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Can Sarcopenia Quantified by Ultrasound of the Rectus Femoris Muscle Predict Adverse Outcome of Surgical Intensive Care Unit Patients and Frailty? A Prospective, Observational Cohort Study

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Abstract

Objective—To compare sarcopenia and frailty for outcome prediction in surgical intensive care unit (SICU) patients.

Background—Frailty has been associated with adverse outcomes and describes a status of muscle weakness and decreased physiological reserve leading to increased vulnerability to stressors. However, frailty assessment depends on patient cooperation. Sarcopenia can be quantified by ultrasound and the predictive value of sarcopenia at SICU admission for adverse outcome has not been defined.

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Methods—We conducted a prospective, observational study of SICU patients. Sarcopenia was diagnosed by ultrasound measurement of rectus femoris cross-sectional area. Frailty was diagnosed by the Frailty Index Questionnaire based on 50 variables. Relationship between variables and outcomes was assessed by multivariable regression analysis NCT02270502.

Results—Sarcopenia and frailty were quantified in 102 patients and observed in 43.1% and 38.2%, respectively. Sarcopenia predicted adverse discharge disposition (discharge to nursing facility or in-hospital mortality, odds ratio 7.49; 95% confidence interval 1.47–38.24; $P = 0.015$) independent of important clinical covariates, as did frailty (odds ratio 8.01; 95% confidence interval 1.82–35.27; $P = 0.006$); predictive ability did not differ between sarcopenia and frailty prediction model, reflected by a likelihood ratio of $\chi^2 = 21.74$ versus 23.44, respectively, and a net reclassification improvement (NRI) of -0.02 ($P = 0.87$). Sarcopenia and frailty predicted hospital length of stay and the frailty model had a moderately better predictive accuracy for this outcome.

Conclusions—Bedside diagnosis of sarcopenia by ultrasound predicts adverse discharge disposition in SICU patients equally well as frailty. Sarcopenia assessed by ultrasound may be utilized as rapid bedside modality for risk stratification of critically ill patients.

Keywords

frailty; risk prediction; sarcopenia; surgical intensive care unit; ultrasound

High value in healthcare can be characterized as desirable health outcomes accomplished at decreased dollars spent.¹ Critical care services cost continue to increase rapidly, rising to \$81.7 billion in 2005 from \$56.6 billion in 2000, which represents 0.7% of the US Gross Domestic Product.^{2,3}

The availability of reliable outcome predictors of surgical critically ill patients may help improve the value of care. Providing information on expected length of hospitalization, and risk for functional dependence at discharge and mortality may help patients and relatives make informed decisions about their goals of care.⁴ Prehospital functional status or physiological capacity is not typically included in instruments we use to predict outcomes in critically ill patients.^{4,5}

Frailty is the status of decreased physical and cognitive reserve leading to increased vulnerability to stressors.⁶ The frail phenotype is characterized by changes in mobility, muscle mass, nutritional status, strength, and endurance.⁷ Although strongly correlated with age,⁸ frailty is not an inevitable part of aging.⁶ Within the geriatric population, frailty occurs with a prevalence of up to 43%⁹ and has been shown to predict discharge to institutional care, mortality, and hospital length of stay (LOS).^{10,11}

Although it is intuitive to conclude that frail patients are predisposed to adverse outcomes in the surgical intensive care unit (SICU), supporting data are sparse.¹² There is a paucity of objective, point of care testing to identify those patients in the SICU who are frail. Current measures of frailty have not been well suited for decisions involving the acute risk and rationale for surgical intervention. The frailty index (FI) quantifies the accumulation of physiologic deficits.¹³ Assessment of the FI is time consuming and requires adequate communication with the patient to obtain the self-reported measure.¹² Sarcopenia (low

skeletal muscle mass) is a key element of frailty,¹⁴ which translates to higher healthcare utilization and mortality.¹⁵ Computed tomography (CT)-based measurements of the psoas and temporalis muscles have been shown to correlate with patient outcomes.^{16,17} However, not all patients in the SICU have or are eligible for CT scans of these anatomic locations during their hospitalization.

Our aim was to evaluate whether simple noninvasive assessment of sarcopenia by ultrasound, which does not rely on patient cooperation, may be a viable bedside tool to predict outcomes among critically ill surgical patients. Our research hypothesis was that sarcopenia and frailty both comparably well predict adverse discharge disposition and duration of hospitalization of SICU patients.

METHODS

Study Population and Setting

The study was approved by the Institutional Review Board of Partners Healthcare (Protocol#2014P000249). Written informed consent was obtained from all patients before study participation. Admissions were screened daily to identify patients (older than 18 years) who were expected to stay in the SICU for at least 24 hours. Patients transferred from a skilled nursing facility were excluded from the study, as were patients with preexisting paralysis (Fig. 1). The study was performed in 2 SICUs at a large academic medical center between June 12 and October 29, 2014.

Study Protocol

Consecutive critically ill patients were approached within 72 hours of SICU admission for enrollment in the study. Ultrasound images of rectus femoris (RF) muscle were obtained for each patient on enrollment day. Patients were deemed ready to file the FI questionnaire if they were alert and calm Richmond Agitation-Sedation Scale¹⁸ score between -1 and +1), not delirious [negative Confusion Assessment Method intensive care unit (ICU)]¹⁹ and proved capacity to follow 2-step instructions. In patients who did not meet these criteria, information on their preadmission conditions was obtained from proxies. Muscle strength was assessed by manual muscle testing once patient's arousal and capacity to follow commands were sufficient.²⁰

Data Collection

On SICU admission, patients' characteristics [age, sex, race, ethnicity, height, weight, admission diagnoses, Charlson comorbidity index (CCI),²¹ number of prescription medications²²] were noted. Admission laboratory data (creatinine, hemoglobin, sodium level, international normalized ratio, and pH), vital signs [systolic blood pressure, heart rate, body temperature, and Glasgow Coma Scale (GCS)] were recorded as well as illness severity [Acute Physiology Chronic Health Evaluation (APACHE) II score]⁵ and severity of organ dysfunction [Sequential Organ Failure Assessment (SOFA) score].⁴ SOFA scores were obtained on SICU admission and on the third SICU day. At the time of discharge from hospital, following variables were collected: duration of mechanical ventilation, requirement for vasopressor support, blood transfusions, and renal replacement therapy. Baseline

nutritional status was assessed using the variables described in the Short Nutritional Assessment (unintentional weight loss, decrease in appetite, and supplemental drinks or tube feeding).²³ With an exploratory intention, we analyzed hospital costs incurring from admission until hospital discharge using the internal cost-accounting database at the study's institution as a function of sarcopenia.

Muscle Ultrasound

Rectus femoris cross-sectional area (RF_{CSA}) was measured by B-mode ultrasonography using a 3 to 12 MHz transducer array (Philips Ultrasound, Bothell, WA) as previously described.^{24,25} All measurements were made by a single investigator, a medical student (Noomi Mueller) who was trained by a radiologist (Florian J. Fintelmann). Patients were positioned supine in 30° -upper body elevation, with legs extended and muscles relaxed. The point that represented 60% of the distance from the anterior superior iliac spine to the superior border of the patella was identified. The ultrasound probe was positioned perpendicularly along the superior aspect of the right thigh and transverse images of the RF were obtained (Fig. 2). A copious amount of gel was applied to minimize tissue compression. The inner echogenic line of the RF was traced manually on a frozen image and RF_{CSA} calculated by planimetric technique provided by the vendor (Phillips Medical Systems, Bothell, WA). All measurements were made on the screen of the ultrasound unit at the bedside. Patients in whom the lines of the RF muscle were not well defined due to soft-tissue edema were excluded ($n = 3$).²⁶ To test the accuracy of measurements, 9 patients underwent repeat measurements of right RF_{CSA} on 2 separate occasions during the same day. The mean (SD) bias and 95% limits of agreement were -0.08 (0.44) cm^2 and -0.94 to -0.78 cm^2 .²⁷ Intraclass correlation coefficient was 0.96. Two educational tools for the training of novice operators are provided (see video and text file, Supplemental Digital Content 1 and 2, <http://links.lww.com/SLA/A916>, <http://links.lww.com/SLA/A917>). We also quantified the time required to obtain the RF_{CSA} in 6 ultrasound novices (students) who performed repeated ultrasound measurements of the RF muscle in healthy volunteers. Operator experience was defined as total number of RF ultrasound measurements performed by a novice operator.

Analysis of Muscle Data

Normal muscle mass differs by sex.^{28,29} Therefore, we adjusted ultrasound-measured RF_{CSA} for sex using published skeletal muscle mass values of lower body of healthy adults.³⁰ RF_{CSA} of female patients were multiplied with the coefficient 1.484, whereas male patients represented the reference group (adjustment coefficient = 1). Sex-adjusted RF_{CSA} was used for further statistical analysis.

Sarcopenia was defined based on receiver-operating characteristic curve analysis determining the discrimination of frailty by sex-adjusted RF_{CSA} . The optimal cutoff value of sex-adjusted RF_{CSA} was identified using Youden index³¹ and allowed us to divide our patient population into sarcopenic versus nonsarcopenic.

Frailty Index

Frailty was determined with the 50 item FI by Joseph et al¹⁰ obtained from the Canadian Study of Health and Aging,³² using 50 preadmission frailty items, including baseline functional dependence, social support, nutrition, comorbidities, depression, and patient demographics. The FI was calculated as the number of frailty items present in the patient divided by the total number of items ($n = 50$). Frailty was defined by a FI of 0.25 or higher. Patients were stratified into 2 groups as frail or nonfrail based on their FI.¹⁰

Muscle Strength Testing

A member of the study team (Noomi Mueller or Stephanie D. Grabitz) tested 12 muscle groups by manual muscle testing: shoulder abductor, elbow flexor, wrist extensor, hip flexor, knee extensor, and ankle dorsiflexor muscles bilaterally.²⁰ Each muscle group was scored on the Medical Research Council Scale (MRC), ranging from 0 (paralysis) to 5 (normal muscle strength). For each patient, an average strength score across all muscles tested was calculated, and if <4 (antigravity strength), muscle weakness diagnosed.³³

Outcome Measures

Our primary outcome measure was adverse discharge disposition defined as discharge to a skilled nursing facility (not including discharge to rehabilitation center) or in-hospital mortality.¹⁰ None of our patients came from skilled nursing facilities. Secondary outcomes included SICU LOS and hospital LOS.

Statistical Analysis

This trial was registered in clinicaltrials.gov as a study to investigate the predictive value primarily of frailty and sarcopenia (NCT02270502). This manuscript is focused on the predictive value of sarcopenia on adverse discharge disposition. Sample power calculation was based on the outcome adverse discharge disposition. Based on pilot data, we expected an adverse discharge rate of 15%.³⁴ We calculated that a sample size of 100 patients would provide $>80\%$ power to detect an association between sarcopenia and adverse discharge disposition (correlation coefficient $r = 0.3$) with a 2-sided α error of 0.05.

Descriptive data were reported as means (SDs) for continuous, as medians (interquartile ranges) for ordinal and as proportions for categorical variables.

To evaluate whether sarcopenia predicts outcome, regression models were constructed. The following clinically relevant covariates were defined a priori and included in all models: age, APACHE II score, CCI, serum creatinine, hemoglobin level, and GCS at admission. We used logistic regression models to evaluate the predictive ability of sarcopenia, frailty, and poor nutritional status for adverse discharge disposition. Zero-truncated Poisson regression was used to evaluate predictive ability for the secondary outcomes SICU and hospital LOS. Absence of multicollinearity was confirmed by testing variance inflation factors.

Predictive abilities of the multivariable risk prediction models (frailty prediction model vs sarcopenia prediction model and malnutrition prediction model vs sarcopenia prediction model) were compared. χ^2 values were calculated for each prediction model. For the binary

primary endpoint adverse discharge disposition, we further used the risk reclassification approach of Pencina et al.³⁵ The NRI was generated by balancing the proportion of patients whose risk was more accurately classified using the sarcopenia compared with the frailty prediction model against the proportion of patients whose risk was less accurately classified.³⁶ Patients were divided into 4 risk groups for adverse discharge, of less than 25%, 25 to less than 50%, 50 to less than 75%, and 75% or higher. We then calculated the number of patients who were reclassified into either higher- or lower risk categories using the sarcopenia rather than the frailty prediction model. Reclassification analysis was also conducted to compare the predictive ability of the malnutrition prediction model with the sarcopenia prediction model.

To evaluate whether the predictive ability of the sarcopenia model changed when further including frailty into the model, we subtracted the log likelihoods of the nested models for each outcome and determined a *P* value with 1° of freedom (df).

All further analyses were conducted with an exploratory intention. To evaluate the association between skeletal muscle ultrasound and frailty, as well as between skeletal muscle ultrasound and nutritional status, Spearman rank analysis of sex-adjusted RF_{CSA} versus FI and Short Nutritional Assessment score were performed. Negative predictive values of sarcopenia for frailty and for poor nutritional status were calculated.

To characterize the learning curve of the novice operators, we generated a linear mixed model (compound symmetry) including “operator experience” (1–18), “number of volunteer measured” (1, 2, or 3), “assessment side” (right vs left), and “number of repeat measurement” (1, 2, or 3) as repeated independent variables and “time to obtain a RF_{CSA}” as the dependent variable. We tested for a main effect of “operator experience” on the “time to obtain a RF_{CSA}.” To assess the degree of operator variability, we calculated the intraclass correlation coefficient for measurements of the novices.

Data were analyzed with STATA 13 (Stata, College Station, TX), SPSS 22.0 (SPSS, Chicago, IL), and SAS version 9.4 (SAS Institute Inc., Cary, NC). A 2-sided *P* value of less than 0.05 was considered statistically significant.

RESULTS

In total, 111 consecutive critically ill patients were prospectively enrolled, of whom 102 patients successfully completed sarcopenia and frailty assessment and were included in our analyses (Fig. 1). As quantified by muscle ultrasound, mean sex-adjusted RF_{CSA} amounted 5.9 (2.1) cm², with 43.1% of patients (n = 44) having sarcopenia. Mean FI was 0.23 (0.12) and 38.2% of patients (n = 39) met the criteria for frailty. Malnutrition was diagnosed in 37.3% of patients (n = 38). In 96 patients who underwent strength assessment, mean MRC score was 4.7 (0.4), with 6.3% of patients (n = 6) having global muscle weakness. In 20.8% of patients, MRC score could not be successfully obtained on enrollment day due to inadequate ability to conduct the volition-dependent test. More than two-thirds of patients were admitted to the SICU after a major surgical procedure, with thoracic, vascular, and abdominal surgery being the most common interventions (Table 1). During their SICU stay,

37.3% of patients ($n = 38$) were mechanically ventilated, with an average time on ventilator support of 3.11 (4.5) days. Patient characteristics are provided in Table 2.

Sarcopenic Phenotype on the Surgical Intensive Care Unit

Sarcopenic patients admitted to the SICU had a higher burden of comorbidities, increased muscle weakness, and were older than patients with no sarcopenia. Within the patient group aged less than 50 years, 18.2% ($n = 4$) had sarcopenia. At time of admission to the SICU, vital signs did not differ between groups, whereas APACHE scores were higher in patients with sarcopenia. SOFA scores obtained on the day of SICU admission did not differ between groups, but were higher in sarcopenic compared with nonsarcopenic patients on day 3 after admission ($P = 0.01$). Hospital costs of patients with sarcopenia were found to be 42.2% higher than mean costs of nonsarcopenic patients ($P < 0.001$).

Sarcopenia: a Biomarker of Frailty?

A significant association was found between the sex-adjusted RF_{CSA} and FI (Spearman coefficient -0.52 , $P < 0.001$, Fig. 3) as well as between sex-adjusted RF_{CSA} and nutritional status (Spearman coefficient -0.48 , $P < 0.001$). The area under the receiver operating characteristic curve for the sex-adjusted RF_{CSA} to predict frailty was 0.75. The cutoff value with maximal sensitivity and specificity for the diagnosis of frailty corresponded to the RF_{CSA} threshold of 5.2 cm^2 (sensitivity 73%, specificity 69%). Absence of sarcopenia had a negative predictive value of 79.3% for frailty and of 75.9% for malnutrition.

Primary Outcome Adverse Discharge Disposition

A total of 17.6% of patients (18 patients) had an adverse discharge disposition (13 to a skilled nursing facility and 5 in-hospital deaths; Table 2). All patients who died in the hospital were sarcopenic. After including the covariates age, APACHE II score, CCI, creatinine, hemoglobin, and GCS in a multivariable regression model, sarcopenia was found to be an independent predictor of adverse discharge disposition [odds ratio (OR) 7.49; 95% confidence interval (CI) 1.47–38.24; $P = 0.015$; Fig. 3, Table 3], as was sex-adjusted RF_{CSA} (OR 0.30; 95% CI 0.14–0.66; $P = 0.003$). Frailty also predicted adverse discharge disposition (OR 8.01; 95% CI 1.82–35.27; $P = 0.006$; Fig. 3, Table 3), as did poor nutritional status (OR 3.80; 95% CI 1.04–13.86; $P = 0.043$).

The predictive ability of the sarcopenia model was very similar to the frailty prediction model. The χ^2 values of the sarcopenia and frailty models amounted to $\chi^2 = 21.74$ and 23.44. In particular, the clinically meaningful risk classification of patients showed that the 2 prediction models did not significantly differ, with an NRI of -0.02 (95% CI -0.31 to 0.26 ; $P = 0.87$). Among 18 patients who experienced an adverse discharge disposition, 3 patients were reclassified to a higher clinical risk category and 3 patients were reclassified to a lower clinical risk category by the sarcopenia prediction model. Among 84 patients who did not experience an adverse discharge disposition, 10 patients were reclassified into a lower and 12 into a higher clinical risk category (Table 4).

Further, when adding frailty to the sarcopenia prediction model, the model performance was not statistically improved for the outcome adverse discharge disposition (δ -2Log Likelihood = 2.688, $df = 1$; $P = 0.10$).

Predictive ability did not differ between the sarcopenia and the malnutrition prediction model, reflected by a likelihood ratio $\chi^2 = 21.74$ versus 19.02, respectively, and an NRI of -0.01 (95% CI -0.30 to 0.30 ; $P = 0.98$).

In addition, sarcopenia predicted discharge to skilled nursing facility (OR 5.05; 95% CI 1.01–25.24; $P = 0.048$) independent of important clinical covariates, as did frailty (OR 5.32; 95% CI 1.18–23.98; $P = 0.03$), and poor nutritional status, but the latter trend did not reach statistical significance (OR 2.35; 95% CI 0.62–8.87; $P = 0.21$).

Secondary Outcomes

In this patient cohort, mean SICU LOS was 4.6 (4.4) days and hospital LOS 10.8 (8.8) days (Table 2). After including the covariates age, APACHE II score, CCI, creatinine, hemoglobin, and GCS in a multivariable regression model, sarcopenia independently predicted hospital LOS [incidence rate ratio (IRR) 1.37; 95% CI 1.19–1.58; $P < 0.001$], as did sex-adjusted RF_{CSA} (IRR 0.91; 95% CI 0.88–0.95; $P < 0.001$). For the endpoint SICU LOS, sarcopenia did not reach statistical significance after all covariates were included into the regression model (IRR 1.13, 95% CI 0.90–1.43; $P = 0.29$). Frailty was found to be independent predictor of SICU LOS (IRR 1.49; 95% CI 1.17–1.89; $P = 0.001$) and hospital LOS (IRR 1.57; 95% CI 1.35–1.82; $P < 0.001$).

The predictive ability of the sarcopenia model was similar to the frailty prediction model. The sarcopenia prediction model had a moderately lower likelihood ratio test (likelihood ratio $\chi^2 = 75.85$ vs 85.47 for SICU LOS and 142.17 vs 158.42 for hospital LOS, for the sarcopenia vs the frailty prediction model). Further, when adding frailty to the sarcopenia prediction model, the model performance was significantly improved for SICU LOS (δ -2Log Likelihood = 4.821, $df = 1$; $P = 0.03$) and hospital LOS (δ -2Log Likelihood = 11.773, $df = 1$; $P < 0.01$).

Operators' Learning Curve

Each of the 6 novice operators conducted a total of 18 measurements on 3 volunteers. The mean (SD) of “time to obtain a RF_{CSA}” was 63.15 (41.10) seconds and a main effect of “operator experience” on the “time to obtain a RF_{CSA}” was found ($P < 0.001$; times required performing the first and final measurements amounted 152.33 (65.58) and 46.67 (24.53) seconds, respectively; see eFigure, Supplemental Digital Content 3, <http://links.lww.com/SLA/A918>). The intraclass correlation coefficient of measurements was 0.988.

DISCUSSION

In this prospective cohort study of patients admitted to the surgical ICU, we found that sarcopenia as measured by bedside ultrasound and frailty predicted poor outcomes of critically ill patients. Predictive abilities of the sarcopenia and the frailty prediction model

were equally good, particularly for the primary outcome adverse discharge disposition. For the secondary outcome duration of hospitalization, frailty was a slightly better predictor. Bedside skeletal muscle ultrasound on admission, a rapid and easy method that does not require patient cooperation, may be used for risk stratification of SICU patients.

Predictive Value of Sarcopenia

Sarcopenia defined by ultrasound of the RF muscle predicted adverse discharge disposition and hospital LOS in our cohort of critically ill patients. Our findings are in line with previous studies performed in hospitalized surgical patients with no critical illness. Our data support the work of Reisinger et al²³ who quantified muscle mass by preoperative CT imaging using the L3 muscle index in patients undergoing colorectal surgery and found that sarcopenia diagnosed by CT predicts adverse postoperative outcome. Similarly, in a population of elderly patients undergoing emergency surgery, sarcopenia as measured by abdominal CT predicted adverse disposition.³⁷

Further, our findings add to a retrospective study by Moisey et al¹⁵ reporting that sarcopenia in critically ill trauma patients as assessed by CT is associated with mortality and ICU utilization. CT imaging cannot be performed as a screening method on every SICU patient due to high cost, radiation exposure, and dangers of transportation.³⁸ In our prospective study, we were able to demonstrate the predictive value of muscle ultrasound, a low-cost imaging modality free of ionizing radiation that can be conducted at the bedside by SICU staff with minimal training. Ultrasound of the RF muscle was recently applied in an ICU population to characterize the pathogenic process of acute skeletal muscle wasting during critical illness.³⁹ In another study, ultrasound-measured decrease in muscle thickness was correlated with LOS of immobilized ICU patients, but lack of standardized timing of the muscle ultrasound exam makes the data hard to interpret.⁴⁰ Our study is the first to evaluate the predictive abilities for adverse outcome of sarcopenia as diagnosed by bedside ultrasound in the SICU. Interestingly, sarcopenia did not predict duration of SICU stay. In our institution, SICU discharge depends on both patients' conditions and bed availability. Our data show that sarcopenia is associated with higher need for institutional care after discharge, representing higher disease burden, and functional dependence after hospitalization. Our study adds to the existing literature that sarcopenia quantified easily by bedside ultrasound methods predicts poor outcome of surgical critically ill patients.

Physiological Correlates of Poor Functional Status in the Surgical Intensive Care Unit

Before surgery and critical illness, a loss of reserve may lead to homeostatic imbalance, which in turn may impair recovery and healing of SICU patients.¹² Frail patients may have a lower functional capacity and decreased ability to mobilize at baseline. Thus, they are vulnerable against severe physiologic stressors, predisposing them to functional dependence at discharge and death.

Several important factors contribute to the process of sarcopenia, such as a state of generalized inflammation, dysregulation of the endocrine system as well as an altered protein metabolism and gene expression.⁴¹ A lack of regular physical activity and chronic malnutrition causing a negative nitrogen balance further enhance the loss of muscle mass.⁷

The cycle of frailty is a downward spiral with the clinical signs of a decline in muscle mass, strength, endurance, and energy expenditure.⁷ We believe that sarcopenia is a relevant element of frailty as it captures all these clinical signs. Sarcopenia constitutes a main risk factor for adverse health-related outcome.

Predictive Value of Frailty

Our data show that frailty is an important prognostic factor of patients admitted to the SICU. These results add to the findings of 2 recent multicenter studies performed in ICU patients ages 50 years and 65 years, which showed that frailty is associated with a greater risk of mortality and adverse events.^{42,43} In accordance with the described prevalence of frailty between 23 and 41% in the ICU, we found that frailty was common at SICU admission, affecting more than one-third of patients. Bagshaw et al⁴² and Le Maguet et al⁴³ quantified frailty in the ICU with the Clinical Frailty Scale, a 1 to 9 points rating tool based on clinical judgment. Here, we measured frailty by means of the FI. Unlike these studies, we included critically ill patients of all ages into our study, to evaluate whether frailty is a widely generalizable outcome predictor of SICU patients. Similar to previous reports,⁴⁴ we also observed that some younger patients (<50 years) are frail, emphasizing that frailty and age are distinct variables and cannot be used interchangeably.

Comparison of Risk Stratification by Sarcopenia and Frailty

When comparing the accuracy of risk prediction by use of the NRI, no significant difference was found between the sarcopenia and the frailty prediction model for the primary outcome adverse discharge. Likelihood ratio tests showed that the predictive abilities of the 2 models were similar and adding frailty to the sarcopenia model did not improve prediction. Both variables, sarcopenia and frailty, may equally well help us to understand the varying vulnerability to surgical intervention of patients of the same chronological age.

For the secondary outcome duration of hospitalization, the frailty models had moderately better predictive accuracy.

Sarcopenia: a Biomarker of Frailty?

Sarcopenia and frailty are not the same variables, but frailty is associated with sarcopenia and both variables predict adverse discharge of SICU patients equally well. There is no standardized method of measuring frailty. Various tools exist, such as the phenotype of frailty by Fried et al,⁷ the Clinical Frailty Scale,⁶ and the FI³²—each providing a useful risk assessment. It is interesting that many physicians still seem to assess frailty subjectively from the “end of the bed,” a relatively unreliable approach.⁴⁵ In our study, we used a FI composed of 50 variables based on the Canadian Study of Health and Aging.¹⁰ Another established method of assessing impaired functional status is the evaluation of muscle strength.³³ In our patients, manual muscle testing could not be performed early after admission in one-fifth of cases due to impaired patient cooperation. Consequently, voluntary muscle strength measurement is not the most favorable method for risk adjustment of surgical ICU patients. Low muscle mass or sarcopenia is considered a key element of frailty and has recently been used to assess frailty in patients with peripheral artery disease.⁴⁶ We found that muscle cross-sectional area was significantly correlated with the FI. Absence of

sarcopenia provided a negative predictive value of 79% to exclude frailty. Our data suggest that the 2 proposed approaches regarding the concept of frailty capture related, but not identical groups of individuals. In our patients, poor nutritional status was associated with sarcopenia. Our exploratory findings add to a study by Reisinger et al²³ reporting that sarcopenia, frailty, and poor nutritional status predict postoperative sepsis in patients undergoing colorectal cancer surgery. Sarcopenia measured by nonvolitional ultrasound methods may be used as biomarker for frailty and poor nutritional status to predict outcome of critically ill patients unable to follow commands.

Our data show that ultrasound of the RF muscle is a reliable method with a very low level of operator variability, which can be rapidly learned by nonprofessional staff to predict adverse discharge disposition.

Sarcopenic Phenotype on the Surgical Intensive Care Unit

Patients with sarcopenia had higher APACHE II scores at admission compared with patients without sarcopenia. Organ dysfunction did not differ at SICU admission, but was more severe in sarcopenic compared with nonsarcopenic patient on the third SICU day, emphasizing the importance of the biomarker sarcopenia as a predictor for the recovery process in critical illness. Upon admission to the SICU, sarcopenic patients were older and had more comorbidities. Of note, neither age nor comorbidity index independently predicted adverse discharge in our patient population underlining the superiority of biological over chronological age in predicting poor outcomes.⁸ In an exploratory analysis, we found 42.2% higher mean costs of care in sarcopenic patients compared with costs of nonsarcopenic patients, which supports the findings of a retrospective study indicating sarcopenia is predictor of payer and hospital costs in patients undergoing major surgery.⁴⁷

Clinical Implications

Risk prediction is important for resource allocation and quality assessment of healthcare by bringing predicted and reached outcomes into perspective.⁴⁸ In surgical critical care, each patient's risk-to-benefit ratio needs to be evaluated to define the optimal treatment plan following an individualized approach to patient care. To optimize the value of surgical care, we need to avoid the outcome adverse discharge disposition, which we characterized in this study as in-hospital mortality or discharge to a skilled nursing facility in patients who were functionally independent before admission.¹⁰ Information on risk of postoperative mortality or functional dependence at discharge may help patients and/or relatives make informed decisions about goals of care. Our data suggest that sarcopenia can be utilized for risk stratification in SICU patients. Muscle ultrasound is a valid and simple technique that could also be used for longitudinal assessment of treatment success. Future studies may use this technique to individualize postoperative interventions that may reduce the risk for an adverse discharge disposition related to critical illness, such as early mobilization,⁴⁹ optimized nutritional support,⁵⁰ and reduction of sedation and opioid dose.

Strength and Limitations

The strengths of the current study include that we present a prospective cohort study in surgical critically ill patients, with standardized data assessment and application of relevant

statistical methods such as reclassification, to evaluate the predictive ability of sarcopenia, a biomarker for frailty and poor nutritional status, as diagnosed by ultrasound. We introduce a noninvasive, rapid and nonvolitional bedside tool for risk stratification in surgical ICU patients.

We had several limitations in the current study. We did not evaluate the predictive value of sarcopenia and frailty for long-term outcomes and on quality of life. However, information on discharge disposition and expected duration of hospitalization is valuable, as these measures are associated with quantity and quality of survival of critical illness as well as increasing healthcare expenditures.^{51,52} Moreover, due to impaired ability of our SICU patients to communicate, we accepted that proxies file the frailty questionnaire. A good agreement between functional status reported by patients versus proxies has been reported. Finally, our results were obtained at 2 SICUs of a single academic medical center and it is unknown whether the results of this study are applicable in other settings.

CONCLUSIONS

In this prospective study in surgical critically ill patients, we found that sarcopenia and frailty predict adverse discharge disposition as well as duration of hospitalization. Predictive abilities of the sarcopenia and frailty prediction model were very similar, particularly for the outcome adverse discharge. Skeletal muscle ultrasound on admission, a method that does not require subject cooperation, may be used as a biomarker for frailty to predict poor outcomes of patients admitted to the surgical ICU.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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FIGURE 1.

Patients' flow through the study. *Manual muscle testing could not be completed during SICU stay in 6 patients due to delirium (n = 3), patient refusal (n = 1), transfer (n = 1), and mortality (n = 1).

FIGURE 2.

Representative transverse ultrasound image of the rectus femoris muscle acquired with a 3 to 12 MHz linear transducer (Philips Medical Systems, Bothell, WA) using musculoskeletal settings. F, femur; VI, vastus intermedius; VL, vastus lateralis; VM, vastus medialis.

FIGURE 3.

Frailty and sarcopenia are associated variables that equally well predict adverse discharge disposition. A, Relationship between sarcopenia and adverse discharge disposition defined as discharge to skilled-nursing facility or in-hospital mortality. B, Relationship between frailty and adverse discharge disposition. C, Scatterplot of frailty index versus cross-sectional area of rectus femoris muscle as measured by ultrasound. A significant correlation was found between the frailty index and sex-adjusted cross-sectional area of rectus femoris muscle (Spearman $r = -0.52$, $P < 0.001$).

TABLE 1**Surgical Intensive Care Unit Admission Diagnoses**

Diagnosis	N (%)
Postoperative patients	72 (70.6)
Thoracic surgery	24 (23.5)
Vascular surgery	17 (16.7)
Abdominal surgery	15 (14.7)
Orthopedic surgery	12 (11.8)
Transplant surgery	5 (4.9)
Neurologic surgery	2 (2.0)
Trauma	18 (17.6)
Hemodynamic instability	17 (16.7)
Respiratory failure	5 (4.9)
Sepsis	5 (4.9)
Pancreatitis	2 (2.0)
Bowel obstruction	1 (1.0)

Characteristics and Outcome Measures of Study Population (n = 102), by Sarcopenia and by Frailty Status

TABLE 2

Variables	All Patients (n = 102)	Sarcopenic Patients (n = 44)	Nonsarcopenic Patients (n = 58)	Frail Patients (n = 39)	Nonfrail Patients (n = 63)
Demographics					
Age (years), mean (SD)	61.9 (15.8)	70.3 (14.0)	55.5 (14.1)	67.7 (14.0)	58.3 (15.9)
Age range	21–89	21–89	21–79	28–85	21–89
<50, No (%)	22 (21.6)	4 (9.1)	18 (31.0)	4 (10.3)	18 (28.6)
Male sex, No (%)	62 (60.8)	31 (70.5)	31 (53.4)	26 (66.7)	36 (57.1)
White race, No (%)	94 (92.2)	42 (95.5)	52 (89.7)	38 (97.4)	56 (88.9)
Less than high school, No (%)	7 (6.9)	6 (13.6)	1 (1.7)	4 (10.3)	3 (4.8)
BMI (kg/m ²), mean (SD)	26.9 (4.8)	25.6 (4.5)	27.8 (4.8)	27.4 (4.9)	26.5 (4.7)
Underlying and acute illness					
Frailty index, mean (SD)	0.23 (0.12)	0.29 (0.11)	0.17 (0.10)	0.34 (0.08)	0.15 (0.06)
Sex-adjusted RF _{Csa} (cm ²), mean (SD) *	5.9 (2.1)	4.1 (0.8)	7.2 (1.8)	4.8 (1.3)	6.6 (2.3)
MRC strength score, mean (SD) *	4.7 (0.4)	4.5 (0.4)	4.8 (0.3)	4.5 (0.5)	4.8 (0.4)
Muscle weakness, No (%) *	6 (6.3)	5 (12.2)	1 (1.8)	4 (11.1)	2 (3.3)
CCI score, median (IQR)	5 (2–7)	6.5 (4–8)	4 (1–6)	7 (5–8)	3 (1–5)
APACHE II score, median (IQR)	10 (7–15)	12 (8–16)	9 (6–12)	12 (8–17)	9 (6–13)
SOFA score, SICU admission, median (IQR)	4 (1–6)	3.5 (1–7)	4 (2–6)	4 (2–7)	3 (1–6)
SOFA score, day 3, median (IQR)	2 (0–4)	3 (1–5.5)	2 (0–3)	2 (1–5)	1 (0–4)
ASA status of 3, No (%)	66 (64.7)	31 (70.5)	35 (60.3)	32 (82.1)	34 (54.0)
No of prescription drugs, mean (SD)	7.9 (5.7)	10.6 (5.6)	5.9 (5.0)	11.6 (5.1)	5.7 (4.9)
SICU admission vital signs					
Systolic BP (mm Hg), mean (SD)	127.7 (21.5)	126.0 (21.1)	129.0 (21.8)	123.9 (21.1)	130.1 (21.5)
Heart rate (beats/min), mean (SD)	82.2 (17.3)	81.6 (20.1)	82.6 (15.1)	81.7 (18.2)	82.5 (16.9)
Body temperature (°F), mean (SD)	98.0 (1.0)	97.9 (1.0)	98.1 (1.0)	97.9 (0.8)	98.1 (1.1)
GCS score, median (IQR)	15 (11–15)	15 (10–15)	15 (11–15)	14 (10–15)	15 (11–15)
SICU admission laboratory data					
Creatinine (mg/dL), mean (SD)	1.1 (0.7)	1.2 (0.7)	1.0 (0.7)	1.4 (1.0)	0.9 (0.3)
Hemoglobin (mg/dL), mean (SD)	10.6 (2.2)	10.3 (2.0)	10.8 (2.4)	9.8 (1.9)	11.1 (2.3)
pH, mean (SD)	7.34 (0.1)	7.33 (0.1)	7.35 (0.1)	7.35 (0.1)	7.34 (0.1)

Variables	All Patients (n = 102)	Sarcopenic Patients (n = 44)	Nonsarcopenic Patients (n = 58)	Frail Patients (n = 39)	Nonfrail Patients (n = 63)
Sodium of >144 mmol/L, No (%)	4 (3.9)	2 (4.5)	2 (3.4)	2 (5.1)	2 (3.2)
INR, mean (SD)	1.2 (0.4)	1.3 (0.5)	1.2 (0.3)	1.3 (0.5)	1.2 (0.2)
SICU treatment intensity					
Mechanical ventilation, No (%)	38 (37.3)	19 (43.2)	19 (32.8)	19 (48.7)	19 (30.2)
Tracheostomy, No (%)	5 (4.9)	3 (6.8)	2 (3.4)	2 (5.1)	3 (4.8)
Vasoactive medication, No (%)	55 (53.9)	26 (59.1)	29 (50.0)	24 (61.5)	31 (49.2)
Renal replacement therapy, No (%)	7 (6.9)	6 (13.6)	1 (1.7)	7 (17.9)	0
Blood transfusion, No (%)	39 (38.2)	20 (45.5)	19 (32.8)	19 (48.7)	20 (31.7)
Outcome variables					
Adverse discharge, No (%)	18 (17.6)	15 (34.1)	3 (5.2)	14 (35.9)	4 (6.3)
Hone, No (%)	57 (55.9)	17 (38.6)	40 (69.0)	12 (30.8)	45 (71.4)
Rehabilitation, No (%)	27 (26.5)	12 (27.3)	15 (25.9)	13 (33.3)	14 (22.2)
Skilled nursing facility, No (%)	13 (12.7)	10 (22.7)	3 (5.2)	9 (23.1)	4 (6.3)
In-hospital mortality, No (%)	5 (4.9)	5 (11.4)	0	5 (12.8)	0
Length of stay					
SICU (days), mean (SD)	4.6 (4.4)	5.6 (5.6)	3.8 (3.0)	6.1 (6.2)	3.6 (2.3)
Hospital (days), mean (SD)	10.8 (8.8)	13.3 (11.2)	8.9 (5.8)	14.6 (11.7)	8.4 (5.0)

* n = 96.

ASA indicates American Society of Anesthesiologists; BMI, body mass index; BP, blood pressure; INR, International Normalized Ratio; IQR, interquartile range; No, number.

TABLE 3

Multivariate Regression Analyses for the Outcome Adverse Discharge Disposition (n = 102)

Adverse Discharge Disposition	Variable	OR	95% CI	P
	Sarcopenia	7.49	1.47–38.24	0.015
	Age	1.00	0.95–1.06	0.98
	APACHE II score	1.08	0.96–1.21	0.22
	CCI score	1.09	0.82–1.46	0.56
	Creatinine	0.70	0.26–1.94	0.50
	Hemoglobin	1.13	0.80–1.62	0.49
	GCS	0.86	0.69–1.06	0.15
	Frailty index 0.25	8.01	1.82–35.27	0.006
	Age	1.03	0.98–1.08	0.33
	APACHE II score	1.12	0.98–1.27	0.09
	CCI score	0.99	0.73–1.35	0.94
	Creatinine	0.53	0.19–1.47	0.23
	Hemoglobin	1.15	0.83–1.61	0.40
	GCS	0.95	0.76–1.18	0.63

TABLE 4

Risk Reclassification Comparing the Sarcopenia and the Frailty Prediction Model Among Patients With and Without an Adverse Discharge Disposition (n = 102)

	Sarcopenia Prediction Model: Risk Categories for Adverse Discharge Disposition					
	Frailty Prediction Model: Risk Categories for Adverse Discharge Disposition	<25% Risk No	25 to <50% Risk No	50 to <75% Risk No	>75% Risk No	Total Number No
In 18 patients who had adverse discharge						
<25% risk		3	2	0	0	5
25 to <50% risk		2	5	1	0	8
50 to <75% risk		0	1	4	0	5
>75% risk		0	0	0	0	0
Total		5	8	5	0	18
In 84 patients who did not have adverse discharge						
<25% risk		60	12	0	0	72
25 to <50% risk		5	1	0	0	6
50 to <75% risk		1	3	1	0	5
>75% risk		0	0	1	0	1
Total number		66	16	2	0	84

Predictive accuracies of the sarcopenia compared with the frailty prediction model were similar, as reflected by a net reclassification improvement of 0.02 (95% CI 0.31 to 0.26, $P = 0.87$).

No indicates number of patients.