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ORIGINAL ARTICLE

Long-term mortality and functional outcome after prolonged paediatric intensive care unit stay

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Abstract

We performed a retrospective, observational study of patients who had spent > 14 days in the paediatric intensive care unit (PICU) of our hospital from 2011 to 2013. Specifically, long-term mortality, functional outcome, and PICU resource occupancy were examined. All prolonged-stay patients in our study were < 15 years of age. Favourable outcomes were defined as a Pediatric Overall Performance Category (POPC) score of 1–2, and unfavourable outcomes as a POPC score of 3–6 or death. During the study period, there were 1082 PICU admissions involving 805 patients, 111 (13.8%) of whom had one or more prolonged PICU stays. Among these patients, 100 (90%) survived to PICU discharge and 92 (83%) survived to hospital discharge. At the 3-year follow-up, the survival rate was 75% (77/102; nine patients were lost to follow-up) and the favourable outcome rate was 43% (44/102) (57% among survivors). Prolonged PICU-stay patients accounted for 50.5% of the PICU patient-days. Extremely prolonged stays (≥ 28 days) correlate with low favourable outcome rates ($P = 0.03$), but did not correlate with mortality rates ($P = 0.16$).

Conclusion: Although prolonged PICU-stay patients utilized many PICU resources, most survived at least 3 years, and > 50% of the survivors had a favourable functional outcome (POPC score).

What is Known:
- *The number of patients with prolonged paediatric intensive care unit (PICU) stays is increasing.*
- *These patients utilize many resources and are at high risk for mortality and disabilities.*

What is New:
- *Although prolonged-stay patients accounted for 50% of PICU patient-days, their 3-year survival rate and favourable functional outcome rate (based on Pediatric Overall Performance Category scores) were relatively high.*
- *Extremely prolonged stays (≥ 28 days) correlate with low favourable functional outcomes but not with mortality.*

Keywords Long-term outcome · Mortality · Pediatric Overall Performance Category · Prolonged · Resource · Paediatric intensive care units

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Abbreviations

IQR	Interquartile range
PICUs	Paediatric intensive care units
PIM2	Paediatric index of mortality 2
POPC score	Pediatric Overall Performance Category score

Introduction

While 50% of patients are discharged after spending less than 2 days in a paediatric intensive care unit (PICU) [18], others require stays longer than 13 days. The number of patients with prolonged PICU stays is increasing [13], and such patients not only utilize many PICU resources [9, 16, 18], but also are at high risk for mortality [3, 13, 16] and disabilities [12, 14]. Although the short-term mortality rate of prolonged-stay

patients has decreased, the proportion of survivors with moderate or severe disabilities has increased significantly [12]. Additionally, mortality and disability rates of prolonged-stay patients continue to increase after discharge from PICUs [14]. Therefore, knowledge of the long-term functional and survival outcomes after prolonged PICU stays is important.

Although several studies reported the long-term outcomes of patients admitted to PICUs [1, 2, 5–8, 10, 14, 15, 20], only a few focused on long-term outcomes after prolonged PICU stays [3, 13, 16, 21]. In the study published by Pollack et al. in 1987, 58% of prolonged-stay (> 13 days) patients died or became severely disabled within 1 year after PICU discharge [16]. However, owing to improvements in PICU care, which have enabled more patients to survive, a re-evaluation of long-term outcomes after prolonged stays is necessary. We therefore determined long-term mortality rates, PICU resource occupancy rates, and functional outcomes in patients with prolonged PICU stays (> 14 days) in Japan.

Materials and methods

Design and setting

We performed a retrospective, observational study of paediatric patients admitted to the PICU at a tertiary children's hospital (Osaka Women's and Children's Hospital) in Japan between January 2011 and December 2013. The PICU had eight beds during the study period for medical and surgical paediatric patients. There was no step-down unit in the hospital during the study period. Approximately 400 patients were admitted to the PICU annually, 70% of whom were admitted after surgical procedures including approximately 190 cardiac surgeries. Trauma patients were not cared for in the PICU.

Inclusion and exclusion criteria

We included all paediatric patients aged < 15 years with at least one prolonged PICU stay (defined as > 14 consecutive days in the PICU). For patients with multiple stays, functional outcomes were assessed only after the first stay.

Data collection

All data were retrospectively collected from the medical records of the patients. The retrieved data included the following demographic characteristics and outcome measures: age and body weight on admission to the PICU, sex, genetic abnormalities, underlying diseases, type of admission, paediatric index of mortality 2 (PIM2) [19], duration of mechanical ventilation, duration of PICU stay (expressed as number of patient-days), and survival status during the PICU stay, the hospital stay, and 3 years after the PICU stay. Data relating to outpatient follow-up care (rehabilitation and home care support) were also collected.

Clinical endpoints

The primary endpoints were mortality and functional outcome. Functional outcome was quantified by using the Pediatric Overall Performance Category (POPC) scoring system. POPC scores were categorized as follows: good (1), mild disability (2), moderate disability (3), severe disability (4), vegetative state or coma (5), and brain death (6) [4]. A favourable outcome was defined as a POPC score of 1–2, and an unfavourable outcome was defined as a POPC score of 3–6 or death.

Mortality rates and functional outcomes were determined 3 years after the first PICU admission. Patients transferred to other hospitals were not included in the follow-up analyses as they were difficult to contact. Via POPC scoring, we also assessed the functional status of all patients ≥ 1 month of age prior to the onset of the disease that led to PICU admission. Mortality rates and POPC scores were based on data in the medical records, as independently assessed by two physicians. When the POPC score differed between the two physicians, the physicians discussed the results until an agreement was reached.

PICU resource occupancy

To assess PICU resource occupancy, we determined the total number of mechanical ventilation days and the total number of PICU patient-days. This was done for all patients with prolonged PICU stays and all patients with PICU stays of any length; the former value was divided by the latter value to calculate the occupancy rate. We also determined the total number of PICU patient-days according to the length of the PICU stay (15–20 days, 21–27 days, or ≥ 28 days).

Statistical methods

Categorical variables were evaluated using the chi-square test, or when any expected counts were < 5, Fisher's exact test. Continuous variables were evaluated using the Wilcoxon rank-sum test. Statistical significance was defined as $P < 0.05$. The statistical analyses were conducted using JMP version 10.0 software (SAS Institute Inc., Cary, NC, USA) and R version 3.3.2 software (R Foundation for Statistical Computing, Vienna, Austria).

Informed consent

This study was approved by the ethics committee of the Osaka Women's and Children's Hospital (No. 1063). The need for

informed consent was waived owing to the retrospective nature of the study.

Results

Patient characteristics

During the study period, there were 1082 PICU admissions (805 patients < 15 years of age), 135 of which led to a prolonged PICU stay (> 14 days). Among the 805 patients, 111 (13.8%) had one or more prolonged stays: 97, one prolonged stay; 9, two prolonged stays; 2, three prolonged stays; 1, four prolonged stays; and 2, five prolonged stays.

The median age of the 111 prolonged-stay patients was 2 months (IQR [interquartile range 25th–75th], 0–29) and the median body weight was 3.9 kg (IQR, 2.8–8.2); 48 (43%) patients were male. Twenty-six (23%) patients had genetic abnormalities including trisomy 21 ($n = 5$), 22q11.2 deletion syndrome ($n = 4$), Kabuki syndrome ($n = 2$), Apert syndrome ($n = 2$), Miller-Dieker syndrome ($n = 2$), and others ($n = 11$). Fifty-eight (52%) patients had a cardiovascular disease, 18 (16%) had a neurological/muscular disease, 16 (14%) had a respiratory disease, 7 (6%) had a haematological/oncological/immunological disease, and 4 (4%) had a digestive tract disease. The median PIM2-predicted mortality rate was 5.2% (IQR, 2.4–9.6).

Long-term mortality

Figure 1 shows the flow chart of patient outcomes. Among the 111 patients with prolonged PICU stays, 100 (90%) survived to PICU discharge, 92 (83%) survived to hospital discharge, and 6 (5%) died after hospital discharge. Excluding the nine patients lost to follow-up owing to transfer to other hospitals, the 3-year survival rate was 75% (77/102). The 3-year follow-up evaluations were conducted as close as possible to the anniversary of the initial admission to the PICU; the median difference was 26 days (IQR, 12–51). Among the patients examined, 43% (44/102) had a favourable functional outcome (POPC score 1–2) at the 3-year follow-up and 57% (58/102) had an unfavourable outcome (POPC score 3–6 or had died).

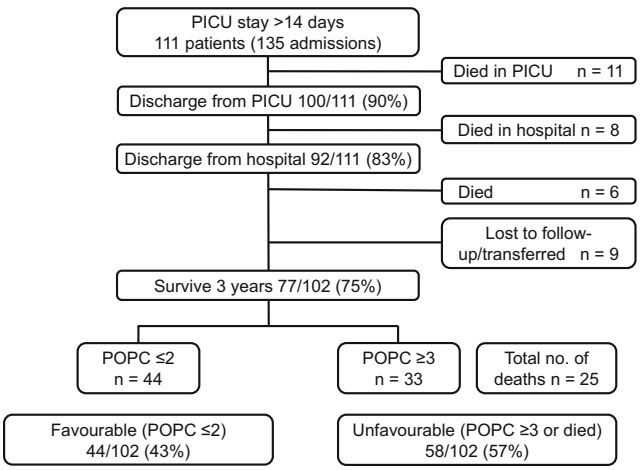

Fig. 1 Flow chart of patient outcomes. PICU paediatric intensive care unit, POPC Pediatric Overall Performance Category

Table 1 shows the baseline characteristics of the prolonged-stay PICU patients with favourable and unfavourable 3-year functional outcomes. Male patients ($P = 0.01$), patients with genetic abnormalities ($P = 0.002$), and patients with multiple prolonged PICU stays ($P = 0.03$) were more frequent in the unfavourable outcome group. Moreover, the median durations of mechanical ventilation ($P < 0.001$) and PICU stay ($P = 0.004$) were longer in the unfavourable outcome group.

Figure 2 shows the proportion of favourable functional outcomes, unfavourable functional outcomes, and deaths according to the duration of the PICU stay. Although not statistically significant, increases in the mortality and unfavourable outcome rates 3 years after PICU discharge paralleled increases in the duration of the stay (both P values = 0.07). Patients with extremely prolonged stays (≥ 28 days) had a lower favourable outcome rate than did those with shorter stays ($P = 0.03$), but a similar mortality rate ($P = 0.16$).

Functional status

The 58 patients who were ≥ 1 month of age at the time of PICU admission were evaluated both before (functional status) and 3 years after (functional outcome) admission. Pre-admission and follow-up POPC scores were favourable in 19/58 (33%) and 22/58 (38%) patients, respectively ($P = 0.70$) (Table 2). Three of the 19 (16%) patients with favourable pre-admission scores died, whereas 12 (63%) had favourable follow-up scores. Additionally, 10/39 (26%) patients with unfavourable pre-admission scores had favourable follow-up scores (mean POPC score 3.1 vs. 1.7; $P = 0.02$).

PICU resource occupancy

During the study period, patients with prolonged PICU stays (13.8% of all PICU patients) accounted for 4362/8632 (50.5%) PICU patient-days and 3369/5289 (63.7%) mechanical ventilation days. Patients with prolonged PICU stays of 15–20 days, 21–27 days, and ≥ 28 days occupied 839/8632 (9.7%), 699/8632 (8.1%), and 2824/8632 (32.7%) PICU patient-days, respectively.

Discussion

The present study determined long-term mortality rates, functional outcomes, and resource use in patients with prolonged PICU stays. At the 3-year follow-up, 75% of these patients

Table 1 Baseline characteristics of prolonged-stay patients with favourable and unfavourable outcomes 3 years after admission to the paediatric intensive care unit

Patient characteristics	All[a] $n = 111$	Favourable (POPC score 1–2) $n = 44$	Unfavourable (POPC score 3–6 or death) $n = 58$	*P* value
Median age, months (IQR)	2 (0–29)	0.5 (0–8)	4 (0–37)	0.07
Median body weight, kg (IQR)	3.9 (2.8–8.2)	3.3 (2.6–6.9)	4.2 (2.9–10)	0.19
Male, number (%)	48 (43)	26 (59)	20 (34)	0.01*
Genetic abnormality, number (%)	26 (23)	4 (9)	21 (36)	0.002*
Underlying disease category, number (%)				0.35
Cardiovascular	58 (52)	27 (61)	29 (50)	
Neurological/muscular	18 (16)	2 (5)	11 (19)	
Respiratory	16 (14)	8 (18)	8 (14)	
Haematological/oncological/immunological	7 (6)	2 (5)	4 (7)	
Gastrointestinal	4 (4)	2 (5)	2 (3)	
None	8 (7)	3 (7)	4 (7)	
Admission post-surgery, number (%)	47 (42)	22 (50)	22 (38)	0.22
Elective admission, number (%)	52 (47)	23 (52)	27 (47)	0.69
Median PIM2 predicted mortality rate, % (IQR)	5.2 (2.4–9.6)	4.1 (2.3–8.1)	6.3 (3.2–12)	0.05
Multiple prolonged PICU stays, number (%)	14 (13)	2 (5)	11 (19)	0.03*
Median duration of mechanical ventilation, day (IQR)	17 (12–27)	15 (10–22)	26 (15–49)	< 0.001*
Median duration of PICU stay, day (IQR)	24 (18–36)	22 (17–34)	32 (21–56)	0.004*

Patient characteristics and outcomes were compared between patients with favourable and unfavourable outcomes at the 3-year follow-up. *Statistically significant ($P < 0.05$). [a] All patients included the nine patients lost to follow-up. *IQR* interquartile range, *PIM2* paediatric index of mortality 2, *PICU* paediatric intensive care unit, *POPC score* Paediatric Overall Performance Category score

were alive, and 43% had a favourable functional outcome as defined by the POPC score. We also found that patients with prolonged PICU stays occupied more than half of the PICU patient-days and mechanical ventilation days.

There is no standardized definition of a prolonged PICU stay. Previous studies defined it as ≥ 28 days [3, 13] or ≥ 30 days [21]; in these studies, the long-term mortality rate was 35–50% and the unfavourable outcome (death or impaired capacity) rate was approximately 60%. However, ≥ 28 days may be too restrictive as it applies to only 1–3% of the PICU population [3, 13]. Therefore, to better represent this population, we defined a prolonged stay as > 14 consecutive days. This definition may be particularly relevant in Japan, where hospitals are not reimbursed for stays > 14 days. Moreover, its use may help improve the outcomes and resource utilization rates of prolonged-stay patients, hence providing a rationale for revamping existing reimbursement policies.

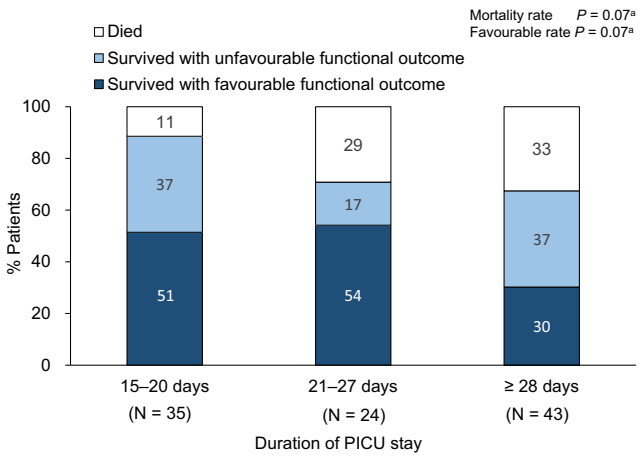

Fig. 2 Outcomes according to the duration of the prolonged paediatric intensive care unit (PICU) stay. The outcomes were determined 3 years after admission to the PICU. [a]*P* values were calculated among the three duration groups (15–20 days, 21–27 days, and ≥ 28) days using Fisher's exact test

The 3-year survival rate (75%) and favourable functional outcome rate (POPC score 1–2; 43% in all prolonged-stay patients) in our study were similar to those in a study conducted over three decades ago (1-year follow-up rates of 76% and 42%, respectively) [16]. In that study, a prolonged PICU stay was defined as > 13 days, and a favourable outcome as alive without severe disabilities.

When we only considered patients with extremely prolonged stays (≥ 28 days, $n = 43$), the mortality rate was 33% (14/43) and the favourable functional outcome rate was 30% (13/43). These values are similar to or lower than those in previous studies (35.2–49.8% for mortality and 27% for favourable outcome) [3, 13]. The proportion of patients with extremely prolonged PICU stays was higher in our study (5.3%) than previous studies (1.0–3.1%) [3, 13]. Possible

Table 2 Post-admission functional outcome according to pre-admission functional status

Pre-admission functional status	Favourable 3-year outcome (POPC score 1–2) $n = 22$	Unfavourable 3-year outcome (POPC score 3–6 or death) $n = 36$
Favourable (POPC score 1–2), *n* (%)	12 (55)	7 (19)
Unfavourable (POPC score 3–6), *n* (%)	10 (45)	29 (81)

Post-admission outcome differed significantly according to pre-admission functional status ($P = 0.009$). *POPC* Pediatric Overall Performance Category

reasons for this difference include more severe illness in our patient population and our more rigorous, conservative discharge policy. Therefore, studies that consider disease severity are warranted.

Prolonged-stay patients accounted for only 13.8% of all patients admitted to our PICU during the study period. However, they utilized a disproportionate share of the resources: approximately 50% of the PICU patient-days and 60% of the ventilator days. Others also reported high rates of PICU resource occupancy by prolonged-stay patients [9, 11, 13]. However, the relatively high long-term survival rate and favourable functional outcomes in our study appear to justify the heavy usage of PICU resources by prolonged-stay patients.

Although achieving a high long-term follow-up rate is difficult, doing so is important for ensuring the reliability of the results, as is the timing of the follow-up. In the present study, the 3-year follow-up rate was 92% (102/111), with only nine patients lost to follow-up. This high rate may reflect the routine assessment of developmental status in 94% of our paediatric patients by specialists at our institution and is consistent with previously reported rates of 94% (219/233) [13] and 72% (138/193) [3] at 4 years (median) and 6.3 years (mean), respectively. Another study reported a follow-up rate of 91% (42/46), albeit after only 1 year [16].

Our study compared functional status before PICU admission and functional outcome at the 3-year follow-up in patients aged ≥ 1 month. The percentage of patients with a favourable status before admission was similar to the percentage of patients with a favourable outcome at follow-up. Of note, 10/39 (26%) patients with an unfavourable pre-admission status had a favourable follow-up outcome. One of these patients had no underlying disease. Nine had a cardiovascular disease, and eight of the nine received cardiovascular surgery. We speculate that cardiovascular surgery accounted in part for the improved functional outcomes.

The present study had some limitations. First, it was a retrospective, observational, single-centre study. As such, it relied on medical records (which may have been inaccurate or incomplete) rather than first-hand examinations for POPC scoring. Moreover, owing to its small sample size, its results may not be entirely generalizable. Second, two factors may have influenced the PICU resource utilization and outcome results: the individual practice patterns of the clinicians at our hospital (PICU admission/discharge decisions are based on the clinical condition of the patient rather than established criteria) and the type of post-discharge care (rehabilitation, home care, or both in 27%, 39%, and 19% of the 77 surviving patients, respectively).

Third, we did not assess changes in POPC scores in patients aged < 1 month at the time of PICU admission. Accurate assessment of POPC scores is challenging and prone to bias in neonates and very young children. Previous studies also excluded very young children from similar analyses [3, 13, 16, 21] or did not perform comparisons [3, 16]. Hence, we cannot definitively say whether the unfavourable outcomes in our study reflected prolonged PICU stays, the patient's inherent condition on admission, or the conditions of patients aged < 1 month at the time of admission.

Fourth, there were two significant differences between the nine patients lost to follow-up and the remaining patients: the former weighed more than the latter on admission and more often had a neurological/muscular disease (data not shown). The other characteristics (Table 1), however, were similar. Finally, although POPC scoring is easy to accomplish and comparable to other functional status scoring systems [17], it may lack the precision required for accurate evaluation of long-term functional outcomes. Therefore, studies using other outcome measures are required for confirmation.

Despite these limitations, this is the first report in this decade of long-term mortality and functional outcome after prolonged PICU stays (> 14 days). Importantly, mortality rates and functional outcomes were relatively favourable. Of note, we achieved a high follow-up rate of 92% after 3 years, presumably owing to routine assessment of developmental status by specialists at our institution.

Conclusions

While 13.8% of the prolonged PICU-stay (> 14 days) patients occupied half of the PICU patient-days, 75% of them survived for at least 3 years, and more than half of the survivors had favourable functional outcomes as defined by POPC scores. These results might justify the high utilization of PICU resources by such patients. However, studies determining the

long-term outcomes of prolonged PICU-stay patients in different settings and using different outcome measures are needed.

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Authors' contributions NM contributed to the conception and design of the study, the acquisition and analysis of the data, the drafting of the manuscript, and the critical revision of the manuscript for important intellectual content.

TH contributed to the conception and design of the study, the acquisition and analysis of the data, and the drafting of the manuscript, and played a large role in the writing of the manuscript.

YI contributed to the conception and design of the study, the interpretation of the data, and the revision of the manuscript.

YS contributed to the conception and design of the study, the interpretation of the data, and the revision of the manuscript.

MT contributed to the conception and design of the study, the interpretation of the data, and the revision of the manuscript.

All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study, formal consent was not required.

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