Sarcopenia is a predictor of outcomes in very elderly patients undergoing emergency surgery

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Background. *With the increasing aging population, the number of very elderly patients (age ≥ 80 years) undergoing emergency operations is increasing. Evaluating patient-specific risk factors for postoperative morbidity and mortality in the acute care surgery setting is crucial to improving outcomes. We hypothesize that sarcopenia, a severe depletion of skeletal muscles, is a predictor of morbidity and mortality in very elderly patients undergoing emergency surgery.*

Methods. *A total of 170 patients older than the age of 80 underwent emergency surgery between 2008 and 2010 at a tertiary care facility; 100 of these patients had abdominal computed tomography images within 30 days of the operation that were adequate for the assessment of sarcopenia. The impact of sarcopenia on the operative outcomes was evaluated using both univariate and multivariate analysis.*

Results. *The mean patient age was 84 years, with an in-hospital mortality of 18%. Sarcopenia was present in 73% of patients. More sarcopenic patients had postoperative complications (45% sarcopenic versus 15% nonsarcopenic,* P = .005*) and more died in hospital (23 vs 4%,* P = .037*). There were no differences in duration of stay or requirement for intensive care unit postoperatively. After we controlled for confounding factors, increasing skeletal muscle index (per incremental cm^2/m^2) was associated with decreased in-hospital mortality (odds ratio ~0.834, 95% confidence interval 0.731–0.952,* P = .007*) in multivariate analysis.*

Conclusion. *Sarcopenia was independently predictive of greater complication rates, discharge disposition, and in-hospital mortality in the very elderly emergency surgery population. Using sarcopenia as an objective tool to identify high-risk patients would be beneficial in developing tailored preventative strategies and potentially resource allocation in the future. (Surgery 2014;156:521-7.)*

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With the increasing aging population, the number of very elderly patients undergoing emergency surgery is increasing. Postoperative complications can result in longer hospital stays, need for intensive care, greater resource expenditure, and increased mortality. Evaluating patient-specific risk factors for postoperative morbidity and mortality in the acute care operative setting is crucial in clinical decision-making and improving outcome. To identify those at greater risk of postoperative morbidity and mortality, clinicians have used grading systems such as the American Society of Anesthesiologists (ASA) classification and body mass index (BMI) with mixed success.

Frailty, a lack of physiologic reserve to tolerate acute stress on the body, recently has been suggested to be a stronger predictor of operative

outcome[1,2]; however, current assessments of frailty are criticized to be subjective, and there is no consensus on the best method of measuring frailty.[2] A more objective measurement of frailty possibly comes in the form of sarcopenia, severe depletion of skeletal muscle, measured by quantifying skeletal muscle mass in a cross sectional imaging study.[3-6] Recent literature has associated sarcopenia with worse outcomes in patients undergoing operation for resection of primary and metastatic colorectal cancer, pancreatic cancer, and liver transplantation,[3,4,6-8] The presence of sarcopenia also predicts greater mortality in patients with cirrhosis, stage III melanoma, and in those awaiting liver transplantation.[9-11]

Despite recent research into the effect of sarcopenia on outcomes of cancer and transplant surgery, there are few data involving the acute care surgery patient population. Given the diversity of presenting pathology in this group, an objective and patient-specific predictor of adverse outcome is a valuable tool to assist in preoperative discussions, improving operative outcomes, and to assist in postoperative resource planning.

In this study, we investigated the prevalence of sarcopenia in patients undergoing acute operative care. The objective of this study was to answer the following questions: (1) Does sarcopenia impact in-hospital mortality in patients older than the age 80 undergoing emergency surgery? (2) Does sarcopenia impact duration of stay, complications, and discharge disposition in this patient population? We hypothesize that sarcopenia is associated with increased mortality as well as the development of postoperative complications. In the analysis, in addition to the use of the standard threshold for sarcopenia, the skeletal muscle index (SMI, per incremental cm^2/m^2) as a continuous variable is used to assess impact of muscle wasting on outcomes.[12]

METHODS

This study was approved by the Health Research Ethics Board at the University of Alberta. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (ie, STROBE) guideline for reported retrospective cohort studies.[13]

Study design and setting. We conducted a retrospective cohort study of all patients who underwent an emergency general surgical operation between 2008 and 2010 at a single academic tertiary care hospital with a dedicated Acute Care Surgical Team (University of Alberta, Edmonton, Canada). Inclusion criteria included age greater than 80 years and adequate clinical and computed tomographic (CT) information for sarcopenia assessment within 30 days of an emergent operation. Patients were excluded from this analysis if they underwent an elective procedure, were <80 years of age, or missing clinical or radiograph data for the analysis of sarcopenia.

Clinical assessments. Patient data recovered from electronic medical records included sex, age, weight, height, date of admission/discharge, date of operation, type of procedure, comorbidities, discharge disposition, presence and type of complication, medications, and ASA scores preoperatively.

Patient variables, outcomes, and confounders. The exposure of interest in this study was sarcopenia (see the section "Assessment of sarcopenia"). The primary outcome was in-hospital mortality. Secondary outcomes included complications, duration of intensive care unit (ICU) and hospital stay, and requirement for placement postindex hospital stay. The Charlson Comorbidity Index (CCI) was calculated as previously described.[14] Covariates included in multivariable analysis included age, sex, and medical comorbidity as reflected by the ASA score.[15]

Sarcopenia assessment. Sarcopenia was assessed by measuring total lumbar skeletal muscle cross-sectional area at the level of L3 using CT and normalizing for height to acquire the SMI.[16] A cross-sectional image at the level of L3 is first identified from the CT image group. The image is analyzed with SliceOmatic V4.3 (TomoVision, Montreal, Quebec, Canada) to demarcate and quantify different tissue types using predetermined Hounsfield Unit (HU) thresholds. The HU threshold used for skeletal muscles was −29 HU to 150 HU.[12] All skeletal muscles at the level of L3 were quantified, which includes the psoas, erector spinae, quadratus lumborum, transverse abdominis, external and internal obliques, and rectus abdominis. Two trained observers, who were blinded to the patient outcomes, reviewed separately all images to confirm identification of skeletal muscle groups manually before the software computed the cross-sectional areas by quantifying the pixels falling into the skeletal muscle thresholds. Total cross-sectional area of skeletal muscles at the level of L3 was normalized to height to acquire the SMI (cm^2/m^2). Sarcopenia was defined as L3 SMI≤38.5 cm^2/m^2 for women and ≤52.4 cm^2/m^2 for men based on a CT sarcopenia study.[5] The gray level image, a measure of the muscle attenuation in HU, also was recorded.

Statistical analysis. Statistical analysis was performed using IBM SPSS version 19 (2010; SPSS Institute, Chicago, IL). In the event of missing

values, data were not replaced or estimated. Data were analyzed via the use of descriptive statistics to characterize demographics and other clinical variables. Categorical variables were compared by the χ^2 test or Fisher exact test (<5 subjects). For continuous variables, normally distributed variables were reported as means with standard deviations (SD) and compared by the Student *t* test. Non-normally distributed continuous data were reported as medians with interquartile ranges (IQR) and compared by Wilcoxon rank sum test. Survival was defined as the dichotomous outcome, alive at hospital discharge.

Multivariable analysis. To control for variables that may confound the effect of sarcopenia (SMI) on in-hospital mortality, a multivariable logistic regression analysis was performed. The prespecified prognostic variables included age, sex, ASA score, and SMI. Model performance was assessed using the c-statistic (plotted as area under receiver operator curve [AUROC]) and the Hosmer-Lemeshow test for goodness of fit. Multivariate associations are reported as odds ratios (OR) with 95% confidence interval.

RESULTS

Characteristics and outcomes of patients undergoing emergency operation. Between January 2008 and December 2010, 170 patients older than the age of 80 underwent emergency operation at the University of Alberta Hospital. Of these, 113 (66%) of these patients had abdominal CT images within 30 days of operation. One hundred (59%) had CT images of acceptable quality at the level of L3 for analysis using our graphic analysis program and comprised the final cohort for data analysis.

Most emergency operative procedures were colon resection (22.9%), small bowel resection (19.4%), laparotomy (15.9%), cholecystectomy (10.6%), incarcerated or strangulated hernia repair (8.8%), and bleeding or perforated peptic ulcer disease (5.3%).

The patient demographics and descriptive data are outlined in Table I. The mean patient age was 84.1 (SD 3.6) years, and 51% were male. The median BMI was 25 (IQR 22–27) kg/m^2. Mean ASA score of patients undergoing surgery was 3.2 (SD 0.6). The mean CCI was 2.5 (SD 1.9). Sarcopenia was present in 73% of patients observed. The mean skeletal muscle cross-sectional area was 111 (24) cm^2, whereas the mean SMI after we normalized for height was 39.4 (6.6) cm^2/m^2. The mean muscle attenuation was 19 (SD 9) HU.

Overall complications, duration of stay, and mortality. Of the overall 100 patients in this cohort, 37% experienced at least one postoperative complication, and 29% required ICU care postoperatively. The overall median duration of hospital stay was 13 days (IQR 8–24), whereas overall in-hospital mortality was 18%.

Table I. Baseline characteristics of 100 patients >80 years who underwent emergency surgery

Demographics	*Number (%) or mean (SD) or median (IQR)*
Age	84.1 (3.6)
Sex, male	51 (51%)
Metrics	
Height, m	1.67 (0.11)
Weight, kg	68 (59–82)
Body mass index, kg/m^2	25 (22–27)
Gray level image, HU	19 (9)
Skeletal muscle surface area, cm^2	111 (24)
Skeletal muscle index, cm^2/m^2	39.4 (6.6)
ASA score	3.2 (0.6)
Charlson Comorbidity Index	2.5 (1.9)
Sarcopenia	
Present	73 (73%)
Outcomes	
Duration of hospital stay	13 (8–24)
ICU postoperatively	29 (29%)
Complications	37 (37%)
In-hospital mortality	18 (18%)
Discharge disposition	
Died in hospital	18 (18%)
Transferred to another hospital	34 (34%)
Rehabilitation	3 (3.0%)
Assisted care	7 (7%)
Home with services	13 (13%)
Home without services	25 (25%)

Categorical variables presented as numbers. Normally distributed variables presented as mean (SD). Non-normally distributed variables presented as median (IQR).
ICU, Intensive care unit; *IQR*, interquartile range.

Univariate analysis: Sarcopenic versus nonsarcopenic patients. Univariate comparisons of sarcopenic ($n = 73$) and nonsarcopenic ($n = 27$) patients were performed (Table II). Male sex was associated with sarcopenia (18.5% nonsarcopenic versus 63% sarcopenic, $P < .001$). There was no difference in mean muscle attenuation (gray level image) (18.5 vs 20.7 HU, $P = .27$) or the mean total cross-sectional muscle surface area (109 [22] vs 117 [28] cm^2, $P = .11$) in sarcopenic compared with nonsarcopenic patients. ASA scores did not differ between sarcopenic and nonsarcopenic patients (3.2 [0.6] vs 3.2 [0.7], $P = .96$). CCI scores also did not differ between sarcopenic and nonsarcopenic patients (2.6 [SD 1.9] vs 2.1 [SD 1.8], $P = .23$). There were no differences in duration of stay (13 [8–25] vs 10

Table II. Univariable analysis comparing patients with and without sarcopenia

Demographics	*No sarcopenia (27)*	*Sarcopenia (73)*	P *value*
Age, y	83.6 (2.9)	84.3 (3.9)	.30
Male	5 (18.5%)	46 (63%)	<.001*
Metrics			
Height, m	1.62 (0.10)	1.69 (0.11)	.001
Weight, kg	65 (59–73)	70 (59–82)	.88
Body mass index, kg/m^2	25 (24–28)	24 (22–27)	.12
Gray level image, HU	20.7 (8.5)	18.5 (8.9)	.27
Skeletal muscle surface area, cm^2	117 (28)	109 (22)	.11
Skeletal muscle index, cm^2/m^2	44.4 (6.7)	37.6 (5.6)	<.001*
ASA score	3.2 (0.7)	3.2 (0.6)	.78
Charlson Comorbidity Index	2.1 (1.8)	2.6 (1.9)	.23
Outcomes			
Duration of hospital stay	10 (5–19)	13 (8–25)	.15
ICU postoperatively	5 (18.5%)	24 (32.9%)	.22
Complications	4 (14.8%)	33 (45.2%)	.005*
In-hospital mortality	1 (3.7%)	17(23.2%)	.037*
Discharge disposition			.043*
Died in hospital	1 (3.7%)	17 (23.2%)	
Transferred to another hospital	7 (25.9%)	27 (37.0%)	
Rehabilitation	0 (0%)	3 (4.1%)	
Assisted care	3 (11.1%)	4 (5.5%)	
Home with services	5 (18.5%)	8 (11.0%)	
Home without services	11 (40.7%)	14 (19.2%)	

*Statistical significance $P < .05$.
Categorical variables compared using χ^2 (Fisher exact for $n = 5$ values). Normally distributed variables presented as mean (SD) and comparison made with Student *t* test. Non-normally distributed variables presented as median (interquartile ranges) and compared with non-parametric Wilcoxon rank sum test.
ICU, Intensive care unit.

[5–19] days, $P = .15$) and requirement for ICU care postoperatively (33% vs 19%, $P = .22$) between sarcopenic and nonsarcopenic patients. More sarcopenic patients had postoperative complications (45% vs 15%, $P = .005$) and died in the hospital (23 vs 4%, $P = .037$). The discharge disposition was then examined in sarcopenic compared with nonsarcopenic patients. Sarcopenic patients were less likely to go home without services; instead, they required more transfers to rehabilitation centers or subacute hospitals ($P = .043$).

Multivariable analysis: Impact of sarcopenia (SMI) on in hospital mortality. A multivariable logistic regression model for postoperative mortality was developed (Table III). There were no significant interaction terms. The c-statistic (ie, how well the model distinguishes between in-hospital survivors and non-survivors) was 0.873 demonstrating good predictive accuracy (Fig). Age (univariable logistic regression $P = .244$) was not included in the final model. SMI and ASA score were found to impact in-hospital mortality. After we controlled for confounding, increasing SMI (per incremental cm^2/m^2) was associated with decreased in-hospital mortality (OR ~0.834, 95% confidence interval 0.731–0.952, $P = .007$). ASA score (per unit increase) was associated with increased in-hospital mortality (OR ~22.56, 95% confidence interval 4.33–117.68, $P < .001$). Sex was not statistically important in the final model ($P = .128$).

DISCUSSION

As our population ages, an increasing number of the elderly will require emergency surgery. This study is the first to examine the effect of sarcopenia on the outcomes in very elderly patients undergoing emergency surgery. Our study demonstrates that sarcopenia is common in the very elderly operative patients, comprising almost 80% of the population. As hypothesized, sarcopenia is an important independent predictor of mortality and the development of post-operative complications. Each incremental SMI was protective after we controlled for confounding by ASA and sex. Additionally, the presence sarcopenia predicted discharge disposition after emergency surgery.

Other studies have found sarcopenia to negatively impact survival in patients undergoing operation for metastatic cancers and liver transplantation.[9-11] Given that the emergency operative procedures varied from appendectomy to bowel resections for advanced colorectal

Table III. Multivariable analysis of in hospital mortality for patients >80 years undergoing emergency operation

	Univariate (n = *100)*			*Multivariate* (n = *84, c = 0.871)*			
	OR	*95% CI*	P *value*	*Included in model?*	*OR*	*95% CI*	P *value*
Age	1.082	0.948–1.235	.244	No			
Sex, female	1.050	0.378–2.913	.925	Yes	0.297	0.062–1.417	.128
SMI, cm^2/m^2	0.884	0.799–0.978	.017*	Yes	0.834	0.731–0.952	.007*
ASA class	10.421	2.976–36.495	<.0001*	Yes	22.56	4.33–117.68	<.001*

*Statistical significance at alpha = 0.05 (*P* value).
ASA, American Society of Anesthesiologists; *95% CI*, 95% confidence interval; *OR*, odds ratio; *SMI*, skeletal muscle index.

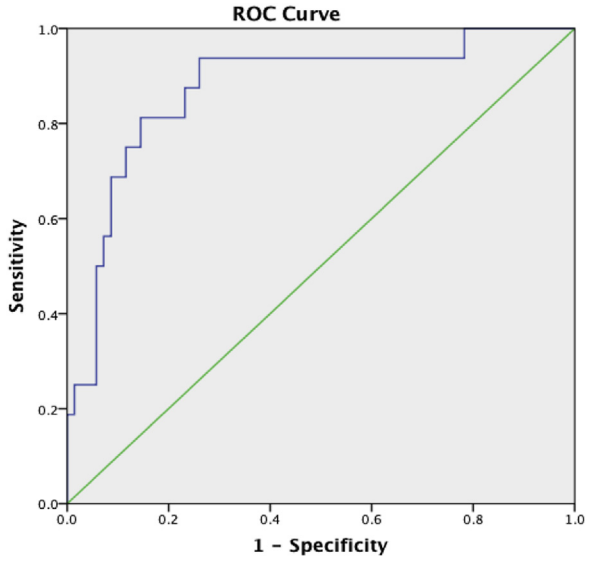


Fig. AUROC for multivariable model predicting in-hospital mortality using sex, SMI (cm^2/m^2), and ASA score. AUROC (c-statistic) = 0.873. Final model included 85 patients (16 had missing data).

carcinoma, suggesting that sarcopenia as a prognosticator can be generalized to the acute care surgical patients who have a variety of presenting pathology.

ASA scores were highly predictive of patient mortality in both univariate and multivariate analysis. The strengths of the ASA score are its quick determination on admission and its low cost; however, ASA scores are subjective measurements and can be inconsistent between evaluators.[17] Given our elderly patient population, the mean ASA score was 3.2 with SD of 0.6. ASA scores are given in increments of 1, which unfortunately does not offer predictive value among a large proportion of our patients who scored 3.

SMI as a continuous variable was shown to be protective for mortality in the elderly patient population undergoing surgery independently of sex and ASA score in multivariate analysis; therefore, SMI could be an objective assessment tool to distinguish risks among those who have the same ASA score. One possible explanation is that ASA scores assess patient based on cardiopulmonary risks and status whereas sarcopenia is a measure of nutritional and functional status. Whereas cardiopulmonary risks could influence immediate mortality perioperatively, the presence of sarcopenia can be used to predict whether the patient has the physiological reserve to tolerate and recover adequately from surgery. In univariate analysis ASA scores are not statistically correlated with the presence of sarcopenia, providing support that ASA and sarcopenia measures separate patient-specific factors. The measurement of sarcopenia has the potential to join the suite of preoperative assessments used routinely to evaluate operative candidacy, especially in the very elderly patient population.

Interestingly, sarcopenic patients did not require a longer hospital stay or increased duration in the ICU compared with nonsarcopenic patients. This observation, however, could be confounded by various factors. First, because of the limited size of the patient population in this study, those sarcopenic patients who died shortly after surgery will underestimate the duration of stay. Second, the discharge date we obtained for our study population only applied to their discharge from University of Alberta Hospital where their operation was performed. Many sarcopenic patients required transfer to another hospital for further inpatient care and recovery and thus could underestimate the length of stay of our sarcopenic patient population.

With regard to ICU admission, perhaps sarcopenic patients experienced an increased incidence of complications that did not require ICU admission. Sarcopenia may be more reflective of nutritional status, being more predictive of infections and ability to recover from surgery. Sarcopenic

patients displayed a trend of worsening discharge disposition and required more rehabilitation and greater level of care after their stay. This information has implications in improving preoperative discussions, targeted preventative strategies, and eventually resource allocation.

The etiology of muscle wasting is complex and it is difficult to distinguish age-related muscle wasting and disease-related muscle wasting. A previous study in a colorectal cancer population demonstrated that patients with sarcopenia had more comorbidities than patients with sarcopenia of the same age.[6] Age and CCI of the patients in this study did not have a correlation with presence of sarcopenia. It is notable that similar findings have been found in other studies. For example, in cancer patients, sarcopenia was an independent predictor when performance status, stage, age, sex, and cancer site are controlled for and in cirrhotic patients sarcopenia was an independent predictor of survival when Model For End-Stage Liver Disease score was taken into account.[18,19] Because all patients in this study were older than the age of 80 years, perhaps due to the survival effect, relative differences in age in this group did not contribute to the presence of sarcopenia. Male sex was correlated highly with the presence of sarcopenia. Whether this indeed the case for the elderly operative patient population may require larger study population to confirm. Other than limited sample size, another possible explanation is that the threshold we are using does not translate well to our population. The threshold to determine sarcopenia is sex dependent and was derived from a younger cancer patient population.[5] These thresholds may be overestimating sarcopenic patients in elderly male patients selectively.

The presence of sarcopenia is not limited to underweight patients. In univariate analysis, the mean BMI of sarcopenic patients did not differ from that of nonsarcopenic patients. The average BMI of sarcopenic patient was 24, the same as the mean BMI of the entire study population. A traditional marker of risk, BMI <18.5 is increasingly rare in the contemporary surgical population even among the very elderly. These findings are consistent with previous literature, where sarcopenia occurs throughout a range of BMI scores independent of generalized wasting.[5]

In this study, the survival analysis was not performed using predetermined threshold values to classify individual patients as sarcopenic or not; rather we included muscularity (SMI) as a continuous variable thereby relating the full range of variation of this feature to predict the outcome. Many researchers characterize their patients as being sarcopenic (ie, below a threshold level of muscle depletion), and we also did this in the descriptive characterization of our population. The thresholds we used originally were derived from optimum stratification of SMI also at the level of L3, using the most significant *P* values to define sex-specific thresholds for mortality in cancer patients.[5] These thresholds have been used in multiple investigations in patients with cancer and nonmalignant disease[10,11] and thus provide a benchmark against which the prevalence of severe muscle depletion can be compared across populations. Currently, however, given the paucity of information in the emergency surgical literature on sarcopenia and evidence-based cutoffs, we believe there is utility in using information from other patient populations in the literature. Future multicenter studies would be useful to determine clinically relevant sarcopenic cut-offs for the elderly emergency surgery population.

Limitations of this study includes its retrospective nature and comments on association and not causation can only be made. Because this was a small single-center study there is potential selection bias in choosing candidates for operation.

In conclusion, sarcopenia is common in the very elderly surgical population and is a strong independent predictor of the development of in-hospital complications and mortality. It is also suggestive of the need for rehabilitation postoperatively. Assessment of sarcopenia using CT image analysis is a readily available and feasible possibility. Using sarcopenia as an objective tool to identify high-risk patients would be beneficial in developing tailored preventative strategies, assist in preoperative discussions and potentially resource allocation in the future.

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