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The Association between Functional Status and Health-Related Quality of Life Following Discharge from the Pediatric Intensive Care Unit

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Abstract

Background: Despite one third of children with acquired brain injury (ABI) experiencing new functional impairments following critical care admission, there is limited research investigating the impact of new functional impairments upon overall health-related quality of life (HRQOL) or among important HRQOL domains.

Objectives: We aimed to investigate the association between new functional impairments, measured by the Functional Status Scale (FSS), and HRQOL in pediatric patients with ABI after critical care.

Methods: We conducted a secondary analysis of a prospective, observational study of 275 children aged 2 months- 18 years with ABI. Primary exposure evaluated was change in FSS from baseline at hospital discharge categorized per prior work (no change; 1-2 point increase; 3 point increase). Primary outcome was overall HRQOL 6-months after hospital discharge measured by the Pediatric Quality of Life Inventory (PedsQL) total score. Secondary outcomes were PedsQL

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domain scores. PedsQL total and domain scores were transformed into age-standardized z-scores for analyses. Multiple linear regression models evaluated the association between FSS change category and HRQOL (overall and domain z-scores) when controlling for demographic and clinical characteristics, and reported as β -coefficients with 95% Confidence Interval (CI).

Results: Complete data were analyzed for 195 (71%) children, including 127 with traumatic brain injury. New functional impairment was common with 32 (16%) patients experiencing FSS increases ≥ 3 , 50 (26%) patients with FSS increases of 1-2 points, and 113 (58%) patients with no change from pre-hospital baseline. The majority of children (63%) demonstrated HRQOL ratings ≥ 1 standard deviation below healthy age-based standards (z-scores ≤ -1). Regression models demonstrated older age, female sex, presence of comorbidities, and pre-admission cardiopulmonary resuscitation were all significantly associated with poorer overall HRQOL (all $p < 0.05$). FSS increase ≥ 3 at discharge was significantly associated with worse overall HRQOL at follow-up ($\beta = -1.07$; 95% CI = -1.63, -0.52) when controlling for the aforementioned significant factors, and significantly improved model fit (p-value for change = .001). Similar findings in secondary analyses were found for physical domain scores, with FSS increase showing significant association with worse physical HRQOL scores and improvements in model fit. Change in FSS was not significantly associated with other HRQOL domain scores (emotional, social, school, psychosocial).

Conclusions: Many children with ABI after critical care experience new functional impairments (FSS increases) and worse HRQOL than healthy peers. FSS increase at discharge is a significant risk factor for worse HRQOL in the months after hospital discharge, and improves HRQOL models beyond illness and demographic variables alone.

Keywords

Pediatric; Critical Care; Post-Intensive Care Syndrome; Outcomes; Brain Injury

Introduction

In the United States, approximately 300,000 children are admitted each year to the Pediatric Intensive Care Unit (PICU). Around 20% of PICU admissions are for acquired brain injury (ABI) that stems from primary neurologic insults, such as traumatic brain injury (TBI), status epilepticus, infectious and inflammatory conditions, stroke, and cardiac arrest [1]. These PICU patients frequently require critical care interventions, have a prolonged hospital admission, and have high rates of mortality [1]. Relatedly, one third of ABI patients have a new functional disability at hospital discharge [1], far surpassing disability rates among other PICU cohorts [2], and reflecting the high risk of poor outcomes in these children.

The Functional Status Scale (FSS) is a physician-rated scale assessing six domains of functioning that combines to form a total score ranging from 6 (normal) to 30 (very severe dysfunction)[2]. It was created to provide an age-independent, objective and efficient measure of functional abilities and new disabilities after PICU admission [3]. Additionally, the FSS was shown to be advantageous in that it is more sensitive to measuring changes within moderate to severe dysfunction categories compared to the commonly used Pediatric Overall Performance Category (POPC) and Pediatric Cerebral Performance

Category (PCPC) scales [3]. FSS changes ≥ 3 from baseline correlate with moderate to severe impairments in adaptive function [2, 3]. Approximately 13% of children with ABI diagnoses requiring PICU admission have new severe disabilities (FSS increases ≥ 3) at hospital discharge [1], but it is unclear how these changes impact broader health domains or important constructs like health-related quality of life.

A need for understanding the impact of new functional disabilities across multiple domains of functioning is highlighted by the dearth of research quantifying outcomes of ABI diagnoses within the Post-Intensive Care Syndrome (PICS) framework [4, 5], as impairment occurs across several health domains. Briefly, PICS can impact patients in acute and chronic ways, even years after discharge from the PICU [1, 6] and manifests as post-PICU morbidities within the domains of physical health, cognitive health, emotional health, and social health [7, 8]. Research has shown these domains to be highly integrated with moderate to strong correlations between domain measures [9, 10].

A lack of a streamlined multimorbidity and multidomain measure of PICS contributes to our limited understanding of sequelae of critical care and ABI. Health-related quality of life is not a proxy for PICS, but overlaps with many of the same domains of interest to offer a broad measure of overall health. Specifically, the Pediatric Quality of Life Inventory (PedsQL) core scales assess physical, emotional, social, and school functioning domains. Furthermore, this measure is feasible, valid and sensitive to change in a PICU population [11]. Several patterns of health-related quality of life outcomes have emerged in recent research. Studies have determined that critical illness and TBI populations present with worse health-related quality of life compared to healthy and demographically-matched controls. TBI populations demonstrated poorer health-related quality of life in the acute phase (e.g., up to 43% at 6-months [12-17]), and continued impairments 12-months or more post-discharge [14, 15, 18-20]. Prior studies of health-related quality of life in PICU and trauma populations identified differences between racial/ethnic groups [11, 21], low socioeconomic status [21, 22], age [17, 21], and premorbid comorbidities [12, 14, 15, 23] as demographic variable associated with poorer health-related quality of life. Illness related variables including, increased illness severity (e.g., Glasgow Coma Scale; [16, 21, 24]), need for critical care interventions (e.g., mechanical ventilation; [11, 12, 22]), admission diagnosis (e.g., trauma, cardiovascular; [12, 15, 20, 22]), extended length of stay [23, 25] [24], chronic health and psychosocial conditions post-discharge [14, 22-24], have also been associated with poorer health-related quality of life. Further, while the FSS may capture new functional impairments as determined by a medical physician, the impact of those impairments on a child's life likely vary and may differentially impact broader aspects of their everyday activities including emotional, social, and school functioning. The association between new functional impairments and health-related quality of life after PICU discharge and ABI have not been studied. Understanding this relationship is paramount to providing appropriate post-PICU care and implementing interventions aiming to improve long-term health outcomes [26]. Identifying the impact of new functional impairments on quality of life may assist in more targeted referrals and resource allocation, and highlight the need for follow-up after discharge to increase early access to interventions that can support patients in their recovery (e.g., therapy, family support, school support services).

The primary aim of the current study was to determine the utility of a feasible and increasingly utilized measure of functional status, the FSS, to predict changes in health-related quality of life in the acute recovery period after PICU discharge when controlling for relevant illness and child related variables. We hypothesized that changes in the FSS from pre-morbid function would be significantly associated with poorer overall health-related quality of life. A secondary aim of this study was to explore the association between changes in FSS and domain scores of the PedsQL measures to explore the impact of new functional disabilities after PICU admission on a broad range of health domains.

Methods

Participants and Procedures

We performed a secondary analysis of a prospective observational study of consecutive children aged 2-months to 18-years admitted to the PICU between July 2018 and April 2020 for ABI surviving to hospital discharge. A total of 324 patients were eligible for follow-up. Five patients died, and 275 (85%) eligible patients completed a follow-up. Eighty patients were excluded from analysis for missing or incomplete outcomes data (see Supplemental Table 1). We analyzed data for 195 children (71%) who completed an acute follow-up visit through the Pediatric Critical Care and Neurotrauma Recovery Program (PCCNRP) between 1- and 6-months post-discharge. The referral and follow-up patterns and program details for the PCCNRP have been previously described [9, 27-29]. The Institutional Review Board at Oregon Health & Science University approved the study procedures with a waiver of consent.

Measures

Demographic and Critical Illness-Related Variables.—Electronic medical records were used to obtain age, sex, race, ethnicity, and insurance status. Illness- and hospitalization-related variables included admission diagnosis, disease severity, and time since discharge. Admission primary diagnosis was categorized as the following: trauma, hypoxic ischemic encephalopathy (HIE) from cardiopulmonary arrest, status epilepticus, infectious or inflammatory disease, stroke, or other (hydrocephalus, osmotic demyelination, strangulation with loss of consciousness). Disease severity was evaluated by need for any critical care intervention specific to the PICU setting (i.e., mechanical ventilation, neurosurgical intervention, vasopressor, central venous line placement, arterial line placement, intracranial pressure monitor, dialysis, refractory status epilepticus, extracorporeal support, in-hospital cardiopulmonary resuscitation [CPR]), admission Glasgow Coma Scale (GCS), length of overall hospital and PICU stays, and discharge to inpatient rehabilitation. Medical record review was used to determine whether the patient had pre-morbid chronic conditions in any of three categories: medical (e.g., congenital heart disease, cerebral palsy, epilepsy), psychiatric (e.g., anxiety, depression), or neurodevelopmental (e.g., learning disability, attention-deficit/hyperactivity disorder). Chronic condition variables were dichotomized for analysis consistent with prior work given the wide range of conditions identified [1, 30]. Receipt of CPR was recorded both pre-admission and during hospitalization from medical records. The use of electroencephalography and presence of any seizure during admission were recorded from

medical records separate from critical care interventions for refractory status epilepticus as they can occur in any hospital setting.

Functional Status Scale (FSS)—The primary exposure evaluated in this study was functional change at discharge from baseline using the FSS, which assesses six domains of functioning with scores for each domain ranging between 1 (normal) and 5 (very severe dysfunction) with total scores ranging from 6 to 30 [2]. The six domains include mental status, sensory functioning, communication, motor functioning, feeding, and respiratory status. FSS scores were categorized consistent with prior work showing a FSS change ≥ 3 corresponded to a moderate or severe functional limitation on the Adaptive Behavior Assessment Scale, 2nd Edition [2, 31, 32]. For this study, we used three FSS change categories consistent with prior work: no change from pre-admission baseline; increase of 1 or 2 points; increase ≥ 3 points [1-3]. Pre-admission baseline FSS was determined by a PICU attending during hospitalization, and evaluated again by PCCNRP physicians at hospital discharge and during follow-up appointments as described in prior work [1, 9].

Health-Related Quality of Life.—The primary outcome measure of this study was overall health-related quality of life. This measure was administered at the follow-up appointment between 1 and 6 months after hospital discharge. PedsQL 4.0 Generic Core Scales [33] is a measure of health-related quality of life in youth 2-18 years of age reported by parent/caregiver proxies. The PedsQL is a standardized 23-item measure in which caregivers rate how often their child has experienced problems across different functional domains within the past two weeks on a five-point Likert scale. Specific domains assessed include physical, emotional, social, and school functioning. Individual items are adjusted to be developmentally-appropriate across age ranges and yield a total score [33]. As the measure differs across the age range of the study, z-scores were calculated using previously published reference scores for a healthy pediatric population to convert our sample's total and domain scores into z-scores, representing the number of standard deviations each individual participant was from an age-standardized healthy children [33]. The PedsQL has been validated for use within a PICU population and has demonstrated good construct validity and responsiveness to change [11]. Internal consistency for the PedsQL in our sample was excellent ($\alpha=0.86-0.95$).

The PedsQL Infant Scales [34] were used to assess health-related quality of life in infants 1-24 months of age. The PedsQL Infant Scales are two standardized questionnaires that comprise 36-items for infants 1-12 months and 45-items for youth 13-24 months in which caregivers rate how often their child has experienced problems within different functional domains on a five-point Likert scale. Domains assessed include physical health and psychosocial functioning within the past two weeks. Individual items are adjusted to be developmentally-appropriate across the two age ranges and both questionnaires yield a total score [34]. Previously published reference scores for healthy infant populations were used to convert our sample's total and domain summary scores into z-scores to represent the number of standard deviations each individual participant was from age-standardized healthy children [34]. Previous research in infants revealed excellent internal consistency

and discriminant validity [34]. Internal consistency on the PedsQL Infant Scales in our sample was excellent ($\alpha=0.93-0.95$).

Data Analyses

Descriptive statistics were used to describe sociodemographic and illness-related characteristics, and primary predictor (e.g., FSS change from baseline) and outcome (e.g., PedsQL) variables. The majority of continuous variables were not normally distributed and reported as median with interquartile range (IQR). We used chi-square and Mann-Whitney U tests to compare our final sample to those with missing or incomplete data to assess for bias in our results (see Supplemental Table 1). We used chi-square and Kruskal Wallis tests to compare variables across FSS groups at both hospital discharge (Table 1) and follow-up (Supplemental Table 2) in order to assess for confounding variables related to the FSS group. A Bonferroni correction was used given the multiple time points assessed, defining significance at $p<.025$ for these analyses. Results of this analysis showed nearly identical results at the two time points and strong collinear relationships between FSS change from baseline at discharge and FSS change from baseline at follow-up. Thus, we chose to focus our subsequent analyses on the FSS change at discharge as this would provide a more useful predictor variable for clinicians aiming to determine need for follow up and risk for impaired quality of life.

We used simple linear regression to evaluate demographic and clinical variables in relation to our primary outcome of health-related quality of life total z-score for the full sample. The PedsQL total score represents the same construct across developmental modules and has been used as a primary outcome variable in previous health-related quality of life literature using infant, school-aged, and teen modules [35,36]. Results were reported as β coefficients with 95% confidence interval (95% CI). Some continuous predictors were log transformed prior to entering into regressions given non-normal distributions. FSS change scores were dummy coded (no change, 1-2 point change, 3 point change) with no change being used as our reference group in regressions. Hierarchical multiple linear regression was used to determine how change in FSS score at discharge explains variance in health-related quality of life at follow-up. The model included entry of relevant covariates in Step 1 and changes in FSS from baseline in Step 2. Regression models were evaluated via adjusted R^2 and stepwise R^2 change with addition of FSS change categories at the $p<.05$ level. Potential covariates and confounders were identified from bivariate analyses described above at a significance level of $p<.05$. As the primary analysis for this study was to evaluate variance explained by FSS change, variables were tested individually for collinearity with FSS change at discharge and in the multivariable model for multicollinearity, and variables were excluded if the variance inflation factor was >5 . We additionally explored multiple linear regression models for subscale z-scores for Physical Health Summary (infant PedsQL), Psychosocial Health (infant PedsQL), Physical Function, Emotional Function, Social Function, and School Function (Supplemental Tables 3-8). Given the limitation of sample size for these secondary analyses, we maintained the same variable selection for the total score regression described above. IBM SPSS Version 26 was used to complete all statistical analyses.

Results

Table 1 shows the characteristics of the 195 children evaluated following critical care for ABI. The most common diagnosis was trauma (65%), followed by infectious and inflammatory disease (12%), status epilepticus (7%), stroke (6%), hypoxic ischemic brain injury from cardiac arrest (6%), and other (4%). The majority of the patient participants were male (59%) and had Medicaid insurance (52%). Forty-four (23%) patients had one or more prior comorbid medical (14%), psychiatric (4%), or neurodevelopmental (10%) disabilities, but only 5% of the patients had an abnormal baseline FSS score (i.e., >6). Most patients (n=114, 59%) required at least one critical care intervention, including 31% (n=61) requiring intubation and mechanical ventilation. The cohort with missing or incomplete data (Supplemental Table 1) was more likely to identify as White and have a lower GCS on admission.

At hospital discharge, 32 (16%) patients had a FSS increase from baseline ≥ 3 , 50 (26%) patients had a FSS increase from baseline of 1 or 2 points, and 113 (58%) patients had no change in FSS from baseline. Changes from baseline to discharge were noted in patients among all FSS domains including: mental status (n=9), sensory (n=38), communication (n=27), motor (n=43), feeding (n=40), and respiratory (n=7). Analyses revealed significant associations between FSS increases from baseline and multiple demographic and clinical variables (Table 1) including non-trauma diagnoses, lower admission GCS, longer length of stay, need for critical care intervention (both as a group and all individual interventions), any seizure, and discharge to rehabilitation (all $p < .01$). FSS change at discharge was also significantly associated with z-scores for PedsQL total and physical domain scores. While not reaching statistical significance, trends between greater FSS increase from baseline at discharge and lower z-scores in the other PedsQL domains were also noted (Table 1).

Most patients (n=123; 63%) had lower health-related quality of life when compared to healthy age-matched norms as reflected by negative z-scores. In fact, 43% had PedsQL total z-scores more than one standard deviation below reference norms (z-score < -1), and 21% had z-scores more than two standard deviations below reference norms (z-score < -2). Simple linear regression revealed multiple clinical and demographic variables were significantly associated with PedsQL total z-scores (Table 2), including age, sex, comorbidities, length of stay, and pre-admission CPR. Time from discharge to follow-up was not associated with PedsQL total z-score. Changes in all FSS domains were associated with reductions in PedsQL total z-score.

Multiple linear regression was performed primarily to evaluate the contribution of FSS increase from baseline at discharge to models of health-related quality of life at follow-up. Clinical and demographic variables tested in models included age, sex, pre-admission comorbidities, log length of stay, rehabilitation discharge, pre-admission CPR and change in FSS score categories at discharge. Length of stay and rehabilitation discharge were not significant in step one models, exhibited collinearity with change in FSS, and were removed. The final model (Table 3) revealed that older age, female sex, presence of comorbidities, and pre-admission CPR were all significantly associated with poorer health-related quality of life as reflected by lower total PedsQL z-scores. Results of the primary analysis also showed a

significant increase in model R^2 (p-value of change =.001) with the addition of FSS change categories at discharge, and significant worsening in the total PedsQL z-score for children with FSS increases 3 points at discharge compared to no FSS change ($\beta = -1.07$; 95% CI = -1.63, -0.52).

We also explored multiple linear regression models for health-related quality of life domains using PedsQL domain z-scores (Supplemental Tables 3-8) with the same covariates as above. In children over age 2 years, FSS increase from baseline at discharge of any magnitude was independently associated with worse physical health z-scores compared to no FSS change and increased model R^2 by 10% (p-value change <.001). While FSS increases from baseline at discharge produced negative β -coefficients in the other domain score models for children over age 2 years, the addition of FSS change categories did not significantly increase R^2 in the emotional, social, or school domain models (change R^2 ranged 2-3% in each model). Among infants 2 years, FSS increase from baseline at discharge 3 points was particularly impactful to physical health z-scores ($\beta = -2.11$; 95% CI = -3.32, -0.9), and produced a significant increase in model R^2 with the addition of FSS categories to the model (increase R^2 20%; p-value change = .002). Infant psychosocial health was also associated with FSS increase 3 points ($\beta = -1.23$; 95% CI = -2.35, -0.12), but addition of FSS categories to the model did not reach statistical significance (R^2 change =9%; p-value=.08).

Discussion

Children surviving critical care for ABI have high rates of new functional impairments and reduced health-related quality of life when compared to healthy age-normed populations. The present study contributes to the pediatric critical care and ABI literature by providing novel information regarding the contribution of new functional impairment at hospital discharge measured by FSS to models of health-related quality of life months after discharge. Overall, our findings revealed that a decline in functional status at discharge, particularly FSS increase from baseline 3 points, was associated with significantly poorer health-related quality of life for survivors of ABI when adjusting for relevant demographic and clinical variables. The addition of change in FSS categories significantly improved multivariable models of overall health-related quality of life beyond models with illness and demographic data alone. FSS change categories were particularly impactful for models of physical health domains, which is conceptually aligned with what is measured through the FSS. Our results show that timely follow-up is needed for children with new functional impairments measured by FSS as interventions could be provided in follow-up aimed at improving long-term global health outcomes such as health-related quality of life.

Examination of our sample's PedsQL scores in comparison to healthy age-matched norms and other studies focused in pediatric critical care and trauma populations enhance our main findings. Nearly half of participants in our study experienced a PedsQL Total score that was one standard deviation below healthy norms [33, 34], highlighting the impact of PICU admission for ABI on health-related quality of life and the need to identify risk factors to ensure proper follow-up and intervention. PedsQL outcome scores in a mixed PICU sample with prolonged length of stay (28 days) were found to be even lower than

our patients on the PedsQL Total, Physical, Social, and School subscales [23]. Our study included a broader PICU population with regard to illness severity and length of stay, which likely accounts for differences in our cohort PedsQL scores. While the majority of other studies on health-related quality of life show impairments in this construct up to several years post-discharge, some note smaller rates of impairment compared to our sample. This likely reflects the high variability in measures of health-related quality of life used in the extant literature that limits comparisons across studies. However, the PedsQL has been identified as a preferred tool for measuring health-related quality of life within pediatric critical care [22], and our findings suggest that impairment in health-related quality of life is frequent in our post-PICU sample. We used the PedsQL scales as part of a broader examination at follow-up, offered to all critical care survivors of ABI at our institution, to screen for morbidities across PICS domains, and determine need for longitudinal follow-up. Our analyses indicated symptomatology across the domains measured by the PedsQL, which aligns with domains in the PICS framework, and may serve as a useful screening measure in outcomes work.

In addition to our main findings discussed above, our study revealed that illness and child-related variables are all associated with patient health-related quality of life in the acute recovery phase, which is consistent with previous literature in TBI and PICU cohorts [11, 12, 20-25]. We found, in addition to FSS change, that sex, comorbidities, age and pre-admission CPR uniquely contributed to models of total health-related quality of life z-scores. Sex was predictive of all health-related quality of life domain z-scores in the pediatric age group with parents rating female youth as having reduced health-related quality of life compared to their male counterparts. Sex differences were demonstrated in prior work with a different measure of health-related quality of life, but not with the PedsQL, and were hypothesized to reflect a number of factors including hormonal differences and socialized expression of emotional and physical symptomatology [37]. A similar interpretation of findings could be proffered here for our sample and the PedsQL. Alternatively, males may experience significant symptoms and reduced quality of life, but patients and/or parents under-recognize or under-report these difficulties in boys.

The presence of chronic conditions has also been shown to portend worse health related quality of life in prior work [12, 14, 15, 23, 38], which is consistent with our findings. Others found measures of severity of illness like increased length of stay and need for critical care interventions (e.g., mechanical ventilation) were significantly associated with reduced health-related quality of life [11, 12, 22-25]. In our bivariate analysis, we found measures of severity of illness were associated with change in FSS, but did not uniquely contribute to explaining variance in health-related quality of life regression models. It is possible that change in FSS is able to capture much of the variance from these measures; however, prior studies on health-related quality of life have not included FSS change to compare directly to our work. We also found pre-admission CPR was significantly associated with reduced health-related quality of life after discharge. This finding was interesting as CPR has been shown to increase risk of FSS change and physical disability [1], but its significant contribution to health-related quality of life models without significantly confounding FSS estimates is highly suggestive that other factors like the emotional and family impact of pre-hospital CPR, also plays a role. Nonetheless, our

broad ABI cohort differs from prior studies of PICU and trauma populations, which likely contributes to differences in risk factors for reduced health-related quality of life.

Also of interest, our analyses demonstrated both similarities and differences between our pediatric and infant (<2 years) age groups. Analyses in both age groups demonstrated that FSS increase from baseline at discharge was associated with total and physical function domain z-scores on the PedsQL measures. However, results showed larger shifts in FSS from premorbid function were needed to impact health-related quality of life outcomes in an infant compared to older children and adolescents. While older age was an independent risk factor for reduced overall health related quality of life in our primary analysis using the entire cohort, age was not a significant factor in any of the secondary domain evaluations. Covariates for the physical (sex, CPR), emotional (sex, comorbidity), social (sex, comorbidity), and school (sex, comorbidity) domains retained significance as in the primary analysis in children over age 2 years; however, none of these covariates were significant in infant models of physical and psychosocial health domains. Findings may reflect reduced power in the secondary domain analyses or differences in items in the PedsQL 4.0 Core and the PedsQL Infant Scales. Findings may also capture differences in developmental expectations, more difficulty observing symptoms in infants who have a number of skills still emerging, or a reduced range of pre-existing skills. Future research is needed to confirm our findings with respect to age, and longitudinal work should examine whether these associations persist as the infant and young child ages. When taken together, our findings highlight the need for providers engaged in post-PICU follow-up to consider child, illness, and injury related variables as well as the new functional impairments that can impact recovery.

We focused our analyses on FSS change from baseline at hospital discharge as FSS changed minimally within the 6-month timeframe of this study for patients after discharge, and time from discharge was not associated with FSS group or quality of life score. Previous studies have suggested that both morbidity and mortality increased after discharge. Among a broad PICU sample, one study showed increased morbidity from 5.2% to 6.5% from discharge to 6-month follow-up, and mortality rates increased from 3.9% to 7.8% [31]. Another study found that rates of morbidity and mortality double at 3-year follow-up for PICU survivors. Differences are likely due to the different populations and time points studied [32]. Our study focuses on a primary ABI cohort known to suffer higher rates of new disability at discharge (33%) and decline in functional status compared to other PICU populations [1-3]. These patients may also have different trajectories of FSS changes after discharge, however more research is needed. Most patients in our study were evaluated within 3-months of hospital discharge, so improvements or declines in FSS could be seen with more longitudinal follow-up. Our findings show functional ability measured by the FSS at discharge is an important predictor of health-related quality of life in the months after discharge— this finding will likely translate to broader PICU populations given the wide applicability of FSS, and deserves further study.

FSS change at discharge made an important contribution to models of health-related quality of life in our study. Changes in FSS contributed most significantly to physical health domains on the PedsQL, which is not surprising given FSS was developed as a marker of

functional abilities that are heavily dependent on physical markers of health (e.g., motor, feeding, sensory). Emotional, social, and school health domains can be impacted by physical health morbidities, and this likely explains the finding in our study that FSS increases at discharge showed trends for worsening z-scores across these domains (Table 1). However, these estimates did not achieve significance in domain regression models as there are several other experiential and patient-level factors that contribute to these health domains that are not captured by physical function alone. FSS change at discharge may serve as an important predictor for post-hospital health-related quality of life particularly in physical measures, but other variables are needed to fully appreciate the breadth of morbidities experienced by PICU and ABI survivors to improve prediction of morbidity in other health domains encompassed by PICS.

Our study has several limitations to consider. Our single center study captured a large number of all ABI survivors at our tertiary academic institution, but there are known differences in pediatric ABI populations in PICU's across regions and centers that may limit generalizability [39, 40]. Only 10% of our population required inpatient rehabilitation after discharge, reflecting the broad illness severity of our population and study, that would also be distinct from studies on outcomes collected in the rehabilitation setting. We additionally utilized a parent-proxy report for health-related quality of life that may differ from patient self-report; however, our use of parent-proxy report allowed comparison of health-related quality of life across a wide age range representative of the ABI population. Additionally, the PedsQL is a subjective measure of health-related quality of life intended to report global well-being that can be influenced by a myriad of factors not directly related to the illness or injury, making it difficult to capture all of the variance in regression models. We do not have a measurement of premorbid health-related quality of life for our sample, which limits our ability to fully evaluate the direct contributions of FSS on the PedsQL within the context of these additional factors that may contribute to global well-being. The PedsQL is also not a proxy for PICS and does not measure important morbidity in all PICS domains, including cognitive function and post-traumatic stress, relevant to critical care and trauma populations. No currently available measure is able to capture all PICS domains simultaneously as a measure of overall health after discharge from the PICU, and measures targeting different PICS domains may find distinctive relationships between FSS and outcomes. The FSS also includes a limited number of domains assessed that may not capture all PICS-related sequelae. However, it was selected as the best functional status measure for our study sample given its validation in PICU samples and ability to capture greater variability in functional status among children with more severe injuries compared to other functional status measures (e.g., WeeFIM)[41]. Our study shows important relationships between a widely available measure of PICU morbidity, the FSS, and overall health-related quality of life.

Conclusions & Future Directions

Children surviving critical care for ABI suffer high rates of new functional impairment and show health-related quality of life well below that of age-normed peers. FSS change at discharge, particularly an increase 3 points, is an independent risk factor for worse health-related quality of life in these children, along with older age, female sex, chronic

comorbidity, and pre-admission CPR. The addition of change in FSS significantly improves model performance beyond patient and clinical factors alone, and is particularly impactful to health-related quality of life domains measuring physical health. Additional research is needed to understand how FSS changes impact overall health and individual domains longitudinally, as impact may change over time as children return to their daily lives or their expectations change, such as with return to school. Children with declines in functional status at hospital discharge represent a cohort of children at risk for worse health-related quality of life that would benefit from close follow-up and interventions to improve recovery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1. Demographic and clinical characteristics among Functional Status Scale change groups at hospital discharge

	All patients N=195 (%)	No FSS Change n=113 (%)	FSS increase 1-2 n=50 (%)	FSS increase 3 n=32 (%)	P-value
Age in years at admit, Median (IQR)	6.3 (1.1,11.0)	6.7 (1.7,11.1)	5.1 (0.6,12.2)	6.3 (1.3, 10.3)	.71
Admission Diagnosis					<.001
Trauma	127 (65%)	86 (76%)	29 (58%)	12 (38%)	
Infectious/Inflammatory	24 (12%)	7 (6%)	11 (22%)	6 (19%)	
Cardiac Arrest	11 (6%)	5 (4%)	3 (6%)	3 (10%)	
Status epilepticus	13 (7%)	11 (10%)	1 (2%)	1 (3%)	
Stroke	12 (6%)	3 (3%)	4 (8%)	5 (16%)	
Other	8 (4%)	1 (1%)	2 (4%)	5 (16%)	
Male sex	114 (59%)	67 (59%)	30 (60%)	17 (53%)	.80
White Race	145 (74%)	85 (75%)	36 (72%)	24 (75%)	.62
Hispanic ethnicity	34 (17%)	15 (13%)	10 (20%)	9 (28%)	.13
Medicaid insurance	101 (52%)	58 (51%)	25 (50%)	18 (56%)	.85
Length of Stay, Median days (IQR)					
Critical care	1.6 (0.9,4.3)	1.1 (0.8,1.8)	2.0 (1.1, 4.3)	9.2 (5.0,20.1)	<.001
Hospital	3.6 (1.5,10.1)	1.7 (1.1, 3.6)	6.6 (3.5,10.1)	18.1 (11.8,30.8)	<.001
Pre-admission Chronic Comorbidity, Any	44 (23%)	29 (26%)	7 (14%)	8 (25%)	.24
Medical	28 (14%)	16 (14%)	5 (10%)	7 (22%)	.33
Psychiatric	7 (4%)	4 (4%)	2 (4%)	1 (3%)	.98
Neurodevelopmental	19 (10%)	14 (12%)	4 (8%)	1 (3%)	.26
Admission Glasgow Coma Scale, Median (IQR)	15 (14,15)	15 (14,15)	15 (12,15)	6.5 (4.5,11)	<.001
Pre-admit cardiopulmonary resuscitation	14 (7%)	5 (4%)	3 (6%)	6 (19%)	.02
Critical care intervention, any	114 (59%)	47 (42%)	36 (72%)	31 (97%)	<.001
Seizure during admission	28 (14%)	6 (5%)	11 (22%)	11 (34%)	<.001
Electroencephalography during admission	37 (19%)	10 (9%)	10 (20%)	17 (53%)	<.001
Discharge to inpatient rehabilitation	20 (10%)	0	4 (8%)	16 (50%)	<.001
Days since discharge to follow-up, Median (IQR)	50 (37, 76)	49 (37, 71)	61 (36, 80)	50 (41, 70)	.74
PedsQL total z-score, Median (IQR)	-0.76 (-1.81, 0.35)	-0.41 (-1.41, 0.54)	-0.76 (-2.13, 0.37)	-1.80 (-2.90, -0.68)	.001

	All patients N=195 (%)	No FSS Change n=113 (%)	FSS increase 1-2 n=50 (%)	FSS increase 3 n=32 (%)	P-value
PedsQL subscale z-scores, Median (IQR)					
Physical	n=136 -0.30 (-1.64, 0.27)	n=82 0.14 (-1.11, 0.65)	n=31 -1.26 (-1.97, -0.11)	n=23 -1.64 (-2.08, 0.18)	.001
Emotional	-0.72 (-1.86, 0.41)	-0.44 (-1.86, 0.70)	-0.72 (-1.58, 0.13)	-1.01 (-1.86, 0.24)	.28
Social	-0.46 (-1.52, 0.59)	-0.29 (-1.17, 0.59)	-0.46 (-1.87, 0.24)	-1.87 (-2.22, -0.11)	.05
School	-0.88 (-2.01, 0.35)	-0.88 (-1.73, 0.54)	-0.88 (-2.01, -0.03)	-1.44 (-2.58, -0.17)	.29
Infant PedsQL subscale z-scores, Median (IQR)					
Physical Health Summary	n=59 0.27 (-1.06, 1.26)	n=31 0.43 (-0.46, 1.26)	n=19 0.76 (-0.56, 1.26)	n=9 -2.47 (-3.13, -.22)	.005
Psychosocial Health Summary	0.16 (-1.13, 0.85)	0.16 (-0.43, 0.93)	0.46 (-0.53, 0.85)	-1.36 (-2.15, -0.43)	.06

Table 2. Simple linear regression evaluating overall quality of life (total PedsQL z-score)

	Beta coefficient (95% Confidence Interval)	p-value
Age in years at admission	-0.06 (-0.10 - -0.03)	.001
Diagnosis		
Trauma (reference)	ref	ref
Infectious/Inflammatory	-0.26 (-0.93 - 0.42)	.45
Status epilepticus	-0.06 (-0.97 - 0.85)	.90
Cardiac arrest	-0.76 (-1.71 - 0.19)	.12
Stroke	-0.47 (-1.38 - 0.44)	.31
Other	0.69 (-0.41 - 1.79)	.22
White race	0.20 (-0.29 - 0.70)	.42
Hispanic ethnicity	-0.39 (-0.96 - 0.18)	.17
Medicaid insurance	-0.40 (-0.83 - 0.03)	.07
Male sex	0.69 (0.26 - 1.12)	.002
Length of Stay		
Critical care (Log days)	-0.93 (-1.38 - -0.47)	<.001
Hospital (Log days)	-0.65 (-1.05 - -0.24)	.002
Pre-admission chronic comorbidity, any	-0.68 (-0.92 - -0.44)	<.001
Admission Glasgow Coma Scale (Log score)	1.33 (-0.71 - 3.36)	.20
Pre-admit cardiopulmonary resuscitation	-1.12 (-1.94 - -0.30)	.008
Critical care intervention, any	0.30 (-0.14 - 0.74)	.18
Seizure during admission	-0.38 (-0.99 - 0.24)	.23
Electroencephalography during admission	-0.18 (-0.73 - 0.37)	.52
Discharge to inpatient rehabilitation	-0.70 (-1.39 - -0.01)	.05
Days since discharge to follow-up, Median (IQR)	0.00 (-0.01 - 0.01)	.85
Change in Functional Status Scale total at discharge:		
No change (reference)	ref	ref
Increase 1-2 points	-0.31 (-0.80 - 0.19)	.22
Increase 3 points	-1.18 (-1.77 - -0.60)	<.001

	Beta coefficient (95% Confidence Interval)	p-value
Functional Status Scale domain changes at discharge:		
Increase mental status 1 (n=9)	-0.97 (-1.99 - 0.06)	.06
Increase sensory 1 (n=38)	-0.65 (-1.19 - -0.11)	.02
Increase communication 1 (n=27)	-0.95 (-1.56 - -0.33)	.003
Increase motor 1 (n=43)	-0.72 (-1.24 - -0.21)	.01
Increase feeding 1 (n=40)	-0.76 (-1.28 - -0.23)	.01
Increase respiratory 1 (n=7)	-1.35 (-2.50 - -0.20)	.02

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Table 3.

Multivariable model evaluating overall (total PedsQL) quality of life z-scores

	Step 1 Beta coefficient (95% Confidence Interval)	Step 2 Beta Coefficient (95% Confidence Interval)
Age in years at admission	-0.05 (-0.09 - -0.01)	-0.05 (-0.09 - -0.02)
Male sex	0.60 (0.18 - 1.01)	0.56 (0.15 - 0.96)
Pre-admission chronic comorbidity	-0.49 (-0.99 - 0.01)	-0.52 (-1.01 - -0.03)
Pre-admission cardiopulmonary resuscitation	-1.14 (-1.93 - -0.35)	-0.85 (-1.63 - -0.07)
Functional Status Scale change at discharge		
No change	--	Ref
Increase 1-2	--	-0.39 (-0.86 - 0.08)
Increase 3	--	-1.07 (-1.63 - -0.52)

Step 1 model statistics: F= 8.08, p-value <.001; R2 = .147; adjusted R2=.128

Step 2 model statistics: F= 8.22, p-value <.001; R2 = .210; R2 change =.063; F change= 7.41, p-value change = .001; adjusted R2=.184