma the underlying health status has a significant impact on overall mortality. This study aims to assess if CT evaluation of skeletal muscle quality could be a risk stratification tool in the ED for these patients. **Methods:** Retrospective observational study between January 2018 and September 2021, including consecutive patients ≥ 65 years admitted to the ED for a major trauma (defined as Injury Severity Score > 15). Muscle quality analysis was made by specific software (Slice-O-Matic v5.0, Tomovision®, Montreal, QC, Canada) on a CT-Scan slice at the level of the third lumbar vertebra. **Results:** 263 patients were included (72.2% males, median age 76 [71-82]), and 88 (33.5%) deceased. The deceased patients had a significantly lower skeletal muscle area density (SMAd) compared to survivors. The multivariate Cox regression analysis confirmed that SMAd < 38 at the ED admission was an independent risk for death (adjusted HR 1.68 [1.1 – 2.7]). The analysis also revealed that, among the survivors after the first week of hospitalization, the patients with low SMAd had an increased risk of death (adjusted HR 3.12 [1.2 – 7.9]). **Conclusions:** The skeletal muscle density evaluated by a CT scan at ED admission could be a valuable risk stratification tool for patients ≥ 65 years with major trauma. In patients with SMAd < 38 HU the in-hospital mortality risk could be particularly increased after the first week of hospitalization.

Keywords: Emergency Department; Major trauma; Trauma in elderly; Injury Severity Score; older adults; CT scan muscle quality assessment; skeletal muscle area; skeletal muscle density

1. Introduction

The progressive aging of the global population presents significant challenges for health systems [1,2], as the number of older people is increasing faster than that of any other age groups in nearly all countries [2]. Consequently, a growing number of older adults are presenting to the Emergency Department (ED) with traumatic injuries [3–5]. In the US in 2016, adults ≥ 65 years accounted for about

1/3 of all trauma patients, with a case fatality rate much higher than the younger population, and similar trends have been reported in the European Union [6,7].

Older adults with trauma often present a higher number of comorbidities and suffer from more complex clinical conditions compared to younger patients [8,9]. Independent of other factors, these patients are indeed more prone to experience heart, pulmonary, and renal complications [10,11]. Moreover, particularly when emergency surgery is required, overall mortality increases with age, doubling in patients aged ≥ 80 years old [12,13].

Nevertheless, chronological age and comorbidities do not always truly reflect the overall health status of older patients. To better access this population, the concept of frailty has been introduced, defined as a state of increased vulnerability to stressors and characterized by a progressive declined physiological function and reduced strength, increasing the risk of adverse outcomes [14,15]. However, a complete frailty assessment needs a comprehensive geriatric assessment, which could be difficult to obtain in the ED, particularly in the case of major trauma.

Sarcopenia, define as the age-related loss of muscle mass and function [16,17] shares several clinical features with frailty [18] and could be used as a marker of increased frailty. Both sarcopenia and frailty are closely associated with poor nutritional status [19], and have been linked to worse clinical outcomes in elderly patients [20–22]. Various methods can be used to evaluate sarcopenia and radiology plays a prominent role, even though there is a lack of consensus on their standardization [23,24]. Nevertheless, computed tomography (CT) offers an objective and reproducible means of assessing both sarcopenia and overall frailty [25].

This study aims to investigate the association between skeletal muscle quality and mortality in older patients admitted to the ICU for major trauma.

2. Materials and Methods

This is a monocentric observational cohort study conducted in the ED of a teaching hospital in central Italy, with a catchment area of about 1.8 M inhabitants, and about 80k patients admitted per year. The institutions held a trauma center treating about 2k major traumas per year.

This retrospective observational study aimed at evaluating the association between radiological parameters and in-hospital mortality.

The study enrolled all consecutive patients ≥ 65 years who were admitted to our ED for major trauma between January 2018 and September 2021. Major trauma was defined based on an Injury Severity Score (ISS) ≥ 16 .

Given the observational nature of the study and its retrospective design, no a priori sample size calculation was performed. Instead, we included all eligible consecutive patients aged ≥ 65 years who presented with major trauma (ISS ≥ 16) and met the inclusion criteria during the predefined study period (January 2018 to September 2021). This approach was chosen to ensure the representativeness of the sample and to reduce selection bias.

The final sample size reflects the real-world incidence of major trauma in older adults presenting to our Emergency Department, which serves a high-volume trauma center with approximately 2,000 major trauma cases per year. Stratification into outcome-based groups (e.g., survivors vs. non-survivors; early vs. late mortality) was performed post hoc, based on clinical endpoints.

For each patient, hospital-based, electronic health records were used to collect all the demographic and clinical data. Patients with minor injuries were excluded from the study. Additional exclusion criteria included the absence of an abdominal CT scan at ED admission and the presence of severe intramuscular haemorrhage at the level of the third lumbar vertebra, which could impair accurate muscle assessment on CT.

2.1. Study Variables

Upon presentation to the ED, for each patient, the following informations were collected for each patient:

- Demographic data, including age and sex;
- Physiological parameters at ED admission including Glasgow Coma Scale, Respiratory rate, Systolic blood pressure;
- Acute Injury Scale (AIS) scores and the Injury Severity Score (ISS). The scores were blindly calculated for each patient by three authors (MP, LF, GT) based on the clinical records and the radiological findings.
- Information about clinical history and comorbidities was assessed with the Charlson Comorbidity Index (CCI), a validated score used to predict the risk of death one year after hospitalization in patients with a high comorbidities burden.
- The average length of stay (LOS) was calculated from the time of the ED admission to the time of discharge or death.
- Laboratory tests, including hemoglobin, white blood cells, platelet count, fibrinogen, prothrombin time, partial thromboplastin time, glucose, creatinine, urea, nitrogen, and blood gas analysis results (pH, lactates, bicarbonates)
- Assessment of muscle quality. Body composition analysis was performed on a single axial CT-Scan slice (DICOM image format) at the level of the third lumbar vertebra (L3), using specific software (Slice-O-Matic v5.0, Tomovision®, Montreal, QC, Canada). Image analysis was performed by two investigators with over five years imaging experience and blinded to outcomes, to minimize the introduction of bias. The cross-sectional area of skeletal muscle (SMA), subcutaneous adipose tissue (SAT), and visceral adipose tissue (VAT) were analyzed based on pre-established thresholds of Hounsfield Units (HU): SMA - 29 to 150, SAT - 190 to -30, and VAT - 150 to -50. Skeletal muscle area density (SMAd) was calculated by finding the mean of the HU of SMA. Similarly, the mean HU density was calculated for VAT (VATd), and SAT (SATd)[21]. Supplementary Figure S1 shows a sample of the CT images used for the calculations.

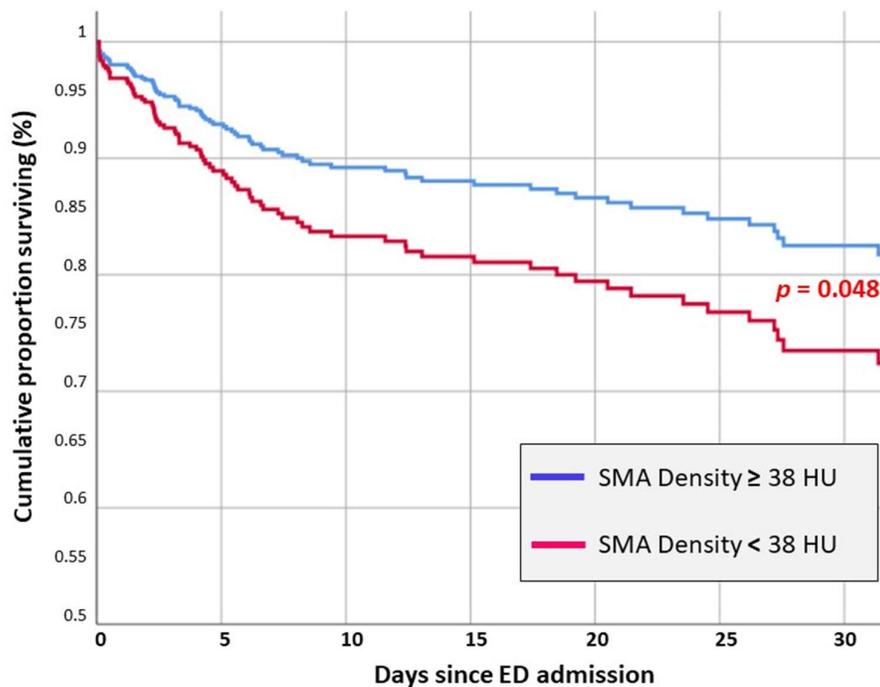


Figure 1. Survival.

2.2. Study Endpoints

The primary study endpoint of the study was all-cause in-hospital death.

Secondary endpoints included early mortality (defined as mortality within 7 days since admission) and the late mortality (defined as mortality that occurred >7 days since admission).

2.3. Statistical Analysis

This was a retrospective observational study aimed at evaluating the association between radiological parameters and in-hospital mortality.

Continuous variables were reported as median [interquartile range, IQR] and were compared with univariate analysis by the Mann-Whitney U test. Categorical variables were reported as absolute numbers (percentage) and were compared by Chi-square test (with Fisher's test if appropriate). Receiver operating characteristic (ROC) curve analysis was used to estimate the performance of the evaluated radiological parameters in predicting in-hospital death. The Youden index was used to estimate the optimal cut-off threshold associated with the defined outcomes. The areas under the ROC curve were compared by the DeLong method. Significant variables in the univariate analysis were entered into a multivariate Cox regression model to identify the independent predictors of in-hospital death. The single items included in combined variables (i.e. APACHE II score and CCI) were not included in multivariate models to avoid overfitting and factor overestimation. Furthermore, to improve the parameter estimation and the model fitting, the continuous variables were dichotomized according to the cut-off values identified by ROC analysis. Early and late mortality were evaluated in separate multivariate Cox regression models, by considering only the events that occurred <7 days and ≥ 7 days, respectively, and considering as "censored" cases the remaining deaths. A p-value of 0.05 was regarded as significant in all the analyses.

Data were analyzed using IBM SPSS statistics for Windows, Version 25 (IBM Corp. Armonk, NY, USA) and MedCalc Statistical Software version 19.2.1 (MedCalc, Ostend, Belgium).

2.4. Ethical Approval

The study was conducted according to the principles expressed in the Declaration of Helsinki and its later amendments. All patients gave their informed consent to participate in the study. The research protocol was approved by the Institutional Review Board of Fondazione Policlinico Universitario "A Gemelli" IRCCS – Rome (#0025817/22; Study ID: #5121).

3. Results

3.1. Study Cohort and Baseline Characteristic

A total of 263 patients (179 males, 72.2%) were enrolled in the study. The median age was 76 years [71 – 82]. The enrolled patients had a median ISS 26 [20–33]; the AIS was highest for head and neck injuries (3, ranging from 2 to 5). As expected, the enrolled patients had several comorbidities, and the median CCI was 4 [3–5]. Overall, 175 patients survived (66.5%), with a median length of hospital stay (LOS) of 15.5 days [6.2 – 29.4] (Table 1).

Table 1. Clinical characteristics of the patients in the study cohort and comparison between deceased vs. survivors.

	All Patients n 263	Survived n 175	Deceased n 88	p value
Age	76 [71-82]	75 [69-81]	78 [74-85]	<0.001
Sex (male)	179 (72.2%)	132 (75.4%)	47 (64.4%)	0.088
<i>Injury severity</i>				
ISS	26 [20-33]	25 [17-33]	29 [25-33]	<0.001
AIS Head Neck	3 [2-5]	3 [0-4]	5 [4-5]	<0.001
AIS Face	0 [0-2]	0 [0-2]	0 [0-1.5]	0.724
AIS Chest	2 [0-4]	2 [0-4]	0 [0-3]	0.066
AIS Abdomen	0 [0-0]	0 [0-2]	0 [0-0]	0.124
AIS Pelvi-Extremity	0 [0-2]	1 [0-3]	0 [0-2]	0.028
AIS External	0 [0-1]	1 [0-1]	0 [0-1]	0.027
APACHE II	20 [15-26]	17 [14-21]	27 [24-30]	<0.001
<i>Laboratory Values at ED admission</i>				
Hb (mg/dL)	12.8 [11.2-14]	13.1 [11.4-14.2]	11.9 [10.2-13.5]	<0.001
WBC (*10 ⁹)	13.2 [9.19-16.84]	13.3 [9.48-16.47]	12.6 [9-19.5]	0.638
PLT	205 [156-257]	208 [169-253]	183 [148-268]	0.319
Fibrinogen	287 [250-335]	285 [252-327]	290 [244-365]	0.421
aPTT	28.6 [25.5-34.4]	27.2 [24.9-31.7]	33.6 [28.5-39.5]	<0.001
Glucose	158 [133-207]	152 [131-200]	170 [135-209]	0.081
Creatinine (mg/dL)	1.01 [0.8-1.26]	1 [0.8-1.23]	1.05 [0.8-1.36]	0.437
BUN (mg/dL)	20 [17-24]	20 [17-24]	20.5 [18-28.8]	0.574
Lactate (mmol/L)	2.5 [1.8-3.5]	2.5 [1.8-3.4]	2.7 [1.7-7.8]	0.725
<i>Muscular parameters at CT scan evaluation</i>				
SMA	151.2 [122.5 / 170.5]	153.8 [127.7 / 169.8]	140.5 [112.3 / 173.9]	0.204
VAT Area	144.3 [77.2 / 218.9]	158.9 [87.9 / 222.3]	128.3 [77.9 / 202.1]	0.112
SAT Area	150.9 [110.2 / 207.5]	154.4 [113.3 / 211.45]	142 [98.67 / 191.1]	0.119
SMA Density	41.6 [34.72 / 47.8]	41.9 [35.9 / 48.1]	37.9 [32.2 / 45.7]	0.009
VAT Density	-83.4 [-87.2 / -78.0]	-83.9 [-87.9 / -79.5]	-82.5 [-86.1 / -75.6]	0.047
SAT Density	-85.0 [-89.0 / -78.9]	-85.7 [-89.8 / -80.0]	-82.6 [-87.8 / -77.8]	0.029
<i>Comorbidities</i>				
CCI	4 [3-5]	4 [3-5]	4 [3-5]	0.053
History of CAD	19 (7.7%)	14 (8%)	5 (6.8%)	1.000
Congestive Heart Failure	5 (2%)	2 (1.1%)	3 (4.1%)	0.154
Peripheral Vascular Disease	26 (10.5%)	17 (9.7%)	9 (12.3%)	0.649
Cerebrovascular Disease	13 (5.2%)	8 (4.6%)	5 (6.8%)	0.534
Dementia	8 (3.2%)	5 (2.9%)	3 (4.1%)	0.696
COPD	30 (12.1%)	25 (14.3%)	5 (6.8%)	0.134
Diabetes	3 (13.7%)	24 (13.7%)	10 (13.7%)	1.000
Chronic Kidney Disease	20 (8.1%)	10 (5.7%)	10 (13.7%)	0.043
Malignancy	17 (6.9%)	13 (7.4%)	4 (5.5%)	0.784

Abbreviations: : Hb – Hemoglobin; WBC – White Blood Cells; PLT – Platelets; aPTT – activated Partial Thromboplastin Time; APACHE – Acute Physiology and Chronic Health Evaluation; BUN – Blood Urea Nitrogen; AIS – Acute Injury Scale; ISS - Injury Severity Score; HU – Hounsfield units; CCI – Charlson Comorbidity Index; COPD – Chronic Obstructive Pulmonary Disease; SMA – Skeletal muscle area; VAT – Visceral adipose tissue; SAT – Subcutaneous adipose tissue.

The 88 patients deceased during hospitalization whwrw significantly older than survivors, although gender distribution and overall comorbidity burden, as measured by CCI, were similar between the groups (Table 1). As expected, deceased patients had a higher ISS compared to survivors

(19 [25 – 33] vs. 25 [17 – 33], $p < 0.001$), with the most pronounced differences observed in head and neck injuries. Similarly, the APACHE II score was significantly higher in non-survivors compared to survivors (27 [24-30] vs. 17 [14-21], $P < 0.001$) (Table 1).

Among the laboratory parameters assessed at the ED admission, deceased patients had lower Hb values and higher derangement of coagulation (Table 1), reflecting the possible relationship between acute bleeding and worse outcomes.

3.2. Muscular Quality Assessment

Comparing the muscular and adipose tissue at the level of the 3rd lumbar between the deceased and survivors, the two groups had similar SM, VAT, and SAT areas (Table 1). However, the mean tissue density as expressed by Hounsfield units (HU), was significantly different between the groups. The deceased had lower SMA density (37.9 [32.2 / 45.7] vs. 41.9 [35.9 / 48.1] vs. $p = 0.009$), and higher VAT density (-82.5 [-86.1 / -75.6] vs. -83.9 [-87.9 / -79.5], $p = 0.047$), and SAT density (-82.6 [-87.8 / -77.8] vs. -85.7 [-89.8 / -80.0], $p = 0.029$) (Table 1).

Evaluating these parameters by ROC analysis, SMAd showed the best association with in-hospital death with an AUROC of 0.599, followed by SATd and VATd (AUROC 0.582 and 0.575, respectively) (Table 2). There were no significant differences among the AUROC (SMAd vs SATd z statistic 0.326, $p = 0.744$; SMAd vs. VATd z statistic 0.458, $p = 0.657$; VATd vs SATd z statistic 0.220, $p = 0.825$). According to the Youden index J, the best discriminating values for the prediction of in-hospital death were < 38 HU for SMAd, > 77 HU for VATd, and > 83 HU for SATd. However, these thresholds had limited sensitivity and specificity (Table 2).

Table 2. Receiver Operating Characteristics (ROC) analysis for the association between continuous variables and in-hospital death. The Youden index J was used to find the optimal cut-off value to dichotomize the variable.

	ROC Curve Area	<i>p</i> value	Youden Index Cut-Off Value	Sensitivity [95% CI]	Specificity [95% CI]
Age	0.638 [0.577 – 0.696]	<0.001	> 75	69.3 [58.6 – 78.7]	52.0 [44.3 – 59.6]
ISS	0.649 [0.588 – 0.707]	<0.001	< 24	82.9 [73.4 – 90.1]	42.9 [35.4 – 50.5]
APACHE II	0.939 [0.902 – 0.964]	<0.001	> 22	82.9 [73.4 – 90.1]	86.9 [80.9 – 91.5]
aPTT	0.727 [0.669 – 0.780]	<0.001	> 31.6	64.7 [53.9 – 74.7]	74.8 [67.8 – 81.1]
<i>Muscular CT scan parameter</i>					
SMA Density	0.599 [0.537 – 0.658]	0.038	< 38	52.3 [41.4 – 63.0]	73.1 [65.9 – 79.6]
VAT Density	0.575 [0.513 – 0.635]	0.047	> -77	31.8 [22.3 – 42.6]	82.8 [76.4 – 88.1]
SAT Density	0.582 [0.520 – 0.643]	0.026	> -83	51.4 [40.2 – 61.9]	63.4 [55.8 – 70.6]

Abbreviations: CCI – Charlson Comorbidity Index; ISS – Injury Severity Score; aPTT - activated partial thromboplastin time; APACHE - Acute Physiology and Chronic Health Evaluation; SMA – Skeletal muscle area; VAT – Visceral adipose tissue; SAT – Subcutaneous adipose tissue.

3.3. Multivariate Analysis for Survival

The multivariate Cox regression model revealed that SMAd < 38 HU was an independent risk factor for in-hospital death in our cohort (HR 1.68 [1.02-1.05]) (Supplementary Figure S2). Together with SMAd, independent risk factors for poor outcomes were: ISS > 24 (HR 2.8 an increased aPTT at ED admission (HR 1.04 [1.02-1.05]), a higher injury severity according to ISS (HR 1.02 [1.01-1.04]), and older age (HR 1.04 [1.01-1.08]) (Table 3, Supplementary Figure S2).

Table 3. Multivariate Cox regression analysis of the variables associated with all-cause in-hospital death. To improve model fitting and parameter estimation, the continuous variables were dichotomized by a cut-off chosen by ROC analysis Youden index J.

Variable	Beta	Wald	Odds Ratio [95% CI]	p
Age > 75 years	0.327	1.330	1.39 [0.79 – 2.42]	0.249
ISS > 24	1.054	12.905	2.87 [1.61 – 5.10]	<0.001
APACHE II > 22	2.048	45.426	7.75 [4.27 – 14.07]	<0.001
aPTT > 31.6"	0.579	5.251	1.78 [1.09 – 2.93]	0.022
SMA Density <38 HU	0.519	4.836	1.68 [1.06 – 2.67]	0.028
SAT Density > -83 HU	0.149	0.311	1.16 [0.68 – 1.96]	0.577
VAT Density > -77 HU	0.197	0.466	1.22 [0.69 – 2.14]	0.495

Abbreviations: aPTT – activated Partial Thromboplastin Time; ISS - Injury Severity Score; HU – Hounsfield units; SMA – Skeletal muscle area; VAT – Visceral adipose tissue; SAT – Subcutaneous adipose tissue.

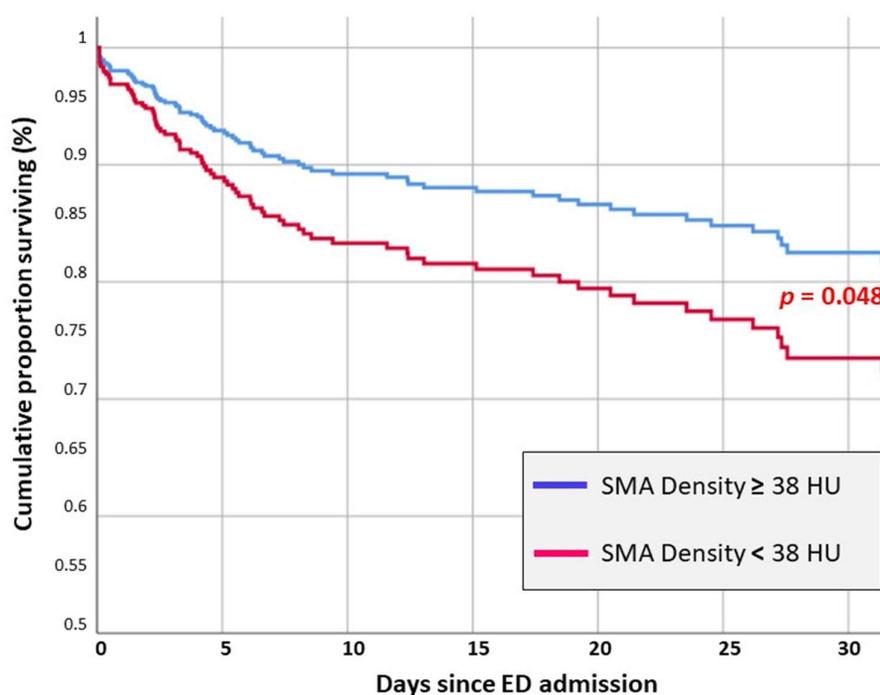


Figure 2. Overall survival.

3.4. Early and Late Mortality Analysis

When considering only the patients deceased within the first week since admission, the Cox regression analysis confirmed APACHE II score >22, ISS >24, and aPTT >31.6" as independent risk factors for in-hospital death. In these patients, muscle quality parameters were not significantly associated with death (Table 4, Figure 1).

Interestingly, when considering only the deaths in patients surviving the first week of hospitalization, only APACHE II >22 and SMAd <38 were associated with in-hospital death (Table 4). In particular, the analysis revealed that patients with SMAd <38 had about a three-fold, increased risk of death during the later phase of the hospitalization (HR 3.12 [1.23 – 7.88]), independent of other clinical factors (Figure 1B).

4. Discussion

The main finding of the present study is that in patients aged ≥ 65 years with major trauma, reduced skeletal muscle density was independently associated with in-hospital mortality, regardless of other clinical characteristics.

Although the role of muscle mass in trauma patients is well established, most studies have focused on the recovery phase, linking higher muscle mass to better outcomes [26]. However, this is mainly due to the known loss of muscle mass during prolonged hospitalization and does not specifically address muscle quality [27].

In a 2021 study by Xi *et al.*, it was reported that in patients who experienced abdominal trauma, poorer skeletal muscle quality was linked to increased length of hospital stay and increased number of complications [28]. Although definitive conclusions cannot be drawn, pre-existing nutritional status is likely to play a contributory role. The importance of nutrition in preserving skeletal muscle is well known [29] and nutritional interventions are now a mainstay in the treatment of elderly patients who are affected by sarcopenia. It could be tempting to suggest that poor skeletal muscle quality is simply a proxy for malnutrition, which is the real determinant for worse clinical outcomes, but, likely, other mechanisms could also play a role [30, 31].

Muscle quality and mass are influenced by systemic inflammation, which impairs regeneration and promotes fat accumulation, further exacerbating inflammation [31–33]. Inflammation also promotes the increase of adipose tissue, which could be in itself a trigger for further inflammation [33]. Both increased adiposity and inflammation have been linked to complications and worse outcomes in trauma patients [30].

Also, it has been speculated that muscle mass could be associated with social and economic factors, which could in turn play a role in the worse outcomes experienced by this group of patients [34,35]. However, our study does not include data to explore or confirm this hypothesis.

An additional interesting finding was the different adipose tissue distribution (both visceral and subcutaneous) in deceased patients (Table 1). Although adipose tissue in the elderly population has been associated with increased inflammation [33], it is important to note that reduced adipose tissue may also result from malnutrition [36]. On the other hand, some authors have reported that contrary to common sense, an increased adipose tissue could be linked to malnutrition and sarcopenia [37]. However, the data derived from our cohort does not give final clues on this point. In our cohort, while the SATd and VATd values were significantly different between survivors and controls (Table 1, 2), the characteristics of the adipose tissue did not prove to be independent risk factors for poor outcomes in the multivariate analysis (Table 3).

Interestingly, our analysis showed that short-term mortality (<7 days) was mostly primarily correlated with trauma severity, advanced age, and coagulation abnormalities (Table 4). Late mortality was higher in the group with poor muscle quality and the difference was higher as the length of hospital stay increases (Supplementary Figure 2). Interestingly, the rate of infectious complications such as pneumonia and sepsis were not significantly different among those who survived and those who did not, suggesting that low muscle quality in itself may have played a key role in increasing mortality. As is well known, sarcopenia increases the risk of experiencing trauma in geriatric patients, which is associated with a significant burden in terms of mortality and morbidity in modern societies [38].

Table 4. Multivariate Cox regression analysis of the variables associated with the risk of in-hospital death (all cause) within (model 1) and after (model 2) seven days since admission.

Model 1 – Factors affecting mortality risk within 7 days since admission				
Variable	Beta	Wald	Hazard Ratio [95% CI]	p
Age > 75	0.632	3.837	1.88 [1.00 – 3.54]	0.050
ISS > 24	1.320	10.186	3.74 [1.66 – 8.41]	0.001
APACHE II > 22	1.528	18.736	4.61 [2.31 – 9.20]	<0.001
aPTT > 31.6''	0.684	5.019	1.98 [1.09 – 3.61]	0.025

SMA Density <38 HU	0.239	0.724	1.27 [0.73 – 2.20]	0.395
SAT Density > -83 HU	-0.047	0.019	0.89 [0.48 – 1.88]	0.891
VAT Density > -77 HU	-0.243	0.408	0.78 [0.37 – 1.65]	0.523

Model 2 – Factors affecting mortality risk starting from 7 days since admission. The cases deceased within days were considered as “censored” in this regression model.

Variable	Beta	Wald	Hazard Ratio [95% CI]	p
Age > 75	0.167	0.162	1.18 [0.52 – 2.66]	0.688
ISS > 24	0.669	2.370	1.95 [0.83 – 4.57]	0.124
APACHE II > 22	3.096	22.637	22.11 [6.18 – 79.15]	<0.001
aPTT > 31.6”	0.064	0.016	1.06 [0.39 – 2.90]	0.900
SMA Density <38 HU	1.137	5.771	3.12 [1.23 – 7.88]	0.016
SAT Density > -83 HU	-0.350	0.386	0.71 [0.23 – 2.12]	0.534
VAT Density > -77 HU	-0.019	0.001	0.98 [0.29 – 3.34]	0.976

Abbreviations: aPTT – Partial Thromboplastin Time; ISS - Injury Severity Score; HU – Hounsfield units; SMA – Skeletal muscle area; VAT – Visceral adipose tissue; SAT – Subcutaneous adipose tissue.

In our cohort, the skeletal muscle quality, and specifically the overall muscle density, was significantly associated with late mortality. While it is somewhat intuitive that patients with higher muscle mass may recover better from trauma than sarcopenic patients, our data revealed that good muscle quality may be an even more important predictor of outcomes than traditionally recognized factors such as comorbidities and advanced age.

As expected, the study also confirmed that the APACHE II score could be a reliable tool for stratifying mortality risk in trauma patients ≥ 65 years [39]. Predictably, both the type and severity of trauma were linked to mortality. In particular, higher ISS values and elevated AIS scores for the head and neck were significantly associated with worse outcomes [40, 41]. Lastly, the factors associated with acute bleeding such as lower Hb and mainly an increased aPTT, showed a high correlation with in-hospital mortality in our cohort, particularly for the early mortality (Table 3, 4). Indeed, although rapid control of bleeding and coagulation are currently the mainstay of trauma resuscitation, the overall mortality among bleeding trauma patients is still high [42]. Moreover, the mortality of these patients could be not limited to the very short term due to exsanguination, but can also occur later in the clinical course [42-45]. On the other hand, it is worth noting that in older adults the use of anticoagulants is more common than in the general population and is associated with increased bleeding risk, overall increased mortality, and the need for a post-hospital care facility [46].

Comorbidities burden is usually considered one of the main determinants of worse outcomes in trauma patients, particularly for older adults. As reported in a study by *Gioffrè-Florio et al.* [38], comorbidities such as osteoporosis are linked to worse outcomes in patients who experience a fall. At the same time, other authors have even designed specific comorbidity indexes for trauma patients [47]. In our population, we observed that Chronic Kidney Disease (CKD) was the only comorbidity associated with an increase in mortality, but the overall number of comorbidities, evaluated through the CCI, was not significantly higher. This latter finding, which is not consistent with the literature, could be due to the specific older population, and to the different methods to assess comorbidity in different studies [48]. Interestingly, in our sample patients who experienced higher mortality showed lower levels of hemoglobin. Anemia has been known to be associated with higher mortality in elderly trauma patients and has been linked to a higher prevalence of CKD, which could be consistent with our population [49]. At the same time, CKD is linked to sarcopenia, and its development in patients with CKD is multifactorial and it may occur independently of weight loss or cachexia [50].

5. Limitations

Our study presented some limitations, particularly due to its retrospective design, which does not allow us to draw any definite conclusions on the causal link between skeletal muscle quality and prognosis. At the same time, although we found an association, the mechanisms underlying it are

not clear and were not investigated in the present study. Finally, while the overall severity of trauma and multiple clinical parameters were taken into consideration, still several potential confounders could not be addressed in the present analysis. In particular, key variables related to the patient's inflammatory status and nutritional condition—which may significantly influence both muscle quality and clinical outcomes—were not available in the dataset and could not be assessed.

6. Conclusions

Our study demonstrated that in patients ≥ 65 years admitted to the ED for major trauma, muscle quality assesment by CT scan at admission could serve as an effective tool for prognostic risk stratification.

Moreover, our study highlights that the prognosis is influenced not merely by muscle mass, but more importantly by muscle quality, as assessed by average muscle density on a CT scan. This is particularly relevant since muscle quality is strongly linked to nutritional status, possibly highlighting the importance of nutritional status in elderly patients.

Overall, reduced skeletal muscle quality (SMAd <38 HU) was demonstrated to be an independent risk factor for in-hospital mortality in older adults, particularly in the late phase of the clinical course.

Author Contributions: MC and LC conceived and designed the study. GP, MC, and LLR extracted and interpreted the radiological images, MP, AP, and GT performed the data collection, MC, AP, and GDM drafted and reviewed the manuscript, MC, MP, and CS analyzed and interpreted the results, MCM, AG, and FF supervised the project and guarantee for the data integrity.

Funding: This research received no external funding.

Institutional Review Board Statement: The research was approved by the local IRB of Fondazione Policlinico Universitario Gemelli, IRCCS, Rome (Protocol 5121 - IRB #0025817/22 – on March 8, 2022), and conducted according to the principles expressed in the Declaration of Helsinki and its later amendments (Tokio 2004). Due to the retrospective and anonymized design, the patient consent was waived.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Data will be available upon reasonable request from the corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

ED	Emergency Department
CT	Computed Tomography
ISS	Injury Severity Score
AIS	Acute Injury Scale
CCI	Charson Comorbidity Index
LOS	Length of Stay
SMA	Skeletal Muscle Area
SAT	Subcutaneous Adipose tissue
VAT	Visceral Adipose tissue
HU	Hounsfield Units
SMAd	Skeletal Muscle Area Density
VATd	Visceral Muscle Area Density
IQR	Interquartile Range
ROC	Receiver Operating Characteristic
CKD	Chronic Kidney Disease

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