Body Composition and Acquired Functional Impairment in Survivors of Pediatric Critical Illness

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Objectives: To identify whether body mass and composition is associated with acquired functional impairment in PICU survivors.

Design: Retrospective dual-cohort study.

Setting: Single multidisciplinary PICU.

Patients: Two distinct PICU survivor cohorts: 432 unselected admissions from April 2015 to March 2016, and separately 92 patients with abdominal CT imaging at admission from January 2010 to December 2016.

Interventions: None.

Measurements and Main Results: Admission body mass index and Functional Status Scale scores at admission, PICU discharge, and hospital discharge were obtained for all patients. Acquired functional impairment was defined as increase greater than or equal to 3 in Functional Status Scale from baseline. Patients were classified as having: "temporary acquired impairment" (acquired impairment at PICU discharge recovering by hospital discharge), "persistent acquired impairment" (acquired impairment at PICU discharge persisting to hospital discharge), and "no acquired impairment." CT scans were analyzed for skeletal muscle and fat area using National Institute of Health ImageJ software (Bethesda, MD). Multinomial logistic regression analyses were conducted to identify associations between body mass index, muscle and fat indices, and acquired functional impairment. High baseline body mass index was consistently predictive of persistent acquired impairment in both cohorts. In the second cohort, when body mass index was replaced with radiologic anthropometric measurements, greater skeletal muscle, and visceral adipose tissue indices were independently associated with persistent acquired impairment at hospital discharge (adjusted odds ratio, 1.29; 95% CI, 1.03–1.61; $p = 0.024$ and adjusted odds ratio, 1.13; 95% CI, 1.01–1.28; $p = 0.042$, respectively). However, this relationship was no longer significant in children with PICU stay greater than 2 days.

Conclusions: In PICU survivors, baseline body mass and composition may play a role in the persistence of acquired functional impairment at hospital discharge. Characterization and quantification

of skeletal muscle and fat deserves further study in larger cohorts of PICU children. (*Crit Care Med* 2019; 47:e445–e453)
Key Words: adipose tissue; body mass index; critically ill children; functional status; skeletal muscle

Mortality from pediatric critical illness has declined from approximately 11% to 5% in the past few decades, accompanied by an increase in functional impairment from 8% to 18% in children surviving critical illness (1). Approximately a third of all patients experience a newly acquired functional impairment at PICU discharge, and in some, impairment improves by hospital discharge (2–4). However, 10–13% of patients admitted to the PICU do not recover by 6 months post discharge, and their functional impairment can persist up to 3 years post PICU stay (1–3). Children with impairments following PICU have persistent healthcare needs and are more likely to be readmitted, which can exhibit significant burden on their caregivers and healthcare resource utilization (1).

The pathophysiology of functional impairment following critical illness is currently unclear. Past studies have not differentiated between the risk factors for functional trajectories. Understanding the factors associated with different trajectories of functional impairment and recovery may elucidate possible mechanisms of functional impairment in critically ill children.

In adults, long-term functional impairment and weakness in survivors have been associated with acute skeletal muscle wasting during critical illness (5–7), suggesting a role for anthropometry and nutritional status in functional impairment. Higher baseline body mass index (BMI) appears protective—critically ill adults with higher BMI appear to have less functional impairment and better recovery (8, 9). CT scans in adults suggest that the protective effects of high BMI may be attributable to greater skeletal muscle mass and quality (10, 11). In critically ill children, low or high BMI have been associated with greater risk of mortality, infections, and ventilator requirement in critically ill children (12–14). However, in children with severe sepsis, BMI was not found to be associated with change in functional status (14). Whether specific components of skeletal muscle and fat are associated with functional impairment in survivors of pediatric critical illness has not been investigated.

The aim of our two-cohort study was to identify the association between body mass and composition and functional impairment in critically ill children. We hypothesized that, as in adults, greater BMI is associated with recovery from functional impairment, and that this is attributable to a greater skeletal muscle mass at baseline.

MATERIALS AND METHODS

Two retrospective cohorts were studied, comprising of first all consecutive admissions to the PICU of a tertiary hospital (KK Women's and Children's Hospital, Singapore), and second of children admitted to the same PICU with available abdominal CT scans. No sample size calculations were undertaken as this was an exploratory study based on convenience sampling. Both study cohorts were approved by the SingHealth centralized institutional review board with a waiver for informed consent. The Strengthening of the Reporting of Observational Studies in Epidemiology checklist was followed in the conduct and reporting of this study (15).

Cohort 1

Patients 1 month to 18 years old admitted to the PICU between April 2015 and March 2016 were included, with repeat admissions excluded. Nonsurvivors at hospital discharge were additionally excluded as the focus of this work is on critical care survivorship.

Baseline Data Collection

Baseline demographics, medical history, and PICU admission information were retrieved from medical notes. Covariates were defined a priori based on previous published literature (2, 16). Illness severity was calculated using the Pediatric Index of Mortality (PIM) 3 percent probability of death (17). The presence of complex chronic disease was determined using the classification by Feudtner et al (18) Version 2, as these patients have increased healthcare requirements and poorer PICU outcomes (19). C-reactive protein (CRP) levels at PICU admission were extracted for information on inflammatory status. BMI was calculated using PICU admission weight and height and converted to age and gender-specific BMI *z* scores (20, 21). Patients were classified as having a low (*z* score < –2), normal (*z* score –2 to 2), or high (*z* score > 2) BMI.

Outcome–Functional Status and Acquired Impairment

Functional status was measured using the Functional Status Scale (FSS), a 5-point scale (1 to 5) rating across six domains (mental, sensory, communication, motor, feeding, and respiratory), with increasing scores indicating worse functional status (22). The FSS was scored by two investigators (C.O., S.S.) using data extracted systematically from medical records (23). Inter-rater reliability for hospital discharge FSS was assessed in a random subgroup of patients ($n = 50$) using Kappa statistic, Bland-Altman plots, Pearson's *r*, and intra-class correlation coefficient (ICC) based on an absolute agreement, two-way random-effects model (24).

Acquired impairment, or a new impairment in function, was defined as an FSS increase of greater than or equal to 3 between 2 time-points (18). We examined change in FSS scores at PICU and hospital discharge, and a priori defined three outcome groups:

1) Temporary acquired impairment: patients with new functional impairment at PICU discharge but not at hospital discharge,
2) Persistent acquired impairment: patients with new functional impairment at PICU discharge and at hospital discharge, and
3) No new acquired impairment.

Statistical Analysis

Multinomial logistic regression analysis was used to determine associations between baseline characteristics and outcome. Univariate analyses were conducted to determine individual associations between baseline variables and functional impairment group. Due to small numbers in each group, admission category and race were collapsed into two groups each (neurologic injury vs others, Chinese vs non-Chinese). All variables significant at the *p* value of less than 0.10 level for either temporary or persistent acquired impairment were entered into a backward stepwise multivariate regression analysis with an entry and removal probability of *p* value of less than 0.05 and *p* value of less than 0.10 respectively. Sensitivity analysis was also conducted in a subgroup of patients with PICU stay of greater than 2 days to determine whether similar associations were observed in patients requiring greater medical support. In patients with CRP levels available, the relationship between CRP levels and outcomes was explored. All data were analyzed using IBM SPSS Version 20.0 (IBM Corp, Armonk, NY) with statistical significance set at *p* value of less than 0.05.

Cohort 2

Patients 1 month to 18 years old admitted from January 2010 to December 2016 were included if they had a baseline abdominal CT scan, defined as one taken a day before or within the first 4 days of their PICU admission (10). Only the first admission was used, and nonsurvivors were excluded. Baseline characteristics, BMI, and functional outcome were retrieved from medical records per cohort 1. FSS scores at baseline, PICU discharge, and hospital discharge were scored by a single investigator (C.O.).

Analysis of CT Scans

Skeletal muscle and fat were derived from single cross-sectional CT images, which have been shown to correlate with whole-body muscle and fat volumes (25, 26). Single slice images at the level of the third lumbar vertebrae (L3) were extracted in accordance with adult protocols (27). Images were excluded if they were of poor quality or had motion artifacts present. ImageJ software (National Institute of Health, Bethesda, MD) was used to analyze the images according to published protocols by two observers (C.O., A.Z.H.C.) (28). Briefly, skeletal muscle and fat areas were measured using commonly reported thresholds of –29 to 150 Hounsfield units (HUs) for skeletal muscle, –190 to –30 HU for intramuscular adipose tissue (IMAT) and subcutaneous adipose tissue (SCAT), and –150 to –50 HU for visceral adipose tissue (VAT) (**Fig. 1**). Skeletal muscle quality was determined by skeletal muscle density (SMD), that is, the mean attenuation of the delineated muscle measured in HU (29). The observers were trained by a radiologist in the delineation of skeletal muscle and fat, and uncertainties in manual delineation were verified with the radiologist. Inter-rater reliability was conducted on a random sample of skeletal muscle area (SMA) and IMAT ($n = 20$) using Bland-Altman plots, Pearson's *r*, and ICC based on an absolute agreement, two-way random-effects model (24).

To compare SMA across patients, a skeletal muscle index (SMI) was calculated by dividing the area by the square of the height in meters (cm^2/m^2). Indices were similarly created for IMAT (IMATi), VAT (VATi), and SCAT (SCATi) (27).

Statistical Analysis

Multinomial logistic regression analysis was used to determine the association between BMI and functional outcome group, adjusting for significant factors found in cohort 1. BMI was then replaced with skeletal muscle and fat indices to determine their association with functional outcome, first individually, then collectively in a multiple regression analysis. Sensitivity analyses were repeated as per cohort 1. The correlation between CRP levels and adipose tissue indices were explored. Predicted probability curves for outcome groups were also explored in relation to skeletal muscle and fat indices.

RESULTS

Cohort 1

Four-hundred thirty-two patients were included (**Table 1**; and **Table S1**, Supplemental Digital Content 1, http://links.lww.com/CCM/E471). Excluded patients are detailed in **Figure S1** (Supplemental Digital Content 1, http://links.lww.com/CCM/E471). There was no significant difference between survivors and nonsurvivors in terms of age and BMI (**Table S2**, Supplemental Digital Content 1, http://links.lww.com/CCM/E471). Rates of temporary acquired impairment and persistent acquired impairment in this cohort were 29.9% ($n = 129$) and 7.2% ($n = 31$), respectively. Inter-rater reliability of FSS scores is reported in **Figure S2** (Supplemental Digital Content 1, http://links.lww.com/CCM/E471).

Univariate and multivariate analyses are shown in **Table S3** (Supplemental Digital Content 1, http://links.lww.com/CCM/E471). In a multivariate model, high BMI was predictive of persistent acquired impairment (adjusted odds ratio [aOR],

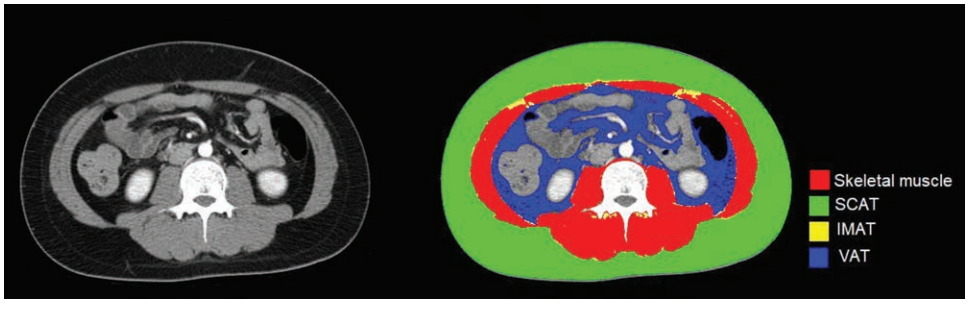


Figure 1. Example of a CT scan at the level of the third lumbar vertebrae. IMAT = intramuscular adipose tissue, SCAT = subcutaneous adipose tissue, VAT = visceral adipose tissue.

TABLE 1. Cohort 1 Versus Cohort 2 Patient Characteristics

Patient Variables	Cohort 1 (*n* = 432)	Cohort 2 (*n* = 92)	*p*
Age, yr, median (IQR)	3.3 (0.3–8.7)	8.9 (5.5–12.4)	< 0.001
Male gender, *n* (%)	263 (60.9)	58 (65.1)	0.699
Race, *n* (%)			0.801
Chinese	240 (55.6)	50 (54.3)	
Malay	94 (21.8)	18 (19.6)	
Indian	42 (9.7)	12 (13.0)	
Other	56 (13.0)	12 (13.0)	
Body mass index category, *n* (%)			0.136
Low	85 (19.7)	11 (12.0)	
Normal	305 (70.6)	68 (73.9)	
High	42 (9.7)	13 (14.1)	
Feudtner's complex chronic conditions, *n* (%)	223 (51.6)	47 (51.1)	0.926
Baseline Functional Status Scale, median (IQR)	6.0 (6.0–7.0)	6.0 (6.0–6.0)	0.030
Elective admission, *n* (%)	182 (42.1)	15 (16.3)	< 0.001
Admission category, *n* (%)			0.713
Respiratory	88 (20.4)	14 (15.2)	
Neurologic	108 (25.0)	25 (27.2)	
Cardiovascular	116 (26.9)	25 (27.2)	
Other	120 (27.8)	28 (30.4)	
Neurologic injury, *n* (%)	107 (24.8)	25 (27.2)	0.596
Pediatric Index of Mortality 3 probability, %, median (IQR)	1.0 (0.4–2.2)	2.5 (1.4–5.1)	< 0.001
Outcome group, *n* (%)			0.035
No acquired impairment	272 (63.0)	45 (48.9)	
Temporary acquired impairment	129 (29.9)	36 (39.1)	
Persistent acquired impairment	31 (7.2)	11 (12.0)	
PICU stay, d, median (IQR)	1.4 (0.9–3.1)	3.5 (1.8–7.0)	< 0.001
Hospital stay, d, median (IQR)	6.8 (4.0–14.0)	19.0 (9.1–45.8)	< 0.001
Mechanical ventilation days, median (IQR)	0 (0–1.1)	0.5 (0–3.7)	0.012

IQR = interquartile range.

4.24; 95% CI, 1.47–12.19; $p = 0.007$). No significant association was observed between BMI and temporary acquired impairment. The distribution of BMI group across impairment category and domains are shown in **Figures S3** and **S4**, ***a*** and ***b*** (Supplemental Digital Content 1, http://links.lww.com/CCM/E471). The association between high BMI and persistent acquired impairment remained significant in the subgroup of patients with PICU stay greater than 2 days (aOR, 4.33; 95% CI, 1.03–18.27; $p = 0.046$). In patients with CRP levels upon admission ($n = 198$), there was no significant association between CRP and temporary or persistent morbidity (OR, 1.00; 95% CI, 1.00–1.01; $p = 0.257$ and OR, 1.00; 95% CI, 0.99–1.01; $p = 0.811$, respectively).

Cohort 2

Ninety-two patients were included (**Table S4**, Supplemental Digital Content 1, http://links.lww.com/CCM/E471). Details of excluded patients are listed in **Figure S5** (Supplemental Digital Content 1, http://links.lww.com/CCM/E471). Thirty-six (39.1%) and 11 (12.0%) experienced temporary and persistent acquired impairment, respectively. Median SMI, IMATi, and VATi were 36.0 cm^2/m^2 (interquartile range [IQR], 31.6–41.8 cm^2/m^2), 0.84 cm^2/m^2 (IQR, 0.32–1.66 cm^2/m^2), and 6.3 cm^2/m^2 (IQR, 3.1–11.9 cm^2/m^2), respectively, whereas median SMD was 52.6 HU (IQR, 44.4–60.3 HU). Inter-rater reliability are detailed in **Figure S6** (Supplemental Digital Content 1, http://links.lww.com/CCM/E471). BMI *z* score was

moderately correlated with SMI, IMATi, and VATi (Pearson's $r = 0.44$, $p < 0.001$; $r = 0.37$, $p < 0.001$; and $r = 0.35$, $p = 0.001$, respectively).

Similar to cohort 1, high BMI was associated with persistent acquired impairment (aOR, 12.12; 95% CI, 1.37–272.3; $p = 0.038$) (**Table S5**, Supplemental Digital Content 1, http://links.lww.com/CCM/E471). Replacing BMI with muscle and fat indices demonstrated that greater SMI, IMATi, VATi, and TATi were all significantly associated with persistent acquired impairment, whereas lower SMD was significantly associated with temporary acquired impairment (**Table 2**). Due to multicollinearity, fat indices were not entered into the regression equation simultaneously. VATi was included as the model had the largest R^2 of 0.527. This model demonstrated that greater SMI and greater VATi were independently associated with persistent acquired impairment (aOR, 1.29; 95% CI, 1.03–1.61; $p = 0.024$ and aOR, 1.13; 95% CI, 1.01–1.28; $p = 0.042$, respectively). Gender was not found to be significant and was

TABLE 2. Multinomial Logistic Regression of CT Scan Variables in Cohort 2

	Temporary vs No Acquired Impairment		Persistent vs No Acquired Impairment	
CT Variables	**aOR (95% CI)**	***p***	**aOR (95% CI)**	***p***
Univariate regression analysis				
SMI	1.01 (0.95–1.07)	0.780	1.17 (1.03–1.32)	0.016
SMD	0.95 (0.90–0.99)	0.029	0.95 (0.88–1.04)	0.270
IMATi	1.19 (0.85–1.68)	0.315	2.07 (1.19–3.60)	0.010
VATi	1.03 (0.99–1.09)	0.162	1.11 (1.03–1.20)	0.010
Subcutaneous adipose tissue index	1.01 (1.00–1.03)	0.093	1.04 (1.01–1.07)	0.023
Total adipose tissue index	1.01 (1.00–1.03)	0.079	1.03 (1.01–1.06)	0.008
SMA:IMAT ratio	1.00 (1.00–1.00)	0.774	1.00 (1.00–1.01)	0.867
SMA:VAT ratio	1.00 (0.99–1.01)	0.647	0.99 (0.88–1.11)	0.858
SMA:TAT ratio	0.75 (0.51–1.10)	0.137	1.00 (0.82–1.23)	0.981
VAT:SCAT ratio	1.53 (0.55–4.28)	0.419	0.97 (0.17–5.60)	0.967
Multiple regression analysis				
SMI	1.02 (0.96–1.08)	0.494	1.28 (1.03–1.58)	0.026
VATi	1.04 (0.99–1.09)	0.096	1.16 (1.04–1.31)	0.009
SMI	1.04 (0.97–1.11)	0.254	1.21 (1.05–1.39)	0.007
SMD	0.95 (0.90–0.99)	0.017	0.90 (0.81–1.01)	0.075
SMI	1.04 (0.98–1.11)	0.207	1.29 (1.03–1.61)	0.024
SMD	0.95 (0.89–1.00)	0.054	0.96 (0.84–1.10)	0.574
VATi	1.01 (0.95–1.07)	0.804	1.13 (1.01–1.28)	0.042
Multiple regression analysis - subgroup (PICU stay > 2 d)				
SMI	1.00 (0.94–1.07)	0.969	1.22 (0.99–1.50)	0.061
VATi	1.02 (0.97–1.07)	0.475	1.13 (1.01–1.26)	0.037
SMI	1.00 (0.94–1.08)	0.950	1.15 (1.01–1.32)	0.039
SMD	0.98 (0.93–1.03)	0.458	0.94 (0.85–1.05)	0.261
SMI	1.01 (0.94–1.08)	0.876	1.22 (0.99–1.51)	0.067
SMD	0.98 (0.92–1.05)	0.615	0.99 (0.87–1.13)	0.907
VATi	1.01 (0.95–1.07)	0.755	1.12 (0.99–1.26)	0.062

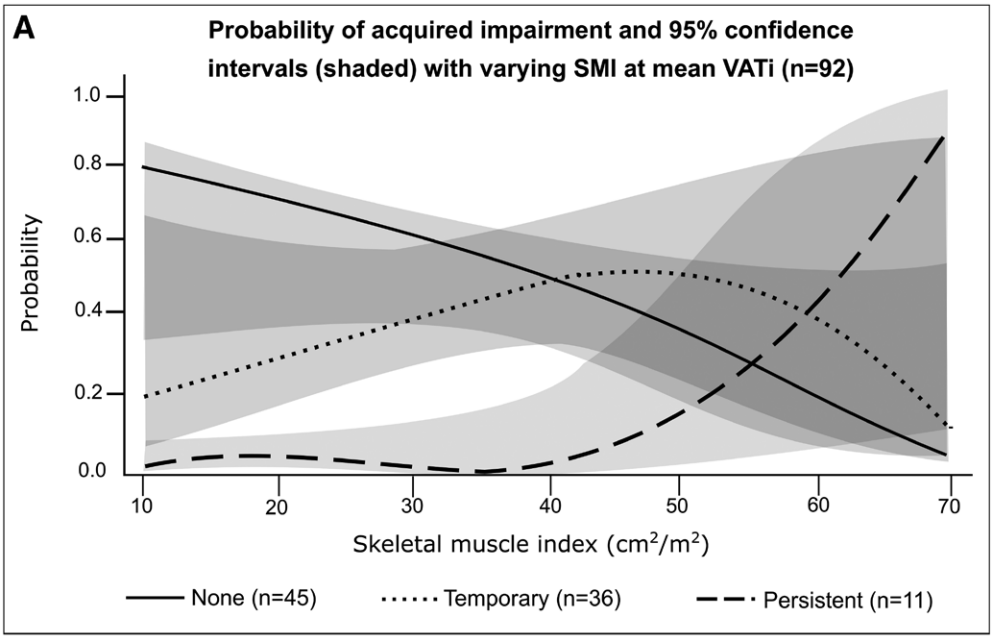
aOR = adjusted odds ratio, IMATi = intramuscular adipose tissue index, SMD = skeletal muscle density, SMI = skeletal muscle index, VATi = visceral adipose tissue index.

Odds ratios adjusted for neurologic injury, Pediatric Index of Mortality 3 probability, age, and race.

dropped from the model ($p = 0.305$). In patients with CRP available ($n = 46$), there was also no significant association between CRP levels and VATi (Pearson's $r = –0.02$; $p = 0.896$), IMATi ($r = –0.01$; $p = 0.925$), or SCATi ($r = 0.01$; $p = 0.968$).

In patients with PICU stay greater than 2 days, high BMI remained significantly associated with persistent acquired impairment (OR, 29.1; 95% CI, 1.39–610.9=8; $p = 0.030$). However, after replacing BMI with SMI, SMD, and VATi, CT indices were no longer significantly associated with persistent acquired impairment (Table 2).

Adjusted probability curves for acquired impairment across varying levels of SMI and VATi are shown in **Figure 2**. At a mean VATi of 10.6 cm^2/m^2, probability of persistent acquired impairment remains low across the observed SMI range until approximately 60 cm^2/m^2, where the probability of persistent acquired impairment exceeds that of temporary acquired impairment (Fig. 2*A*). At a mean SMI of 37.1 cm^2/m^2, a similar trend is observed with increasing VATi until approximately 70 cm^2/m^2 (Fig. 2*B*). With increasing VATi and SMI, there is greater probability of persistent acquired impairment at a lower SMI and VATi, respectively (**Fig. 3**, ***A*** and ***B***).



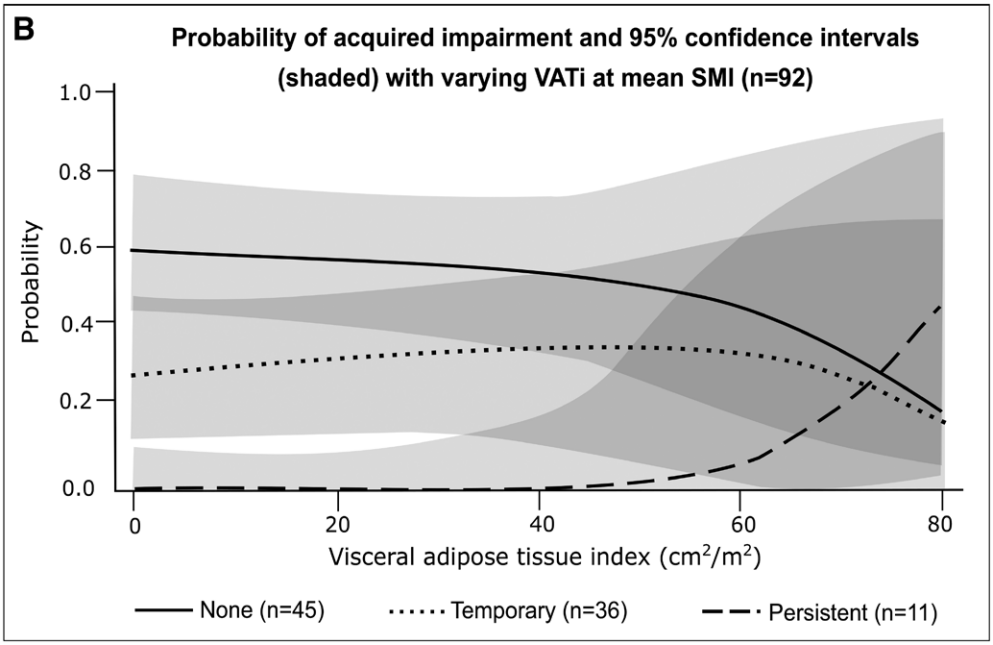


Figure 2. Probability curves for no impairment, temporary acquired impairment, and persistent acquired impairment at varying levels of skeletal muscle index (SMI) and mean visceral adipose tissue index (VATi) (**A**) and varying VATi and mean SMI (**B**).

DISCUSSION

Functional impairment is a growing problem in pediatric critical illness, yet its mechanisms and pathophysiology are not yet clearly understood. To our knowledge, this is the first study to explore the role of anthropometry and functional impairment in critically ill children using both general measures as well as imaging of specific muscle and fat components. We demonstrated a functional trajectory where a significant proportion of children experienced new functional impairment at PICU discharge (37–51%), with a much smaller proportion of experiencing persistent functional impairment at hospital discharge (7–12%). We hypothesized that greater BMI would be associated with lower rates of persistent impairment, which could be attributed to higher baseline skeletal muscle. On the contrary, we found that high baseline BMI was significantly associated with persistent acquired functional impairment at hospital discharge in two independent cohorts. Body composition analyses demonstrate that two different anthropometric phenotypes—high skeletal muscle mass and high visceral fat mass—were independently associated with persistent acquired functional impairment in PICU survivors. However, in children with greater than 2 days of PICU stay, this relationship no longer remained significant, limiting the generalizability of our findings to children with greater illness severity.

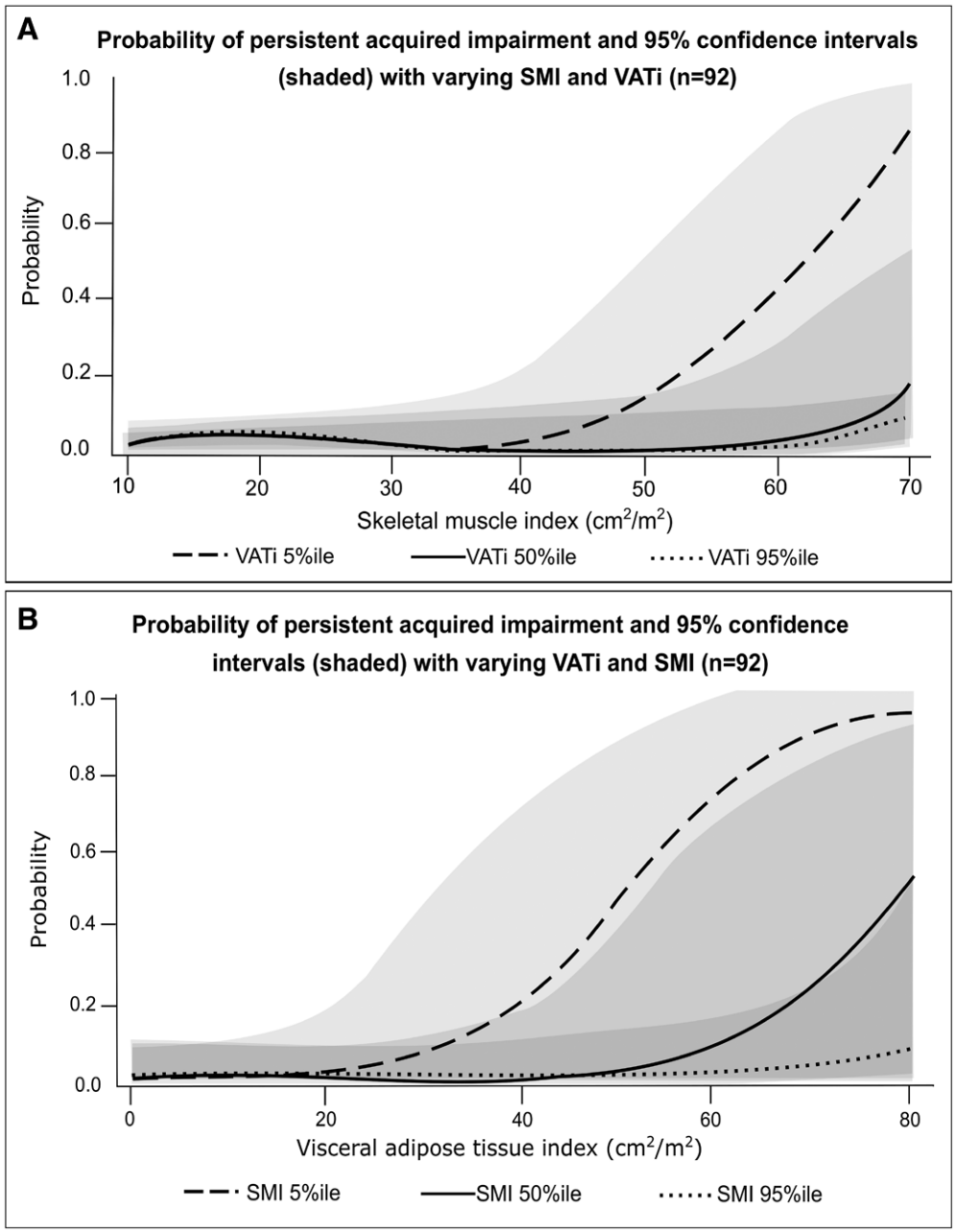


Figure 3. Probability curves persistent acquired impairment at varying levels of skeletal muscle index (SMI) (**A**) and visceral adipose tissue (VATi) (**B**).

BMI is often used as a marker of nutritional status and risk and has been recommended as a part of routine nutritional assessment in critically ill children (30). Both low and high BMI have been associated with worse outcomes (12–14). Other pediatric and adult cohorts have found a protective effect of high BMI during critical illness, a phenomenon known as the "obesity paradox" (31–34), suggesting the insufficient granularity of weight or BMI alone in reflecting body composition (10, 35). Thus, individual components of skeletal and fat have been studied to understand the relationship between body mass and outcomes (10). Adipose tissue secrete adipokines such as tumor necrosis factor-α and interleukin-6 which interfere with skeletal muscle structure and induce muscle wasting (36, 37), of which VAT appears to have greater pro-inflammatory activity (38). In our cohort, replacing BMI with CT indices demonstrated that increased VAT was associated with a greater risk for persistent acquired impairment, even after adjusting for possible confounders. However, we were unable to demonstrate an association between adipose tissue and inflammatory response in our study as CRP was only measured in 61% of cohort 2, and no other inflammatory cytokines were measured. Nevertheless, the role of VAT in association with skeletal muscle changes during critical illness deserves further study and should be coupled with cytokine measurements.

A second phenotype, greater baseline skeletal muscle mass, was also independently associated with persistent acquired impairment, contrary to adults where lower skeletal muscle mass was associated with poorer outcomes (10). It is possible that children with greater skeletal muscle mass were more active pre-morbidly and may have experienced a greater loss of mass due to immobility during the PICU stay, that is, the most active will be most affected. Unfortunately, baseline activity and longitudinal muscle changes were not captured in our study. Of note, in the adult study where lower SMA was associated with worse outcomes, patients had a much longer ICU stay and ventilator requirement (10). Our study constituted comparably smaller numbers with children who were less sick, and thus our findings regarding skeletal muscle mass and functional impairment should be interpreted with caution. Indeed, in our subgroup of sicker patients with PICU stay greater than 2 days, the relationship between baseline skeletal muscle and persistent acquired impairment no longer remained significant.

Skeletal muscle mass appears to be a greater predictor of persistent acquired impairment than skeletal muscle quality, defined by SMD. In adults, skeletal muscle quality decreases during critical illness, and lower baseline muscle quality has been shown to

be independently associated with greater risk of 6-month mortality and longer hospital stay (11, 39). Typically, the presence of fatty infiltrates in skeletal muscle increases with age, resulting in decreasing muscle quality (40). In our cohort, median baseline SMD (52 HU; IQR, 38.6–56.9) was much higher than that reported in adults (approximately 30 HU). The lack of predictive ability of muscle quality measures in our cohort may be due to either the relatively higher SMD observed in children as compared with adults, or poor fidelity of SMD to differentiate skeletal muscle quality in children in regards to function.

With decreasing rates of mortality, functional impairment has been suggested as the main outcome measure in critical illness studies (41). However, there is still much variability in the timing and tools to measure functional status (42). We used the FSS in this study due to its ease of scoring and feasibility of obtaining these scores from medical records, as well as its ability to demonstrate impairments in various domains (23, 43). Our rates of acquired functional impairment are slightly higher than that reported in other studies (5% at hospital discharge) using the same functional measure (3, 44), but lower than the recently published "WeeCover" study (81.5% at PICU discharge) (2), which used a different functional tool. This suggests that FSS may under-detect impairments in patients with mild morbidities, shown by the large ceiling effects observed (71–83% at baseline, 20–23% at PICU discharge, and 57–64% at hospital discharge). Of note, in the "WeeCover" study, the greatest deficit and slowest recovery occurred in the mobility function domain (2). Motor function was also the most commonly impaired domain at hospital discharge in our population. Given the close relationship between skeletal muscle and physical function (45, 46), it appears even more important to study the skeletal muscle changes in order to better understand the problem of functional impairment in PICU children.

There are several limitations of our study. First, the retrospective nature of our study limits the accuracy of our data to that of medical records and restricts our ability to control for certain factors such as inflammatory status. Second, our single-center study utilizing convenience sampling limits its external validity. A large majority of our cohort had no impairments or transient impairments that resolved by hospital discharge (Table 1; 93% and 88% of cohorts 1 and 2, respectively). The association between radiographic body composition variables and outcomes were based on a very small number of patients with actual deterioration. Hence, these relationships will need to be further examined in larger populations with prospective evaluation of body composition. However, CT scans carry a significant radiation dose, which limits body its use in children for body composition assessments. The association between body composition and outcomes needs to be explored using alternative, safe bedside methods (47). Indeed, the low frequency of CT scans in our cohort suggested inadequate power in cohort 2. Based on a persistent impairment rate of 5.4% reported in the literature (3), an alpha of 0.05 and power of 0.90, 213 patients would be required for a multiple regression model and up to 10 predictors. Further, the correlation between CT L3-derived skeletal muscle and whole-body skeletal muscle has not been validated in children, only in adults (26). However, MRI studies showed that skeletal muscle volume increases proportionally in the trunk and extremities with age; thus, skeletal muscle derived from a single abdominal slice is also highly correlated with whole-body skeletal muscle volume in children (48–50). Age differences were present; however, measures of muscle and fat mass were normalized for size, minimizing this effect. Although other differences were seen between cohorts (e.g., PIM 3), these were corrected for.

CONCLUSIONS

Preadmission body mass and composition may play an important role in the persistence of acquired functional impairment in survivors of pediatric critical care and deserves further study in a larger, sicker group of patients. Quantifying and characterizing individual skeletal muscle and adipose tissue components may impact on future interventional trial methodology (e.g., different requirements of nutritional and physical therapy) and needs to be further delineated in observational work.

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