Skeletal Muscle Changes, Function, and Health-Related Quality of Life in Survivors of Pediatric Critical Illness

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OBJECTIVES: To describe functional and skeletal muscle changes observed during pediatric critical illness and recovery and their association with health-related quality of life.

DESIGN: Prospective cohort study.

SETTING: Single multidisciplinary PICU.

PATIENTS: Children with greater than or equal to 1 organ dysfunction, expected PICU stay greater than or equal to 48 hours, expected survival to discharge, and without progressive neuromuscular disease or malignancies were followed from admission to approximately 6.7 months postdischarge.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Functional status was measured using the Functional Status Scale score and Pediatric Evaluation of Disability Inventory–Computer Adaptive Test. Patient and parental health-related quality of life were measured using the Pediatric Quality of Life Inventory and Short Form-36 questionnaires, respectively. Quadriceps muscle size, echogenicity, and fat thickness were measured using ultrasonography during PICU stay, at hospital discharge, and follow-up. Factors affecting change in muscle were explored. Associations between functional, muscle, and health-related quality of life changes were compared using regression analysis. Seventy-three survivors were recruited, of which 44 completed follow-ups. Functional impairment persisted in four of 44 (9.1%) at 6.7 months (interquartile range, 6–7.7 mo) after discharge. Muscle size decreased during PICU stay and was associated with inadequate energy intake (adjusted β, 0.15; 95% CI, 0.02–0.28; $p = 0.030$). No change in echogenicity or fat thickness was observed. Muscle growth postdischarge correlated with mobility function scores (adjusted β, 0.05; 95% CI, 0.01–0.09; $p = 0.046$). Improvements in mobility scores were associated with improved physical health-related quality of life at follow-up (adjusted β, 1.02; 95% CI, 0.23–1.81; $p = 0.013$). Child physical health-related quality of life at hospital discharge was associated with parental physical health-related quality of life (adjusted β, 0.09; 95% CI, 0.01–0.17; $p = 0.027$).

CONCLUSIONS: Muscle decreased in critically ill children, which was associated with energy inadequacy and impaired muscle growth postdischarge. Muscle changes correlated with change in mobility, which was associated with child health-related quality of life. Mobility, child health-related quality of life, and parental health-related quality of life appeared to be interlinked.

KEY WORDS: critically ill children; functional status; health-related quality of life; skeletal muscle; ultrasonography

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Outcome trends of pediatric critical illness in the past 3 decades illustrate decreasing mortality rates with a rise in functional impairments (1). These functional impairments contribute to the "Post-Intensive Care Syndrome in pediatrics," significantly affecting healthcare costs, caregiver burden, family functioning, and health-related quality of life (HRQOL) (2). Impairments occur mainly in three areas—physical/functional, neurocognitive, and psychologic (3). In a recent study of functional trajectory in pediatric critical care survivors, impairments in physical function appear more common and persistent than cognitive impairments (4).

Functional impairment following critical illness has been widely studied in adults. Adult survivors of acute respiratory distress syndrome reported persistent impairment in function and HRQOL, attributed to muscle loss and weakness during ICU stay (5). Imaging modalities such as ultrasonography and CT have now demonstrated acute decreases in skeletal muscle size and fat infiltration into skeletal muscle (6, 7). These skeletal muscle changes correspond with decreases in strength and function following ICU stay (6, 8).

In critically ill children, ultrasound imaging has captured decreases in skeletal muscle size during critical illness (9, 10). However, ultrasound studies focused on post-PICU discharge muscle changes have not yet been described. It is also unknown whether changes in skeletal muscle are associated with decreases in function or HRQOL in critically ill children or their parents.

We aimed to describe functional and skeletal muscle changes in critically ill children from PICU admission to posthospital discharge. Secondary aims were to explore factors associated with muscle change and the association between muscle changes and functional impairments in PICU survivors, as well as survivor and parental HRQOL.

MATERIALS AND METHODS

Subjects

We conducted a prospective observational study of children 1 month to 18 years admitted to a tertiary mixed medical-surgical-cardiac PICU in Singapore. Subjects were recruited between January 2015 and October 2018 if they had greater than or equal to 1 organ dysfunction (2005 International Pediatric Sepsis Consensus Conference criteria [11]), expected PICU admission greater than or equal to 48 hours and expected survival greater than or equal to 1 year postdischarge. Due to manpower constraints, recruitment was conducted on weekdays, subject to the availability of a study team member to obtain consent. Children with oncological or progressive neuromuscular disease were excluded as these conditions could affect long-term skeletal muscle changes (12, 13). Subjects were followed throughout PICU stay, at hospital discharge, and once 6–12 months postdischarge.

A second cohort of age- and gender-matched healthy children, defined as physically active children without preexisting disease, were recruited from outside the hospital for comparison of survivors postdischarge. This study was approved by the SingHealth Centralized Institutional Review board with appropriate informed consent (Reference: 2014/2073). This study was registered with ClinicalTrials.gov (NCT03730844) and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist was used in reporting this study (14).

Measurements

Clinical Data. Baseline characteristics were recorded including presence of complex chronic conditions defined by Feudtner et al (15). PICU data collected included admission reason, Pediatric Index of Mortality (PIM) 3 illness severity score, maximum organ dysfunction score by the Pediatric Logistic Organ Dysfunction 2 score, duration of mechanical ventilation, and sedation (11, 16, 17). Daily energy and protein intakes were collected and compared with requirements calculated by the Schofield equation and American Society for Parenteral and Enteral Nutrition recommendations, respectively, expressed as percent adequacy (18, 19). Energy adequacy was defined as meeting two-thirds of energy requirement during PICU stay (19). Our unit protocol aims to initiate enteral nutrition within 48 hours of admission, reach full feeds within 12–16 hours thereafter. Parenteral nutrition is initiated if feeds are not tolerated. There were no institutional changes in sedation, mechanical ventilation, and early mobilization during this time.

Function and HRQOL. Functional and HRQOL measurements and their time points are shown in **Table 1**. In PICU subjects, global functional status was assessed using the Functional Status Scale (FSS), while specific functioning in daily activities, mobility, and social/cognitive function were assessed using the Pediatric Evaluation of Disability Inventory—Computer Adaptive Test (PEDI-CAT) (20, 21). Impairments in global function were

TABLE 1.
Functional and Muscle Assessments and Time Points

Assessments	PICU Admission (Baseline)	PICU Stay	PICU Discharge	Hospital Discharge	Postdischarge
Ultrasound	✓[a]	✓	✓	✓	✓
Functional Status Scale	✓[b]	–	✓	✓	✓
Pediatric Evaluation of Disability Inventory–Computer Adaptive Test	✓[b]	–	–	–	✓
Pediatric Quality of Life Inventory	✓[b]	–	–	✓	✓
Short Form-36 questionnaire	–	–	–	✓	✓

[a]Within 48 hr of admission.
[b]Based on preadmission function.
Dashes indicate not available.

defined as an increase in greater than or equal to 3 FSS points from baseline (20). Child physical and psychosocial HRQOL was measured using the Pediatric Quality of Life Inventory (PedsQL) generic core scales Version 4.0 (> 2 yr) and Infant and Toddler Scales Version 1.0 (≤ 2 yr). These were completed by the child (> 13 yr) or parent (≤ 13 yr or unable to comprehend) (22). Parent physical and mental HRQOL was measured using the Short Form-36 (SF-36), completed by the primary parent (23). In healthy children, PedsQL and PEDI-CAT were assessed at a single outpatient clinic visit. In all measurement tools, higher scores indicated better function except for the FSS, where higher scores indicate worse function.

Muscle Ultrasound. Quadriceps ultrasound was conducted within 48 hours of PICU admission, day 3, 7, and 10, at PICU and hospital discharge, and postdischarge (procedure detailed in **online supplement**, http://links.lww.com/CCM/G286). In healthy children, ultrasound measurements were at a single time point. Properties studied include rectus femoris cross-sectional area (RF_{CSA}), rectus femoris echogenicity (RF_{ECHO}), and quadriceps fat thickness (**Fig. e1**, http://links.lww.com/CCM/G286). Ultrasound measurements were captured and measured by a single observer (C.O.). Intra-rater measurements for RF_{CSA} were conducted in a random subgroup of 26 patients.

Statistical Analysis

Paired *t* tests or Wilcoxon signed-rank tests were used to compare parameters at various time points and between subjects and controls. Change in function and HRQOL from baseline were calculated at PICU discharge, hospital discharge, and postdischarge. Postdischarge, PedsQL, and PEDI-CAT scores were also compared with age- and gender-matched controls. Parental SF-36 domain-specific, Mental Component Summary (MCS), and Physical Component Summary scores were compared with local norms (24, 25). Box plots and error bars were used for pictorial summary.

Regression analysis was used to identify factors associated with muscle loss. According to guidance by Lederer et al (26), we controlled for historical factors associated with muscle changes (i.e., age, admission body mass index [BMI] *z* score, baseline FSS score, and PIM 3 score) (10). In addition, variables significant at the *p* value of less than 0.10 level in the univariable analyses were considered for the multiple regression model. Associations between change in ultrasound parameters and function were explored using regression analysis, controlling for age, baseline function, and PIM 3 score. Associations between function and HRQOL were analyzed controlling for age, PIM 3 score, and presence of complex chronic conditions. Model fit was assessed using R^2 and *F*-statistic, and multicollinearity was determined if the variance inflation factor was greater than 3. Data were analyzed using IBM SPSS Version 20.0 (IBM Corp, Armonk, NY) with a two-tailed test and significance of *p* value of less than 0.05. At each time point, missing data were excluded from analysis. Characteristics of those completing follow-up were compared with those lost to follow-up.

RESULTS

Of the 77 subjects who consented, four died in hospital and were excluded from analysis (**Fig. 1**). Forty-four of

73 survivors completed follow-up at a median of 6.7 months (interquartile range [IQR], 6.0–7.7 mo) post-PICU discharge (**Table 2**). Muscle ultrasound measurements demonstrated high intraoperator reliability (intraclass correlation coefficient, 0.999; 95% CI, 0.997–0.999) (**Fig. e2**, http://links.lww.com/CCM/G286).

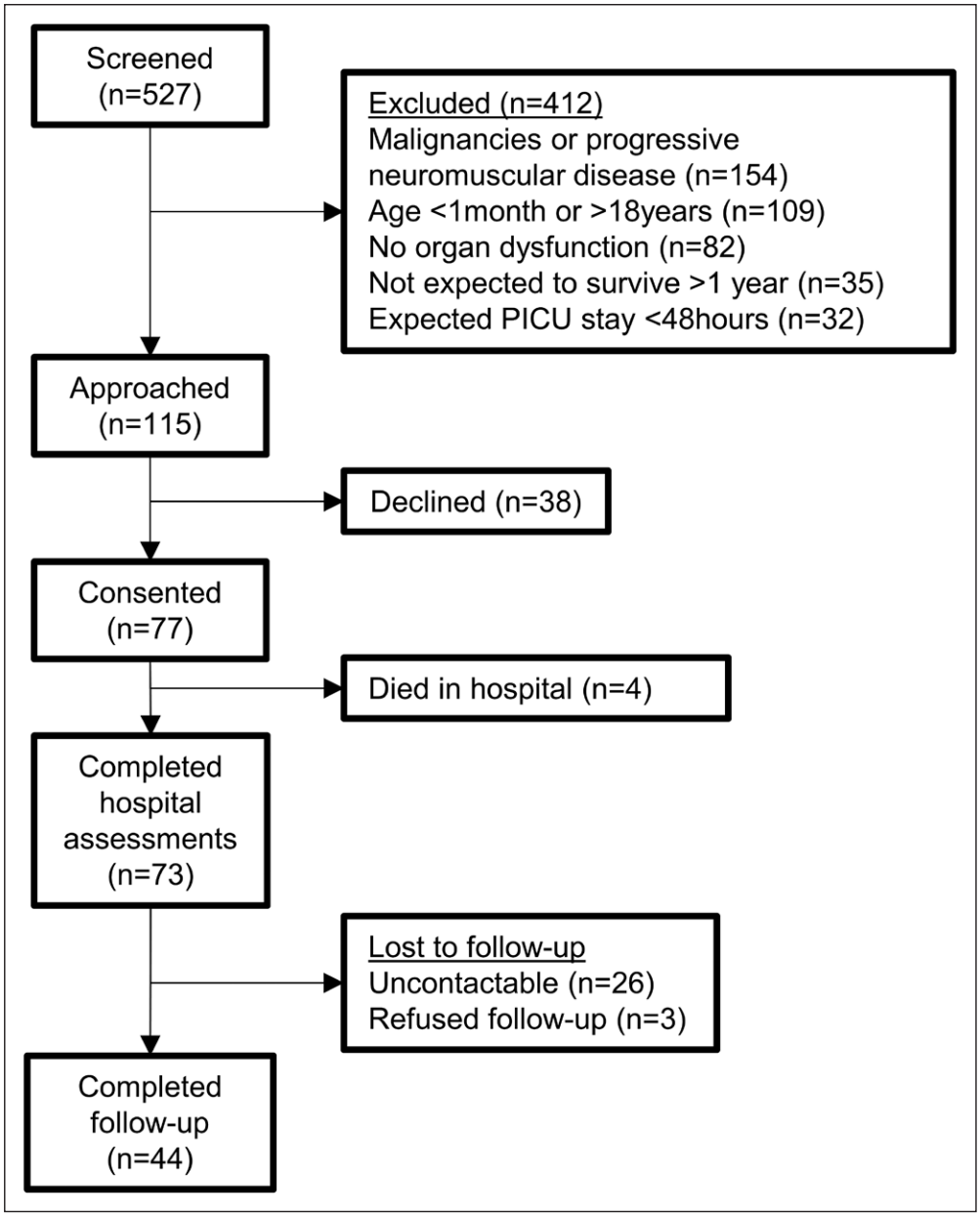

Figure 1. Study flowchart depicting recruitment and subject assessments at various time points.

PICU and Hospital Muscle and Functional Changes

At PICU discharge, FSS scores worsened by 2.0 points (IQR, 0–5.0 points; $p < 0.001$; **Fig. 2**), resulting in global functional impairment in 35 of 73 patients (47.9%). RF_{CSA} decreased by 6.2% (95% CI, 0.9–11.6%; $p = 0.003$), translating to a decrease of 2.4% (95% CI, 0.3–4.4%) per day. In 11 children with PICU stay greater than or equal to 10 days, peak muscle loss occurred on day 3, returning to baseline thereafter (**Fig. e3**, http://links.lww.com/CCM/G286). Patients did not demonstrate significant change in RF_{ECHO} or quadriceps fat thickness. Lower admission BMI *z* score was associated with muscle loss (**Table e1**, http://links.lww.com/CCM/G286). Controlling for age, baseline BMI *z* score, and baseline FSS score, for every percent decrease in energy adequacy during PICU stay, there was a 0.14% loss in muscle (95% CI, 0.01–0.26; $p = 0.033$) (**Table e2**, http://links.lww.com/CCM/G286). Inadequate energy intake was associated with more muscle wasting (–9.9% [95% CI, –15.6% to –4.1%] vs 2.5% [95% CI, –9.3% to 14.2%]; $p = 0.034$) (**Fig. 3**; and **Table e3**, http://links.lww.com/CCM/G286).

By hospital discharge, only 10 of 73 (13.7%) still had global functional impairment. There was also an overall recovery of muscle size, with a change in muscle size of –1.0% (95% CI, –7.5% to 5.5%; $p = 0.752$) from baseline. However, child HRQOL worsened, with a greater decline in physical compared with psychosocial scores (29.0 [IQR, 71.0–9.4] vs 15.0 [IQR, 33.3–0.04]; $p < 0.001$). At PICU and hospital discharge, RF_{CSA} change was not associated with change in FSS scores, controlling for age, baseline FSS score, and PIM 3 probability (**Table e4**, http://links.lww.com/CCM/G286).

Postdischarge Muscle and Functional Changes

Child Muscle, Function, and HRQOL. At follow-up, four of 44 (9.1%) still experienced global functional

TABLE 2.
Baseline Participant Characteristics for Total and Follow-Up Group

Variables	Baseline (*n* = 73)	No Follow-Up Group (*n* = 29)	Follow-Up Group (*n* = 44)	*p*
Age, yr	3.1 (0.8–9.2)	4.7 (1.8–9.7)	2.7 (0.6–9.2)	0.269
Male gender, *n* (%)	39 (53.4)	15 (51.7)	24 (54.5)	0.813
Weight, kg	14.6 (7.5–30.3)	15.9 (10.2–31.0)	12.7 (6.7–29.0)	0.230
Height, cm	98.0 (68.0–135.0)	105.0 (84.5–135.5)	90.0 (63.0–133.3)	0.189
Body mass index *z* score	−0.73 (−1.79 to 0.42)	−0.27 (−1.91 to 0.72)	−0.78 (−1.79 to 0.21)	0.569
Complex chronic disease, *n* (%)	28 (38.4)	6 (20.7)	22 (50.0)	0.012
Pediatric Index of Mortality 3 % probability	0.80 (0.40–2.20)	0.50 (0.30–1.45)	1.16 (0.53–2.28)	0.051
PICU stay, d	3.9 (2.0–12.3)	3.3 (0.3–11.9)	5.5 (1.9–12.6)	0.358
Post-PICU hospital stay, d	3.0 (2.0–8.0)	2.0 (2.0–6.0)	4.0 (2.0–9.0)	0.147
MV required, *n* (%)	55 (75.3)	19 (65.5)	36 (81.8)	0.165
MV days	1.4 (0.1–8.0)	1.1 (0–8.4)	1.6 (0.2–8.0)	0.772
Reason for admission				0.641
Cardiovascular	42 (57.5)	17 (58.6)	25 (56.8)	
Respiratory	17 (23.3)	7 (24.1)	10 (22.7)	
Neurologic	9 (12.3)	4 (13.8)	5 (11.4)	
Others	5 (6.8)	1 (3.4)	4 (9.1)	
Rectus femoris cross-sectional area, cm^2				
Below 6 yr	1.39 (0.69–2.53)	2.15 (1.20–2.71)	1.35 (0.57–2.40)	0.211
6 yr and above	2.46 (1.72–4.49)	3.94 (1.96–6.22)	2.26 (1.61–2.53)	0.055
Fat thickness, cm	1.02 (0.79–1.39)	0.99 (0.78–1.42)	1.04 (0.79–1.39)	0.803
Rectus femoris echogenicity	29.5 (23.8–41.0)	31.6 (24.3–41.3)	29.1 (23.7–39.6)	0.553
Energy adequacy, %	46.9 (24.3–76.5)	50.8 (13.0–88.2)	46.0 (27.0–63.0)	0.981
Protein adequacy, %	41.4 (9.4–67.8)	34.0 (0–83.5)	43.6 (14.3–63.3)	0.633

MV = mechanical ventilation.
Data are presented as median (interquartile range) unless otherwise specified. *p* values are for comparisons between those with and without follow-up.

impairment, without significant differences in PICU characteristics in those with or without persistent global functional impairment (**Table e5**, http://links.lww.com/CCM/G286). There was no significant change in daily activities (median T score change –2.0 [IQR, –8.0 to 8.0]; $p = 0.278$), mobility (0 [IQR, –12.0 to 13.0]; $p = 0.293$), or social/cognitive function scores (0 [IQR, –6.0 to 10.0]; $p = 0.826$) from baseline (**Table e6**, http://links.lww.com/CCM/G286). However, scores remained lower in survivors than in healthy controls (**Table e7**, http://links.lww.com/CCM/G286). Child HRQOL improved between discharge and follow-up,

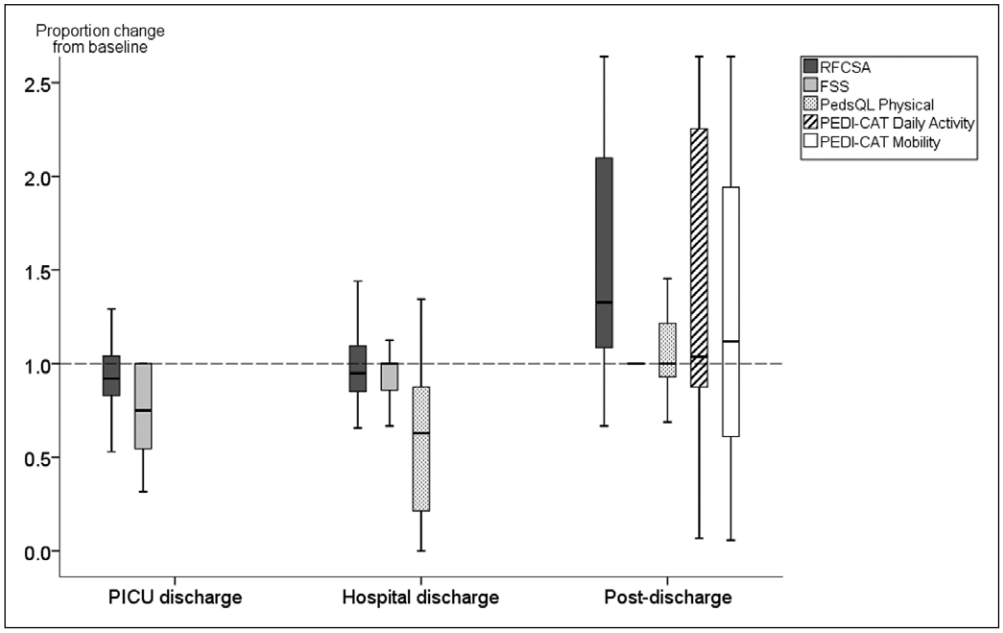

Figure 2. Proportion change in muscle, physical function, and physical health-related quality of life from baseline. *Bars* represent muscle size, functional status, and health-related quality of life scores in proportion to baseline values at three time points: PICU discharge ($n = 73$), hospital discharge ($n = 73$), and postdischarge ($n = 44$). Values above 1.0 (*dotted line*) demonstrate an improvement, while values below 1.0 demonstrate a worsening of values. FSS = Functional Status Scale, PEDI-CAT = Pediatric Evaluation of Disability Inventory—Computer Adaptive Test, PedsQL = Pediatric Quality of Life Inventory, RF_{CSA} = rectus femoris cross-sectional area.

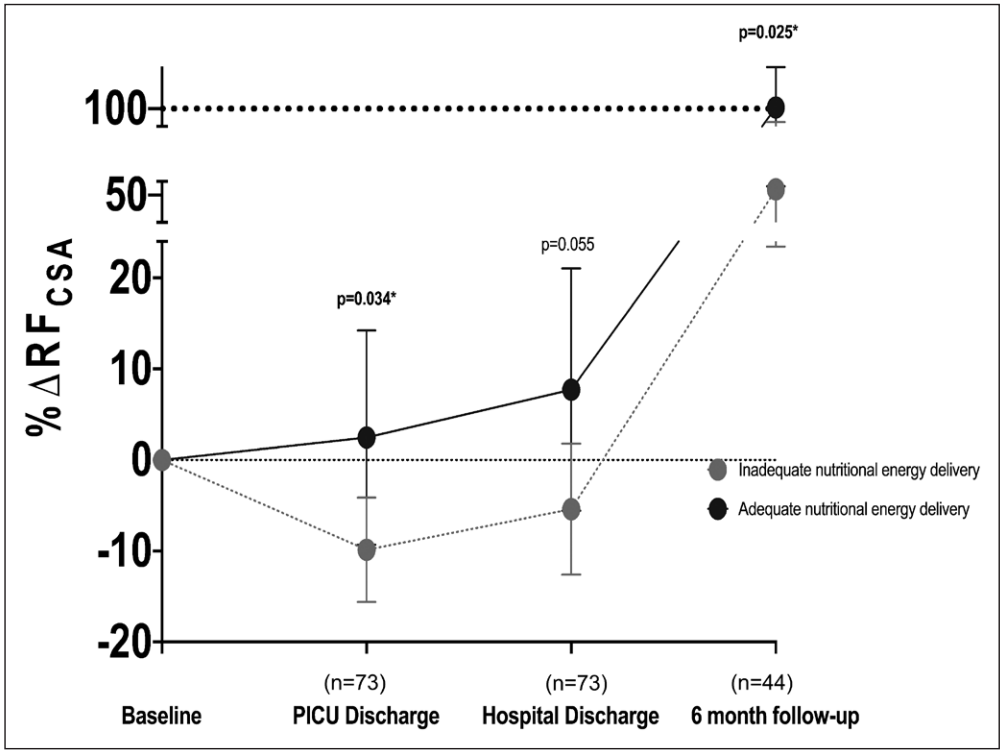

Figure 3. Longitudinal rectus femoris cross-sectional area (RF_{CSA}) change from baseline. *Asterisks* demonstrate significant differences in muscle size change between patients with and without adequate nutritional energy delivery. Values presented are mean and 95% CIs.

resulting in no significant overall change in scores from baseline.

Muscle size increased by 64.6% (95% CI, 38.7–90.4%; $p < 0.001$) from baseline. RF_{CSA} loss during PICU stay was associated with a smaller RF_{CSA} postdischarge (**Table e9**, http://links.lww.com/CCM/G286). Compared with age- and gender-matched controls, RF_{CSA} was lower in survivors while weight, height, and BMI *z* score were not significantly different (Table e7, http://links.lww.com/CCM/G286). This remained significant in a sensitivity analysis of survivors without any baseline global functional impairment ($n = 34$) (2.10 cm^2 [IQR, 1.72–2.97 cm^2] vs 2.85 cm^2 [IQR, 1.99–4.35 cm^2]; $p = 0.034$). Quadriceps fat thickness increased by 20.1% (95% CI, 4.6–35.6%; $p = 0.012$) while RF_{ECHO} showed no significant change (**Figs. e4** and **e5**, http://links.lww.com/CCM/G286).

At follow-up, increase in muscle size was associated with improvements in mobility scores (adjusted β, 0.05; 95% CI, 0.01–0.09; $p = 0.046$) (**Table e10** and **eFig. e6**, http://links.lww.com/CCM/G286). Improvements in mobility function were also associated with improvements in child physical HRQOL (**Table e11**, http://links.lww.com/CCM/G286).

Parental HRQOL. Parental physical HRQOL scores did not change significantly from hospital discharge (−1.81; 95% CI, −5.00 to 1.38; $p = 0.254$). However, parental mental HRQOL scores improved (10.95; 95% CI, 5.78–16.1; $p < 0.001$), specifically in the role-emotional and mental health domains (**Table e8**, http://links.lww.com/CCM/G286). Fifty percent and 16% of parents had MCS scores less than or equal to 1 SD below norm at hospital discharge and postdischarge, respectively. Child physical HRQOL were associated with parental physical HRQOL scores (**Table e12**, http://links.lww.com/CCM/G286).

DISCUSSION

Our study aimed to explore the physical sequelae across the continuum of body structure, function, and participation in critically ill children and its relation to parent and child HRQOL. We described functional and skeletal muscle changes throughout critical illness and recovery in children. Muscle change from baseline to follow-up was associated with mobility function. Mobility was in turn associated with child's physical HRQOL, which subsequently correlated with parental physical HRQOL.

Trajectory of Function and Muscle Changes

Global functional impairment in our cohort followed a similar trajectory to that reported in the literature, where rates are greatest at PICU discharge, improving with time but remaining persistent in a small proportion of survivors at 6–12 months postdischarge (4, 27). We did not find differences in baseline or PICU characteristics between those with and without persistent functional impairment, likely due to our small numbers. However, there was a trend toward persistent functional impairment in those with younger age and longer PICU stay, consistent with other studies (28, 29).

Muscle changes followed a similar trajectory to that of global function, as decreases in muscle size were observed at PICU discharge, recovering thereafter. In our cohort, muscle size decreased at 2.4% per day, comparable to that reported in adults (2–3% per day [6]) and slightly higher than that reported in children (1.5% per day [9, 10]). In contrast, fat thickness or muscle echogenicity did not significantly change. Echogenicity changes have been reported in critically ill adults representing the development of myonecrosis and myosteatosis (7, 30) and have been associated with impairments in strength (8). While this highlights a gap for future research into the specific differences between adults and children as regards tissue cell death and ultrasound echogenicity sensitivity, our findings suggest limitations in the use of RF_{ECHO} monitoring in critically ill children.

While no published values of RF_{CSA} growth in children exist, data from lower limb muscle mass and rectus femoris thickness changes suggest an expected growth rate of 15–20% over 6 months (31, 32). RF_{CSA} growth in our cohort were greater (65% [95% CI, 39–90%] over 6 mo), although muscle size remained significantly smaller in PICU survivors compared with age- and gender-matched controls. A possible explanation is the delay between onset of critical illness and baseline muscle measurement (taken within 48 hr of PICU admission), during which significant muscle loss may have already occurred, resulting in a smaller than expected baseline value and a larger than expected postdischarge growth. Alternatively, this rapid increase may be a physiologic response to acute muscle wasting during childhood growth. The rapid rate of muscle change reinforces the need for future ultrasound studies to capture muscle measurements as early as possible to provide accurate information on baseline muscle size. Our results also highlight an important characteristic of children—their constant state of growth. Unlike in adults, where the goal is for muscle size to return to baseline, muscle recovery in children appears to require growth that exceeds age-expected rates. Overall, the changes in muscle size observed are clinically relevant due to its association with functional status in critically ill children at follow-up, which occurred in the mobility domain. This mirrors findings associating muscle with physical function in adults and suggests a potential use for muscle ultrasound in determining early changes in physical function.

Associative Factors of Muscle Change

Two observations in regard to nutrition arose from our study. First, higher admission BMI *z* score was associated with less muscle wasting, greater decrease in fat thickness and an increase in muscle echogenicity. This suggests possible differences in endogenous sources of energy utilization between low and high BMI groups during critical illness—higher baseline fat stores may promote mobilization of fat and protect against muscle

wasting during critical illness, although muscle quality is not preserved. This "obesity paradox" theory has been demonstrated in adult mice, where obese mice experienced similar weight loss but more fat and less muscle loss compared with lean mice (33). Second, greater energy adequacy was associated with less muscle wasting in our cohort, contrary to reports in adults, possibly due to metabolic differences between children and adults (34, 35). Animal studies of muscle metabolism demonstrate high protein turnover rates in infancy, decreasing exponentially with age (36, 37). Growth in children is highly dependent on anabolic agents (e.g., growth hormone and insulin-like growth factor 1) (38, 39), which are themselves highly dependent on nutritional adequacy (40, 41). Rates of energy adequacy in our study (47%) are comparable to that reported in a large multicenter cohort (42), highlighting a gap in nutritional practice worldwide. Efforts focusing improving nutritional adequacy may reduce muscle wasting during PICU stay and help modify postdischarge function. This hypothesis is strengthened by findings that amino acid, as opposed to energy supplementation, drove worse outcomes in a supplementary parenteral nutrition trial (43, 44). However, these theories remain to be evaluated in randomized interventional studies. In critically ill adults, trials have failed to show benefits of increased energy provision on postdischarge function (45, 46), suggesting a complex relationship between nutrient metabolism and critical illness inflammation that is currently not completely understood. Future nutritional trials will require careful design to account for various factors including timing of nutrition, anthropometric heterogeneity while preventing overfeeding (47).

Implications on HRQOL

HRQOL is increasingly recognized as an important outcome in critical care. HRQOL declined significantly in our cohort during hospital stay, similar to other PICU HRQOL studies (48, 49). Physical HRQOL was significantly associated with mobility in survivors, a reminder that functional limitations have an impact on perceived health status. In addition, poorer patient physical HRQOL was associated with poorer physical HRQOL of parents, a possible indication of the physical toll that parents experience during their child's care. Such impairments in physical health have been reported in mothers caring for children with physical limitations, particularly those requiring help with transfers (50). This highlights a potential focus area of patient and caregiver support during the PICU stay and recovery. A possible way may be through family support protocols and active involvement of caregivers in rehabilitation, which has been shown to reduce depression in family members (51).

Limitations and Future Directions

A limitation of our study was the smaller sample size than other PICU functional follow-up studies (4, 52), albeit larger or comparable to acute PICU muscle ultrasound studies (9, 10). Only 60% completed follow-up, although our follow-up rates were comparable to that reported in other PICU follow-up studies (60% vs 53–80%) (4, 52, 53), suggesting the feasibility of follow-up studies measuring a combination of muscle, function and HRQOL. Another limitation is that our cohort may not be representative of other PICU cohorts. Illness severity scores were lower than others reported in the literature (0.8% risk of mortality vs average 3–7%) (4, 17), although based on both adult and pediatric data, sicker patients are likely to experience a greater degree of skeletal muscle wasting during PICU stay (6, 10). Our patients were also primarily of a cardiac diagnosis (57.5%), and those who completed follow-up were more likely to have a preexisting complex chronic condition compared with those who dropped out. This could have impacted on the degree of impairment and recovery, evident by nonsignificant changes in HRQOL and PEDI-CAT scores between baseline and follow-up. These factors limit generalizability and extrapolation of muscle recovery data to other PICU cohorts. Selection bias may also have been present due to the use of convenience sampling and the lack of data about those who did not consent to our study. Last, parental HRQOL was assessed using SF-36 questionnaires, which reflects generic health status and may not adequately reflect parental stress and anxiety. Furthermore, we did not assess parental HRQOL at baseline, limiting assessment of change from baseline. Questionnaires focusing on aspects of stress and anxiety conducted at baseline and longitudinally may better represent the impact of pediatric critical illness on their caregivers.

To our knowledge, this is the first study to report skeletal muscle changes using ultrasonography throughout critical illness and recovery and associate muscle with

functional changes in survivors and the subsequent consequences for parents. Our study demonstrates the importance and feasibility of combining muscle and functional assessments in PICU survivors. Our data also presents the hypothesis that nutrition provision is a potentially modifiable aspect of PICU care that could be explored in future trials on muscle wasting, possibly in combination with other rehabilitative interventions.

CONCLUSIONS

Critically ill children experience impairments in function and reductions in rectus femoris size during PICU stay. Muscle loss correlated with less overall muscle growth at 6 months postdischarge, which was associated with less improvements in mobility. Patient mobility function, physical HRQOL and parental HRQOL appear interlinked. Further study of longitudinal muscle, functional, and HRQOL changes in critically ill children are warranted.

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