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Mortality in very long-stay pediatric intensive care unit patients and incidence of withdrawal of treatment

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Abstract *Background:* The mortality for children with prolonged stay in pediatric intensive care units (PICU) is much higher than overall mortality. The incidence of withdrawal or limitation of therapy in this group is unknown. *Purpose:* To assess mortality and characteristics of children admitted for ≥28 days to our ICU, and to describe the extent to which limitations of care were involved in the terminal phase preceding death. *Methods:* For the period 2003 to 2005 clinical data were collected retrospectively for children with prolonged stay (defined as ≥28 days) in a medical/surgical PICU of a university children's hospital. *Results:* In the PICU, 4.4% of the children (116/2,607, equal gender, mean age 29 days) had a prolonged stay. Median (range) stay was 56 (28–546) days. These children accounted for 3% of total admissions and occupied 63% of total admission days. Mortality during admission for this group was five times higher (22%) than the average PICU mortality rate of 4.6%. Withdrawal or limitation of therapy preceded 70% of deaths. *Conclusions:* Children with prolonged stay in the PICU have a significantly high risk of mortality. Death is typically preceded by limitation of care.

Keywords Long-stay patient · Pediatric intensive care unit · End of life · Mortality · Limitations of care

Abbreviations

LSP	Long-stay patient
PICU	Pediatric intensive care unit

Introduction

Critical appraisal of the effectiveness of different modes of treatment and demands for more cost-efficient hospital processes have focused attention on the duration of care in an intensive care unit (ICU), an environment which necessarily provides high levels of care and therefore requires substantial operating budgets [1–3]. Median stay for most patients is 2 days [4, 5], but a small minority need to stay much longer and use resources in excess of their numeric proportions [6]. Long stay in the pediatric ICU is usually defined as stay longer than 12–13 days [1, 3, 7]. A special subgroup is formed by patients with very prolonged stay, longer than 30 days [7, 8].

The few reports available on outcomes of long-stay pediatric ICU patients demonstrate higher mortality and morbidity compared with short-stay patients [3, 6, 9, 10]. Withdrawal and limitation of medical care is associated with 14-75% of deaths in neonatal and pediatric intensive care [11–13]. These issues have been extensively discussed in the past decade [8, 11, 12, 14–16] and have been the subject of ongoing public discourse. The extent to which limitations of care actually contribute to death in very long-stay pediatric ICU patients is not known. The aim of the present study was to assess characteristics and mortality of very long-stay patients in our unit and to describe how often treatment was limited and/or withdrawn.

Methods

Data collection and definitions

The ICU of the Erasmus MC-Sophia Children's Hospital, Rotterdam, is a level III interdisciplinary intensive care unit for children in The Netherlands, providing all pediatric and surgical subspecialties (except direct cardiopulmonary bypass). All patients, including newborns with major congenital anomalies, admitted from 1 January 2003 until 31 December 2005 were retrospectively identified using the computerized patient data management system. Long-stay patients were defined as those admitted for at least 28 continuous days. The reason for this cutoff point was that 28 days is three times the median length of stay in our unit. Whenever a long-stay patient was readmitted, only the first admission was included in the study. The following clinical data were collected from hospital medical records and our patient data management system: age, sex, presence and number of congenital malformations, reason for admission, and diagnosis. Both data systems are used by nursing and medical staff.

Primary outcome was death during admission. Deaths during operations or other procedures were classified as intensive care deaths. Cause of death was categorized as [13]: brain death, do-not-resuscitate, failed cardiopulmonary resuscitation, withdrawal or limitation of therapy [17–20].

Retrospectively, every patient's death was classified according to four categories:

1. Brain death (BD): when criteria for brain death were fulfilled.
2. Do-not-resuscitate (DNR): when a previously ordered DNR document was available.
3. Failed resuscitation (RES): when advanced life support failed.
4. Withdrawal or limitation of therapy (W/LT): when, by agreement between family and medical staff, present level of life-sustaining treatment (LST) was limited and/or inotropes/mechanical ventilation removed.

Main diagnoses were categorized into six groups: disorders of the respiratory system, gastrointestinal disorders, multiple congenital abnormalities, neurological disorders, cardiac disease, and others. Data on survival, limitations of therapy, and withdrawal of therapy were collected. Decisions regarding do-not-resuscitate (DNR) and limitation/withdrawal of life-sustaining therapy (W/LT) were taken by a multidisciplinary team. As described earlier [21, 22] families were involved in all cases.

Severity of illness on admission was measured by PRISM III score according to Pollack et al. published in 1996, which was calculated from physiological data that included the most abnormal values in the first 12 h and second 12 h of PICU stay.

In the terminal phase, patients were not transferred to a different ward. Instead, optimal palliative care was offered in a separate part of the intensive care unit. When needed or requested by the medical team and/or parents, the institutional Ethics Review Board was consulted. Approval from this board for the present study was waived due to its retrospective character.

Setting

The setting for this study was a 34-bed multidisciplinary tertiary level III pediatric ICU with extra corporeal membrane oxygenation (ECMO) facilities, including a 6-bed step-down unit. This ICU is part of a 250-bed pediatric university hospital with a referral population of 4,000,000 and staffed full-time by intensive care specialists with basic training in pediatrics or anesthesiology.

Data analysis

Data are presented as mean ± standard deviation (SD) or median (interquartile range [IQR] or range) where appropriate and were analyzed by using SPSS software (SPSS version 12.0 for Windows, 2005, Chicago, IL).

Results

During the study period 2,607 patients were admitted on 3,700 occasions for a total of 16,013 admission days. Of this group 4.4% (116/2,607) patients were identified as very long-stay patients, responsible for 3.4% (126/3,700) of total admissions and consuming 63% (10,055/16,013) of admission days. One hundred and six long-stay patients were admitted once, seven were admitted twice, and three were admitted three times.

Demographic and care characteristics of long-stay patients are summarized in Table 1. Clinical diagnoses were: disorders of the respiratory system (29, 25%), gastrointestinal disorders (23, 20%), multiple congenital abnormalities (19, 16%), neurological disorders (18, 15%), cardiac disease (18, 15%), and others (9, 8%).

Table 1 Demographic characteristics of long-stay patients

Demographic characteristics	Long-stay patients $N = 116$	Long-stay nonsurvivors $N = 25$	Long-stay survivors $N = 91$
Admissions	126	25	111
Fraction of total admissions (%)	3	2.6	0.6
Males (%)	57	60	58
Age median (months) (IQR 25)	1	1	1
Mean age (months)	29	29	29
Mortality (%)	22	–	–
Surgical patients (%)	37	36	34
Median ventilation (days) (IQR 25)	30	33	45

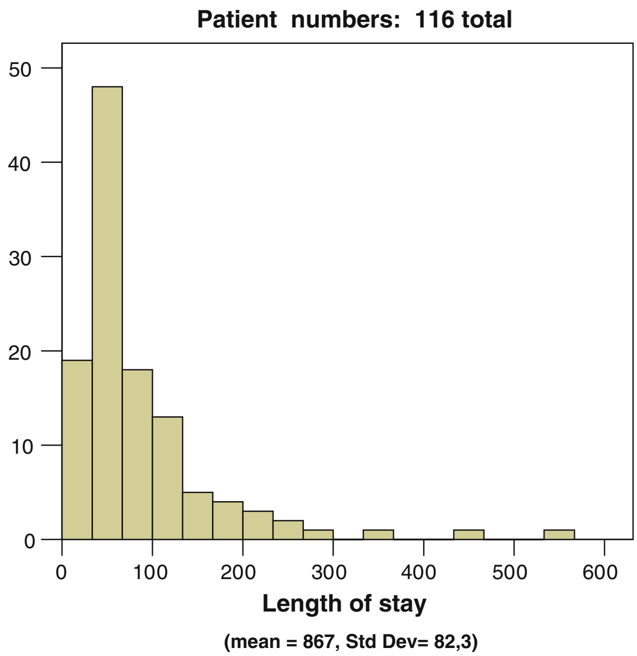

Fig. 1 Length of intensive care unit stay in days for a total of 116 long-stay patients

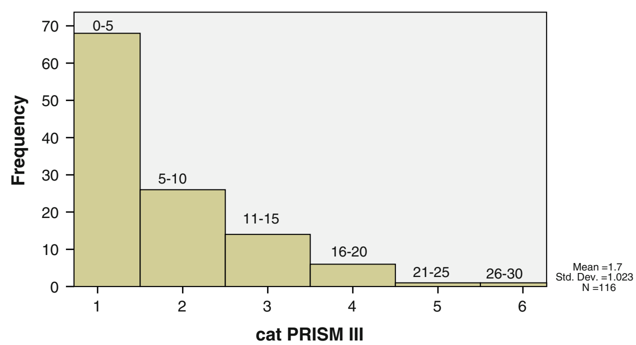

Fig. 2 PRISM III score among long-stay patients

Their median length of stay was 56 (IQR 37–108) days. Distribution of length of stay is shown in Fig. 1. Outliers were three patients admitted for more than 300 days, the longest stay being 546 days. PRISM III scores are shown in Fig. 2. The majority of the long-stay patients (58%) had a PRISM III score between 0 and 5. Ninety-four patients (81%) had a maximum PRISM III score of 10.

During the study period 4.6% (120/2,607) of the total patient group died during admission; 21% (25/120) of them were very long-stay patients. The mortality rate of long-stay patients was higher compared with short-stay patients [22% (25/116) versus 3.8% (95/2,491), $p < 0.001$]. The characteristics of long-stay survivors and nonsurvivors are shown in Table 2. Neonates accounted for half of the patient population in both groups. The most common diagnoses among the long-stay nonsurvivors were multiple congenital anomalies (7/25, 28%) and cardiovascular disease (7/25, 28%). Multiple congenital anomalies was the most frequent diagnosis among the long-stay survivors as well (25/91, 27%), followed by diseases of the respiratory system (22/91, 24%).

Table 2 Characteristics of nonsurvivors and survivors

	Nonsurvivors	Survivors
Patient numbers	25	91
Patients no./total admissions	25	91/101
Male (%)	60	58
Median age (days)	29	34
Median length of stay (days)	67	54
Patient admission days	2,538	7,517
Neonate (%)	52	47
Ex-premature (%)	8	5
Diagnosis (%)		
Resp.	2/25 (8%)	22/91 (24%)
Cardio.	7/25 (28%)	7/91 (8%)
Gastro.	4/25 (16%)	17/91 (18%)
Neuro.	4/25 (16%)	14/91 (15%)
Others.	1/25 (4%)	6/91 (7%)
MCA[a]	7/25 (28%)	25/91 (27%)

[a] Multiple congenital anomalies

The specific primary diagnoses which led to long stay are presented in Table 3. A total of 101 readmissions were counted for 91 survivors. Comparing different

Table 3 Specific primary diagnosis among long-stay patients

Primary diagnosis	Nonsurvivors	Survivors
Dilated/restricted cardiomyopathy	2	1
Congenital heart disease	7	6
Acquired arrhythmia	0	1
Congenital airway/pulmo. disease	1	4
Acquired airway/pulmo. disease	0	5
Congenital gastrointestinal malformations	3	12
Acquired gastrointestinal disease	0	4
Congenital hypotonia	1	5
Status epilepticus (therapy resist)	1	1
Acquired neurological disease	0	1
Central hypoventilation	0	1
Infantile encephalopathy	1	3
Psychomotor retardation eci	1	1
Metabolic disease	1	2
Trauma	0	1
Sepsis	0	1
Malignancy	0	4
Multiple congenital anomalies	7	25
Congenital diaphragmatic hernia	0	12
Hematological/vascular disease	0	1
Total	25	91

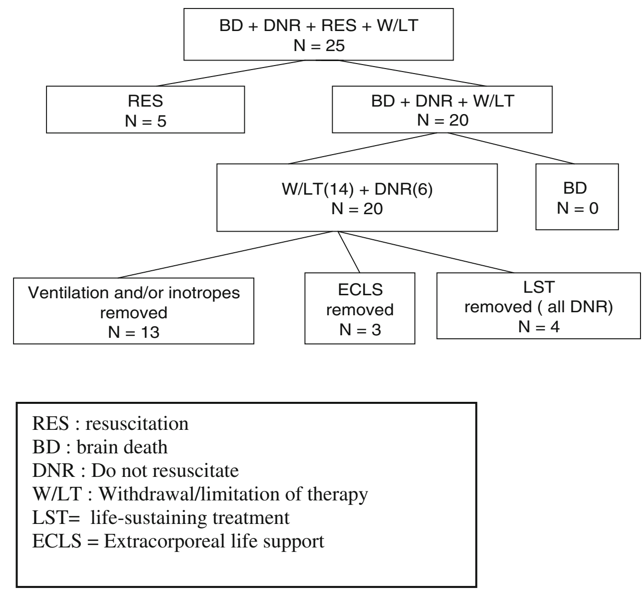

Fig. 3 Nonsurvivors end-of-life flow diagram in different patient groups, in which all nonsurvivors are categorized according to mode of death. RES: resuscitation, BD: brain death, DNR: do not resuscitate, W/LT: withdrawal/limitation of therapy, LST: life-sustaining treatment; ECLS: extracorporeal life support. In addition the W/LT and DNR group ($n = 20$) is categorized by different ICU dependent treatments which they had been receiving

diagnosis between survivors and nonsurvivors showed no statistical significance ($p = 0.999$).

Figure 3 shows a flow diagram in which end-of-life categories are shown for nonsurvivors. No patients were included in the category of brain death. Among 25 deaths, 6 patients had DNR status. Active withdrawal of support occurred in 12 patients: 2 with DNR orders and 10 without. Three patients were removed from extracorporeal life support (ECLS): one patient after 12 days ECMO and two cardiac patients with refractory shock. Table 4 summarizes characteristics in terms of mode-of-death category and end-of-life treatment.

All end-of life meetings between the medical team and family which resulted in limitations of treatment, DNR or withdrawal were documented. The cause of death was well documented in all the charts, including an electronic patient data management system which has been used by both nursing and medical staff members. Consensus between caregivers and medical team regarding the end-of-life meetings was reached in all cases. All parents were physically present with their child when passing away, except one parent couple who, with respect to their religious restrictions, unfortunately could not be present at the time of death.

Discussion

In this study the group of very long-stay patients (LOS ≥28 days) forms only a small proportion of the total cohort (3%), but they are responsible for a considerable part of admission days (63%). The mortality rate for this group was five times higher than that for the total cohort.

We found that our very long-stay patients consumed a high proportion of total admission days, which is consistent with earlier studies performed in adult and pediatric ICUs (LOS >12 days) [3, 7, 20]. The overall mortality rate in our ICU is comparable to the mortality rates reported by European and North American studies [1, 4, 13]. We reported a much higher mortality rate in very long-stay patients (defined as >28 days) compared with short-stay patients. It is difficult to compare this mortality with earlier reports, as these were studies of long-stay patients (defined as 7–30 days) [3, 6, 9, 10]. However, it is still lower than the ICU mortality documented among adults following very long stay (32%) [7].

Previous analysis by Marcin et al. [1] of diverse PICUs in the USA indicates that, among other factors, PRISM III score between 10 and 33 was predictive of long stay in their population. Given that PRISM III score has not been evaluated amongst European long-stay patients, we considered these scores in our study sample. The majority (81%) of our long-stay patients did have a PRISM III score between 0 and 10, which is at the lower range of the score and might be explained by the unique case mix of our ICU and the PRISM III score not being population independent.

Table 4 Characteristics in mode-of-death categories

	BD	DNR	W/LT	RES
Number	0	6	14	5
Age (years) mean (SD)		2.3 (4.9)	2.5 (5.6)	2.4 (5.3)
Age (years) median (range)		0.0 (0.0–3.9)	0.0 (0.0–1.5)	0.0 (0.0–6.0)
LOS (days) mean (SD)		82 (72)	102 (134)	123 (51)
LOS (days) median (range)		48 (39–136)	62 (33–107)	131 (75–167)
Initial ICU admission diagnosis (*n*)				
Resp		3	7	–
Cardiac		–	4	–
Resp + Cardiac		–	1	–
Resp + Surgery		2	2	–
Neurology		1	–	–
End-of-life treatments and characteristics				
Ventilated patients (*n*)		6	14	–
Ventilation days 80–100%		4	12	–
Tracheostomy		2	4	–
Noninvasive ventilation		–	–	
Multiple congenital anomaly		4	5	–
Dialysis		–	–	–

DNR do not resuscitate
RES (failed) resuscitation
W/LT withdrawal/limitation of therapy
BD brain death

The few studies available of adults who required at least 28–30 days of ICU care generally report reasonable to relatively good chance of hospital and long-term survival, with some disability during daily activities [7, 23–27]. Friedrich et al. [7] reported a 32% ICU mortality and a 58% hospital survival rate among their very long-stay patients. Most survivors were discharged to their previous place of residence, which was considered as an important indicator of quality of life.

A high proportion of deaths in this study were preceded by end-of-life discussions, resulting in withdrawal or limitation of life-sustaining treatment. So far, however, there are no guidelines or protocols to facilitate the decision-making process when establishing appropriate boundaries concerning the extent of medical care. Once certainty about the diagnosis and prognosis has been obtained, it is vital that a prominent member of the interdisciplinary teams informs the parents and evaluates whether the treatment given is in the child's best interest [12, 15, 22, 28, 29]. If disagreement occurs between the parents and the view held by the medical team, this conflict can be mediated according to the guidelines of the Dutch Pediatric Society, reported in the early 1990s and available to all its members. Fortunately disagreement did not occur in our patient group.

Optimal palliative care was provided in a separate part of the intensive care unit without transferring the patient to a different ward. In the holistic approach towards our patients we appreciate continuous care given by the same care providers. Caring for families with a child awaiting the end of life creates a situation where an inevitable death demands the involved care providers to continue a close relationship, especially when a long stay has been involved.

The retrospective character of the study is a limitation. It was conducted in a mixed ICU population, which limits its generalizability and application to other centers. Moreover, our unit's infrastructure and the lack of separate high-dependency units within our hospital may have had a decisive influence on our findings. The issue of generalizability, given the different population and institutional setting, has also been raised by Friedrich et al. in 2006 when evaluating an adult ICU population [7]. They described the unique character of their data, which may not be applicable to other centers with a different view on health care organization [7]. Having an intermediate/step-down unit and long-term ventilatory facilities apart from the intensive care might yield other results (for example, shorter ICU length of stay). The 28-day minimum length of stay we defined may limit the applicability of our findings to other patient populations with severe congenital malformations with shorter length of stay but also high mortality.

Notwithstanding the limitations of this type of investigation, we believe that our data on very long-stay patients will raise awareness of this matter and contribute towards the improvement and establishment of appropriate goals of care. Long-term survival, functional outcomes, and quality of life are important aspects of PICU patients that need more study. Pediatric follow-up data in long-stay patients are limited and contradictory [3, 6].

In conclusion, the high mortality rate and frequent application of a "withholding" approach shown in this study emphasizes the necessity of timely care assessment, when a patient's stay in the pediatric ICU exceeds 28 days. A multidisciplinary team should then discuss possibilities of cure and care based on current and predicted future suffering. We recommend the use of a transparent individualized protocol to guide the treatment team towards boundaries of care.

Ongoing investigation is needed to point out the different indications and justifications of limitations of treatment for pediatric ICU patients with prolonged length of stay. Early identification of patients at risk of very long stay and recognition of their high risk of mortality and potential consequences for future therapeutic modalities should be incorporated into the activities of teams working at the pediatric ICU.

Conflict of interest statement None.

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