Functional Recovery in Critically Ill Children, the "WeeCover" Multicenter Study

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Objectives: To evaluate functional outcomes and evaluate predictors of an unfavorable functional outcome in children following a critical illness.

Design: Prospective observational longitudinal cohort study.

Setting: Two tertiary care, Canadian PICUs: McMaster Children's Hospital and London Health Sciences.

Patients: Children 12 months to 17 years old, admitted to PICU for at least 48 hours with one or more organ dysfunction, were eligible. Patients not expected to survive, direct transfers from neonatal ICU and patients in whom long-term follow-up would not be able to be conducted, were excluded.

Interventions: None.

Measurements and Main Results: The primary endpoint was functional outcome up to 6 months post PICU discharge, measured using the Pediatric Evaluation of Disabilities Inventory Computer Adaptive Test. Secondary outcomes included predictors of unfavorable functional outcome, caregiver stress, health-related quality-of-life, and clinical outcomes such as mortality, length of stay, and PICU-acquired complications. One hundred eighty-two patients were enrolled; 78 children (43.6%) had functional limitations at baseline and 143 (81.5%) experienced functional deterioration following critical illness. Ninety-two (67.1%) demonstrated some functional recovery by 6 months. Higher baseline function and a neurologic insult at PICU admission were the most significant predictors of functional deterioration. Higher baseline function and increasing age were associated with slower functional recovery. Different factors affect the domains of functioning differently. Preexisting comorbidities and iatrogenic PICU-acquired morbidities were associated with persistent requirement for caregiver support (responsibility function) at 6 months. The degree of functional deterioration after critical illness was a significant predictor of increased hospital length of stay.

Conclusions: This study provides new information regarding functional outcomes and the factors that influence meaningful aspects of functioning in critically ill children. Identifying patients at greatest risk and modifiable targets for improvement in PICU care guides us in developing strategies to improve functional outcomes and tailor to the rehabilitation needs of these patients and their families. (*Pediatr Crit Care Med* 2018; 19:145–154)

Key Words: critical care; function; outcomes; pediatrics; recovery

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Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/pccmjournal).

Drs. Choong and Fraser, Ms. Cameron, and Ms. Simpson contributed to the acquisition of the data. Dr. Choong drafted and edited the article. All authors contributed to the conception and design of the study, the analysis and interpretation of the data, and final approval of article and accountability for all aspects of the work.

Supported, in part, by the Innovation Fund from Hamilton Academic Health Sciences Organization (principal investigator [PI]: Dr. Choong), and the Academic Medical Organization of Southwestern Ontario (PI: Dr. Fraser). Dr. Gorter received funding from a Patient-Centered Outcomes Research Institute grant (consultation fee) and Wiley publishers (Deputy Editor Child Care Health & Development), and he disclosed that he holds the Scotiabank Chair in Child Health Research. Dr. Khetani received funding from CanChild Centre for Childhood Disability Research, and she disclosed that she is lead author of the original Young Children's Participation and Environment Measure (YC-PEM) that was used in this study. Dr. Khetani is affiliated with CanChild Centre for Childhood Disability Research where the YC-PEM is licensed for commercial distribution and receives a portion of sales revenue. The remaining authors have disclosed that they do not have any potential conflicts of interest.

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DOI: 10.1097/PCC.0000000000001421

A "good" outcome following a critical illness has traditionally been measured by survival. However, in the context of the current high survival rates in critically ill children, mortality may not be the most appropriate quality indicator of pediatric critical care (1). The overwhelming majority of children admitted to PICUs in developed countries survive their critical illness and return home to recover with their families and communities. Current evidence indicates that "functioning" (i.e., one's physical, cognitive and psychosocial capacities, and ability to perform activities of daily living and participation in life situations) (2) is a more meaningful and important outcome to patients and families (3). However, patient important outcomes are rarely used as primary outcomes in clinical trials in critical care (4). A specific challenge in pediatric critical care is the paucity of research on functional outcomes and the factors that influence functional recovery in the general population of critically ill children (5). Previous data from our pilot study suggest that certain aspect of function may be more or less affected by critical illness, which in turn influences a child's overall recovery over time (6). The objectives of this study were to evaluate functional outcomes and predictors of unfavorable functional outcome, in children who survive a critical illness.

METHODS

This prospective observational longitudinal cohort study received institutional research ethics approval and was conducted at two tertiary care, university-based PICUs in Ontario, Canada: McMaster Children's Hospital and Children's Hospital, London Health Sciences Centre, Ontario. Informed parental consent and patient assent or consent where appropriate were obtained for participation in this study.

Participants

In order to enroll children at potential risk of functional decline and avoid participants who were less sick with short PICU stays (6), eligible patients were children over 12 months to 17 years old who were admitted to the PICU for at least 48 hours, had dysfunction in one or more organs at admission (as measured by Pediatric Logistic Organ Dysfunction [PELOD] 2 [7]), and were restricted to bed rest or not being mobilized in the first 48 hours of PICU admission. Patients were excluded if they were: 1) transferred directly from neonatal ICU, 2) previously enrolled in this study, 3) not able to complete long-term follow-up (e.g., lived out-of-region or had a language barrier), and 4) not expected to survive the current PICU admission.

Outcomes of Interest

The primary endpoint was functional outcome, measured longitudinally at PICU discharge, 3 and 6 months post PICU discharge. We applied the World Health Organization International Classification of Functioning, Disability and Health: Child and Youth version (ICF-CY) framework and used the Pediatric Evaluation of Disabilities Inventory Computer Adaptive Test (PEDI-CAT) Speedy version as a primary measure of child functioning (8). This electronic patient and/or parent-reported outcome measure is reliable and validated in children from birth to 20 years and captures functional performance in four key domains: daily activities, mobility, social/cognitive, and responsibility (9). The first three domains evaluate activity dimensions of function and performance of discrete tasks, whereas the responsibility domain measures one's ability to participate and engage in multistep life tasks or the requirement of caregiver support to do so (8). The Speedy ("Precision") version provides an efficient Computer Adaptive Test score, while maintaining precision. This generic functional outcome measure can be used across all clinical diagnoses, conditions, and community settings (10). PEDI-CAT is reported as a scaled score (recommended to assess change in functional domains over time) and normative scores (referenced to general population for age).

Secondary outcomes of interest were as follows: 1) predictors of unfavorable functional outcome; 2) measures of additional important determinants of health and functioning at 3 and 6 months post PICU discharge: health-related quality-of-life (HRQoL) as measured by KIDSCREEN (11), and parental/family caregiver stress as measured by the Pediatric Inventory for Parents (PIP) (12), a disease-related parenting stress measure (13); 3) PICU clinical outcomes, that is, duration of ventilation, length of stay, mortality, PICU and hospital readmission rates up to 6 months post PICU discharge; and 4) the occurrence rate of specific PICU-acquired complications (undesirable and unintended clinical conditions, distinct from the diagnosis requiring admission to PICU), that is, PICU-acquired weakness, delirium, new onset pressure ulcers, joint contractures, and poor glycemic control. These critical illness–acquired complications were selected based on evidence of an association with unfavorable functional and neurocognitive recovery in adults (14). The patient-reported outcome measures were administered by interview to parents and patients when appropriate. Details of the measurement tools and definitions for each of the PICU-acquired complications are outlined in the **Supplemental Appendix** (Supplemental Digital Content 1, http://links.lww.com/PCC/A588).

Sample Size

We designed this study to determine the predictors of unfavorable functional outcome, defined as the proportion of patients whose function did not return to baseline 6 months post PICU discharge. We estimated the sample size using the data from the WeeCover Pilot study, where 58% patients experienced unfavorable functional outcome (15). Based on planned multiple regression analyses with 10 planned predictors, the rule of 10–15 patients for each predictor variable (16), and factoring a possible loss to follow-up rate of 20%, we estimated a total sample size of 180 participants to create stable models for prediction of unfavorable functional outcome.

Analysis Plan

Baseline demographics and descriptive PICU outcomes were summarized using counts (%) for categorical variables and mean (SD) or median (interquartile range [IQR]) for continuous data as appropriate. Estimates of change in function scores were

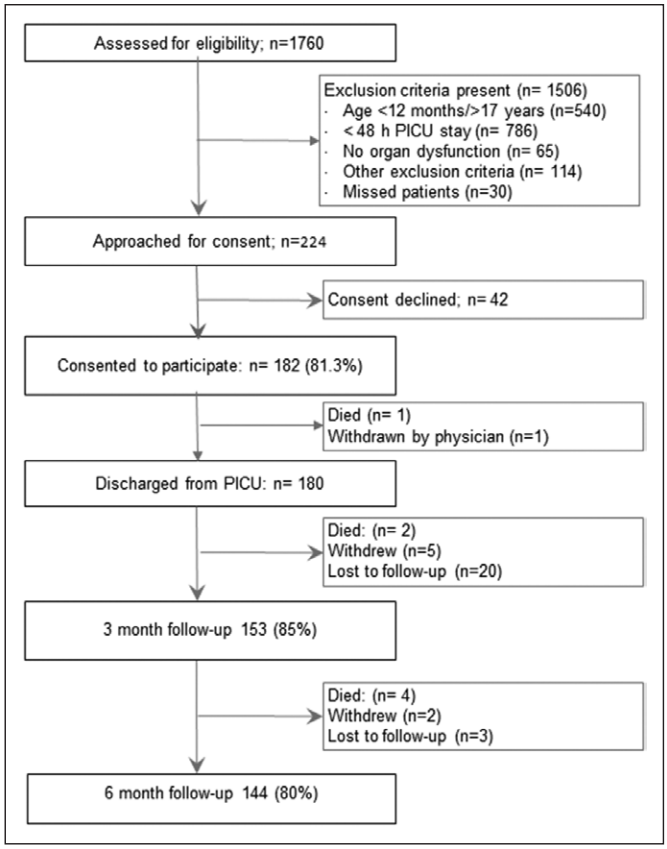

Figure 1. Patient enrollment and follow-up rate.

reported as mean (95% CI) (17). Functional deterioration and functional recovery were defined by the magnitude of change in PEDI-CAT scaled scores from baseline, where larger positive scores denote greater functional deterioration and slower functional recovery respectively. Functional recovery to baseline was defined as improvement in PEDI-CAT scaled scores to within 5% of their baseline score for each respective domain.

We assessed the following predictors of functional outcome based on available evidence, clinical relevance, and hypothesized association with functional outcome (18–21): baseline patient characteristics (age, gender, baseline function, and preexisting comorbidity), critical illness factors (admission diagnosis, severity of critical illness, and presence of PICU-acquired complications), and additional factors hypothesized to influence functional recovery (length of stay and caregiver stress) (18). Given the heterogeneity and numerous possible admission diagnoses and based on previous evidence (19), we chose to evaluate sepsis and neurologic insult on PICU admission as potential risk factors. Preexisting comorbidity was assessed based on adult data suggesting that this was the most important factor for HRQoL and functions after critical illness in adults (22).

We conducted exploratory multivariable analyses using regression methods to determine associations between predictor variables and functional outcome and hospital length of stay. As the PEDI-CAT measures four domains of function, we treated each domain as separate continuous outcomes in our analyses. The criterion for statistical significance was set at alpha equals to 0.05. We assessed model assumptions by examining the residuals. We also examined the presence of multicollinearity among the predictors and removed the predictors with high collinearity. The regression results were reported as estimates of model coefficients (95% CI) and associated *p* values. All statistical analyses were conducted using RStudio version1.0.143 (Based on R version 3.4.0, Boston, MA).

RESULTS

A total of 182 patients were enrolled between August 2014 and January 2016. As one participant died and another withdrew prior to PICU discharge, we enrolled an additional two beyond the originally planned 180 participants. Follow-up was completed in 153 participants (85%) and 144 participants (80%) at 3 and 6 months, respectively (**Fig. 1**). The PEDI-CAT was completed primarily by parents and by 20 patients (10.1%) at baseline. The KIDSCREEN was completed by only six patients. Baseline demographics for the 182 patients enrolled are presented in **Table 1**. The median (IQR) age was 7.1 years (2.9–13.4 yr), and 52% were male. One hundred twenty-three patients (68.7%) had a preexisting comorbidity, 56.8% of whom consisted of an underlying neurologic condition (e.g., seizure disorder, cerebral palsy, chronic encephalopathy).

Primary Outcome

Overall, 78 participants (43.6%) were functioning below expected for age in one or more domains at PICU admission (Table 1). This increased to 143 participants (85.1%) at PICU discharge (**Table 2**). Seventy-three children (55.7%) were still functioning below expected for their age at 6 months. One hundred thirty-seven patients (81.5%) experienced functional deterioration in one or more domains due to their critical illness. Functional outcome trajectories following critical illness for each of the four domains are displayed in **Figure 2**. Overall, 92 (67.1%) experienced some recovery in one or more domains of function by 6 months; however, residual limitations remain in each functional domain; 32 patients (24%) still had not returned to baseline mobility function 6 months post PICU discharge. **Figure 3** presents the proportion of patients who had not returned to their baseline function for each functional domain at 6 months post PICU discharge.

Predictors of Functional Outcome

Functional Decline at PICU Discharge. PELOD-2 was excluded from the regression model due to high collinearity with Pediatric Risk of Mortality III. Multivariable regression analyses revealed that higher baseline function and presence of a neurologic insult at PICU admission were independent predictors of worse functional decline overall at PICU discharge (**Table 3**). Increasing severity of illness and PICU-acquired morbidities were risk factors for greater decline in social and cognitive function. Increasing severity of illness revealed the same direction of relationship to worsening functional outcomes in the other three domains. Age, sex, and sepsis were explored in the model but not found to be significant risk factors for functional decline.

TABLE 1. Baseline Characteristics at PICU Admission

Demographic Variables	No. of Patients (n = 182)
Age (yr), median (IQR)	7.2 (2.9–13.4)
Gender, male, *n* (%)	95 (52.2)
Primary diagnostic category at admission, *n* (%)	
Respiratory failure	65 (35.7)
Sepsis	26 (14.3)
Postsurgical care	22 (12.1)
Trauma	21 (11.5)
Cardiac	2 (1.1)
Neurologic	16 (8.8)
Endocrine	3 (1.7)
Nephrologic	2 (1.1)
Burns	3 (1.7)
Hypovolemic/hemorrhagic shock	2 (1.1)
Malignancy	10 (5.5)
Other	8 (4.4)
Preexisting comorbidity[a], *n* (%)	125 (68.7)
Neurologic	71 (56.8)
Respiratory	42 (33.6)
Malignancy	16 (12.8)
Endocrine	15 (12.0)
Cardiac	12 (9.6)
Other	20 (16.0)
Pediatric Risk of Mortality III[b] at admission, median (IQR)	7 (3–11)
Pediatric logistic Organ Dysfunction 2[c] at admission, median (IQR)	5 (3–6)
Baseline functioning as measured by PEDI-CAT[d] scaled scores, mean (SD)	
Daily activities	52 (13)
Mobility	59 (15)
Social/cognitive	60 (12)
Responsibility	43 (14)
Patients with low baseline functioning (PEDI-CAT[d] normative score < 2 SD for age), *n* (%)	
Overall	78 (43.6)
Domain specific, *n* (%)	
Daily activities	55 (30.7)
Mobility	70 (39.1)
Social/cognitive	52 (29.1)
Responsibility	42 (23.5)

IQR = interquartile range, PEDI-CAT = Pediatric Evaluation of Disability Inventory Computer Adaptive Test.

[a]Preexisting comorbidity refers to an underlying medical condition present prior to PICU admission. Patients may have > 1 condition. "Neurologic" indicates underlying neurologic condition, e.g., epilepsy, cerebral palsy, chronic encephalopathy.

[b]Pediatric Risk of Mortality Score, third generation; based on the first 12 hr of PICU stay (range 0–74).

[c]Pediatric Logistic Organ Dysfunction 2 score (range 0–33).

[d]PEDI-CAT. The scaled score is criterion referenced and recommended for assessing change in function over time. Normative scores describe the child's functional performance in comparison with other children of the same age (by 1 yr intervals).

Functional Recovery at 6 Months Post PICU Discharge. Higher baseline function and increasing age were associated with a slower functional recovery across all domains at 6 months. Other factors affected functional recovery to varying degrees: neurologic insult was associated with slower recovery in mobility and activities, while increasing severity of illness primarily affected children's abilities to regain independence in performing social/cognitive tasks. Preexisting comorbidity and the development of PICU-acquired complications were associated with poorer recovery in responsibility (i.e., persistent need for caregiver support in managing tasks). Sepsis, sex, PICU length of stay, and parental stress at PICU discharge were explored in the model but not found to be predictive of functional recovery.

Predictors of Hospital Length of Stay. Multivariable regression analyses for hospital length of stay are presented in **Table 4**, using decline in daily activities domain as one of the predictors. Regression tables exploring the three other functional domains as predictors showed a similar direction in each domain as with daily activities and are included in **Supplemental Appendix Table 1** (Supplemental Digital Content 2, http://links.lww.com/PCC/A589). The greater the degree of functional decline following critical illness, a neurologic insult, the development of PICU-acquired complications, and higher parental stress at PICU discharge were all independently associated with a longer duration of hospitalization. Worsening function as a result of critical illness increases hospital length of stay by 2% for each one point decline in functioning, whereas a neurologic insult at admission and the presence of one or more PICU-acquired complication increases the hospital length of stay by as much as 42% and 28%, respectively.

Secondary Outcomes

The PIP-Frequency and PIP-Difficulty parenting stress scores indicated that events contributing to stress were

TABLE 2 . Functional and Clinical Outcomes

Functional Performance	PICU Discharge ($n = 168$)	3 Mo ($n = 141$)	6 Mo ($n = 131$)
PEDI-CAT[a] scaled scores, mean (SD)			
Daily activities	44.4 (11.2)	51.3 (12.2)	52.6 (11.9)
Mobility	46.2 (12.7)	56.8 (13.0)	57.9 (13.4)
Social/cognitive	55.9 (12.9)	60.5 (11.5)	61.4 (10.8)
Responsibility	36.3 (12.4)	43.0 (13.2)	43.3 (12.4)
PEDI-CAT[b] normative score < 2 SD in 1 or more domains, *n* (%)	143 (85.1)	80 (56.7)	73 (55.7)
Caregiver Stress: Pediatric Inventory for Parents[c], median (IQR)	**PICU Discharge**	**3 Mo**	**6 Mo**
Frequency score	135.0 (116.0–154.0)	108.5 (87.0–135.2)	100.0 (75.0–121.0)
Difficulty score	118.0 (97.0–141.0)	95.5 (67.8–126.3)	90.5 (61.3–118.5)
Low health-related quality-of-life, *n* (%) with KIDSCREEN[d] T scores < 1SD		**3 Mo**	**6 Mo**
Physical well-being		44 (31)	36 (27)
Psychologic well-being		42 (30)	27 (21)
Moods and emotions		8 (6)	5 (4)
Autonomy and parent relation		19 (13)	9 (7)
Social support and peers		58 (41)	52 (40)
School environment		6 (4)	2 (2)
Clinical Outcomes		***n* = 180**	
Duration of mechanical ventilation (invasive and/or noninvasive), median (IQR)		4.0 (2–8)	
Ventilator-free days[e]		26.0 (23–28)	
Length of PICU stay		7 (4–12)	
Length of hospital stay		17.5 (10–29)	
PICU-acquired complications, *n* (%)		109 (60.6)	
PICU-acquired weakness		40 (22.5)	
Pressure ulcers		35 (19.7)	
Grade 2 and above		24 (13.3)	
Delirium		21 (11.8)	
Poor glycemic control		68 (37.8)	
New onset joint contractures		1 (0.6)	
Deep venous thrombosis		2 (1.1)	
No. of PICU-acquired complications in affected patients, *n* (%)			
1 only		61 (56)	
2 only		35 (32)	
3 or more		13 (12)	
Readmission rate in 6 mo, *n* (%)			
Hospital		63 (35)	
Subset admitted to PICU		41/63 (65.1)	

IQR = interquartile range, PEDI-CAT = Pediatric Evaluation of Disability Inventory Computer Adaptive Test.

[a]PEDI-CAT, the scaled score is criterion referenced and recommended for assessing change in function over time.

[b]PEDI-CAT normative scores (T score) compares functional performance with other children of the same age (by 1 yr intervals). Data are presented for the *n* (%) with normative scores < 2 SD for age.

[c]The Pediatric Inventory for Parents measure contains 42 medically related situations and thoughts that may contribute to parenting stress. Using a five-point Likert scale, each item is rated according to frequency of occurence (frequency score) and how difficult/stressful the event is (difficulty scores). Scores range from 42 to 210 with higher scores indicating greater parenting stress.

[d]KIDSCREEN is a health-related quality-of-life (HRQoL) score, reported as T scores (scale means of 50; SD < 1SD indicates lower HRQoL than reference population for age).

[e]Ventilator-free days is the number of days alive and free of invasive mechanical ventilation at day 30 post PICU admission.

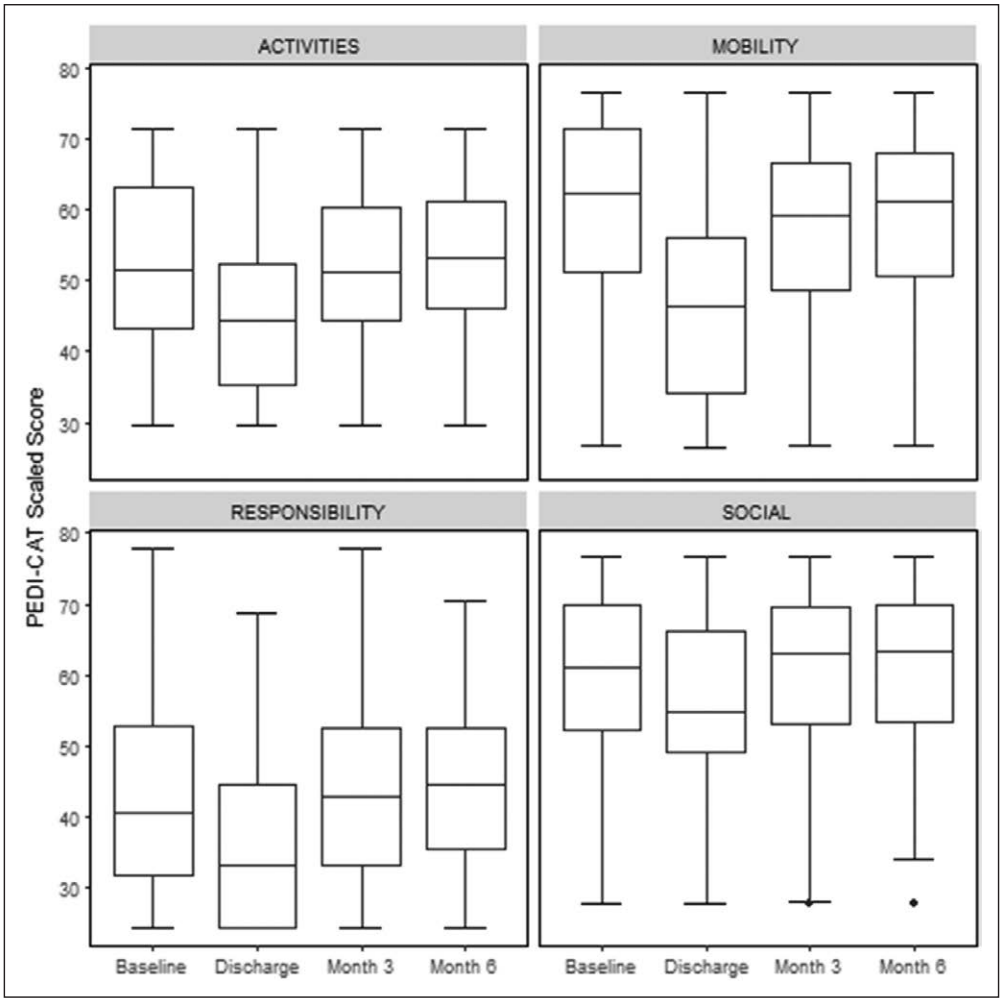

Figure 2. Functional outcome trajectories 6 mo following critical illness. Pediatric Evaluation of Disability Inventory Computer Adaptive Test (PEDI-CAT) median and interquartile range scaled scores are presented for each of the four key functional domains, at each time point.

frequent and perceived as difficult, particularly at time of PICU discharge, but improved over time (Table 2). HRQoL as measured by KIDSCREEN suggests that physical, psychologic well-being and social support are the domains most affected following critical illness and are still below the referenced population 3 and 6 months post PICU discharge. Clinical outcomes are presented in Table 2. The overall 6-month mortality rate was seven of 182 (3.8%). The majority of deaths (6/7) occurred following PICU discharge (Fig. 1). One hundred nine participants (60.6%) experienced at one or more PICU-acquired complications, 40 (22.5%) of whom developed PICU-acquired weakness. Sixty-three patients (35%) were readmitted to hospital within 6 months of PICU discharge, 41 (65.1%) of whom were admitted to the PICU.

DISCUSSION

Increasing concern for residual morbidities has led to a growing interest in evaluating patient important outcomes in critically ill children (5). This dual-center prospective longitudinal cohort study evaluated functional outcomes using patient-reported outcome measures (23, 24) and demonstrates the following key findings: 1) the majority of children acquire new functional morbidities following a critical illness. Although many demonstrate some functional recovery, a significant proportion still have not returned to baseline function 6 months following PICU discharge; 2) higher baseline functioning prior to critical illness and neurologic insult at PICU admission are the most significant predictors of functional decline following critical illness and a slower functional recovery; 3) greater functional decline following critical illness has a significant impact on hospital length of stay.

Function is important and meaningful to patients and families and therefore has been proposed as a definitive outcome for clinical trials (3). However, measuring function is complex, and the most appropriate measurement tool in critically ill children remains unclear. Prior studies have used numerous measures, including HRQoL tools to capture function (5). The ICF-CY framework clearly defines functioning as a multidimensional construct and is therefore most appropriately evaluated through patient-reported outcome measures (23, 24). We used the PEDI-CAT as our primary measure of functioning in this study because it is a patient- or parent-reported measure, validated against the ICF-CY and can be used across all pediatric age groups (8); it is designed to detect change in a child's abilities to perform functional tasks.

Although there has been research on functional outcomes in specific pediatric subpopulations with traumatic brain injury and congenital heart disease (25, 26), there is little evidence on longitudinal measures of function the general PICU population. This study yields the following important information on functional outcomes in critically ill children. First, we identified that a significant proportion (44%) of critically ill children have baseline functional limitation at admission to PICU, and the majority of children experience a deterioration in their baseline function as a result of their critical illness. Our study reports a higher prevalence of acquired functional impairment at PICU discharge compared with previous studies, which report rates in the range of 10–36% (5, 21, 27, 28). Pinto et

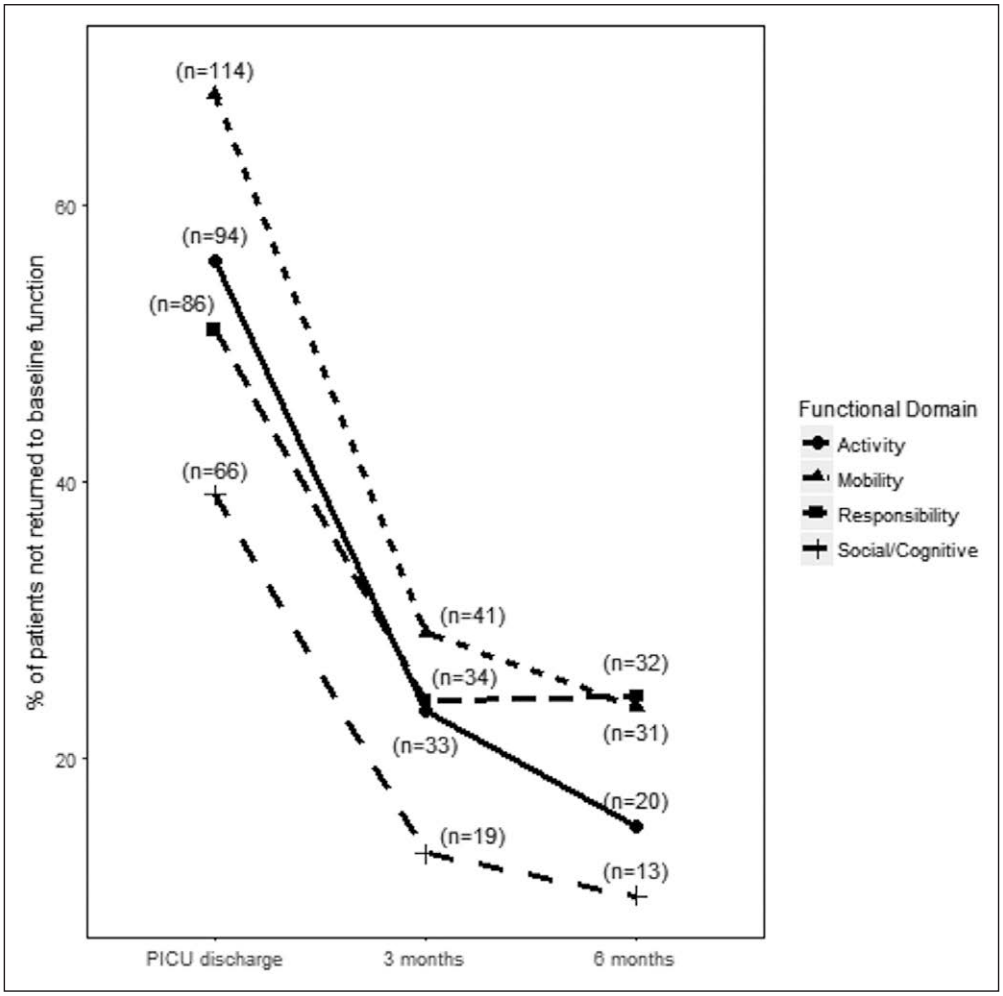

Figure 3. Patients with unfavorable functional outcome. Proportion (*n*) of patients whose function had not returned to within 5% of their baseline Pediatric Evaluation of Disability Inventory Computer Adaptive Test scaled score for each respective domain.

al (27) reported new morbidities in only 5.2% of patients at discharge. This variability may be due to an underestimation in previous studies based on the nature of the measurement tool used, or because of clinician report, as opposed to objective patient/parent-reported tools.

The second important observation from this study is the trajectory of functional recovery as this is one of the few studies that have evaluated functional outcomes on multiple occasions over time, post PICU discharge. Although other studies have identified the prevalence of residual long-term (27, 29), functional morbidities, we were able to determine that the greatest recovery of functional capacities appears to be in the first 3 months post PICU discharge; however, a third of patients had not recovered to baseline function by 6 months.

We found that the greatest predictors of unfavorable functional outcome in this study were higher premorbid function and neurologic insult at PICU admission. Higher functioning patients are at greatest risk of unfavorable functional outcomes because they have more skills and abilities "to lose" and therefore take longer to recover their function, compared with patients with lower functioning at baseline. Although neurologic disorders have previously been identified to be associated with worse clinical PICU outcomes (30), our study confirms that compared with other patient groups, these patients are at the greatest risk of worse functional outcomes at PICU discharge and slow recovery of their mobility and ability to perform activities of daily living at 6 months.

Our findings suggest that critical illness affects different aspects of functioning variably. We found that increasing severity of illness and PICU-acquired complications primarily affected social and cognitive, rather than physical function, and hypothesize the potential adverse influence of delirium and poor glycemic control on this outcome (31, 32). While long-term effects of hyperglycemia are unclear, hypoglycemia is associated with poor neurologic outcome in critically ill infants and children (33). Recent evidence suggests that the prevalence of delirium in critically ill children is similar to adults (34), and delirium is associated with persistent cognitive impairment following ICU discharge (35). Increasing severity of illness was also associated with slower cognitive functional recovery in this study. Previous studies have observed an association with increasing severity of illness and discharge function (20), but few have evaluated the independent impact of severity of illness on functional outcomes and recovery following critical illness. Bone et al (28) reported conflicting results on the effect of illness severity on acquired functional and cognitive disability and suggest that the measurement tools (Pediatric Overall Performance and Pediatric Cerebral Performance Category Scores) used in their study may not objectively discriminate changes in function. We did not find that sepsis was predictive of worse functional outcomes. This may be due to our categorization of all patients with sepsis together for the purposes of regression analyses, irrespective of severity. Similarly, we found that preexisting comorbidities were not predictive of, but appeared to have a reduced risk of functional decline. We also observed that preexisting comorbidities as well as iatrogenic PICU-acquired complications were associated with persistent need for caregiver support (i.e., lower levels of responsibility function for managing

TABLE 3. Multivariable Regression Analyses: Predictors of Functional Outcome According to Each Functional Domain[a]

		Daily Activities		Mobility		Social/Cognitive		Responsibility	
Factors	Comparison	Estimate (95% CI)	*p*	Estimate (95% CI)	*p*	Estimate (95% CI)	*p*	Estimate (95% CI)	*p*
Outcome: functional decline at PICU discharge (change score from baseline to discharge, positive scores indicate greater decline)									
Baseline function[b]	Increase by 1 point	0.3 (0.2–0.4)	< 0.001	0.4 (0.3–0.5)	< 0.001	0.045 (−0.1 to 0.2)	0.43	0.6 (0.1–0.4)	< 0.001
Neurologic insult[c]	Yes vs no	5.4 (2.3–8.6)	0.001	9.4 (5.3–13.5)	< 0.001	6.4 (3.4–9.3)	< 0.001	6.0 (2.7–9.4)	0.001
Preexisting comorbidity[d]	Previously healthy	−4.2 (−7.2 to −1.2)	0.01	−6.1 (−10.0 to −2.2)	0.002	−2.1 (−4.8 to 0.5)	0.11	−2.8 (−5.9 to 0.3)	0.07
PRISM III[e]	Increase by 1 point	0.2 (−0.1 to 0.4)	0.14	0.3 (−0.01 to 0.53)	0.06	0.4 (0.2–0.5)	< 0.001	0.1 (−0.1 to 0.4)	0.22
PICU-acquired complications[f]	Increasing counts	1.4 (−0.4 to 3.2)	0.14	−0.6 (−2.9 to 1.8)	0.64	1.8 (0.2–3.5)	0.03	−0.1 (−0.8 to 3.0)	0.24
Outcome: functional recovery at 6 mo (change score from baseline to 6 mo, positive scores indicate less recovery)									
Baseline function[b]	Increase by 1 point	0.1 (0.04–0.2)	0.004	0.1 (0.04–0.2)	0.01	0.1 (0.1–0.2)	< 0.001	0.1 (0.0–0.2)	0.04
Age (yr)	Increase by 1 yr	0.3 (0.1–0.5)	0.001	0.4 (0.2–0.6)	< 0.001	0.1 (0.0–0.2)	0.08	0.5 (0.3–0.7)	< 0.001
Neurologic insult[c]	Yes vs no	2.6 (0.2–4.9)	0.03	3.9 (1–6.7)	0.01	1.3 (−0.3 to 2.8)	0.12	1.4 (−1.1 to 3.9)	0.26
Preexisting comorbidity[d]	Previously healthy	0.4 (−1.7 to 2.6)	0.74	0.1 (−2.6 to 2.8)	0.93	0.8 (−0.6 to 2.2)	0.26	2.5 (0.3–4.7)	0.03
PRISM III[e]	Increase by 1 point	0.1 (−0.1 to 0.2)	0.40	−0.05 (−0.2 to 0.1)	0.58	0.2 (0.1–0.3)	0.002	−0.1 (−0.2 to 0.1)	0.46
PICU-acquired complications[f]	Increasing counts	0.8 (−0.5 to 2.2)	0.24	1.0 (−0.6 to 2.7)	0.21	0.8 (−0.1 to 1.7)	0.08	1.7 (0.3–3.1)	0.02

PRISM III = Pediatric Risk of Mortality III.

[a]As measured by Pediatric Evaluation of Disability Inventory Computer Adaptive Test (PEDI-CAT) scaled score.

[b]Baseline function: same PEDI-CAT domain was used for the predictor variable in the model as the outcome variable. Results are presented for each domain of function used as the predictor variable in the regression model.

[c]Neurologic insult: admission diagnosis related to neurologic injury, e.g., status epilepticus, traumatic brain injury, CNS sepsis, CNS tumor, or hemorrhage.

[d]Preexisting chronic conditions: underlying comorbidities present prior to PICU admission.

[e]PRISM Score, third generation; based on the first 12 hr of PICU stay (range 0–74).

[f]PICU-acquired complications: presence of any one of the following developing during the PICU admission, counts as one morbidity - PICU-acquired weakness, grade ≥ 2 pressure injury, delirium, poor glycemic control, new onset joint contracture, deep venous thrombosis.

TABLE 4. Multivariable Regression Analyses: Predictors of Hospital Length of Stay

Factors	Comparison	Estimate (95% CI)	*p*
Functional decline[a]	Increase by 1 point	1.02 (1.00–1.03)	0.02
Neurologic insult[b]	Yes vs no	1.37 (0.99–1.89)	0.05
Pediatric Risk of Mortality III[c]	Increase by 1 point	1.01 (0.98–1.03)	0.5
PICU-acquired complications[d]	Increasing counts	1.23 (1.01–1.50)	0.04
Parental stress (Pediatric Inventory for Parents frequency score at PICU discharge)	Increase by 1 point	1.01 (1.00–1.01)	0.005

[a]Functional decline from baseline to PICU discharge, in the daily activities domain. Interpretation: 1.02 = a 2% increase in hospital length of stay for each point decline in function.

[b]Neurologic insult: admission diagnosis related to neurologic injury, e.g., status epilepticus, traumatic brain injury, CNS sepsis, CNS tumor, or hemorrhage.

[c]Pediatric Risk of Mortality Score, third generation; based on the first 12 hr of PICU stay (range 0–74).

[d]PICU-acquired complications: presence of any one of the following morbidities developing during the PICU admission - PICU-acquired weakness, grade ≥ 2 pressure injury, delirium, poor glycemic control, new onset joint contracture, deep venous thrombosis.

Dependent variable is hospital length of stay, log-transformed data are skewed. Results are presented as exponentiated estimated coefficients and 95% CI.

daily tasks) at 6 months. We interpret these findings with caution because preexisting comorbidities was crudely defined in this study and included very heterogeneous systems, diagnoses, and illness severities. Existing literature is conflicted with respect to the impact of comorbidities, with some suggesting that this is a risk factor for acquired functional impairment at PICU discharge (36), while others were not able to demonstrate that comorbidities were a significant predictor (37). Others suggest that the highest rates of morbidity occur in specific groups of patients with underlying diseases, such as childhood cancer, congenital heart disease, and neurologic diagnoses (28, 38). There are no prior studies to our knowledge evaluating comorbidities specifically and "functional recovery" after critical illness in children.

Functional decline following critical illness is important, as it impacts on hospital length of stay. Similarly, PICU-acquired complications significantly increase length of stay and represent and target for quality improvement in pediatric critical care. These are potential modifiable targets for improvement in the delivery of our care. Caregiver stress at PICU discharge for this population was notably higher than previously reported in other childhood diseases (e.g., cancer, sickle cell disease) (39) and was significantly associated with increased hospital length of stay in this study. This relationship has not been previously described in critically ill children but has been observed in other pediatric populations and in caregivers of critically ill adults (40, 41). We speculate that caregiver stress contributes to an increased length of stay, given that this predictor preceded the outcome; however, the impact of long hospital stays on caregiver stress has been demonstrated (41). Caregiver stress can contribute to posttraumatic stress symptoms in children (42), and hence family support and caregiver well-being are important aspects of a child's recovery following critical illness. This study highlights that this is an important and potentially modifiable risk factor to identify in a timely manner, such that management of caregiver stress, social and rehabilitation supports may be instituted early.

We acknowledge the following limitations of this study. We examined functional status up to 6 months hypothesizing that majority experience some recovery in this period and were unable to follow this cohort to possible full functional recovery. We chose to include children expected to be ambulating or mobilizing and therefore excluded infants under 12 months old. Our sample size restricted our regression analyses to a limited number of predictors. We did not conduct HRQoL measurements at the same time points and hence cannot comment on the trajectory of this outcome. Although we identified risk factors, we are not able to draw any conclusions about causation of functional decline from our results. Future planned secondary analyses will evaluate physiotherapy practices and exposure to sedative medications on functional outcome.

CONCLUSIONS

Functional outcome is an important, patient-centered outcome in critically ill children. This prospective longitudinal study contributes new knowledge toward a better understanding of functional outcomes, recovery, and the factors that influence clinically meaningful aspects of functioning in children following a critical illness. It highlights that residual functional morbidity persists and is different for each patient and justifies the importance of follow-up of high risk cohorts after PICU discharge. There is a need to determine the optimal method(s) of measuring and reporting this outcome in critically ill children, in order to advance this field and use function as a patient important outcome measure in interventional trials. Improving our understanding of how aspects of functioning are affected after pediatric critical illness will enable us to identify patients at risk, counsel families, and target rehabilitation and social supports for children and their families. In so doing, we can subsequently design future studies aimed at optimizing functional recovery and ultimately improving the quality of survivorship in critically ill children.

ACKNOWLEDGMENTS

We thank the patients and their families for their participation in this study and for graciously donating their time to this research. We thank Canadian Critical Care Trials Group for the support of and mentorship of this study and the RECOVER Program investigators (https://www.ccctg.ca/Programs/RECOVER.aspx) for their partnership with the WeeCover research program. We also thank the Ontario Ministry of Health Innovation Fund for supporting this study. We thank the CCCTG grants and articles committee and Dr.'s Aimee Sarti and Anne-Marie Guerguerian for their detailed review of the article.

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