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Original article

Validation of the sarcopenia index to assess muscle mass in the critically ill: A novel application of kidney function markers

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SUMMARY

Background & aims: Adverse outcomes for hospitalized patients with sarcopenia are well documented, and identification of patients at risk remains challenging. The sarcopenia index (SI), previously defined as (serum creatinine/serum cystatin C) × 100, could be an inexpensive, readily accessible, objective tool to predict muscle mass and risk for adverse clinical outcomes. The aim of this study was to assess the validity of the SI as a predictor of muscle mass.

Methods: Retrospective study of critically ill adults admitted to Mayo Clinic from 2012 to 2015 with suspected sepsis and an available creatinine and serum cystatin C. Muscle surface area was quantified at the L3/4 vertebral level in patients with an abdominal CT scan (CTMSA). Multivariable regression modeling was used to assess the relationship between SI and CTMSA, as well as short-term clinical outcomes.

Results: The 171 included had a mean weight and body mass index (BMI) of 75.2 ± 16.4 kg and 26.0 ± 4.6 kg/m^2 and abdominal CT scans were available for 81 (47%) patients. The SI correlated with CTMSA (r = 0.40). After adjustment for age, sex, severity of illness, and BMI, SI was independently associated with muscle mass (P = 0.001). A decrease in the SI (indicative of lower muscle mass) was also associated with frailty and worse short-term clinical outcomes.

Conclusion: The SI, a simple calculation from kidney function markers, is a significant predictor of muscle mass in this validation cohort of ICU patients. A low SI was associated with longer hospital length of stay and frailty. Future studies could explore whether the use of SI assists with identifying patients likely to benefit from pharmacotherapy-, nutrition-, or physical therapy-based interventions.

1. Introduction

Sarcopenia is characterized by the loss of muscle mass, strength, and function. Historically, assessment and understanding of sarcopenia were restricted to elderly patients, but recently, more attention has been paid to the prevalence of the disease in patients with chronic comorbid conditions, inflammatory diseases, and critical illness. Prevalence estimates indicate that among patients in the intensive care unit (ICU), sarcopenia may affect up to 60–70% of

Abbreviations: ICU, intensive care unit; CT, computed tomography; DXA, dual-energy x-ray absorptiometry; SI, sarcopenia index; GFR, glomerular filtration rate; AKI, acute kidney injury; BMI, body mass index; BSA, body surface area; APACHE III, acute physiology and chronic health evaluation score; SOFA, sequential organ failure assessment score; ADL, Activities of daily living; CTMSA, CT muscle surface area; SD, standard deviation; IQR, Interquartile range; SMI, skeletal muscle index; HR, Hazard ratio; CI, confidence interval.

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patients [1–3]. In studies of critically ill, mortality rates are 2–4-fold higher among patients with sarcopenia compared to those without, and duration of mechanical ventilation, hospitalization, and resource utilization are higher [1,3].

No single consistent definition for sarcopenia exists in the literature. Several societies and working groups have proposed definitions based on muscle mass and function [4,5]. Information about compromised functional status and muscle strength based on hand grip or gait speed, for example, is often not available in retrospective documentation and even so strength has often been dissociated from muscle mass itself. Muscle mass may be quantified from various imaging techniques [e.g., computed tomography (CT), bioelectrical impedance analysis, dual-energy x-ray absorptiometry (DXA); see also Supplemental Table S1], but using these methods routinely for this purpose is both resource-intensive and impractical for unstable patients. More repeatable, accessible, and inexpensive approaches are necessary to identify sarcopenic critically ill patients.

Kashani and colleagues proposed the sarcopenia index (SI) as a simplified approach to identify patients with reduced muscle mass at risk for poor clinical outcomes [6]. The SI exploits the unique cellular origins of two different markers of glomerular filtration rate (GFR). Creatinine is an endogenous GFR marker whose serum concentration reflects the terminal aspect of muscle catabolism. It is passively eliminated via glomerular filtration, and to a significantly lesser degree, it is actively eliminated via tubular secretion. Cystatin C is an endogenous low molecular weight protein derived from all nucleated cells. It too undergoes glomerular filtration but is neither reabsorbed into systemic circulation nor actively secreted [7]. Among patients with stable renal function, one of the primary determinants of the difference between these two markers is a patient's skeletal muscle mass. The authors demonstrated that in a single sample of 226 critically ill patients the SI was a simple tool that exhibited a good relationship with muscle mass and patient outcomes. To our knowledge, this relationship has not been independently validated in another cohort of ICU patients. Particularly in patients with heightened states of inflammation, as with infections and sepsis, the prevalence of sarcopenia may be higher, and the predictive performance of the SI may differ.

This study aimed to determine whether, in critically ill patients with suspected or documented infections, the SI is a valid marker of muscle mass as defined by the criterion standard of skeletal muscle surface area on abdominal CT scans. In critically ill patients, low skeletal muscle surface area on abdominal CT has been independently associated with relevant clinical outcomes including fewer ventilator-free and ICU-free days and mortality [1].

2. Materials and methods

2.1. Setting and participants

This retrospective study evaluated the SI as a predictor of skeletal muscle mass and outcomes in adults ≥18 years of age admitted to one of three ICUs at Mayo Clinic Hospital, Rochester, MN between March 2012 and May 2015. Data used for this analysis was derived from a prospectively collected cohort of 171 critically ill adults with suspected or documented infections who had both serum creatinine and cystatin C concentrations drawn within the same day [8,9]. Patients excluded from this cohort were individuals with unstable renal function [e.g. evolving or recovering acute kidney injury (AKI), need for renal replacement therapy], a body mass index (BMI) > 40 mg/m^2, a weight < 40 kg or who did not authorize their medical record for review in the state of MN. The Mayo Clinic Institutional Review Board approved the protocol and the requirement for informed consent was waived. Procedures followed were in accordance with the ethical standards of the responsible institutional or regional committee on human experimentation or in accordance with the Helsinki Declaration of 1975 as revised in 1983.

2.2. Measures

Data extracted from the electronic health record included age, sex, race, height, admission weight, body surface area (BSA), BMI, and severity of illness [acute physiology and chronic health evaluation (APACHE III) score, sequential organ failure assessment (SOFA) score within 24-hours of ICU admission]. Data was also gathered on the activities of daily living (ADLs) documented in the 30-days before and up to one year after the SI for the purpose of computing the Frailty Deficit Index, a measure of frailty using the cumulative deficit model developed by Rockwood and colleagues [10]. As previously described, this 32-item instrument tabulates the presence of deficits in 14 ADLs and 18 comorbid conditions to generate a score from 0 (no deficits) to 32 (32/32 deficits) [11,12]. That score is divided by the total items evaluated (e.g. 32) and individuals with a score of 0.25 or greater are considered frail [10]. Patients who were missing more than one measure were excluded from Frailty Deficit Index calculation. In patients with one missing data point scores were calculated using 31 as the denominator.

Creatinine (mg/dL) measurement was assayed using the standardized (isotope dilution mass spectrometry traceable) enzymatic creatinine assay (Roche, Basel, Switzerland). Cystatin C (mg/L) was measured with a particle-enhanced turbidimetric assay (Gentian AS, Moss, Norway). This assay is traceable to the same international certified cystatin C reference material (ERM-DA471/IFCC) used to develop the cystatin C-based CKD-EPI equations. The SI was calculated as [(serum creatinine/serum cystatin C)×100] wherein a low index would indicate that the patient has less skeletal muscle available for serum creatinine production (relatively low numerator) and thus, relative to cystatin C, this would indicate low muscle mass and potentially sarcopenia [6].

Patients were screened for the presence of an abdominal CT scan within 28-days of the creatinine and cystatin C concentrations. The area of abdominal visceral and subcutaneous fat at the L3/4 vertebral level was then measured by a trained study investigator (H.C.) with a validated in-house software program (BodyCompSlicer; [13]). Once the CT image was loaded, the software automatically calculated and placed two boundary lines between subcutaneous fat and abdominal wall/paraspinal muscles and between abdominal wall/paraspinal muscles and visceral fat (Supplemental Fig. S1). The reviewer carefully inspected the boundaries, and manually corrected the boundaries using the mouse–computer interface as necessary. When the correction of boundaries was complete, the software calculated the skeletal muscle area (cm^2) as area containing pixels between two boundaries, and having CT attenuation value of −30 to 150 HU, but excluding the spine and spinal canal. The software automatically created a mask for spine, which was used to exclude spine and spinal canal from being included as muscle (Fig. S1). The area could then be divided by the patient's height (in meters^2) to calculate the corresponding index. This method of using a trained study investigator has previously shown excellent correlation with assessments conducted by a radiology expert [6].

2.3. Data analysis

Continuous data were summarized by using mean ± standard deviation (SD) or median with interquartile range (IQR) depending on distribution. Rank-sum tests and Pearson's chi-square tests were used to compare baseline characteristics between those with and

without a CT scan. For the primary outcome of relationship between the SI and the CT muscle surface area (CTMSA), the Pearson correlation coefficient was used. A linear regression model was fit to determine the independent association between the SI and CTMSA after adjustment for confounders. We also used logistic regression to evaluate CTMSA as a dichotomous endpoint using the sex-adjusted L3 skeletal muscle index (SMI) cut-offs of 43 and 41 cm^2/m^2 for men and women, respectively, when the BMI was <25 kg/m^2 and 53 and 41 cm^2/m^2, respectively, when the BMI was ≥25 kg/m^2 as proposed by Martin [14]. For secondary endpoints of liberation from mechanical ventilation, ICU and hospital discharge, and 28-day and 90-day mortality, Cox-proportional hazards models were used. Results were reported as hazard ratios (HR) with 95% confidence intervals (CI). ICU and hospital length of stay summaries were computed using Kaplan–Meier estimation accounting for the competing risk of death during the stay. A two-sided alpha of 0.05 was considered statistically significant and all analyses were performed with SAS 9.4 and JMP 13.0 software (SAS Institute, Cary, NC).

3. Results

Of the 171 available patients with both a serum creatinine and cystatin C concentration, 87 (51%) had abdominal CT scans within 4 weeks, of which 6 were unable to be reviewed due to image quality. Included patients were 61% male, 97% Caucasian, 82% had sepsis, and the mean ± SD weight and BMI were 75 ± 16 kg and 26 ± 5 kg/m^2, respectively. Cystatin C concentrations were slightly higher in patients with CT scans compared to those without (1.1 ± 0.5 mg/L vs 1.0 ± 0.4 mg/L; P = 0.04). The mean SI was lower in the 81 patients with CT scans (77 ± 25 vs 90 ± 27; P = 0.002). Baseline characteristics were otherwise similar between patients with and without CT scans (Table 1). The median (IQR) time from ICU admission and SI to abdominal CT scan was 1.0 (0.0, 5.0) day and 0.0 (−2.0, 2.0) days, respectively.

3.1. Prediction of muscle mass based on CTMSA

In the 81 patients with CTs, the SI correlated with L3 CTMSA ($r = 0.40$; Fig. 1). In a sensitivity analysis of individuals with a CT scan within 2 days before or after the SI measure (N = 38) the correlation was weaker ($r = 0.21$). Multivariable models which included age, sex, BMI, APACHE III, and, SOFA scores, indicated an independent association between SI and CTMSA (P = 0.001). This model better predicted CTMSA than a similar such model which included serum creatinine adjusted for the same covariates

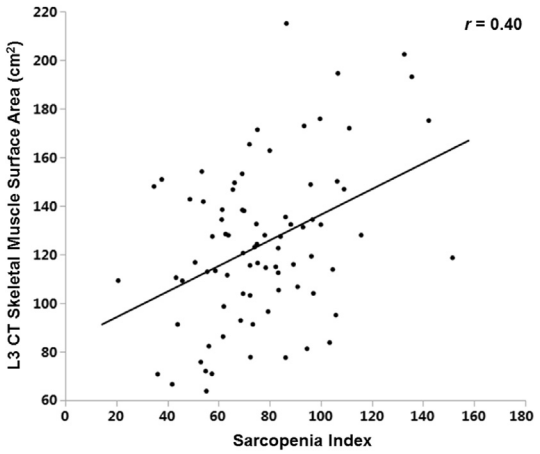

Fig. 1. Correlation between sarcopenia index and skeletal muscle surface area at the L3 level in the 81 patients with an available abdominal CT scan ($r = 0.40$).

Table 1
Baseline patient characteristics and demographic data.

Characteristic	All patients (N = 171)[a]	CT scan[a] (N = 81)	No CT scan[a] (N = 90)	P Value
Age (years)	63.4 ± 16.3	63.8 ± 16.5	63.1 ± 16.3	0.97
Age ≥ 65 years (N; %)	90 (53)	41 (51)	49 (54)	0.62
Male (N; %)	105 (61)	54 (67)	51 (57)	0.18
Caucasian (N; %)[b]	163 (97)	78 (99)	85 (96)	0.22
Weight (kg)	75.2 ± 16.4	76.5 ± 15.8	74.1 ± 16.9	0.31
Body mass index (kg/m^2)	26.0 ± 4.6	26.2 ± 4.8	25.8 ± 4.4	0.63
Body surface area (m^2)	1.86 ± 0.23	1.88 ± 0.21	1.84 ± 0.25	0.26
APACHE III score	65 ± 20	68 ± 21	62 ± 18	0.07
SOFA score	4.8 ± 3.2	5.1 ± 3.5	4.6 ± 2.9	0.54
Charlson Comorbidity Index	5.8 ± 3.8	6.1 ± 3.9	5.5 ± 3.7	0.39
Sepsis (N; %)	141 (82)	66 (81)	75 (83)	0.75
Septic shock (N; %)	35 (20)	20 (25)	15 (17)	0.19
Invasive mechanical ventilation (N; %)	89 (52)	45 (56)	44 (49)	0.38
Renal parameters				
Serum creatinine (mg/dL)	0.9 ± 0.3	0.8 ± 0.3	0.9 ± 0.4	0.68
Cystatin C (mg/L)	1.1 ± 0.4	1.1 ± 0.5	1.0 ± 0.4	0.04
Cockcroft-Gault (mL/min)	99 ± 45	103 ± 47	95 ± 43	0.21
CKD $EPI_{cr-cysC}$ eGFR (mL/min/1.73 m^2)	82 ± 27	81 ± 27	84 ± 27	0.28
Sarcopenia Index	84 ± 27	77 ± 25	90 ± 27	0.002
CT Results				
Skeletal muscle surface area, cm^2	–	124 ± 33	–	–
Skeletal muscle index (SMI), cm^2/m^2[c]	–	42.4 ± 9.8	–	–
Low sex-adjusted SMI (N; %)[d]	–	57 (70)	–	–
Abdominal wall adipose SA, cm^2	–	159 ± 93	–	–
Abdominal visceral adipose SA, cm^2	–	139 ± 99	–	–
Total abdominal SA, cm^2		752 ± 191	–	–

APACHE: Acute Physiology and Chronic Health Evaluation score; SOFA: Sequential Organ Failure Assessment score; CKD-EPI: Chronic Kidney Disease Epidemiology Collaborative; SA: Surface area.

[a] Values expressed as mean ± SD unless noted.

[b] The races of three patients were unknown.

[c] Calculated as (Skeletal muscle surface area in cm^2/height in m^2).

[d] Low sex-adjusted skeletal muscle index calculated as being less than 43 and 41 cm^2/m^2 for men and women, respectively, when the BMI was <25 kg/m^2 and being less than 53 and 41 cm^2/m^2, respectively, when the BMI was ≥25 kg/m^2.

($R^2 = 0.55$ vs $R^2 = 0.48$, respectively; Table 2). Results for the L4 CTMSA were consistent with the L3 findings (SI: $r = 0.36$; creatinine: $r = 0.16$, BMI: $r = 0.31$; R^2 for SI model adjusted for covariates = 0.55, SI P = 0.02).

Fifty seven (70%) patients had a low sex-adjusted SMI. For each 10-unit decrease in the SI, the odds of a low SMI on CT scan increased 1.3-fold (95% CI 1.0, 1.6; P = 0.02) in univariate models. The SI cut offs of 116, 100, 80, 59, and 21 corresponded to a 50%, 60%, 70%, 80%, and 90% probability of low SMI, respectively. An SI cut-off of 106 predicts a low SMI with the greatest sum of the sensitivity and specificity. High sensitivity and high specificity cut-offs (>90%) for SI were 98 and 53, respectively. After adjustment for age, sex, APACHE III score, SOFA score, and BMI, the SI remained independently predictive of low SMI [OR per 10-unit decrease in SI 1.4 (95% CI 1.1, 1.8); P = 0.009].

3.2. Muscle mass and short-term clinical outcomes

Secondary analyses were conducted to explore the relationship between the SI and muscle mass and short-term ICU outcomes. Eighty-nine (52%) patients required endotracheal intubation during the index ICU admission for which the median (IQR) duration of mechanical ventilation was 2.9 (0.7, 6.2) days. Median (IQR) ICU and hospital lengths of stay were 3 (2, 10) days and 15 (8, 36) days, respectively. By 28-days after ICU admission, 32 (19%) patients had died. At day 90, the incidence of mortality was 29%. In the subgroup with CT scans, the incidence of mortality at 28- and 90-days was comparable (16% and 27%, respectively).

In univariate analyses an increase in the SI (indicative of higher muscle mass) significantly predicted ventilator liberation, more rapid discharge from the ICU and hospital, and a lower 90-day mortality. After adjustment for age, sex, severity of illness, and BMI, an SI increase was significantly associated with a shorter length of hospital stay (P = 0.007) (Table 3). In the 81 patients with CT scans, a decrease in SI, CTMSA, and a low SMI were associated with a greater risk of death at 90-days (Table S2). Ninety of the 171 patients had sufficient data within 30 days before or 1 year after the SI to calculate the Frailty Deficit Index [median time between ADL documentation and SI 2.7 (−2.4, 77.7) days]. Overall, 47 (52%) patients were frail and SI was inversely correlated with the frailty score ($r = 0.25$; a higher or "better" SI corresponded to lower or "better" frailty score). The mean ± SD SI was significantly lower in frail patients (79 ± 26 vs 96 ± 27; P = 0.002). In a sensitivity analysis of the 48 patients with ADLs documented within 30-days before SI to no more than 3-days after, indicative of prevalent frailty at the time of the SI, the correlation was strengthened ($r = 0.39$; mean ± SD SI for frail vs not-frail patients 76 ± 23 vs 94 ± 24; P = 0.01).

4. Discussion

In this cohort of 171 critically ill patients with suspected or documented infections, we validated the relationship between the SI and muscle mass as defined by CTMSA. In analyses adjusted for age, sex, severity of illness, and BMI, the SI independently predicted the CTMSA. A low sex-adjusted SMI has previously shown to be an indicator of sarcopenia [14,15]. Per 10-unit decrease in the SI, the odds of a low SMI increased 1.4-fold after adjustment for relevant covariates. A decrease in the SI (indicates lower muscle mass) was also associated with frailty and worse short-term clinical outcomes.

The serum creatinine concentration, the typical bedside assessment tool for trending renal function, is affected by both creatinine production and elimination. Creatinine generation is predominately the product of phosphocreatine metabolism in skeletal muscle and is proportional to muscle mass. In contrast, cystatin C, a low molecular protein in the cystatin superfamily of cysteine protease inhibitors, is produced at a constant rate by all nucleated cells and is passively eliminated via glomerular filtration [16]. Thus among patients with stable renal function, the primary difference between these two markers reflects skeletal muscle mass.

The ratio between creatinine and cystatin C, referred to in this study as the SI, has been explored in stable patients with visceral solid organ transplantation [17,18], amyotrophic lateral sclerosis (ALS) [19], and lung cancer [20]. Among patients with ALS, the SI was significantly lower than among healthy controls and was inversely proportional to disease severity [19]. In 25 patients treated for lung cancers, a low SI was proposed as a screening tool to identify patients with low muscle mass at risk for chemotherapy-toxicity with standard dosing [20]. Although in these studies, the SI was not compared to a criterion standard for muscle mass, the findings are consistent with those by Kim et al. in ambulatory patients with DXA scans who found a strong relationship between a model of weight, creatinine, and cystatin C and measured total body muscle mass (adjusted $R^2 = 0.86$) [21].

Kashani et al. previously extended this work to critically ill patients and demonstrated a strong relationship between SI and muscle mass based on abdominal CT in a single cohort of 226 patients. Sarcopenia is particularly pervasive and devastating in the acutely ill and associated higher mortality, fewer ventilator free days, and longer lengths of stay [1–3]. Recently, in a rigorous multicenter study of 588 acutely ill elderly patients, sarcopenia, defined by low SMI and reduced handgrip strength/walking speed, was associated with a 1.7-fold higher risk for delirium [22]. Our findings independently validate the relationship between the SI and both CTMSA and SMI. We demonstrate the potential role for this inexpensive, minimally invasive approach to identify patients at high risk for adverse outcomes. SI could be used to predict

Table 2
Multivariable linear regression models for CTMSA in patients with CT scans (N = 81).

	Model with SI		Model with Creatinine		Model with BMI	
Model fit (R^2)	0.55		0.48		0.48	
Variable	Estimate (95% CI)	P-Value	Estimate (95% CI)	P-Value	Estimate (95% CI)	P-Value
Age (years)	−0.6 (−0.9, −0.2)	0.003	−0.7 (−1.1, −0.3)	0.002	−0.7 (−1.1, −0.3)	0.001
Male	30.9 (19.6, 42.2)	<0.001	36.3 (23.9, 48.7)	<0.001	36.0 (24.5, 47.6)	<0.001
APACHE III	0.3 (−0.05, 0.6)	0.09	0.2 (−0.2, 0.6)	0.26	0.2 (−0.2, 0.6)	0.25
SOFA	−0.9 (−2.9, 1.1)	0.36	−1.2 (−3.3, 1.0)	0.29	−1.2 (−3.3, 1.0)	0.28
SI (per 10-unit)[a]	3.7 (1.5, 6.0)	0.001	–	–	–	–
Creatinine (mg/dL)	–	–	−1.2 (−22.3, 19.9)	0.91	–	–
BMI (kg/m^2)	2.8 (1.7, 3.8)	<0.001	2.8 (1.6, 4.0)	<0.001	2.8 (1.7, 3.9)	<0.001

SI: Sarcopenia index; BMI: Body mass index; APACHE: Acute Physiology and Chronic Health Evaluation score; SOFA: Sequential Organ Failure Assessment score.
[a] When BMI was removed from the SI model, the R^2 decreased to 0.39 and the estimate (95% CI) and p-values for a 10-unit increase in SI were 3.9 (1.3, 6.4), P = 0.004, respectively.

Table 3
Association between SI (per 10-unit increase) and clinical outcomes in all included patients (N = 171).

Outcome	Unadjusted		Adjusted[a]	
	HR (95% CI)	P-value	HR (95% CI)	P-Value
Ventilator liberation[b]	1.13 (1.03, 1.24)	0.008	1.07 (0.97, 1.19)	0.18
Hospital discharge	1.13 (1.06, 1.20)	<0.001	1.10 (1.03, 1.18)	0.007
ICU discharge	1.10 (1.03, 1.17)	0.003	1.06 (0.99, 1.14)	0.09
28-day all-cause mortality	0.90 (0.78, 1.03)	0.13	0.90 (0.77, 1.06)	0.20
90-day all-cause mortality	0.86 (0.77, 0.97)	0.01	0.90 (0.80, 1.02)	0.11

SI: Sarcopenia index; HR (95% CI): Hazard ratio and 95% confidence interval; ICU: Intensive care unit.
[a] Adjusted for age, sex, APACHE III score, SOFA score, BMI.
[b] Reflects N = 89 patients that underwent invasive mechanical ventilation were included in this analysis.

patients who could benefit from pharmacotherapy-, nutrition- or physical-therapy based interventions either during their ICU stay or upon recovery.

The relationship between the SI and clinical outcomes is less clear. Kashani et al. found a signal between SI and both mortality and duration of mechanical ventilation, but in adjusted analyses the SI did not significantly improve upon existing clinical models [6]. We demonstrated that a higher SI (indicative of higher muscle mass) predicted ventilator liberation, more rapid discharge from the ICU and hospital, and a lower 90-day mortality. In analyses adjusted for age, sex, and severity of illness the only statistically significant association that remained was between the SI and more rapid hospital discharge. The frailty score was inversely correlated with the SI, where a higher or "better" SI corresponded to lower or "better" frailty score. Further study is necessary to understand the association between SI and both objective and patient-reported clinical outcomes.

This study has several limitations. The definitions for sarcopenia vary widely in the literature, but in general, sarcopenia reflects both a reduction in muscle mass and compromised functional status [4]. Little data was available in the electronic health record documentation to characterize the functional aspect of sarcopenia. Previously cystatin C-based estimated GFR, rather than creatinine-based approaches to estimating renal function predicted a 2.4-fold higher risk of reduced muscle strength based on handgrip in ambulatory men 60-years or older [23]. However, this study focused on single-biomarker GFR estimates rather than the ratio of the two biomarkers, the latter of which at steady state reflects the difference in biomarker production rather than elimination. We previously demonstrated that the SI, as defined by the creatinine/cystatin C ratio, exhibits superior performance for muscle mass compared to similar such ratios based on GFR estimates [6]. We also conducted secondary analyses of the relationship between the SI and the Frailty Deficit Index which includes items which assess ability to complete 14 ADLs. Retrospective documentation of ADLs was not available for all patients at consistent time-points so these findings should be considered hypothesis-generating. In the literature, a distinction has been made between "primary sarcopenia," attributed to aging, and "secondary sarcopenia," which is instead a function of disease, inflammation, disuse, or malnutrition. As this was a study of critically ill patients with infections and inflammation, of which 53% were elderly, we are unable to distinguish between these two etiologies. Finally, fluid shifts in critically ill patients may contribute to edema in the intramuscular compartment which we are unable to completely account for in this study. This semi-automated measurement technique used in this study involves manual correction based on anatomic region, thus the effect of subcutaneous edema or ascites was minimized.

5. Conclusion

The SI, a simple calculation from widely available kidney function markers, exhibits a strong relationship with muscle mass in this validation cohort of critically ill patients. Future studies could explore whether the use of SI assists with identifying patients most likely to benefit from supportive care or targeted interventions both during their inpatient stay and at discharge.

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Statement of authorship

EB and KK had full access to all of the data in the study and take primary responsibility for the final content. Design and conduct of the research: EB, JP, HC, CK, OG, EN, NT, KK designed the study. Data collection: EB, HC, MM gathered data on included subjects. Statistical analysis: EB, RD and KK performed the statistical analysis which was reviewed by NT, CK, and OG. Interpretation: All authors reviewed the data and participated in discussions related to interpretation. Wrote paper: EB and KK drafted the manuscript. All authors reviewed and edited the manuscript and have seen and approved the final draft.

Conflict of interest

The authors report no relevant conflicts of interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.clnu.2018.05.031.

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