RESEARCH ARTICLE

Hospital Mortality and Functional Outcomes in Pediatric Neurocritical Care

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ABSTRACT

OBJECTIVES: Pediatric neurocritical care (PNCC) outcomes research is scarce. We aimed to expand knowledge about outcomes in PNCC by evaluating death and changes in Functional Status Scale (FSS) from baseline among PNCC diagnoses.

METHODS: We conducted a 2-year observational study of children aged 0 to 18 years admitted to the ICU with a primary neurologic diagnosis ($N = 325$). Primary outcomes were death and change in FSS from preadmission baseline to discharge. New disability was defined as an FSS change of ≥1 from baseline, and severe disability was defined as an FSS change of ≥3. Categorical results are reported as relative risk (RR) with 95% confidence interval (CI).

RESULTS: Thirty (9%) patients died. New disability ($n = 103$; 35%) and severe disability ($n = 37$; 13%) were common in PNCC survivors. New disability (range 14%–54%) and severe disability (range 3%–33%) outcomes varied significantly among primary diagnoses (lowest in status epilepticus; highest in infectious and/or inflammatory and stroke cohorts). Disability occurred in all FSS domains: mental status (15%), sensory (52%), communication (38%), motor (48%), feeding (40%), and respiratory (12%). Most (64%) patients with severe disability had changes in ≥3 domains. Requiring critical care interventions (RR 2.1; 95% CI 1.5–3.1) and having seizures (RR 1.5; 95% CI 1.1–2.0) during hospitalization were associated with new disability.

CONCLUSIONS: PNCC patients have high rates of death and new disability at discharge, varying significantly between PNCC diagnoses. Multiple domains of disability are affected, underscoring the ongoing multidisciplinary health care needs of survivors. Our study quantified hospital outcomes of PNCC patients that can be used to advance future research in this vulnerable population.

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Patients with pediatric neurocritical care (PNCC) conditions account for 20% of all pediatric critical care admissions in the United States.[1–3] PNCC conditions include traumatic brain injury (TBI), status epilepticus, neuroinfectious and inflammatory conditions, stroke, and cardiac arrest. These patients frequently require critical care interventions, account for billions of dollars in annual hospital costs, and suffer high rates of mortality and morbidity.[4] However, quantification of detailed outcomes among many PNCC diagnoses is scarce and limits intervention research to improve outcomes for these vulnerable children.

Previous research has focused on death and gross outcomes, such as the Pediatric Overall Performance Category or Glasgow Outcome Scale-Extended.[5–10] Although easy to administer, these scales do not provide detail about the type or domain of the disability found and therefore may lack the sensitivity needed for intervention research. The Functional Status Scale (FSS) is a recently validated measure specifically developed to overcome these challenges in pediatric critical care outcomes research by measuring 6 domains of function: mental status, sensory, communication, motor, feeding, and respiratory.[11] Previous work using the FSS shows that 7% of pediatric critical care survivors with a neurologic diagnosis and 11% of patients with traumatic injuries have a change in FSS from baseline of $\geq$3.[12,13] Another study focused on children with TBI requiring critical care intervention showed that 37% had a change in FSS of $\geq$3. This suggests variability in outcomes between neurologic diagnoses,[14] but previous studies have not evaluated FSS among many PNCC diagnoses. Additionally, changes of $\geq$3 in FSS represent substantial impairments in function and a cutoff correlating with moderate or severe impairments in adaptive function[11,15] and underestimate the overall burden of new functional deficits that require ongoing care.

We evaluated hospital outcomes among PNCC admissions by quantifying death and changes in FSS from preadmission baseline both overall and among different PNCC diagnoses. We quantified changes by domain of FSS to provide greater detail on outcomes and explored risk factors for worse outcomes. We hypothesized that rates of disability measured by changes in FSS would vary significantly by primary diagnosis.

METHODS

Study Design and Setting

We conducted an observational study of consecutive children ages 0 to 18 years admitted with a primary neurologic diagnosis to the ICU at an academic tertiary children's hospital and accredited level 1 pediatric trauma center from August 2016 to August 2018. This study was approved by the institutional review board with a waiver of informed consent. Deidentified data will be made available on request.

Participants and Data Collection

The primary exposure was admission diagnosis: TBI, status epilepticus, neuroinfectious and inflammatory diseases (meningitis, encephalitis, abscess or empyema, or demyelinating), stroke (hemorrhagic, ischemic, or cerebral sinus venous thrombosis [CSVT]), and hypoxic-ischemic encephalopathy (HIE) due to out-of-hospital cardiac arrest requiring chest compressions for $>$2 minutes. In patients with multiple diagnoses, the primary diagnosis was used (eg, patients with seizures due to meningitis were classified as infectious). All patients meeting inclusion criteria during daily census review were included in the study. Only characteristics of the first PNCC admission during the study period for a particular patient were included in the analysis.

Demographic and clinical characteristics were collected from electronic medical records and entered into Research Electronic Data Capture prospectively during admission.[16] Preadmission chronic conditions were grouped into system categories (Supplemental Table 4). Pediatric Index of Mortality 2 scores and critical care interventions evaluated illness severity. Interventions included intubation, noninvasive ventilation, central venous catheterization, arterial catheterization, intracranial pressure monitoring, continuous antiepileptic infusion, neurosurgical intervention (eg, decompressive craniectomy and hematoma evacuation), hemodynamic resuscitation or vasopressor use, and in-hospital cardiopulmonary resuscitation (CPR). Interventions were not included if they were used during operative management only (eg, intubation for operation). Seizures were diagnosed clinically and on EEG monitoring. TBI severity was measured by the initial Glasgow Coma Scale (mild complicated 13–15, moderate 9–12, and severe 3–8) recorded in the emergency department. Location and type of TBI were identified from radiology reports, and concurrent nonbrain traumatic injuries were identified from radiology and clinical reports.

Outcomes

The primary outcomes were in-hospital death and change in FSS from baseline. Manner of death was recorded from provider notes. The change from baseline FSS at hospital discharge was used to define disability outcomes and collected for all eligible patients. The FSS is validated for use in pediatric critical care outcomes in children of all ages, has excellent interrater reliability (intraclass correlation coefficient = 0.95),[11] and correlates with the Adaptive Behavior Assessment System–Second Edition.[11] Baseline FSS scores, reflecting patients' preillness function, were documented in the medical record by the treating attending PICU physician within 24 hours of admission per our institution's standard. Discharge FSS scores were inputted into the medical record by a treating attending PICU or neurology physician as part of the PNCC program.[17] Discharge FSS scores reflected the patient's status on the day of discharge. Physicians prospectively inputted FSS on the basis of the 5-category rubric designed by Pollack et al[12] in a tool embedded in the electronic medical record. For this study, we defined new disability as an increase from baseline to discharge FSS total score of $\geq$1 point and new severe disability as an increase of $\geq$3. No patients had improvement from baseline FSS.

TABLE 1 Characteristics and Outcomes of the PNCC Cohort Overall and by Primary Diagnosis

Characteristic or Outcome	All PNCC	TBI	Status Epilepticus	Infectious and/or Inflammatory	Cardiac Arrest	Stroke
	N = 325	*n* = 154	*n* = 71	*n* = 40	*n* = 37	*n* = 23
Age, y, median (IQR)	5.0 (1.3–11.6)	5.5 (1.3–11.7)	3.9 (1.7–8.9)	6.2 (1.8–12.6)	1.2 (0.3–12.6)	9.5 (1.2–15.5)
White race, *n* (%)	253 (78)	130 (84)	53 (75)	27 (68)	24 (65)	19 (83)
Hispanic ethnicity, *n* (%)	49 (15)	19 (12)	15 (21)	6 (15)	3 (8)	6 (26)
Male sex, *n* (%)	198 (61)	101 (66)	40 (56)	23 (58)	22 (60)	12 (52)
Medicaid insurance, *n* (%)	165 (51)	66 (43)	41 (58)	26 (65)	22 (60)	10 (44)
Pediatric Index of Mortality 2 score, median (IQR)	−4.1 (−4.2 to −3.2)	−4.2 (−4.2 to −3.8)	−4.0 (−4.2 to −3.2)	−4.2 (−4.3 to −3.3)	0.5 (−2.8 to 1.9)	−4.3 (−4.7 to −3.2)
Previous critical care admission, *n* (%)	21 (7)	1 (1)	15 (21)	0	4 (11)	1 (4)
Preadmission chronic condition, *n* (%)	96 (30)	16 (10)	51 (72)	5 (13)	13 (35)	11 (48)
Critical care intervention,[a] *n* (%)	184 (56)	68 (44)	34 (48)	28 (70)	36 (97)	13 (57)
Intubation	138 (42)	45 (29)	34 (48)	14 (35)	36 (97)	9 (39)
Central venous line	82 (25)	20 (13)	3 (4)	20 (50)	31 (84)	8 (35)
Arterial line	78 (24)	27 (18)	2 (3)	6 (15)	33 (89)	10 (44)
Neurosurgical intervention	66 (20)	29 (25)	0	17 (43)	0	10 (44)
Hemodynamic intervention	56 (17)	11 (7)	1 (1)	8 (20)	31 (84)	5 (22)
Intracranial pressure monitor	21 (6)	12 (8)	0	4 (10)	0	5 (22)
CPR in hospital	12 (4)	1 (1)	0	0	8 (22)	3 (13)
Infusion of seizure medication	25 (8)	2 (1)	15 (21)	4 (10)	3(8)	1 (4)
Seizure during hospitalization, *n* (%)	68 (21)	10 (7)	31 (44)	14 (35%)	8 (22)	5 (22)
Inpatient nutrition, *n* (%)						
Any parenteral	15 (5)	5 (3)	1 (1)	3 (8)	4 (11)	2 (9)
Any nasogastric or postpyloric feeds	44 (14)	12 (8)	8 (11)	12 (30)	6 (16)	6 (26)
Inpatient consults, *n* (%)						
Physical therapy	141 (43)	68 (44)	18 (25)	28 (70)	11 (30)	16 (70)
Occupational therapy	110 (34)	49 (32)	14 (20)	23 (58)	9 (24)	15 (65)
Speech therapy	54 (17)	17 (11)	6 (9)	15 (38)	5 (14)	11 (48)
Psychology	36 (11)	19 (12)	2 (3)	9 (23)	4 (11)	2 (9)
Hospital days, median (IQR)	3.3 (1.6–8)	2.4 (1.5–5.2)	2.0 (1.3–5.4)	8.1 (6.0–16.4)	2.7 (1.5–7.8)	9.4 (4.4–13.6)
Critical care days, median (IQR)	1.4 (0.8–3.0)	1.0 (0.7–1.9)	1.0 (0.7–2.5)	2.8 (1.5–4.7)	2.7 (1.5–4.4)	3.0 (1.5–6.4)
Mechanical ventilation hours,[b] median (IQR)	37 (5.5–102.8)	11 (108.4–11.2)	10.7 (2.1–57.2)	63.3 (24.9–104)	70.4 (48.5–108)	80 (29.8–136.4)
Hospital mortality, *n* (%)	30 (9)	3 (2)	0	1 (3)	25 (68)	1 (4)
Discharge to inpatient rehabilitation, *n* (%)	29 (9)	11 (7)	4 (6)	8 (20)	0	6 (26)
Baseline FSS, median (IQR); maximum value	6 (6–6); 18	6 (6–6); 14	6 (6–11); 18	6 (6–6); 8	6 (6–6); 15	6 (6–6); 9
Discharge FSS,[c] median (IQR); maximum value	6 (6–8); 27	6 (6–7); 22	7 (6–11); 21	7 (6–8); 15	6.5 (6–8); 26	7.5 (6–9); 27

TABLE 1 Continued

Characteristic or Outcome	All PNCC	TBI	Status Epilepticus	Infectious and/or Inflammatory	Cardiac Arrest	Stroke
	$N = 325$	$n = 154$	$n = 71$	$n = 40$	$n = 37$	$n = 23$
FSS change,[c] median (IQR); maximum value	0 (0–1); 21	0 (0–1); 16	0 (0–0); 15	1 (0–2); 9	0 (0–1); 20	0.5 (0–3); 21
New disability,[c] FSS change, *n* (%)	103 (35)	56 (37)	10 (14)	21 (54)	5 (42)	11 (50)
1 or 2[c]	66 (22)	39 (26)	8 (11)	12 (31)	3 (25)	4 (20)
≥3[c]	37 (13)	17 (11)	2 (3)	9 (23)	2 (17)	7 (30)

[a] Multiple critical care interventions in some patients.
[b] Among patients undergoing mechanical ventilation.
[c] Evaluated among survivors only ($n = 295$).

Statistical Analysis

Descriptive statistics were used, including percentage for categorical variables and median with interquartile range (IQR) for continuous variables, because data were not normally distributed. Demographic and clinical characteristics were compared between survival and disability groups. χ^2 tests for categorical variables (with Fisher's exact correction for expected cell counts <10) and Mann-Whitney *U* tests for continuous variables were used. Bivariate results for categorical variables were reported as relative risk (RR) with 95% confidence interval (CI). The primary analysis compared new disability groups among the overall PNCC cohort. The hypothesized variability in new disability rate by diagnosis was tested by using χ^2 tests. Secondary analyses were conducted to compare the overall cohort by new severe disability and to explore outcomes among individual diagnoses (Supplemental Tables 5–9). All tests were 2 tailed, and significance was defined as $P < .05$. Because secondary analyses were exploratory within limited populations, no adjustment was made for multiple comparisons. All analyses were conducted by using SPSS (version 24.0; IBM SPSS Statistics, IBM Corporation).

RESULTS

Over 2 years, 325 patients had a primary PNCC diagnosis, accounting for 16% of all ICU admissions. Diagnoses included TBI ($n = 154$; 47%), status epilepticus ($n = 71$; 22%), infectious or inflammatory disease ($n = 40$; 12%), HIE ($n = 37$; 11%), and stroke ($n = 23$; 7%). One-third ($n = 96$) had preadmission chronic conditions, which varied by primary diagnosis (Supplemental Table 4). Most (84%) patients had normal baseline FSS (FSS = 6). Severity of illness varied, but 56% received at least 1 critical care intervention, and 25% received 3 or more. Table 1 describes the PNCC cohort and hospital outcomes. Detailed characteristics among each diagnosis are reported in Supplemental Tables 5 through 9.

Thirty (9%) PNCC patients died during hospitalization, most (83%) with HIE. Fourteen deaths (47%) occurred after withdrawal of support, 13 (43%) occurred by neurologic criteria, and 3 (10%) were due to in-hospital cardiac arrest. Among PNCC survivors ($n = 295$), 103 (35%) had a new disability defined as an FSS change from baseline of ≥1 (Fig 1), which varied significantly by diagnosis (range 14%–54%; $P < .001$). Survivors with status epilepticus had less disability (RR 0.4; 95% CI 0.2–0.7), and survivors with infectious and/or inflammatory conditions (RR 1.6; 95% CI 1.2–2.3) had more disability at discharge compared with those with other diagnoses. Thirty-seven (13%) survivors had a new severe disability (FSS change ≥3), particularly among stroke survivors (RR 2.9; 95% CI 1.4–5.8).

Changes in FSS among patients with a new disability ranged from 1 to 21 points (Fig 2). Receiving critical care interventions (RR 2.1; 95% CI 1.5–3.1) and having seizures (RR 1.5; 95% CI 1.1–2.0) during hospitalization were associated with new disability (Table 2). PNCC patients surviving with new disability had significantly longer hospital lengths of stay compared with all ICU admissions (median 8.6 vs 3.8 days) and PNCC survivors without new disability (8.6 vs 2.1 days; both $P < .05$). Six (2%) survivors underwent tracheostomy and gastrostomy placement. Twenty-nine (9%) patients were discharged to inpatient rehabilitation, including 17 (59%) with new severe disability and 12 (41%) with FSS changes of 1 or 2.

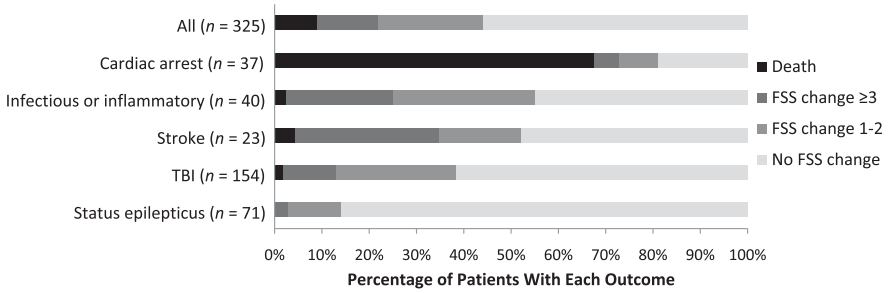

FIGURE 1 Outcomes of children receiving neurocritical care. The chart shows percentages of patients within each diagnosis, with the outcomes of death and new disability being measured by the FSS score change from baseline at hospital discharge.

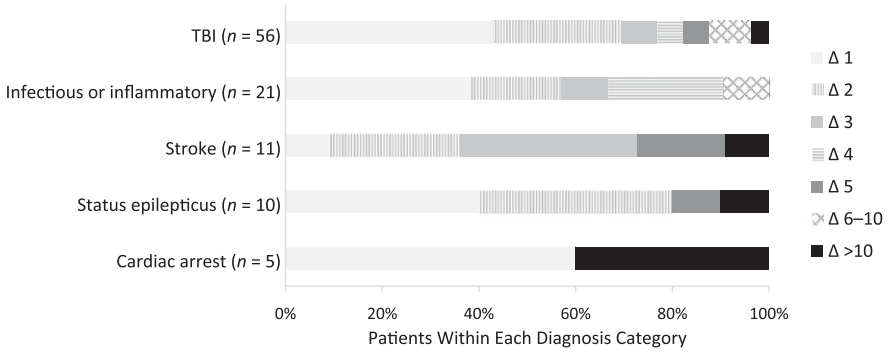

FIGURE 2 FSS change among survivors with new disability. Distribution of FSS total score change from baseline at hospital discharge among diagnosis categories.

Among patients with new disability, fewer changes (≤15%) were found in mental status and respiratory domains compared with sensory (52%), motor (48%), feeding (40%), and communication (38%). Table 3 shows the prevalence of individual FSS domain changes, which varied by diagnosis. Within most FSS domains, changes of 1 were most prevalent Supplemental Fig 3). However, multiple domains were often affected (67% of patients with severe disability had changes in ≥3 separate domains).

TBI accounted for 154 admissions (68% mild complicated, 16% moderate, and 16% severe TBI). Three (2%) patients died, including 2 with severe TBI with nonreactive pupils at admission (neurologic criteria) and 1 with moderate TBI and polytrauma (cardiac arrest). Fifty-six (37%) survivors had a new disability, varying significantly with Glasgow Coma Scale (23% of mild complicated, 58% of moderate, and 72% of severe; $P < .001$). Seventeen (11%) survivors had a new severe disability (5% mild complicated, 17% moderate, 35% severe; $P < .001$). Seizures, frontal lobe injury, contusions, and diffuse axonal injury all increased risk for new disability (all $P \leq .03$; Supplemental Table 5). Other injuries (eg, thoracic, spine, and extremity) increased the risk of new disability compared with isolated TBI (RR 5.3; 95% CI 2.8–10). Only 9 (12%) patients with isolated TBI had new disability.

Patients ($n = 71$) with status epilepticus had better outcomes compared with those with other diagnoses (Table 2). No patients died, 10 (14%) had new disability, and 3% had severe disability. Preadmission epilepsy (54%) and febrile status (23%) were the most common etiologies. Most patients (72%) had preadmission chronic conditions, and 21% had previous ICU admissions. Seizures continued after admission in 31 (44%) patients. Fifteen (20%) patients had refractory status epilepticus requiring infusions of versed or pentobarbital, and this was associated with new disability (RR 5.6; 95% CI 1.8–17.3; Supplemental Table 6).

Among 40 patients with infectious and inflammatory disease, 1 patient with unknown encephalitis died (neurologic criteria), 21 (53%) survivors had new disability, and 9 (23%) had severe disability. Thirty patients had infectious, 7 had inflammatory, and 3 had indeterminate diagnoses (all encephalitis of unknown etiology). Inflammatory and indeterminate diagnoses were associated with increased risk of new disability compared with infectious diagnoses (RR 2.5; 95% CI 1.6–3.9; Supplemental Table 7).

Among 37 HIE patients, 25 (68%) died during hospitalization from withdrawal of life support (48%), neurologic criteria (44%), or subsequent cardiac arrest (8%). Among 12 survivors, 5 (42%) had new disability. Two (17%) survivors had new severe disability, both receiving >30 minutes of CPR and 1 being discharged to hospice. Duration of preadmission CPR ranged from 3 to 102 minutes. Survivors had lower median CPR duration (10 vs 40 minutes; $P = .03$), although 5 survivors received ≥30 minutes of CPR. Two survivors without disability received ≥30 minutes of CPR, 1 with hypothermic submersion injury[18] and 1 with ventricular tachycardia due to myocarditis. New disability among survivors was associated with seizures during admission (RR 4.5; 95% CI 1.3–15.3), younger age, and nonarrhythmia causes of arrest (all $P < .05$; Supplemental Table 8).

Among 23 patients with stroke, 10 had hemorrhagic stroke (all arteriovenous malformations or cavernomas), 9 had ischemic stroke (1 patient with secondary hemorrhage), and 4 had CSVT. One patient with malignant middle cerebral artery stroke died. Half of stroke survivors had new disability, and one-third had severe disability. No CSVT patients had new disability at discharge, whereas hemorrhagic and ischemic stroke had a high prevalence of new disability (55% and 63%, respectively) and new severe disability (43% and 50%, respectively). Although not statistically significant, survival with disability was more common with critical care interventions (RR 2.2; 95% CI 0.8–6.3) and seizures (RR 1.6; 95% CI 0.8–3.6; Supplemental Table 9).

DISCUSSION

Most patients (84%) with PNCC diagnoses have normal FSS at baseline but suffer high rates of death (9%) and new disability (35%) at discharge, including 13% with new severe disability. Outcomes vary significantly with primary diagnosis. PNCC survivors often have functional impairments in multiple FSS domains that require ongoing care after hospital discharge, furthering the burden of PNCC diseases. Increased severity of illness and seizures during admission are associated with worse outcomes, whereas other risk factors varied by diagnosis. This study provides data on new disabilities among individual PNCC diagnoses using the FSS that can be used to advance future research.

We found that nearly 1 in 10 PNCC admissions result in death, confirming results from previous administrative data and point-prevalence studies in PNCC[3,4] and showing that PNCC mortality is substantially higher than rates for other PICU cohorts.[12,19] We also found high rates of morbidity that were consistent with previous reports. Pollack et al[12] reported that 7% of critical

TABLE 2 Characteristics of the PNCC Cohort by Hospital Outcome

Characteristic	Death in Hospital	Survival With Baseline Function	Survival With Any New Disability	Survival With Severe Disability
	$n = 30$	$n = 192$	$n = 103$	$n = 37$
Age, y, median (IQR)	1.7 (0.5–11.6)	4.5 (1.3–10.6)	6.6 (1.7–12.7)	6.6 (2.0–11.4)
White race, *n* (%)	18 (60)[a]	152 (79)	83 (81)	27 (73)
Hispanic ethnicity, *n* (%)	4 (13)	30 (16)	15 (15)	5 (14)
Male sex, *n* (%)	14 (47)	124 (65)	60 (58)	21 (57)
Medicaid insurance, *n* (%)	19 (63)	99 (52)	47 (46)	17 (46)
Pediatric Index of Mortality 2 score, median (IQR)	1.0 (−1.9 to 2.1)[a]	−4.1 (−4.2 to −3.3)	−4.1 (−4.3 to −3.1)	−3.2 (−4.3 to −2.7)
Previous critical care admission, *n* (%)	2 (7)	15 (8)	4 (4)	1 (3)
Preadmission chronic condition,[b] *n* (%)	11 (37)	62 (32)	23 (22)	6 (16)
Admission diagnosis category, *n* (%)				
TBI	3 (10)[a]	95 (50)	56 (54)	17 (46)
Status epilepticus	0[a]	61 (32)	10 (10)[c]	2 (5)[c,d]
Infectious or inflammatory	1 (3)	18 (9)	21 (20)[c]	9 (24)[c]
Cardiac arrest	25 (83)[a]	7 (4)	5 (5)	2 (5)
Stroke	1 (3)	11 (6)	11 (11)	7 (19)[c,d]
Critical care intervention,[e] *n* (%)	30 (100)[a]	82 (43)	72 (70)[c]	29 (78)[c,d]
Intubation	30 (100)[a]	51 (27)	57 (55)[c]	26 (70)[c,d]
Central venous line	29 (97)[a]	14 (7)	39 (38)[c]	25 (68)[c,d]
Arterial line	29 (97)[a]	12 (6)	37 (36)[c]	25 (68)[c,d]
Neurosurgical intervention	3 (10)	32 (17)	31 (30)[c]	16 (43)[c,d]
Hemodynamic intervention	29 (97)[a]	7 (4)	20 (19)[c]	14 (38)[c,d]
Intracranial pressure monitor	2 (7)	5 (3)	14 (14)[c]	9 (24)[c,d]
CPR	9 (30)[a]	0	3 (3)[c]	3 (8)[c,d]
Infusion of seizure medication	2 (7)	11 (6)	7 (11)	5 (14)
Seizure during hospitalization, *n* (%)	8 (27)	32 (17)	28 (27)[c]	9 (24)
Inpatient nutrition, *n* (%)				
Any parenteral	1 (3)	4 (2)	10 (10)[c]	7 (19)[c,d]
Any nasogastric or nasojejunal	1 (3)	9 (5)	34 (33)[c]	22 (60)[c,d]
Inpatient consults, *n* (%)				
Physical therapy	3 (10)[a]	66 (34)	72 (70)[c]	34 (92)[c,d]
Occupational therapy	2 (7)[a]	45 (23)	63 (61)[c]	31 (84)[c,d]
Speech therapy	0[a]	10 (5)	44 (43)[c]	26 (70)[c,d]
Psychology	0	14 (7)	22 (21)[c]	7 (19)
Hospital days, median (IQR)	1.9 (1.2–2.8)[a]	2.1 (1.4–4.6)	8.6 (5–14.3)[c]	14.9 (10.5–20.3)[c,d]
Critical care days, median (IQR)	1.7 (1.2–2.7)	1 (0.7–1.7)	3.1 (1.6–6.2)[c]	6.4 (2.9–12.8)[c,d]
Mechanical ventilation hours, median (IQR)	63.3 (44.2–73.6)	10 (3.5–64.9)	59.2 (16.5–138.7)[c]	137 (72.2–222)[c,d]

New disability is defined by a change in FSS total score of ≥1 from baseline; severe disability is defined by a change in FSS total score of ≥3 from baseline. Groups were compared by using χ^2 tests (with Fisher's exact for cells with expected $N < 10$) for categorical variables and Mann-Whitney *U* tests for continuous variables.

[a] $P < .05$ when comparing the overall PNCC cohort by hospital death.

[b] Multiple preadmission chronic conditions found in 52 (16%) patients overall.

[c] $P < .05$ when compared with survivors without new disability ($n = 192$).

[d] $P < .05$ when compared with all other survivors ($n = 258$).

[e] Multiple critical care interventions in some patients. The neurosurgical intervention category includes decompressive craniectomy or hematoma evacuation; the hemodynamic intervention category includes fluid resuscitation or inotropic or vasopressor support.

care patients with a neurologic diagnosis had FSS changes of ≥3 but noted variability between centers. We found that 13% of all PNCC admissions had FSS changes of ≥3, but this varied from 3% to 33% depending on the diagnosis. A TBI study focused on those receiving critical care interventions showed that 37% had FSS changes of ≥3,[14] similar to the 35% we found in patients with severe TBI. Ahmed et al[13] reported that 11% of all children treated for traumatic injuries requiring pediatric critical care had FSS

TABLE 3 FSS Domain Changes Among Survivors With a New Disability

FSS Domain	All Survivors $N = 103$ (%)		Trauma $n = 56$ (%)		Status Epilepticus $n = 10$ (%)		Infectious and/or Inflammatory $n = 21$ (%)		Cardiac Arrest $n = 5$ (%)		Stroke $n = 11$ (%)	
	Any Δ	$\Delta \geq 3$	Any Δ	$\Delta \geq 3$	Any Δ	$\Delta \geq 3$	Any Δ	$\Delta \geq 3$	Any Δ	$\Delta \geq 3$	Any Δ	$\Delta \geq 3$
Mental status	15 (15)	6 (6)	7 (13)	2 (4)	2 (20)	1 (10)	2 (10)	0	2 (40)	2 (40)	2 (18)	1 (9)
Sensory	53 (52)	4 (4)	37 (66)	1 (2)	3 (30)	0	8 (38)	0	3 (60)	2 (40)	2 (18)	1 (9)
Communication	39 (38)	3 (3)	20 (36)	1 (2)	4 (40)	0	8 (38)	0	2 (40)	1 (20)	5 (46)	1 (9)
Motor	49 (48)	10 (10)	24 (43)	5 (9)	1 (10)	1 (10)	12 (57)	1 (5)	2 (40)	2 (40)	10 (91)	1 (9)
Feeding	41 (40)	9 (9)	18 (32)	4 (7)	6 (60)	1 (10)	7 (33)	1 (5)	4 (80)	2 (40)	6 (55)	1 (9)
Respiratory	12 (12)	2 (2)	6 (11)	1 (2)	3 (30)	1 (10)	0	0	2 (40)	0	1 (9)	0

Columns do not sum to 100% because multiple domains can be impaired per patient. Counts and percentages reflect the number of patients with any change in the FSS domain from the patient's preadmission baseline and the number with changes of 3 or more in each domain. Δ, change in FSS domain from preadmission baseline.
eumatologic diagnoses.

changes of ≥ 3 and that concurrent head injuries increased risk for morbidity. Our study is the first to systematically apply the FSS at the diagnosis level for other nontraumatic PNCC diagnoses.

Similar to previous studies, most children requiring PNCC admission had normal functional baselines in our study.[13,14] Therefore, we also evaluated disability as defined by smaller changes in FSS than previous studies to better quantify the breadth of morbidities these children suffer. Using our definition of FSS increases of ≥ 1 from baseline, the prevalence of new disability after PNCC increased substantially to 35% (range 14%–53% by diagnosis). We believe these small FSS changes are important at the individual patient level when considering risk for ongoing health care needs and reduced quality of life[20–24] and are important considerations for clinicians. Changes of 1 point among previously healthy children are substantial and correspond to suspected hearing or vision loss, need for oxygen or suctioning, need for age-inappropriate help with feeding, or functional impairment of 1 limb depending on the domain affected.[11] These data can be used in future studies aimed at reducing disability after PNCC.

Our study adds granularity to outcomes data by using the FSS. The 6 domains of the FSS offer approximations of activities of daily living and correlate with results of comprehensive adaptive behavior testing.[11] Evaluating outcomes at the FSS domain level, we found that all domains are affected after PNCC, and patients often have disabilities in multiple domains. The wide breadth of morbidities found by using FSS, coupled with knowledge about cognitive, emotional, and psychosocial morbidities after ICU hospitalization,[24–28] suggests that a multidisciplinary approach to patient follow-up is needed to adequately care for these children. Despite the high rate of new disability in multiple domains, $<10\%$ of our patients were discharged to inpatient rehabilitation facilities. Currently few institutions offer systematic follow-up care in PNCC survivors that can provide this type of comprehensive care outside of a rehabilitation setting, although increasing recognition of long-term sequelae is driving the development of longitudinal programs.[3,17,29,30] Our study underscores the need for developing systematic support for patients and families after discharge.

Few interventions have been shown to improve outcomes in PNCC, and intervention studies in this population are hindered by limited knowledge of outcomes and risk factors.[1] With our study, we explored risk factors that could be used to predict outcomes or targeted in future intervention studies. Not surprisingly, markers of illness severity, such as need for critical care interventions, lower Glasgow Coma Scale score in TBI, and increased CPR duration in cardiac arrest, were associated with worse outcomes, similar to previous studies.[14,31–34] However, we also identified seizures during admission as a risk factor for worse outcomes in the overall cohort as well as among individual diagnoses. Seizures may represent worse primary brain injury, but seizures can also lead to secondary brain injury and may serve as a modifiable target to improve outcomes. Although our institution has guidelines for seizure prophylaxis and EEG monitoring in patients with TBI, we did not systematically evaluate EEG for other diagnoses and, notably, may have underdiagnosed subclinical seizure activity. Seizure burden is linked to worse outcomes in the PICU population,[35] and our results further support guidelines for systematic EEG monitoring in PNCC.[36] It remains unknown if interventions targeting seizures can improve outcomes.

Our study has several limitations to consider, including the single-center setting when admission characteristics, treatments, and outcomes in PNCC patients may vary by region and center.[3,4,37–39] Our results are likely comparable to other academic tertiary children's hospitals and level 1 pediatric trauma centers but may not represent PNCC populations at all institutions. PNCC diseases are individually rare, and many of the diagnoses we evaluated had low numbers of admissions, even over 2 years, limiting comprehensive evaluation of risk factors for worse outcomes, particularly among diagnosis subgroups. Future studies should evaluate correlates between FSS changes and neuroimaging, EEG, and biomarkers in larger cohorts to further refine risk factors. Additionally, more than three-quarters of

our patients had normal baseline FSS, but larger studies could explore the development of new disabilities and severity of decline relative to baseline among children with preadmission neurologic impairments. This study was also limited to hospital outcomes, and little data exists on longitudinal outcomes after PNCC, particularly in nontraumatic diagnoses. It is likely that FSS improves or declines in the months after discharge,[40] and future work should evaluate postdischarge FSS to determine potential for recovery and need for ongoing medical intervention after PNCC. Additionally, the FSS does not capture important morbidities, such as those of detailed neuropsychological assessments of cognitive and mental health, or assess impairments in quality of life. Future studies should assess the relationship between FSS and these other important outcomes.

CONCLUSIONS

More than one-third (35%) of PNCC survivors have new disability when evaluating changes in FSS from baseline, and outcomes vary significantly with primary diagnosis. All functional domains measured by the FSS can be affected after PNCC, and patients with new disability often have multiple domains affected concurrently, underscoring the ongoing need for multidisciplinary care after discharge. Future studies should determine the longitudinal course of recovery in FSS after discharge and evaluate risk factors for worse outcomes in larger multicenter populations to identify targets for future intervention.

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