Characteristics and Outcomes of Long-Stay Patients in the Pediatric Intensive Care Unit

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Abstract

Keywords

- children
- pediatrics
- intensive care
- length of stay
- outcome
- long-stay
- mortality

Long-stay patients in the PICU have a higher risk of mortality as compared with non-long-stay patients. We aim to describe mortality and characteristics of long-stay patients and to determine the risk factors for mortality in these children. Total 241 (4.8%) long-stay admissions were identified. Mortality of long-stayers was 48/241 (20%). Higher severity-of-illness score at admission, need for organ support therapies, number of nosocomial infections, and bloodstream nosocomial infection were associated with a higher mortality in long-stay patients in the PICU. Based on multivariate analysis, oncologic diagnosis as a preexisting comorbidity is a strong independent predictor of mortality for long-stay patients.

Background

A small proportion of critically ill children require prolonged admission to the pediatric intensive care unit (PICU). Prolonged length of stay (LOS) in the PICU is generally considered as one that is longer than 12 to 30 days.^{1–5} Approximately 1 to 4.7% of total PICU admissions result in a prolonged LOS.^{1–3,5,6} Even though this is a small percentage, this subset of children requires increased critical care support and resources.^{4,6,7} In addition, compared with other patients, long-stay PICU patients have a higher risk of mortality (15–40%) and long-term morbidity.^{1,2,4,7} The management of these patients can be challenging because of the increased risk of poor outcome and intensive use of PICU resources that are costly. Little is known about the characteristics of these long-stay patients and the associated risks of infection or complications during their PICU stay. Understanding the characteristics and associated risks of long-stay patients in the PICU is crucial to enabling PICU health care providers to plan for critical care services and implement quality improvement initiatives.

In this study, we assessed the characteristics of long-stay (≥ 14 days) PICU patients. Our study aims to assess characteristics and identify risk factors for mortality in this group of patients. We hypothesized that duration of stay and nosocomial infections are risk factors for mortality for long-stay patients in the PICU.

Materials and Methods

The study was conducted in KK Women's and Children's Hospital, one of two tertiary pediatric hospitals in Singapore. Our hospital has 600 general ward beds, 20 high-dependency beds, and 16 PICU beds. The PICU is a multidisciplinary unit that admits more than 700 medical, surgical, and cardiothoracic patients per year. We conducted a retrospective cohort study of all patients admitted from June 2009 through June 2014. Data were collected from our PICU's computerized patient data management system (Intellivue Clinical Information Portfolio [ICIP]). Manual chart review by three investigators (AHPK, QWS, LQZ) was performed. Definitions of terms used in this study were defined a priori to ensure

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accuracy of data extraction. All patients with an LOS of 14 days or more were included in this study. Patient data collected included demographics (e.g., sex, age, severity of illness scores), type of admission (elective or emergency), source of PICU admission, indication for admission, presence of comorbidities (e.g., congenital heart disease, epilepsy, gastroesophageal reflux disease, or chronic lung disease), and presence of chronic care devices on admission (e.g., gastrostomy tube, tracheostomy, noninvasive ventilation, or chronic total parenteral nutrition). Pertinent PICU support data were also collected. These included data on PICU therapies (e.g., invasive mechanical ventilation [MV], dialysis, extracorporeal membrane oxygenation [ECMO], vasoactive medication infusion, need for cardiopulmonary resuscitation [CPR], plasmapheresis, and exposure to antimicrobial therapy). Number of nosocomial infections and complications from PICU stay (e.g., ventilator-associated pneumonia [VAP], catheter-associated urinary tract infection [CAUTI], deep vein thrombosis, and pressure sores) were also collected. VAP was defined as pneumonia occurring more than 48 hours after patients have been intubated and received MV.⁸ Diagnostic criteria used for VAP included fever, increased volume of purulent tracheobronchial secretions, changes in radiographic examination, and a positive microbiologic analysis of respiratory secretions.⁸ We defined endotracheal tube colonization as a positive microbiologic analysis of respiratory secretions with no other diagnostic criteria for VAP. Bloodstream infection was diagnosed with a positive blood culture after 48 hours of PICU admission.⁹ CAUTI was diagnosed with a positive urine culture in which an indwelling urinary catheter was in place for more than 48 hours in the PICU.¹⁰ We considered nosocomial surgical wound infection to be present when positive bacterial cultures from surgical sites after 48 hours of PICU admission led to treatment with appropriate antibiotics. Gastrointestinal complications included gastrointestinal hemorrhage, colitis, peptic ulcer, and pancreatitis. Deep vein thrombosis was diagnosed with radiologic confirmation.¹¹ Pressure sore was diagnosed when there was a visible local damage to the skin due to pressure that was acquired during the PICU stay. Antimicrobial therapy exposure was defined as the number of antimicrobial agent being administered to patient during the PICU stay.

Our primary outcome of interest was PICU mortality. We classified the cause of death into four categories: brain death, failed resuscitation, active withdrawal of life support (e.g., removal of the endotracheal tube), and allowed to die without CPR (e.g., do-not-resuscitate [DNR] status). In our institution, brain death is a clinical diagnosis based on the absence of neurologic function with a known irreversible cause of coma. A patient is diagnosed and certified as brain death when the child fulfills all criteria in accepted brain death guidelines.¹² When a previously ordered DNR document was available, the medical team will consider this as legal order written to withhold CPR or advanced cardiac life support in the event of sudden or impending death. We defined failed resuscitation as the failure to restore return of spontaneous circulation after a period of CPR and

appropriate use of advanced life support. In cases involving active withdrawal of life support due to medical futility, it is usual practice in our unit that an agreement is reached between medical staff and family that present or further life-sustaining treatment was futile and that it is in the best interest of the child to cease life-sustaining treatment. Withdrawal of life support due to medical futility refers to situation whereby life-sustaining support such as MV or ECMO was being removed from patient. Secondary outcomes included discharge disposition, hospital death, and presence of chronic care devices on discharge from PICU. This investigation was approved by the institutional review board without need for informed consent.

Statistical Analysis

Continuous variables were presented as medians with interquartile ranges (IQRs) and categorical variables as absolute numbers and percentages. Continuous and categorical variables were compared with Wilcoxon rank-sum test, McNemars' test, or chi-square test, respectively. Statistical significance was taken as *p* value of less than 0.05 and analysis was performed using Stata 13 software (College Station, Texas, United States).

All variables with *p* value of less than 0.05 in the univariate analysis were included as covariates in a multivariate logistic regression analysis to identify predictors of mortality in long-stay patients. We report the adjusted odds ratio (OR) and 95% confidence interval (CI) in this multivariate analysis.

Results

Characteristics of Long-Stay Admissions

During the study period, there were a total of 5,069 admissions to the PICU with 198 (3.9%) deaths. Of these admissions, 241 (4.8%) admissions, involving 211 patients, had an LOS of 14 or more days (→ **Table 1**) and 81 (1.6%) admissions had an LOS of 28 or more days. Nineteen (9%) long-stay patients stayed twice at the PICU, four (2%) patients stayed thrice, and one (0.5%) had four stays at the PICU for 14 or more days during the study period. Overall PICU mortality rate of these long-stay patients was 20% (48/241) and cumulative hospital mortality was 22% (53/241). Eighty-four (35%) long-stay patients have previous PICU admission and 35 (42%) of these admissions were more than 14 days. One hundred sixteen (55%) patients had comorbidities, 78 (37%) had one comorbidity, and 38 (18%) had two or more comorbidities. In 119 (49%) admissions, patients had one or more preexisting chronic care devices on admission. The three main indications for admission included respiratory (*n* = 92; 38%), cardiovascular (*n* = 69; 29%), and neurologic (*n* = 54; 22%).

In our cohort of long-stay patients, nonsurvivors had longer LOS (27 [IQR 20–43] vs. 21 [IQR 17–33]; *p* = 0.02) and a higher PRISM II (pediatric risk of mortality II) score (15 [IQR 12–22] vs. 13 [IQR 8–20]; *p* = 0.03) compared with survivors. Age at admission, sex, gestational age, previous ICU stay, type of admission, admission source, reason for admission, and preexisting chronic care devices did not differ between survivors and nonsurvivors.

Table 1 Characteristics of long-stay admissions

Demographic characteristics	Long-stay admissions (n = 241)	Long-stay survivors (n = 193)	Long-stay nonsurvivors (n = 48)	p-Value
Admission source, n (%)				0.12
Emergency department	56 (23)	45 (23)	11 (23)	
Ward	112 (46)	86 (45)	26 (54)	
Operating theater	36 (15)	34 (18)	2 (4)	
Other hospitals	37 (15)	28 (15)	9 (19)	
Age (y), median (IQR)	1.37 (0.27–6.35)	1.36 (0.21–5.98)	1.59 (0.37–8.65)	0.47
Emergency admission, n (%)	175 (73)	136 (70)	39 (81)	0.13
Gestational age < 37 wk, n (%)	47 (20)	34 (18)	13 (27)	0.12
Indication for admission, n (%)				0.12
Respiratory	92 (38)	75 (39)	17 (35)	
Cardiovascular	69 (29)	48 (25)	21 (44)	
Gastrointestinal	14 (6)	13 (7)	1 (2)	
Neurologic	54 (22)	48 (25)	6 (13)	
ENT	3 (1)	3 (2)	0 (0)	
Metabolic	5 (2)	3 (2)	2 (4)	
Trauma	3 (1)	2 (1)	1 (2)	
Burns	1 (<1)	1 (<1)	0 (0)	
Length of stay (d), median (IQR)	22 (17–35)	21 (17–33)	27 (20–43)	0.02
Male sex, n (%)	124 (51)	102 (53)	22 (46)	0.38
Need for CPR before PICU admission, n (%)	32 (13)	23 (12)	9 (19)	0.21
Preexisting chronic care devices, n (%)				
Gastrostomy tube	20 (8)	17 (9)	3 (6)	0.56
Chronic ventilation	76 (32)	65 (34)	11 (23)	0.15
Tracheostomy	8 (3)	7 (4)	1 (2)	0.59
Chronic TPN	6 (3)	4 (2)	2 (4)	0.41
Preexisting comorbidity, n (%)	171 (71)	139 (72)	32 (67)	0.47
Number of comorbidity, median (IQR)	1 (0–3)	1 (0–3)	1 (0–2.5)	0.53
Types of comorbidity, n (%)				
Cardiovascular	83 (34)	69 (36)	14 (29)	0.39
Respiratory	47 (20)	38 (20)	9 (19)	0.88
Oncology	21 (9)	10 (5)	11 (23)	< 0.01
Genetic	65 (27)	55 (28)	10 (21)	0.28
Neurology	66 (27)	55 (28)	11 (23)	0.44
Gastrointestinal	64 (27)	53 (27)	11 (23)	0.52
Others	48 (20)	42 (22)	7 (15)	0.35
Previous PICU stay, n (%)				0.62
No	157 (65)	128 (66)	29 (60)	
1–2 times	62 (26)	47 (24)	15 (31)	
≥ 3 times	22 (9)	18 (9)	4 (8)	
PRISM II score, median (IQR)	14 (9–21)	13 (8–20)	15 (12–22)	0.03

Abbreviations: CPR, cardiopulmonary resuscitation; IQR, interquartile range; PICU, pediatric intensive care unit; PRISM, pediatric risk of mortality; TPN, total parenteral nutrition.

Table 2 Treatment modalities for long-stay admissions

PICU modalities	Long-stay admissions (n = 241)	Long-stay survivors (n = 193)	Long-stay nonsurvivors (n = 48)	p-Value
CPR in the PICU, n (%)	17 (7)	10 (5)	7 (15)	0.02
Plasmapheresis, n (%)	4 (2)	3 (2)	1 (2)	0.80
MV, n (%)	229 (95)	181 (94)	48 (100)	0.08
Duration of MV (d) ^a	18 (13–27)	13 (8–20)	26 (18–42)	< 0.01
Vasoactive infusion, n (%)	132 (55)	95 (49)	37 (77)	< 0.01
Duration of vasoactive infusion, days ^a	2 (0–9)	0 (0–7)	7 (2–15)	< 0.01
Dialysis, n (%)	33 (14)	18 (9)	15 (31)	< 0.01
ECMO, n (%)	16 (7)	6 (3)	10 (21)	< 0.01

Abbreviations: CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; MV, mechanical ventilation; PICU, pediatric intensive care unit.

^aSummarized in median (interquartile range).

PICU Treatment Modalities for Long-Stay Admissions

Nonsurvivors were more likely to require dialysis (31 vs. 9%; $p < 0.01$), ECMO (21 vs. 3%; $p < 0.01$), vasoactive infusion (77 vs. 49%; $p < 0.01$), and CPR (15 vs. 5%; $p = 0.02$) during their PICU stay (► **Table 2**).

Secondary Outcomes in PICU Long-Stay Admissions

Total 52 (22%) of the long-stay admissions acquired one or two nosocomial infections during their PICU stay (► **Table 3**). Out of the 16 bloodstream infections, three were catheter-related bloodstream infections (CRBSIs). Twelve (5%) acquired gastrointestinal complication, 25 (10%) acquired deep vein thrombosis, and 12 (5%) developed pressure sore.

In the cohort of long-stayers, nonsurvivors acquired a higher number of nosocomial infections (31 vs. 19%) and specifically, bloodstream infections (15 vs. 5%) as compared with survivors ($p < 0.01$) (► **Table 3**). Long-stay nonsurvivors

were exposed to more number of antimicrobial therapy during their PICU admission compared with survivors (6 [IQR 3–8] vs. 3 [IQR 2–5]; $p < 0.01$). The proportion of endotracheal tube colonization, VAP, urinary tract, and surgical site infections did not differ between survivors and nonsurvivors.

Among 48 deaths, 2 (4%) patients were diagnosed to be brain dead, 28 (58%) had DNR status, 6 (13%) failed resuscitation, and withdrawal of support occurred in 12 (25%). All 28 patients with DNR orders had their DNR status initiated during their PICU stay.

Most long-stay survivors were discharged to inpatient wards (86/193, 96%). Five (3%) were discharged to other hospitals and two (1%) were discharged home. Among the survivors, there were an increased proportion of patients discharged with chronic care devices as compared with admission (► **Table 4**).

Table 3 Secondary outcomes

Secondary outcomes	Long-stay admissions (n = 241)	Long-stay survivors (n = 193)	Long-stay nonsurvivors (n = 48)	p-Value
Nosocomial infections, n (%)				< 0.01
No	189 (78)	156 (81)	33 (69)	
1 infection	42 (18)	33 (17)	9 (19)	
2 infections	10 (4)	4 (2)	6 (12)	
CAUTI	24 (10)	16 (8)	8 (17)	0.64
VAP	17 (7)	11 (6)	6 (13)	0.10
Bloodstream infection	16 (6)	9 (5)	7 (15)	0.01
Surgical site infection	5 (2)	5 (3)	0 (0)	0.26
Endotracheal tube colonization	89 (37)	67 (35)	22 (46)	0.15
No. of antimicrobial therapy				
Median (IQR)	4 (2–6)	3 (2–5)	6 (3–8)	< 0.01

Abbreviations: CAUTI, catheter-associated urinary tract infection; IQR, interquartile range; PICU, pediatric intensive care unit; VAP, ventilator-associated pneumonia.

Table 4 Presence of chronic care devices in survivors upon discharge

Chronic care devices on admission (n = 193)	Chronic care devices on discharge (n = 193)		p-Value ^a
	Yes	No	
Gastrostomy			
Yes	17	5	0.02
No	0	0	
Noninvasive ventilation			
Yes	57	67	<0.01
No	8	60	
Tracheostomy			
Yes	7	32	<0.01
No	0	153	
Chronic TPN			
Yes	2	39	<0.01
No	4	149	

Abbreviation: TPN, total parenteral nutrition.

^aMcNemar's test.

Multivariate Analysis

Based on the univariate analysis, the following variables were entered into the multivariate logistic regression model: continuous variables of PRISM II score and LOS; and the binary variable of preexisting comorbidity, oncology. Having a higher PRISM II score on admission (adjusted OR: 1.04, 95% CI: 1.00–1.08) and oncologic comorbidity (adjusted OR: 6.04, 95% CI: 2.35–15.51) were independent predictors of mortality for long-stay patients (►Table 5).

Discussion

This study assessed the characteristics of patients who stayed at the PICU for 14 or more days and identified risk factors for mortality for long-stay patients in the PICU. Similar to other studies, our study demonstrated that children with prolonged stay in the PICU had higher risk of mortality as compared with short-stay patients.^{1,2,4,7} In our study, the mortality rate in long-stay patients (20%) was approximately five times higher when compared with overall mortality in PICU patients (3.9%).

We found that severity of illness score on admission is associated with the clinical outcome of long-stay patients.

Our findings were consistent with the study performed by Pollack et al,⁷ that severity scores at admission can be a predictor of outcome for long-stay patients in the PICU.

Our study found that oncology comorbidity is a risk factor for mortality in long-stay PICU patients. To the best of our knowledge, there is no literature that compares risk of mortality between long-stay and no-long-stay oncology patients. However, it was shown that patients with pediatric oncology requiring intensive care treatment have a poor prognosis, especially those who develop respiratory failure and/or require cardiovascular support.^{13,14} A study involving 550 patients with pediatric oncology in the PICU reported that these patient's median stay in the PICU was 5 days (range: 1–45 days).¹⁴ The overall mortality rate was 40%, and multiorgan failure due to systemic infection with sepsis was the leading cause of mortality.¹⁴

The rate of nosocomial infection (30%) in our long-stay patients was lower as compared with other studies (75–96%).^{6,15} The higher rate of nosocomial infection in other studies may be due to the inclusion of patients with suspected infection at time of admission to PICU, as the infections of nosocomial origin could not be established.⁶ Our study found that presence of nosocomial infection was associated with mortality of PICU long-stay patients. The number of nosocomial infections acquired by the long-stay patients during their stay in the PICU was associated with mortality ($p < 0.01$). Long-stay nonsurvivors had more bloodstream infections (19 vs. 7%; $p = 0.01$) compared with long-stay survivors. Hence, effective infection control and quality improvement measures addressing the prevention of nosocomial infections, especially bloodstream infections, may further reduce mortality in long-stay patients.

Patients with prolonged PICU stay require higher health care resources consumption as compared with non-long-stay patients.^{4,6,7} Our study showed that with the exception of plasmapheresis therapy, nonsurvivors required more PICU treatment modalities and for a longer duration as compared with survivors. This finding is similar to a previous study that reported that long-stay nonsurvivors had a significantly higher admission and maximum Therapeutic Intervention Scoring System scores.⁷

In our study, most deaths (40/48, 83%) were preceded by a decision to limit life-sustaining treatment (DNR orders; $n = 28$) and withdrawal of life support ($n = 12$). On admission to our PICU, these long-stay patients did not hold a DNR status or a plan for withdrawal. However, during the stay in PICU, the decision was made by family and medical staff to limit or withdraw intensive care. The decision was usually made in view of medical futility. This finding is similar to that

Table 5 Significant independent variables associated with mortality on logistic regression

Variable	Adjusted OR	95% CI	p-Value
PRISM II score	1.038	1.001–1.077	0.043
Length of stay	1.007	0.993–1.022	0.324
Preexisting comorbidity, oncology	6.037	2.349–15.513	< 0.01

Abbreviations: CI, confidence interval; OR, odds ratio; PRISM, pediatric risk of mortality.

described by Naghib et al,² which reported that withdrawal or limitation of therapy preceded 80% (20/25) of deaths in PICU long-stay patients.² Advances in technology and medicine have enabled pediatric intensivists to prolong life, and sometimes beyond the point at which it offers any benefit to the patient and potentially prolongs suffering.¹⁶ If a decision is made to withdraw or limit intensive therapy, the primary focus changes from an interventionist approach aimed at curative to a more patient- and family-directed approach aimed mainly at providing comfort and support to the dying child and the family.¹⁷ Hence, guidelines to facilitate decision-making processes of end-of-life issues and optimal palliative or bereavement programs are paramount to help meet the needs of long-stay patients and their families.² Discussion of end-of-life issues may be initiated earlier especially if risk factors for mortality are present as this may prevent potential prolonged suffering.

This is the first study that examined and described the characteristics and outcomes of long-stay PICU patients in Asia. It revealed a different epidemiologic pattern of patients as compared with the previous studies that were conducted in the United States and Europe.^{2,4-7,15} Most of the studies compared non-long-stay patients with long-stay patients.^{4,5,15} Instead, our study compared long-stay nonsurvivors with survivors and provided new findings on risk factors of mortality in this group of patients. Future studies should evaluate whether the identified risk factors for mortality in our study are similar to those in other PICUs as this will guide clinical decisions in this group of patients.

There are several limitations to this study. Our single-center study limits the potential to generalize results to the wider population of long-stay patients in other PICUs even from the same region. Data were collected retrospectively and may have been subjected to missing data or misclassification.

Conclusion

Although long-stay patients in the PICU represent a small percentage of the overall patients admitted to the PICU, their medical care involved high health care resource utilization with high eventual mortality. This study identified risk factors for increased mortality in these patients. Having a higher severity-of-illness score at presentation, oncologic diagnosis as a preexisting comorbidity, need for organ support therapies, number of nosocomial infection, and acquired bloodstream infections were associated with a higher mortality in long-stay patients in the PICU. Modifiable factors such as prevention of nosocomial infections can potentially reduce mortality rates in this high-risk group of critically ill patients.

Note

This investigation was approved by the SingHealth institutional review board, without need for informed consent. The authors declare that they have no competing

interests. None of the authors received any funding for this study.

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