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Children with Chronic Illness Return to Their Baseline Functional Status After Organ Dysfunction on the First Day of Admission in the Pediatric Intensive Care Unit

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Abstract

Objective—To determine chronic illness outcomes after admission with multiple organ dysfunction syndrome (MODS) for pediatric intensive care unit (PICU) patients.

Study design—We evaluated consecutive PICU admissions from 35 US children's hospitals from 1/2004–12/2005 in the VPICU Performance System (VPS) database. We excluded hospitals with > 10% missing values for MODS variables and patients < 1 month or > 18 years of age. MODS was identified by laboratory and vital sign values from day of admission using International Pediatric Sepsis Consensus Conference (IPSCC) criteria. Chronic illness was identified by secondary diagnoses, classified by modified Delphi method. We evaluated functional outcomes using Pediatric Overall Performance Category (POPC) and Pediatric Cerebral Performance Category (PCPC) scores from PICU admission and discharge.

Results—Of 44,693 admissions, 52.1% had a chronic diagnosis. Chronic diagnoses increased MODS at PICU admission (24.6% versus 12.0%, $p < 0.001$) and mortality (3.7% vs. 1.9%, $p < 0.001$). Patients with a chronic diagnosis had similar changes in POPC and PCPC scores from PICU admission to discharge as previously healthy children. However, outcome in different chronic diagnosis categories was variable.

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Conclusions—Chronic illness increased MODS incidence at PICU admission and impacted all-cause PICU mortality. Although, in aggregate children who survive return to baseline functional status, this varies by chronic illness category.

Keywords

outcomes research; critical care; epidemiology; multiple organ failure; pediatric; chronic disease

Children with chronic illnesses have increased rates of hospitalization, longer duration of hospitalization, a high risk for severe acute illness, and increased utilization of pediatric critical care services compared with previously healthy children. (1–4) As medical technology and therapies have improved over the last two decades, the population of children with a chronic illness who survive and continue to require medical services is growing in number (5–7). Understanding the severity and outcome of critical illness for children with a chronic diagnosis is important for planning preventive strategies, informs decision making for both parents and clinicians, and aids in anticipating future resource utilization. (8) We do not have a clear understanding of the current prevalence and type of chronic illnesses in the US PICU patient population, although prevalence estimates exist for specific categories of chronic illnesses such as congenital/metabolic disorders, technology dependence, and neuromuscular disorders (9–14).

Chronic illness is an established risk factor for severe sepsis in pediatric patients. (15;16) In a previous investigation, we found that patients with mild-moderate impairment in baseline functional status were disproportionately represented in the group of patients presenting with MODS (17). As impaired baseline functional status could reflect those children with chronic illnesses, we hypothesized that children with chronic illnesses may be at greater risk of MODS and have worsening of their functional status after PICU hospitalization.

In this study we examine the impact of chronic illnesses on MODS incidence and several PICU outcomes, including mortality, length of stay, and change in functional outcome score from PICU admission to discharge.

Methods

We used the database and methods described in detail in our previous study. (17) The Virtual PICU Performance System (VPS, LLC®, Alexandria, Virginia) database is a prospective cohort of consecutive PICU patient admissions from 35 pediatric hospitals in the United States. Measures available include: patient demographics, hospital diagnoses, outcome measures such as PICU length of stay and mortality, Pediatric Overall Performance Category (POPC) and Pediatric Cerebral Performance Category (PCPC) (18,19) scores on admission and PICU discharge, and Pediatric Index of Mortality (PIM2) (20), Pediatric Risk of Mortality (PRISMII and PRISMIII) (21) variables from the first day of admission. At the time of this study, hospitals were required to collect PIM2 data elements. Collection of additional severity of illness scores as well as POPC and PCPC scores was optional.

Approval for the research use of this dataset was provided by VPS. This work was performed by the Houston Center for Quality of Care and Utilization Studies at the Michael

E. DeBakey Veterans Affairs Medical Center, Houston, Texas. This study was exempted from IRB approval both at the University of Texas Health Science Center at Houston and at Baylor College of Medicine as it involved the analysis of de-identified patient information.

Global and Cognitive Functional Outcome Scores

The global functional outcome score, the POPC, and the cognitive function outcome score, the PCPC, have been validated for use at time of PICU admission and discharge in the United States (18,19). Both are graded on a 6-point scale with 1 indicating normal functional status and 6 indicating brain death.

Organ Dysfunction Criteria

We classified patients as having a dysfunctional organ system at PICU admission based on the International Pediatric Sepsis Consensus Conference (IPSCC) (22) organ dysfunction criteria using the vital sign and laboratory information available in the VPS database from the day of PICU admission. MODS was defined as the presence of two or more dysfunctional organ systems in a patient, present at PICU admission.

Chronic Illnesses

The presence of a chronic illness was determined by the list of secondary diagnoses assigned to each patient in the VPS database. There are 1051 secondary diagnoses in the VPS panel. A panel of six pediatric intensive care physicians reviewed all possible secondary diagnoses and determined which diagnoses would be classified as chronic using a modified Delphi method. A chronic diagnosis was considered to be any diagnosis that was likely to be chronic in nature, present upon ICU admission, require treatment, and was unlikely to represent an iatrogenic or in-hospital diagnosis. Chronic illness criteria were adapted from the definition of children with special healthcare needs. (23) Four of six panel member agreement established a diagnosis as “chronic”. Subgroup classifications for each secondary diagnosis classified as chronic were pre-assigned through the VPS database. Each subgroup of chronic diagnosis was mutually exclusive as we did not include the same secondary diagnosis in multiple chronic diagnosis subgroups.

Patient Selection

We obtained data for consecutive admissions in the VPS database from January 1, 2004 to December 31, 2005. PIM2 systolic blood pressure values were used to verify consistency of data collection as all patients had PIM2 scores collected. Patients were excluded if they were neonates (less than one month of age), if they were older than 18 years of age, or if they did not have PRISMII or PRISMIII variables recorded as these were necessary to assign organ dysfunction. Hospitals were excluded from analysis if they had more than 10% missing data for PRISMII or PRISMIII systolic blood pressure values. (Figure 1) At the time of this dataset VPS was not collecting an organ failure score.

Statistical Analysis

We compared risk-adjusted mortality for patients who were included and excluded from analysis using PIM2 data. We reported median (25th, 75th percentile) values for variables

with skewed distributions. We assessed group differences in categorical (or ordinal) and non-normal continuous variables using χ^2 and Mann-Whitney rank sum tests, respectively. We assessed the effect of different dysfunctional organ systems on mortality and log-transformed length of stay using χ^2 and Student t-tests, respectively.

We used multivariable logistic regression analysis with patients clustered by hospital of origin to assess the independent effect of each dysfunctional organ system, the number of dysfunctional organ systems, the presence of any chronic diagnosis, the number of chronic diagnoses, and the subgroups of chronic diagnoses on mortality and the development of MODS. We used linear regression to assess the independent effect of each dysfunctional organ system, the number of dysfunctional organ systems, the presence of any chronic diagnosis, the number of chronic diagnoses, and the subgroups of chronic diagnoses on PICU log-transformed length of stay. For both logistic and linear regression models we controlled for patient age, race, and sex. We used generalized linear models with patients clustered by hospital of origin to evaluate the impact of chronic diagnoses and organ dysfunction on change in functional outcome scores from PICU admission to discharge. Statistical analysis was accomplished using Statistical Analysis Systems, version 9.1.3 and STATA 9/SE software.

Results

We previously identified 44,693 PICU admissions from 28 pediatric hospitals, excluding neonates and patients older than 18 years of age, with necessary PIM2, PRISMII, and PRISMIII data recorded. (17) Of those, 48% had POPC and PCPC scores recorded and are examined in this study with regard to functional outcomes. Patients who were excluded from this analysis either due to missing severity of illness scores, or missing functional status scores, had similar PIM2 risk adjusted mortality compared with patients who were included in the analysis [OR 1.0 (95% CI 0.9–1.2)].

Chronic Conditions and MODS

The prevalence of chronic diagnoses was 52.1% in this PICU dataset (Table I). Overall mortality for patients with chronic diagnoses was 3.7% versus 1.9% for patients without a chronic diagnosis ($p<0.001$) (Table I). The incidence of MODS in patients with and without chronic diagnoses was 24.6% and 12.0%, respectively ($p<0.001$) (Table I). Any chronic diagnosis independently increased the risk of MODS at PICU admission in logistic regression analysis [OR 2.3 (95%CI 2.0–2.7)]. Chronic diagnoses increased the overall median PICU length of stay (2.0 days versus 1.2 days, $p<0.0001$) as well as median PICU length of stay when organ dysfunction was present (2.9 days versus 1.9 days, $p<0.001$). When we controlled for the number of dysfunctional organ systems at admission, only patients with more than three chronic diagnoses had an excess risk of mortality [OR 2.1 (95% CI 1.5–3.1)] (Table II).

Patients with chronic diagnoses were more likely to have higher admission and discharge POPC and PCPC scores (Figure 2). The difference in the change in score (delta POPC or PCPC) from PICU admission to discharge comparing patients with and without chronic diagnoses was statistically significant in univariate analysis (Figure 2). However, the

average differences between patients with and without chronic diagnoses in global and cognitive performance were small and appears to be clinically insignificant (Figure 2). In generalized linear models controlling for number of dysfunctional organ systems, baseline functional outcome score, age, sex, and race, patients with chronic diagnoses did not have worse functional outcomes ($p>0.05$) compared with patients without a chronic diagnosis.

Chronic Diagnosis Subgroups

We identified 9 subgroup categories for chronic diagnoses: Respiratory, Cardiac, Hematologic/Oncologic, Neurologic, Immunologic, Transplant, Gastrointestinal/Nutritional, Renal, Genetic/Metabolic, and Other. (Figure 3; available at www.jpeds.com) We further divided the cardiac chronic diagnosis subgroup into either congenital heart disease or non-congenital heart disease and the transplant diagnosis subgroup as bone marrow transplant and solid organ transplant.

Cardiac and neurologic diagnoses were the most common chronic diagnoses with a prevalence of 20.9% and 16.6%, respectively (Figure 3). Patients with cardiac, neurological, metabolic/genetic, hematologic/oncologic, and transplant chronic diagnoses had increased incidence of MODS (Table II) and patients with respiratory, gastrointestinal, renal, immune, and other chronic diagnoses did not. Bone marrow transplant patients had a high independent risk of MODS and the highest independent risk of mortality (Table II). In contradistinction patients with congenital heart disease had the highest risk of MODS and the lowest risk of mortality, even when compared with patients who were previously healthy.

Some chronic diagnosis subgroups were associated with a change from baseline of either global or cognitive outcome score compared with patients without a chronic diagnosis. Patients with congenital heart disease were likely to have improvement in both global and cognitive functional score from PICU admission to discharge ($p<0.003$), as were patients with solid organ transplants ($p<0.05$) when compared with previously healthy children. Patients with pre-existing renal disease had improvement in their cognitive functional score compared with previously healthy children ($p=0.002$). In contrast, patients with non-congenital heart disease, neurologic, immune and oncologic chronic diagnoses had worsening of their global functional score from PICU admission to discharge compared with patients who were previously healthy ($p<0.05$). Patients with pre-existing oncologic diagnosis and neurologic diagnosis also had worsening of their cognitive functional score compared with previously healthy patients. Patients with a diagnosis of bone marrow transplant, if they survived their PICU admission, had similar changes in their global or cognitive functional outcome score from PICU admission to discharge compared with previously healthy patients when adjusted for admission organ failure.

Discussion

In this study, we demonstrate that a majority of patients admitted to the PICU have a chronic illness prior to their PICU admission. This is consistent with previous reports that patients with chronic illnesses have increased risk of severe acute illness and with prevalence estimates of genetic and neuromuscular disorders in the PICU (1;14). Our findings confirm

previous reports that we are increasingly managing patients with complex medical histories and significant chronic illnesses (6,7,24,25). We also show that the presence of a chronic illness is associated with an increased incidence of MODS at PICU admission, it impacts all-cause mortality in the PICU through greater organ dysfunction, and is associated with longer PICU length of stay. Similar relationships have been seen for chronic illnesses and risk for severe sepsis. (16)

We examined the change in functional status from PICU admission to discharge for patients with chronic illnesses, a growing PICU population. Contrary to our original hypothesis, in general, patients with chronic illnesses with MODS were equally likely to return to their baseline functional status as were previously healthy patients with MODS. Thus it is the presence and extent of organ dysfunction which determines outcome of children in the ICU, and not the chronic illness per se, though chronic illness may modulate the risk and outcome of MODS. Specific subgroups of chronic conditions affect the interpretation of these results as some categories of chronic illness have severity-adjusted improvement and others have worsening of functional outcome scores when compared with previously healthy children.

In our study, patients with congenital heart disease and those who received solid organ transplants had functional outcomes which were better than their healthy counterparts with equal admission illness severity. We postulate this is due to chronic organ dysfunction improving after operative cardiac repair or with transplantation in these patient populations. Majnemer et.al studied 131 newborns and young infants at a single center who underwent repair of their congenital heart disease. They found that 58% of newborns and 42% of infants had abnormalities on neurologic exam pre-operatively and that post-operative examination findings were similar (26). That the children in the Majnemer study have neurologic exams which are unchanged pre and post-operatively is likely a better outcome than would be expected based upon admission illness severity, and consistent with our findings. Cole et al found that health related quality of life (HRQOL) improved for all patients after transplantation, consistent with our findings (27).

We also found that bone marrow transplant patients who survived their PICU stay were not more likely to have a poor functional outcome. Previous reports in the literature demonstrate that patients with hematopoietic stem cell transplant (HSCT) continue to have high mortality rates when requiring PICU admission, but that the mortality rates are falling over time (28–30). It is encouraging that the functional outcomes in the patients who do survive are equivalent to previously healthy children.

When we use mortality or functional status alone as indicators of the outcome of patient care, we believe that inappropriate conclusions may be drawn. We propose that it is critical to determine patient complexity (type and number of chronic illnesses, admission illness and severity) for fair comparative outcomes assessment or benchmarking, across institutions.

A limitation particular to our analysis is that we cannot know with complete confidence if the organ dysfunction identified on day one of admission is really “acute”. In other words, a child with a chronic illness may have a chronic physiologic derangement resulting in our assigning a patient to “acute organ dysfunction”. In our study, from 16–33% of all children

identified as having acute organ dysfunction also had the same organ affected by an assigned chronic condition. Prospective evaluation of acute vs. chronic vs. acute on chronic organ dysfunction is necessary to determine with certainty the impact of organ dysfunction and chronic illnesses on outcomes after critical illness in children and our study serves as an initial investigation into this question.

A second limitation to this study, is that we were unable to identify organ failure beyond the first 24 hours, as this information is not routinely collected in the VPS database. However, in the only study to systematically study daily organ failure from Proulx et al, up to 85% of all pediatric organ failure occurs in the first 24 hours of the ICU visit. (31)

We found that children admitted to the PICU with chronic diagnoses have increased incidence of MODS, increased PICU length of stay, and increased PICU mortality due to MODS. The number and type of chronic diagnoses were associated with MODS and mortality as well as the number of dysfunctional organ systems, suggesting that patient complexity is important for MODS risk. Surprisingly, children with chronic diagnoses were as likely as previously healthy children to return to their baseline functional status after MODS.

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Abbreviations Used in This Manuscript

MODS	Multiple Organ Dysfunction Syndrome
PICU	Pediatric Intensive Care Unit
VPS	VPICU Performance System
IPSCC	International Pediatric Sepsis Consensus Conference
POPC	Pediatric Overall Performance Category
PCPC	Pediatric Cerebral Performance Category
PIM2	Pediatric Index of Mortality 2
PRISM	Pediatric Risk of Mortality
OR	Odds Ratio
IQR	Interquartile Range
HRQOL	Health Related Quality of Life
HSCT	Hematopoietic Stem Cell Transplant

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Figure 1.

Data management algorithm

VPS= VPICU Performance System; SBP=systolic blood pressure; POPC= Pediatric Overall Performance Category; PCPC=Pediatric Cerebral Performance Category; PRISM=Pediatric Risk of Mortality

Figure 2.

Baseline and change of functional outcome scores from PICU admission to discharge by presence of chronic diagnoses

POPC= Pediatric Overall Performance Category; PCPC=Pediatric Cerebral Performance Category; PICU=Pediatric Intensive Care Unit; Chronic Diagnosis -= No chronic diagnosis identified; Chronic Diagnosis += At least one chronic diagnosis identified; DeltaPOPC= DischargePOPC-BaselinePOPC; DeltaPCPC=DischargePCPC-BaselinePCPC. ^aPatients with chronic diagnoses had higher baseline POPC and PCPC scores ($p<0.001$) at PICU admission. ^bPatients with chronic diagnoses had greater (worse) changes in POPC and PCPC scores from PICU admission to discharge (Mann Whitney rank sum, $p<0.001$). These differences did not appear clinically significant.

Figure 3.

Prevalence and Type of Chronic Diagnoses in the Pediatric Intensive Care Unit Chronic Diagnosis -= No chronic diagnosis; Chronic Diagnosis += At least one chronic diagnosis; Neuro=Neurologic diagnosis; GI= Gastrointestinal diagnosis; Heme/onc= Hematologic or oncologic diagnosis. *Subgroups of chronic diagnoses which represent combined categories. Transplant category represents both solid organ and bone marrow transplant. Heme/Onc represents both hematologic and oncologic diagnoses. Cardiac subgroup represents both congenital and acquired cardiac disease. Other category includes rheumatologic, endocrine, orthopedic, psychiatric, former premature birth.

Univariate analysis for patients with and without chronic diagnoses

Total N=44693		Chronic Diagnosis + (N)	(%)	Chronic Diagnosis- (N)	(%)	P value
Age (years)		N=23296	100.0	N=21397	100.0	<0.001
1 mos<12mos (Infant)		6638	28.5	4155	19.4	
1-2		4380	18.8	3807	17.1	
3-6		4241	18.2	3646	16.4	
7-10		2674	11.5	2810	12.6	
11-14		3049	13.1	3942	17.7	
15-18		2314	9.9	3037	13.6	0.600
Sex (11 missing)		23290		21392		
Male		13067	56.1	12061	56.4	
Race/Ethnicity						<0.001
Caucasian		13273	57.0	11291	52.8	
African American		3626	15.6	3971	18.6	
Hispanic		2229	9.6	2094	9.8	
Asian		654	2.8	514	2.4	
Other/Mixed/Missing		3514	15.1	3527	16.5	
MODS						<0.001
Present		5731	24.6	2572	12.0	
Number of dysfunctional organ systems						<0.001
0		9567	41.1	13300	62.2	
1		7998	34.3	5525	25.8	
2		4333	18.6	2000	9.3	
3		1183	5.1	481	2.2	
4 or greater		215	0.9	91	0.4	
Died N(%)		852	3.7	407	1.9	<0.001

Table 2

Odds of MODS and Mortality by Number and Type of Chronic Diagnosis

Number of Chronic Diagnoses	Odds of MODS OR(95% CI)	Odds of Mortality OR(95% CI)
0	--	--
1	2.1 (1.8–2.5)	1.0 (1.0–1.5)
2	2.5 (2.0–3.0)	1.3 (1.0–1.6)
3	2.8 (2.2–3.6)	1.3 (0.9–1.9)
4	3.0 (2.3–4.0)	2.1 (1.5–3.1)
Type of Chronic Diagnosis	Odds of MODS OR(95% CI)	Odds of Mortality ^a OR(95% CI)
Cardiac	2.4 (1.8–3.2)	0.7 (0.6–0.9)
Congenital Heart Disease	2.6 (1.9–3.7)	0.5 (0.3–0.7)
Non-Congenital Cardiac	1.5 (1.2–1.8)	2.1 (1.4–3.1)
Neurological	1.5 (1.2–1.8)	1.7 (1.4–2.1)
Respiratory	1.1 (0.8–1.5)	0.6 (0.4–0.9)
Gastrointestinal	1.2 (1.0–1.4)	0.9 (0.6–1.2)
Metabolic/Genetic	1.2 (1.1–1.3)	1.2 (1.0–1.5)
Hematologic/Oncologic	1.4 (1.2–1.6)	2.5 (2.0–3.0)
Renal	1.2 (1.0–1.4)	0.8 (0.4–1.3)
Transplant	2.0 (1.4–2.9)	3.8 (2.2–6.4)
Bone Marrow Transplant	2.5 (1.5–4.1)	9.5 (5.9–15.3)
Solid Organ Transplant	1.9 (1.4–2.5)	2.3 (1.3–4.1)
Immune	1.0 (0.8–1.3)	1.6 (0.9–2.7)
Other	0.9 (0.5–1.5)	2.4 (1.1–5.1)

MODS= Multiple Organ Dysfunction Syndrome; OR= Odds ratio; CI= Confidence interval.

Logistic regression models controlled for patient age, race, sex, number of dysfunctional organ systems, chronic illnesses and were clustered by hospital of origin.

^aRegression model controlled for the number of dysfunctional organ systems.

The referent group for each chronic illness subgroup were patients without a chronic diagnosis.