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Early Protocolized vs. Usual Care Rehabilitation for Pediatric Neurocritical Care Patients: A Randomized Controlled Trial

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TWEET

Early, ICU-based and personalized physical, occupational, and speech and language therapy sessions were feasible and safe in pediatric neurocritical care patients.

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Abstract

Objective—Few feasibility, safety, and efficacy data exist regarding ICU-based rehabilitative services for children. We hypothesized that early protocolized assessment and therapy would be feasible and safe versus usual care in pediatric neurocritical care patients.

Design—Randomized controlled trial.

Setting—Three tertiary care pediatric ICUs in the United States.

Patients—Fifty-eight children between the ages of 3–17 years with new traumatic or non-traumatic brain insult and expected ICU admission > 48 hours.

Interventions—Early Protocolized (consultation of physical [PT], occupational [OT], and speech and language therapy [SLT] within 72 h ICU admission, n=26) or Usual Care (consultation per treating team, n=32).

Measurements—Primary outcomes were consultation timing, treatment type, and frequency of deferrals and safety events. Secondary outcomes included patient and family functional and quality of life outcomes at 6 months.

Main Results—Comparing Early Protocolized (n=26) and Usual Care groups (n=32), PT was consulted during the hospital admission in 26/26 vs. 28/32 subjects (p=0.062) on day 2.4 ± 0.8 vs. 7.7 ± 4.8 (p=0.001); OT in 26/26 vs. 23/32 (p=0.003), on day 2.3 ± 0.6 vs. 6.9 ± 4.8 (p=0.001); and SLT in 26/26 vs. 17/32 (p=0.011) on day 2.3 ± 0.7 vs. 13.0 ± 10.8 (p=.026). More children in the Early Protocolized group had consults and treatments occur in the ICU vs. ward for all three services (all p<.001). Eleven sessions were discontinued early: 9 during PT and 2 during OT, none

impacting patient outcome. There were no group differences in functional or quality of life outcomes.

Conclusions—A protocol for early personalized rehabilitation by PT, OT, and SLT in pediatric neurocritical care patients could be safely implemented and led to more ICU-based treatment sessions, accelerating the temporal profile and changing composition of interventions vs. usual care, but not altering the total dose of rehabilitation.

Keywords

Critical care; Neurologic disorders; Pediatric; Rehabilitation; Outcome

INTRODUCTION

Pediatric intensive care unit (PICU) mortality rates have decreased to 2–4% in the United States while the frequency of new ICU-related morbidities in children and families has been reported to be as high as 30%^{1–7}. Risk factors for the acquisition of ICU-related morbidities are multifactorial and include immobility and underlying diagnoses such as acute neurologic injury^{8–10}. Further, delays in initiating rehabilitation are associated with less functional recovery^{11–14}.

A randomized, controlled trial (RCT) in adults found that early physical and occupational therapy (PT and OT) tailored to patient severity of illness led to shorter time to return to independent activities of daily living, and less delirium and mechanical ventilation days without compromising safety compared to usual care. In addition, quality improvement studies showed that adult neurocritical care patients and PICU patients can tolerate and benefit from ICU-rehabilitative interventions^{15–17}. Data suggest that families and providers are interested in ICU-rehabilitation programs while recognizing important challenges that may be remedied in part through prospective study to inform best practices^{18–22}.

The objective of this study was to demonstrate the feasibility and safety of ICU-based protocolized rehabilitation for pediatric neurocritical care patients in an RCT. We hypothesized that children randomized to the Early Protocol would have more PT, OT, and speech and language therapy (SLT) consultations initiated and therapy sessions provided in the ICU with an acceptable safety profile compared to a Usual Care group.

MATERIALS AND METHODS

Regulatory.

The University of Pittsburgh Institutional Review Board (IRB) approved the RCT (NCT02209935) for the Children's Hospital of Pittsburgh of UPMC. Two other centers received local IRB approval and enrolled patients, including Ann & Robert H. Lurie Children's Hospital of Chicago and Cincinnati Children's Hospital Medical Center. An independent Data Safety Monitoring Board met every 6 months at the University of Pittsburgh. We recruited family, community, clinician, research, administrative, and advocacy stakeholders to participate in the study (Supp Table 1).

Study Period.

Patients were enrolled between February 2015-February 2017.

Recruitment:

We screened for subjects daily in the ICU and approached parents/guardians when criteria were met and the attending physician approved approach.

Enrollment of Patients.

Eligible children were between the ages 3 and 17 years and admitted to the ICU with one of the following acute diagnoses: traumatic brain injury, cardiac arrest, stroke, brain mass (e.g., tumor, arteriovascular malformation), or central nervous system infection/inflammation. Children were enrolled prior to 72 hours of PICU admission, have English speaking parents/guardians, and an expected ICU stay $\leq$ 2 days. Children with a do not resuscitate status, Pediatric Cerebral Performance Category (PCPC) score 4–5 (4=severe disability and 5=persistent vegetative state) prior to their diagnosis, or were not expected to survive $>$ 24 hours were excluded.

Consent and Randomization.

Informed consent was obtained from the subject's parent or guardian and children provided assent whenever appropriate. Subjects were assigned using 1:1 allocation to the Early Protocolized or Usual Care group using a computer-based randomization assignment developed by the study statistician using Statistical Package for the Social Sciences and provided to the site by the study PI. One child was erroneously placed into the Usual Care group when the randomization scheduled called for Early Protocol. After a report was filed with the IRB, this child remained in the Usual Care group for all study interventions and analyses.

Blinding:

The PI and study coordinator were aware of the subject's randomization group. All personnel involved in bedside therapies and child and family outcome assessments were blinded to the subject's randomization group. Children and families were not informed of their group assignment unless requested.

Intervention.

The study intervention was timing of initiation of PT, OT, SLT consultation. The Early Protocolized group had orders for PT, OT, and SLT consultations placed within 72 h of ICU admission. The Usual Care group received PT, OT, and/or SLT consultations per the treating team. Once consulted, PT, OT, and SLT provided care according to their established practices, which are based on a patient's severity and type of illness and developmental status. The treating ICU team does not typically provide additional guidance into application of usual care for PT, OT, or SLT at our institution aside from driving the decision to place the consultation order in the electronic medical record. Thus, some children in the Usual Care group may not receive PT, OT, and/or SLT during their hospitalization. There were no

new therapies introduced in this study and children in both groups received similar care except for the study intervention.

Data Collection.

We collected data from medical charts and from parents/guardians including demographics; functional outcomes; medical condition; ICU treatments and testing results; PT, OT, and SLT in-hospital sessions (treatment type, duration, deferral, and early discontinuation) and safety events. Data were collected at each site and entered into the study database by the study's main research coordinator.

Patient safety.

Patient safety parameters that lead to discontinuation of a therapy session included: 1) abnormal vital sign response to therapy lasting > 2 minutes (e.g., change in systolic blood pressure > 20 mm Hg, heart rate > 20 bpm, respiratory rate greater than the age appropriate range); 2) change pulse oximetry saturation > 10% or oxygen saturation < 90%.; 3) intracranial pressure reading > 20 mmHg; and 4) patient subjective complaint of shortness of breath, pain, lightheaded, nausea, weakness, or palpitations. In addition, therapists used patient severity of illness categories (by respiratory, cardiac, and neurologic systems) to guide therapeutic interventions (Supp Tables 2–3).

Data Management:

The PI, study coordinator, and statistician were the only individuals with direct access to the study database. Data were stored on a password-protected network, with additional periodic secure offsite backups to the database. Data quality was monitored and queries sent to sites regarding missing data or errors in data collection.

Outcome Measures:

Primary outcomes were the feasibility and safety of ICU-based PT, OT, and SLT therapies and therapy details (deferrals, early discontinuations, and types of therapies provided). Deferrals occur when a therapist comes to a patient room for a session but the session is not initiated. Secondary outcomes included the child's physical, cognitive, emotional health outcomes, family functioning, and quality of life (all parent and some patient reported outcomes) (Supp table 4). We recorded disposition at hospital discharge, and ICU and hospital lengths of stay. We obtained consent from two families to video record their experiences with ICU-based rehabilitation.

The site study team assigned the pre-event, hospital discharge, and 6-month PCPC and Pediatric Overall Performance Category (POPC) and Functional Status Scale (FSS) scores using chart review. Six-month outcome assessments were performed by our outcomes team in surviving children over the telephone or during an in-person interview with the parent or guardian during a scheduled outpatient visit. We provided a family incentive payment of \$20 for outcomes completion.

We performed a post-hoc analysis correlating combined group Vineland Adaptive Behavioral Scale (VABS) scores at 6 months with the number of hospital days to PT, OT,

and SLT consultation to explore this relationship given our limited power to assess functional outcomes by randomized group.

Sample size:

The original primary outcome for this RCT was to compare the VABS score between randomized groups at 6 months. However, this outcome was underpowered with the sample size, which was based on an efficacy trial for 175 subjects. Thus, we highlight trial results for safety and feasibility.

Statistical Analyses:

All analyses were conducted using Statistical Package for the Social Sciences. Frequencies and percentages were determined for categorical variables. Data were checked for errors and normality was assessed for all continuous variables using the Kolmogorov-Smirnov test. Continuous data were presented as median (interquartile range [IQR]) since data were skewed. All p -values were 2-sided, and a $p < 0.05$ was considered statistically significant. Group differences in continuous data were compared using the Wilcoxon Rank Sum and Kruskal-Wallis tests. Differences in categorical data were assessed using chi-square analysis with Fisher's exact test when appropriate. All participants were included in outcome analysis using intention-to-treat approach. Missing data were not imputed. Post-hoc analyses were performed using Spearman correlation.

RESULTS

Screening and Enrollment

We screened 923 children for eligibility of which 110 met inclusion criteria (Figure 1). Fifty-eight children were enrolled with 26 in the Early Protocolized group and 32 in the Usual Care group. All children received their assigned intervention and no patient or family withdrew study consent. Primary outcomes were obtained for all children. Prospectively collected secondary outcomes were available for 20/26 (76.9%) patients in the Early Protocolized group and 20/32 (62.5%) patients in the Usual Care group.

Patients and clinical care

Baseline patient characteristics and clinical care variables are presented in Table 1. Group differences included an imbalance in the number of female patients (25% Usual Care vs. 58% Early Protocolized, $p=.024$). There was a non-significant trend toward imbalance in ICU admission diagnoses (TBI: 38% Usual Care vs. 15% Early Protocolized and cardiac arrest: 13% Usual Care vs. 39% Early Protocolized, $p=.154$). Admission pediatric index of mortality (PIM) scores were similar between groups (3.51 [14.7] Usual Care vs. 3.28 [33.9] Early Protocolized, $p=.372$). Many children were treated with extraventricular drains (34%), mechanical ventilation (74%) and epinephrine infusions (31%).

Interventions

PT was consulted in 28/32 (88%) of Usual Care and 26/26 (100%) of Early Protocolized patients during the hospital stay ($p=.178$). PT was consulted during the ICU course for 16/32

(50%) of Usual Care and 23/26 (89%) of Early Protocolized patients ($p<.001$), occurring earlier in the Early Protocolized vs. Usual Care groups in the ICU (median 2 [interquartile range (IQR) 1] vs. 7 [5] days, $p<.001$) (Table 2). The Early Protocolized group had more PT sessions than the Usual Care group in the ICU (180 vs. 134, $p<.001$), and fewer than the Usual Care group on the ward (12 vs. 43, $p=.002$), leading to similar total sessions per patient between the groups (7.7 vs. 7.0, $p=.303$). The most common PT interventions were transfers out of bed (54.3%), bed mobility (60.2%), and side of bed sitting (53.7%) (Supplemental Figure 1). The Early Protocolized group had more transfers (118 vs. 83, $p=.006$), sitting outside of the bed (83 vs. 47, $p=.001$), and less active assist range of motion interventions than children in the Usual Care group in the ICU (19 vs. 33, $p=.026$).

OT was consulted in 23/32 (72%) of Usual Care and 26/26 (100%) of Early Protocolized patients during the hospital stay ($p=.010$). OT was consulted in the ICU for 14/32 (44%) of Usual Care and 22/26 (85%) of Early Protocolized patients ($p<.001$), occurring earlier in the Early Protocolized vs. Usual Care groups in the ICU (2 [1] vs. 7 [6] days, $p<.001$) (Table 2). The Early Protocolized group had more OT sessions than the Usual Care group in the ICU (146 vs. 121, $p<.001$), and but less than the Usual Care group in the ward (30 vs. 70, $p=.018$), leading to similar total sessions per patient between the groups (6.2 vs. 6.4, $p=.830$). The most common OT interventions were bed mobility (67.0%), transfers and activities of daily living (49.5%), and visual skills (49.3%) (Supplemental Figure 2). The Early Protocolized group had less active assist range of motion than children in the Usual Care group (17 vs. 36, $p=.002$).

SLT was consulted in 17/32 (53%) of Usual Care and 26/26 (100%) of Early Protocolized patients during the hospital stay ($p<.001$). SLT was consulted in the ICU for 7/32 (22%) of Usual Care and 24/26 (92%) of Early Protocolized patients ($p<.001$), occurring earlier in the Early Protocolized vs. Usual Care groups in the ICU (2 [1] vs. 10 [15] days, $p<.001$) (Table 2). The Early Protocolized group had more SLT sessions than the Usual Care group in the ICU (83 vs. 21, $p<.001$), and but less than the Usual Care group in the ward (5 vs. 35, $p<.001$), leading to similar total sessions per patient between the groups (4.2 vs. 3.3, $p=.839$). The most common SLT interventions were caregiver education (73.6%), receptive tasks with physical prompt (52.8%), and initiate purposeful communication (50.3%) (Supplemental Figure 3). The Early Protocolized group had less interventions for smell identification (13 vs. 22, $p=.007$), attention via eye opening (22 vs. 40, $p<.001$), fixate/track (4 vs. 34, $p<.001$), localize near/far on fixed object (3 vs. 27, $p<.001$), and sound (26 vs. 35, $p<.001$) but had more imitate sounds/words (42 vs. 14, $p=.013$) than children in the Usual Care group.

Safety events: session discontinuation and deferrals

Overall, 9 PT sessions were discontinued early, 5 for sustained change in systolic blood pressure (4 usual care and 1 early protocol). Two OT sessions and no SLT sessions were discontinued (Table 3). Subjective complaint and two of the three 'other' reasons for discontinuing therapy occurred in the usual care group. In one case, a child had intracranial hypertension just prior to a PT and OT session while receiving nursing care, deferring sessions for the day.

Sessions for PT were deferred on attempt in 21% of cases, for OT in 19% of cases, and 45% for SLT (Table 3). The most common reasons for PT and OT deferral were that the child was not in room at the time therapists arrived for the session followed by nurse request to postpone (for PT) and patient undergoing another treatment (for OT). SLT was deferred most frequently due to nursing request, followed by the child either not being present in the room or undergoing another treatment.

Patient and Family-Centered Outcomes

There were no differences in hospital or ICU lengths of stay, outpatient PT, OT, or SLT prescription, or placement of new technological devices between randomized groups at hospital discharge (Table 4). Although not statistically significant, more children in the Usual Care group (47%) vs. the Early Protocolized group (31%) were admitted to inpatient rehabilitation following their hospital stay.

There were no differences in six-month patient and family functional outcomes or health-related quality of life between randomized groups (Table 5). Within each group, patients had worse quality of life at 6 months compared to their pre-morbid baseline scores (Usual Care: pre-morbid 86 [18] vs. six months 74 [20], $p=.002$ and Early Protocolized: 91 [13] vs. 78 [18], $p=.003$). Similarly, patients had worse adaptive function scores at 6 months on the VABS compared to pre-morbid baseline scores (Usual Care: 100 [22] vs. 86 [21], $p=.004$ and Early Protocolized: 106 [17] vs. 96 [26], $p=.032$).

Exploratory post-hoc analyses

In an exploratory analysis, we combined data from children in both randomized groups to correlate VABS scores at 6 months with the number of hospital days to initial PT, OT, and SLT consultation (Table 6). Higher VABS scores were associated with less ICU days to PT (-0.428 , $p=.015$), OT (-0.366 , $p=.036$), and SLT ($-.600$, $p=.001$).

Next, we examined PT, OT, and SLT interventions by ICU vs. ward location, combining randomized group data (Supp Table 5). Overall, more PT (17 [14] vs. 9 [6], $p=.002$) and OT (17 [15] vs. 10 [12], $p=.013$) sessions were performed in the ICU per patient vs. the ward. There were no differences in the number of SLT sessions by location per patient (16 [15] vs. 12 [15], $p=.265$). For PT, passive range of motion was more common in the ICU (52% vs. 6%) and ambulation (23% vs. 82%) was more common on the ward. For OT, sensory stimulation was more common in the ICU (44% vs. 8%) while transfers and activities of daily living (47% vs. 77%) were more common in the ward. For SLT, more hand over hand assist to touch occurred in the ICU (30% vs. 8%) while fixation and tracking occurred more in the ward (15% vs. 56%). The frequency of session deferrals in the ICU and ward for PT (20% vs. 25%) and OT (17% vs. 22%) were similar. SLT deferrals occurred more frequently in the ICU vs. ward (51% vs. 36%).

Lastly, there were no differences between groups regarding the use of sedatives, narcotics, neuromuscular blockade, or steroids in the ICU (Supp Table 6). There were no differences in nutritional variables between groups during ICU admission including patient weight, calories prescribed, or breakdown of calorie source (e.g., protein, carbohydrate, or fat).

DISCUSSION

To our knowledge, this is the first report of a RCT of protocolized, ICU-based rehabilitation therapies in pediatric neurocritical care patients. The main findings of this study were as follows: 1) Early, protocolized ICU-based rehabilitation therapies were feasible to deliver; 2) More PT, OT, and SLT sessions were performed in the ICU for children in the Early Protocolized group while more PT, OT, and SLT sessions were performed on the ward for patients in the Usual Care patients, resulting in a similar numbers of sessions overall during the hospital stay; 3) Therapies were delivered with relatively good safety profiles; and 4) The frequency of PT, OT, and SLT session deferrals suggests the need for further improvements in education, care delivery and coordination. Additionally, the composition of the PT, OT, and SLT interventions was different by group and location, six-month outcomes were worse than prior to critical illness and similar between randomized groups and in an exploratory post-hoc analysis using pooled data, earlier rehabilitation was associated with better functional outcomes.

Acquisition of new physical, cognitive, and emotional health and quality of life morbidities are increasingly recognized among children and their families surviving critical illness and a framework for Post Intensive Care Syndrome in Children (PICS-p) was recently published to facilitate research on the topic^{3,4,7,14,23}. Risk for new morbidities are multifactorial and includes a child's primary diagnosis and severity of illness, immobility, inflammation, and medications commonly used in the ICU to promote immobility^{8–10}. ICU-related morbidities can synergistically adversely impact an individual's ability to perform activities of daily living, return to school or work, and affect family functioning and quality of life^{24–29}.

RCTs and observational studies in adults with critical illness suggest that ICU-based mobility and cognitive programs can improve outcomes including earlier return to activities of daily living, less delirium and ventilator days, and decrease length of stay and home disposition^{17,30–34}. However, few data exist to support recommendations for routine screening, prevention, and personalized treatment of ICU-related morbidities for children. Some centers have implemented local practice protocols for the delivery of some ICU-rehabilitation services in the absence of pediatric-specific prospective data. A multicenter survey of ICU-rehabilitation practices highlights remarkable variability in approach to usual care (manuscript submitted for review). Published data show that the status quo in PICUs in consulting PT, OT, and SLT therapy is unprotocolized and fraught with challenges towards implementing innovative solutions such as early mobility^{19,35,18,21,36}. Choong et al identified key institutional, patient- and provider-level barriers to early mobility for PICU patients, including the need for physician order and ambiguity in what interventions were safe to provide, many of which were also realized in our study¹⁹. To overcome these barriers and change ICU culture towards valuing recovery as well as resuscitation, there is a vital need for prospective high-quality efficacy evidence, educational tools, human and equipment resources, and implementation strategies³⁷. Family buy-in for early mobility programs for critically ill children is also key, with promising results in a qualitative study^{22,38}.

Our findings that early ICU-based rehabilitation was safe and feasible in pediatric neurocritical care patients align with other studies^{16,39,40}. Centers involved in this work

reported methodical program implementation that started with the formation of multidisciplinary team champions who created evidence and best practice-based protocols, provided multidisciplinary education, and performed quality assurance review. In our study, a multidisciplinary team reviewed the literature and local practices relevant to the provision of PT, OT, and SLT for PICU patients or other patient cohorts if none were available for PICU and codified a severity of illness-based tiered and developmentally-informed approach to daily assessment and treatment plans^{41–43}.

We found it interesting that although more children in the Early Protocolized group had PT, OT, and SLT sessions performed in the ICU compared to the ward, the overall number of sessions throughout the hospital stay was the same (with similar ICU and hospital length of stay). One possible explanation for this finding is that children in the Early Protocolized group, who received earlier assessment and more treatments while in the ICU, had less need for treatments once transferred to the ward. Similarly, children in the Usual Care group received less treatment in the ICU, thus having the need for more therapy in the ward. Supportive of this idea is that, although not statistically significant, more children in the Usual Care vs. Early Protocolized group were discharged from the hospital to inpatient rehabilitation for more intensive treatment, while more children in the Early Protocolized group were discharged home. Another possibility is the imbalance in admitting diagnosis by randomized group – more children with TBI in the Usual Care group and more children with cardiac arrest in the Early Protocolized group - affected consultation decisions by the treating team for the Usual Care group. For example, some clinicians may not request rehabilitative consultations until intracranial pressure monitoring and treatments or other organ supports such as tracheal intubation have been discontinued or until a patient is conscious and able to participate¹⁹. Another possibility is that access to rehabilitation services in the hospital or at a rehabilitation center might depend on a patient's ability to reimburse for those services^{44,45}. Provision of services also depends on therapist and equipment resource availability, which differs between hospitals and even locations within a hospital as usual care practices that do not include ICU patients may not fully provide for resource needs¹⁹.

Our findings have important implications for future efficacy trial design, especially regarding the location, timing, and type of intervention 'dose'. For example, do children who receive earlier therapies improve sooner such that ward and outpatient therapies are not prescribed – only to regress long-term? Our exploratory (pooled) analysis suggested that children who received earlier interventions had superior adaptive functional outcomes at 6 months, but we did not assess longer term outcomes such as back to school functioning. Alternatively, do Early Protocolized interventions need to be delivered across inpatient (ICU, ward, rehabilitation) and outpatient epochs to retain benefits long-term? Or, should the intervention be focused in the ICU period but delivered as part of a multidisciplinary care bundle that includes protocols for sedation and pain⁴⁶? Or should Early Protocolized interventions be delivered with higher intensity (which intervention is key?) compared to Usual Care, the latter which is evolving and center-dependent? And finally, what patient and family centered outcomes and measures should be used to determine whether an intervention was effective?

We enrolled children aged 3–17 years with acute neurocritical care conditions in tertiary care centers and was not powered to examine subpopulations or to determine the efficacy of ICU-based rehabilitation services, which are critically needed. Challenges exist in recruiting and retaining children with critical illness that require planning^{20,47}. Thus, we ask readers to interpret our findings with care when applying Early Protocolized interventions to other populations, including neonates and toddlers, and children with other critical care conditions placing them at increased risk of ICU-related disability such as pediatric acute respiratory distress syndrome, sepsis and multiple organ dysfunction syndrome, transplantation, and cardiac disease. Children with chronic, complex conditions represent a large proportion of the PICU patient population needing prospective study to inform feasibility, safety, efficacy, and best practices.

In response to this need, some centers have initiated follow-up clinics to coordinate care, and a group has published ICU-based consensus-based practice guidelines for early mobility^{48,49}. Governing bodies have published guidelines supporting the need for neurodevelopmental follow up for children with congenital heart disease and prematurity, but we argue that screening, prevention, and treatment of morbidities should begin in the ICU for all children and families at risk of functional disabilities and changes to quality of life^{50,51}.

Study limitations

Disappointingly, this study did not enroll the number of subjects needed and was thus not powered to detect meaningful differences between groups for important patient outcomes or efficacy of Early Protocol vs. Usual Care. PT, OT, and SLT consultation and treatment sessions could not be blinded to the caregivers or patients and families. We were underpowered to find differences in 6-month outcomes. We observed for drift in the usual care group towards earlier rehabilitative therapy consultations, but this did not become problematic. Randomized groups were imbalanced due to underenrollment in addition to a child who was misassigned.

CONCLUSIONS

A protocol for early, personalized rehabilitation by PT, OT, and SLT in pediatric neurocritical care patients could be safely implemented, and led to more ICU-based treatment sessions, accelerating the temporal profile and changing composition of interventions vs. standard care, but not altering the total dose of rehabilitation. Our findings support feasibility and safety of future large scale multi-center RCTs but also raise potentially important considerations for the optimal design of those trials. Validation of the efficacy and optimal implementation of early, ICU-based rehabilitation interventions in the pediatric neurocritical care population and other children at risk of ICU-related disability are critically needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
CONSORT diagram.

PICU, pediatric intensive care unit; LOS, length of stay; PT, physical therapy; OT, occupational therapy; SLT, speech and language therapy; DNR, do not resuscitate

Table 1.

Patient characteristics, devices, and organ supports.

N (%) or median (IQR)	Usual Care, n=32	Early Protocol, n=26	Overall, n=58	p
Age, y	10.6 (4.4)	10.9 (4.0)	10.8 (4.1)	.823
Female sex	8 (25)	15 (58)	23 (40)	.024
ICU admission diagnosis				.154
Traumatic brain injury	12 (38)	4 (15)	16 (28)	
Brain Mass	9 (28)	7 (2)	16 (28)	
Cardiac Arrest	4 (13)	10 (39)	14 (24)	
CNS Infection/inflammation	6 (19)	4 (15)	10 (17)	
Stroke	1 (3)	1 (4)	2 (3)	
Admission PIM score	3.51 (14.7)	3.28 (33.9)	3.44 (16.8)	.372
Admission Glasgow coma scale score				
Motor	4.0 (5.0)	4.5 (5.0)	4.0 (5.0)	.566
Verbal	1.0 (4.0)	1.0 (4.0)	1.0 (4.0)	.637
Eye	1.5 (3.0)	3.0 (3.0)	2.0 (3.0)	.640
Invasive devices present				
Arterial catheter	20 (63)	18 (69)	38 (66)	.718
Central venous catheter	14 (44)	11 (42)	25 (43)	.572
Extraventricular drain	14 (44)	6 (23)	20 (34)	.649
Urinary Catheter	26 (81)	21 (81)	47 (81)	.880
Mechanical Ventilation	32 (100)	21 (81)	43 (74)	.934
Cardiovascular support				
Epinephrine	10 (31)	8 (31)	18 (31)	1.000
Norepinephrine	4 (13)	8 (3)	12 (21)	.143

PIM, Pediatric Index of Mortality; ICU, intensive care unit; CNS, central nervous system

Table 2.

Physical, occupational, and speech and language therapy consultation by hospital location and randomized group.

N (%) or median (IQR)	Usual Care, n=32	Early Protocol, n=26	Overall, n=58	p
PHYSICAL THERAPY				
Consultation, Any initial location	28 (88)	26 (100)	54 (93)	0.178
No. days into stay	5.0 (6.0)	2.0 (1.0)	3.0 (3.0)	<.001
Consultation, ICU initial	16 (50)	23 (89)	39 (67)	<.001
No. days into stay	7.0 (5.0)	2.0 (1.0)	3.0 (3.0)	<.001
Consultation, Ward initial	9 (28)	3 (12)	12 (21)	<.001
No. days into stay	4.0 (7.0)	2.0 (1.0)	3.5 (5.0)	NA
ICU Sessions				
Total number of sessions	134 (43)	180 (57)	314 (100)	<.001
Duration of session, min	31.1 (10.9)	27.3 (9.7)	28.9 (10.4)	.002
Ward Sessions				
Total number of sessions	43 (78.2)	12 (21.8)	55 (100.0)	<.001
Duration of session, min	25.4 (8.8)	25.8 (8.5)	25.4 (8.6)	.817
Total Sessions Per Patient	7.0 (4.7)	7.7 (5.3)	7.4 (5.0)	.303
OCCUPATIONAL THERAPY				
Consultation, Any initial location	17 (53)	26 (100)	43 (74)	<.001
No. days into stay	7.0 (16.0)	2.0 (1.0)	3.0 (4.0)	<.001
Consultation, ICU initial	7 (22)	24 (92)	31 (53)	<.001
No. days into stay	10.0 (15.0)	2.0 (1.0)	2.0 (2.0)	<.001
Consultation, Ward initial	10 (59)	2 (8)	12 (28)	.001
No. days into stay	5.5 (10.0)	2.5 (NA)	2.0 (2.0)	NA
ICU Sessions				
Total number of sessions	21 (20.2)	83 (79.8)	104 (100.0)	<.001
Duration of session, min	30.0 (5.0)	30.0 (15.0)	30.0 (4.4)	.427
Ward Sessions				
Total number of sessions	35 (87.5)	5 (12.5)	40 (100.0)	<.001
Duration of session, min	30.0 (10.6)	52.5 (NA)	30.0 (15.0)	.121
Total Sessions Per Patient	3.3 (3.0)	4.2 (3.5)	3.8 (2.9)	.839
SPEECH/LANGUAGE THERAPY				
Consultation, Any initial location	17 (53)	26 (100)	43 (74)	<.001
No. days into stay	7.0 (16.0)	2.0 (1.0)	3.0 (4.0)	<.001
Consultation, ICU initial	7 (22)	24 (92)	31 (53)	<.001
No. days into stay	10.0 (15.0)	2.0 (1.0)	2.0 (2.0)	<.001
Consultation, Ward initial	10 (59)	2 (8)	12 (28)	.001
No. days into stay	5.5 (10.0)	2.5 (NA)	2.0 (2.0)	NA
ICU Sessions				

N (%) or median (IQR)	Usual Care, n=32	Early Protocol, n=26	Overall, n=58	p
Total number of sessions	21 (20.2)	83 (79.8)	104 (100.0)	<.001
Duration of session, min	30.0 (5.0)	30.0 (15.0)	30.0 (4.4)	.427
Ward Sessions				
Total number of sessions	35 (87.5)	5 (12.5)	40 (100.0)	<.001
Duration of session, min	30.0 (10.6)	52.5 (NA)	30.0 (15.0)	.121
Total Sessions Per Patient	3.3 (3.0)	4.2 (3.5)	3.8 (2.9)	.839

ICU, intensive care unit

Table 3.

Frequency and reason for discontinued and deferred therapy sessions.

Session Deferral	Reason provided	N (%)
Physical therapy n=84/400 (21%)	Patient not in room	20 (23.8)
	Nurse request	15 (17.9)
	Parent request	8 (9.5)
	Patient request	4 (4.8)
	Subjective complaint	4 (4.8)
	Abnormal vitals	1 (1.2)
	Abnormal intracranial pressure	1 (1.2)
	Other	31 (36.9)
Occupational therapy n=61/321 (19%)	Patient not in room	14 (23.0)
	Patient undergoing another treatment	12 (19.7)
	Nurse request	10 (16.4)
	Parent request	7 (11.5)
	Subjective complaint	3 (4.9)
	Abnormal intracranial pressure	2 (3.3)
	Patient request	1 (1.6)
	Other	12 (19.7)
Speech and language therapy n=86/191 (45%)	Nurse request	24 (27.9)
	Patient not in room	13 (15.1)
	Patient undergoing another treatment	11 (12.8)
	Parent request	9 (10.5)
	Subjective complaint	2 (2.3)
	Patient request	1 (1.2)
	Other	26 (30.2)
Session Discontinued	Reason	N
Physical therapy, n=9	Change in systolic blood pressure	5
	Intracranial pressure > 20 mmHg *	1
	Subjective complaint	1
	Other	2
Occupational therapy, n=2	Intracranial pressure > 20 mmHg *	1
	Other	1
Speech and language therapy, n=0	-	0

* Patient re-positioned by nurse prior to start of a combined physical/occupational therapy session

Table 4.

Patient outcomes at hospital discharge.

N (%) or median (IQR)	Usual Care, n=32	Early Protocol, n=26	Overall, n=58	p
ICU length of stay, days	5.0 (9.0)	6.5 (12.0)	5.5 (11.0)	.341
Hospital length of stay, days	11.5 (13.0)	11.5 (13.0)	11.5 (13.0)	.931
Disposition at hospital discharge				.406
Home	16 (50)	15 (58)	31 (53)	
Inpatient rehabilitation	15 (47)	8 (31)	23 (40)	
Long term care facility	0 (0)	1 (4)	1 (2)	
Outpatient therapy prescribed				
Physical	4 (36)	4 (40)	8 (38)	1.000
Occupational	2 (18)	4 (40)	6 (29)	.534
Speech/Language	1 (9)	1 (10)	2 (10)	1.000
New technology dependence				
Cerebrospinal fluid shunt	4 (36)	1 (20)	5 (31)	.942
Percutaneous feeding tube	5 (16)	3 (13)	8 (15)	1.000
Tracheostomy tube	0 (0)	1 (4)	1 (2)	.942

ICU, intensive care unit

Table 5.

Functional and health-related quality of life outcomes.

Median (interquartile range)	Usual Care	Early Protocol	Usual Care vs. Early Protocol p-value	Usual Care p-value	Early Protocol p-value
Pediatric Overall Performance Category					
Pre-morbid	1.00 (0.00), n=32	1.00 (0.00), n=26	.676		
Six months	1.00 (1.00), n=18	2.00 (3.00), n=17	.590		
Pediatric Cerebral Performance Category					
Pre-morbid	1.00 (1.00), n=32	1.00 (0.00), n=26	.294		
Six months	2.00 (2.00), n=18	1.00 (1.00), n=17	.405		
Vineland Adaptive Behavior Scale					
Pre-morbid	99.50 (22.10), n=28	106.12 (17.09), n=22	.340		
Six months	86.33 (20.99), n=18	95.94 (25.86), n=17	.241	.004	.032
PedsQL					
Pre-morbid	85.99 (18.10), n=32	90.71 (12.62), n=26	.402		
Six months	73.97 (19.99), n=18	77.90 (17.73), n=15	.559	.002	.003
McMaster Family Assessment Device					
Pre-morbid	1.48 (.38), n=28	1.67 (.27), n=25	.090		
Six months	1.56 (.35), n=18	1.59 (.32), n=17	.803	.098	.438

The number of patients with outcomes testing data is reported by group and time point.

Table 6.

Exploratory analysis of the correlation between patient and therapy variables with performance on the Vineland Adaptive Behavioral Scale score at 6 months.

Variable assessed	Correlation Coefficient	P-value
PT Sessions Per Patient (Mean), n=35	-.262	.128
OT Sessions Per Patient (Mean), n=32	-.272	.105
SLT Sessions Per Patient (Mean), n=26	-.384	.052
PT Consultation day, n=32	-.428	.015
OT Consultation day, n=33	-.366	.036
SLT Consultation day, n=28	-.600	.001
Age on study day, n=35	-.104	.553
Sex, n=35	.159	.363

PT, physical therapy; OT, occupational therapy; SLT, speech and language therapy