Surviving pediatric intensive care: physical outcome after 3 months

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Abstract Objective: This study investigated the prevalence and nature of physical and neurocognitive sequelae in pediatric intensive care unit (PICU) survivors. Design and setting: Prospective follow-up study 3 months after discharge from a 14-bed tertiary PICU in The Netherlands. Patients and participants: The families of 250 previously healthy children unexpectedly admitted to the PICU were invited to visit the outpatient follow-up clinic for structured medical examination of the child 3 months after discharge; 186 patients were evaluated. Measurements and results: Pediatric Cerebral Performance Category (PCPC) and Pediatric Overall Performance Category (POPC) values were determined at PICU discharge, at the outpatient follow-up clinic, and retrospectively before admission to the PICU. We found that 69% of children had physical sequelae. In 30% of cases these were caused by a previously unknown illness and in 39% by acquired morbidity. In 8% of the children the acquired morbidity was related to complications from PICU procedures. Three months after discharge 77% of the children had normal PCPC scores and 31% had normal POPC scores. Conclusions: Our results indicate that PICU survival may be associated with substantial physical sequelae. Structured follow-up research, preferably by multicenter studies, is warranted in PICU survivors.

Keywords Pediatric intensive care unit · Health status · Follow-up studies · Outcomes research

Introduction

The development of pediatric intensive care has contributed to improved survival in children with critical illness [1, 2]. Traditional outcome measures such as length of stay, number of ventilation days, and mortality are not the only relevant issues. New disease patterns have emerged due to long-term complications and effects of the original illness and its treatment. Physical sequelae, disability, and functional health have become equally important outcome measures in pediatric intensive care unit (PICU) survivors. Awareness of physical sequelae of underlying diseases and intensive care treatment and subsequently their impact on growth and development could lead to improvement in treatment and support after discharge.

Studies on physical sequelae in PICU survivors are scarce. In studies evaluating functional health and quality of life aspects, one third of the evaluated children are in full health 1 year after discharge and 60–80% of the children have good quality of life [3–9]. In 1992 the Pediatric Cerebral Performance Category (PCPC) and the Pediatric Overall Performance Category (POPC) were developed and validated to evaluate outcome in a general PICU population [10, 11]. In 58% and 27% of the studied children, respectively, PCPC and POPC scores at PICU discharge were normal. These scores correlated well with the results of extensive psychometric tests (such as Bayley Scales of Infant Development) performed at one and 6 months after discharge [11, 12].
In multidisciplinary PICU populations reports on outcome are scarce. Historically, outcome research in pediatrics has been based either on an age-specific approach such as follow-up studies of premature infants or on a more disease-oriented approach such as follow-up studies in survivors of cardiothoracic surgery or trauma [13–15]. Evaluative research of adult intensive care survivors has shown the effect of intensive care treatment per se [16–18]. The aim of this study was to evaluate physical and neurocognitive sequelae 3 months after discharge in children who were previously healthy and unexpectedly admitted to the PICU.

**Materials and methods**

This study was carried out between December 2002 and October 2005 as part of an on-going explorative research program on physical and psychological sequelae in children and their parents after an acute and unexpected PICU admission. The PICU of the Emma Children’s Hospital, Academic Medical Center of Amsterdam is a tertiary PICU with 14 beds, admitting medical, surgical, and trauma patients from the greater Amsterdam area. The local ethics review board approved the study protocol.

**Participants**

This study included only previously healthy children who were unexpectedly referred to the PICU with an acute life-threatening illness; we excluded children with known underlying illnesses or scheduled elective surgery. We included all previously healthy patients with respiratory or circulatory insufficiency, all trauma patients irrespective of length of PICU stay, and patients admitted to the PICU for other reasons for 7 days or more. Exclusion criteria were admission due to abuse or self-intoxication and the inability to complete Dutch-language questionnaires. Patient characteristics were obtained from medical records and from the patient data management system.

Of the 250 children eligible for inclusion 186 participated. The parents of 64 did not participate: in 13 cases they refused to participate, in 33 they accepted participation but did not present at the outpatient clinic, and in 18 they did not respond at all. Reasons for refusal included: “everything is going well,” “we have seen too many hospitals,” “we need some rest,” and “we don’t want to remember that time”. Participants and nonparticipants differed only in (a) length of stay, (b) length of ventilation, (c) reasons for admission, and (d) diagnosis at discharge. For example, participants had a longer length of stay and had more ventilation days than nonparticipants; 14 participants stayed in the PICU longer than 21 days and had more than 14 ventilation days (Tables 1, 2).

**Definitions**

The term previously healthy was defined as having no need for medical supervision at anytime before PICU admission. Included were children presenting at the emergency room and directly admitted to the PICU as well as children first admitted to the general ward who deteriorated and

**Table 1** Patient characteristics of PICU admission in participants and nonparticipants

|                        | Participants (n = 186) | Nonparticipants (n = 64) | p-value |
|------------------------|------------------------|--------------------------|---------|
| Age of child, median (years; range) | 1.4 (0.1–17.3) | 1.5 (0.2–15.9) | 0.423 |
| Length of stay in PICU; median (days; range) | 6.0 (1.0–336.0) * | 4.0 (1.0–20.0) | 0.006 |
| Length of artificial ventilation, median (days; range) | 5.0 (0.0–119.0) * | 3.0 (0.0–19.0) | 0.004 |
| Risk of mortality a, median (%; range) | 4.2 (0.2–80.7) | 3.8 (0.2–26.6) | 0.293 |
| Female | 68 (37%) | 23 (36%) | 0.929 |
| Reason for PICU admission * | 77 (41%) | 33 (52%) | 0.001 |
| Respiratory insufficiency | 31 (17%) | 13 (21%) | 0.138 |
| Circulatory insufficiency | 44 (24%) | 9 (13%) | 0.058 |
| Trauma | 22 (12%) | 8 (12%) | 0.770 |
| Neurological disorder | 6 (3%) | 2 (3%) | 0.329 |
| Metabolic disorder | 6 (3%) | 0 (0%) | 0.083 |
| Gastrointestinal disorder | 6 (3%) | 1 (2%) | 0.404 |
| Artificial ventilation | 151 (81%) | 55 (86%) | 0.389 |
| Circulatory support | 46 (25%) | 16 (25%) | 0.966 |
| Neuromuscular blocking agents | 37 (20%) | 18 (28%) | 0.170 |
| Corticosteroids | 69 (37%) | 21 (33%) | 0.757 |
| Central venous catheter | 67 (36%) | 18 (28%) | 0.250 |

* p < 0.05 participants vs. nonparticipants; a Paediatric Index of Mortality II
Table 2 Diagnosis at PICU discharge in participants and nonparticipants

| Diagnosis                        | Participants (n = 186) | Nonparticipants (n = 64) | p-value |
|----------------------------------|------------------------|--------------------------|---------|
|                                  | n          | %      | n    | %      |           |
| Respiratory insufficiency        |            |        |      |        |           |
| Pneumonia                        | 41         | 22     | 19   | 30     | 0.001     |
| Upper airway obstruction         | 19         | 10     | 13   | 20     |           |
| Asthma                           | 13         | 7      | 0    | –      |           |
| Other                            | 4          | 2      | 1    | 2      |           |
| Circulatory insufficiency        |            |        |      |        | 0.001     |
| Congenital heart disease         | 14         | 8      | 0    | –      |           |
| Other cardiac disease            | 4          | 2      | 1    | 2      |           |
| Meningococcal disease            | 11         | 6      | 8    | 12     |           |
| Toxic shock syndrome             | 0          | –      | 4    | 6      |           |
| Other septic shock               | 2          | 1      | 0    | –      |           |
| Trauma                           |            |        |      |        | 0.001     |
| Head trauma                      | 35         | 19     | 7    | 11     |           |
| Other trauma                     | 9          | 5      | 1    | 2      |           |
| Neurological disorder            |            |        |      |        | 0.001     |
| Status epilepticus               | 15         | 8      | 5    | 8      |           |
| Meningitis                       | 3          | 2      | 3    | 5      |           |
| Other                            | 4          | 2      | 0    | –      |           |
| Metabolic disorder               | 6          | 3      | 2    | 3      | –         |
| Gastrointestinal disorder        | 6          | 3      | 0    | –      |           |

* p < 0.05 participants vs. nonparticipants

Participants (n = 186) Nonparticipants (n = 64) p-value

were subsequently admitted to the PICU. Physical sequelae are defined as any physical complaints or abnormalities found at the outpatient follow-up clinic by physical examination. Since all children were previously healthy, they had no physical complaints or abnormalities until shortly before PICU admission. Thus all residual physical complaints or abnormalities had to be related to either the underlying illness or to complications of PICU procedures.

Study protocol

After discharge from the PICU each family received a letter at home explaining the aim and content of the research program. Families were contacted by telephone to invite participation. In cases of failure follow-up letters with tear-off reply slip inviting participation were sent. Written informed consent was obtained from all participating families.

Three months after discharge, all families were invited to visit the outpatient follow-up clinic for structured medical examination of the child. Follow-up at 3 months after discharge was chosen because of psychological follow-up on posttraumatic stress disorder; the results of this assessment will be reported elsewhere. Structured medical examination was performed by semistructured history taking (current health status, well being, social, cognitive and physical functioning and development) and physical examination by one author (H.K.). Complications from PICU procedures such as scars, upper airway obstruction, postthrombotic syndrome and hypoxic-ischemic injury were structurally evaluated [19, 20]. Since many parents mentioned cognitive and behavioral problems spontaneously, these questions were added to the standard interview. Physical and neurocognitive sequelae found at the outpatient follow-up clinic were categorized into two groups: (a) previously unknown pre-PICU morbidity (e.g., a patient admitted to the PICU because of cyanosis caused by an until then not recognized congenital heart defect), (b) acquired morbidity (e.g., a patient with meningococcal infection, suffering from scars and postthrombotic syndrome following central venous catheterization). Acquired morbidity can be related either to the underlying illness for which PICU admission was necessary (scars due to meningococcal infection), to complications of PICU procedures (postthrombotic syndrome), or to a combination of the two. As no validated questionnaires exist to evaluate physical sequelae, we used PCPC and POPC scores to determine the extent of physical and neurocognitive sequelae. PCPC and POPC were determined at PICU discharge, 3 months after discharge, and retrospectively 24 h before admission to the PICU (baseline values) by one of the authors (H.K.).

Data were analyzed using the Statistical Package for Social Sciences, Windows version 11.5. Mann–Whitney and χ² tests were performed to compare participants and nonparticipants with regard to patient characteristics, reason for PICU admission, and diagnosis at discharge.

Results

Structured history taking at the outpatient follow-up clinic revealed concentration problems (9%), behavioral problems (15%), delayed psychomotor development (13%), temporary voice changes (7%), eating problems (9%),
Table 3 Physical sequelae 3 months after discharge in 186 participants (more than one problem per child possible): pre-PICU morbidity is a previously unknown underlying illness that was diagnosed during PICU admission; acquired morbidity is morbidity in a child that was healthy before PICU admission.

|                                      | Pre-PICU morbidity (n = 55) | Acquired morbidity (n = 73) |
|--------------------------------------|-----------------------------|-----------------------------|
|                                      | n   | %   | n   | %   |
| Respiratory problems                 | 21  | 11  | 23  | 12  |
| Circulatory problems                 | 14  | 8   | 0   | –   |
| Neurological problems                | 6   | 3   | 48  | 26  |
| Metabolic disorder                   | 6   | 3   | –   | –   |
| Miscellaneous problems               | 8   | 4   | 14  | 8   |
| Tracheotomy                          | –   | –   | 3   | 2   |
| Scars                                | –   | –   | 17  | 9   |
| Hoarseness                           | –   | –   | 5   | 3   |
| Postthrombotic syndrome              | –   | –   | 7   | 4   |

sleeping problems (9%), and withdrawal symptoms (9%). In 9 of 40 school-age children problems at school were reported. Structured physical examination revealed abnormalities in weight gain (9%), pulmonary auscultation (9%) and neurological (23%) examination, hoarseness after endotracheal intubation (4%), and postthrombotic syndrome after central venous catheterization (4%) and scars (14%).

Of the 186 patients 128 (69%) had persisting complaints 3 months after discharge and 58 (31%) were healthy. Of the 128 children 55 (43%) had a previously unknown underlying illness (pre-PICU morbidity) that was diagnosed during PICU admission. This included patients with congenital anomalies (congenital heart defect, n = 14; metabolic disorder, n = 4), epilepsy (n = 6), and first-attack asthma patients (n = 13; Table 3).

Seventy-three (57%) children were healthy before PICU admission and had acquired morbidity (Table 3). The complaints in these children were diverse, and some children had a combination of problems. Complaints consisted of (a) pulmonary complaints (after admission due to RSV infection) or upper airway problems (tracheotomy) after endotracheal intubation; (b) neurological or neurocognitive problems caused by among other factors, hypoxic-ischemic brain injury, traumatic brain injury, meningitis, or intracerebral bleeding; (c) scars after meningococcal disease, trauma, operations, pleural drains, and (central) venous lines; (d) hoarseness 3 months after extubation (e) postthrombotic syndrome after central venous catheterization; (f) miscellaneous illnesses such as renal insufficiency, adrenal insufficiency, and gastroenterological problems (Table 3). In at least 15 (8%) children morbidity was related to complications from PICU procedures. In the other 61 children with acquired morbidity it was not possible to differentiate between morbidity related to underlying illness, to complications from PICU procedures, or both (Table 3).

Twenty-four hours before PICU admission 177 of the 186 evaluated children (95%) had in retrospect normal PCPC scores and 135 (73%) normal POPC scores (baseline values). The 9 children (5%) with abnormal PCPC scores and 51 (27%) with abnormal POPC scores had presenting symptoms which were not recognized more than 24 h before PICU admission. Figures 1 and 2 show.

Fig. 1 Pediatric Cerebral Performance Category in 186 evaluated children 24 h before PICU admission, at PICU discharge, and 3 months after PICU discharge. Columns from left to right: black, normal; light gray, mild disability; dark gray, moderate disability; white, severe disability; medium gray coma/vegetative state.

Fig. 2 Pediatric Overall Performance Category in 186 evaluated children. POPC scores 24 h before PICU admission, at PICU discharge and 3 months after PICU discharge. Columns from left to right: black, normal; light gray, mild disability; dark gray, moderate disability; white, severe disability; medium gray coma/vegetative state.
that at discharge 46 children (25%) had normal PCPC scores and 2 (1%) normal POPC scores. Three months after discharge 143 children (77%) had normal PCPC scores and 58 (31%) normal POPC scores. Three months after discharge, respectively, 147 (79%) and 93 children (50%) showed PCPC and POPC scores that were the same or improved compared to scores before admission. In respect 39 (21%) and 93 (50%) children’s scores deteriorated (Figs. 1, 2).

Discussion

This is one of the first studies to report the nature and extent of physical sequelae in PICU survivors. Three months after discharge the evaluation of physical and neurocognitive sequelae in PICU survivors showed that only 31% of the evaluated children were healthy while 30% had a previously unknown underlying illness (pre-PICU morbidity), and 39% an acquired morbidity. In at least 8% of these children morbidity was related to complications from PICU procedures. Upper airway disease and pulmonary and neurological problems accounted for some 50% of persisting complaints. Upper airway disease, consisting of upper airway obstruction after endotracheal intubation, or lower airway disease after RSV infection and asthma was found in 47 of 186 evaluated children.

Neurological and neurocognitive sequelae, consisting of delayed psychomotor development, epilepsy, paralyses, and concentration and behavioral disturbances, were found in 54 of 186 evaluated children. Studies evaluating neurocognitive outcome after PICU survival in a structured way are limited [11, 21–23]. To evaluate the extent of neurocognitive sequelae we used PCPC and POPC scores at discharge and at 3 months’ follow-up. At discharge PCPC and POPC scores in our patients were reduced in, respectively, 73% and 91%. Three months later scores had substantially improved. This leads us to believe that long-term follow-up is necessary to evaluate neurocognitive development by structured psychometric testing. In at least 8% of patients morbidity was associated with complications of PICU procedures. Examples include hoarseness due to mucosal damage after endotracheal intubation and impaired growth of extremities due to vascular damage after central venous catheterization. Neither hoarseness nor impaired growth of extremities was ever mentioned spontaneously. In addition, use of medications (corticosteroids, ototoxic drugs, sedatives, and neuromuscular blocking agents) also may lead to long-term sequelae and were not evaluated [24–27].

A number of limitations may have biased the results of this study. First, a considerable number of children were lost due to nonresponse and refusal. Although other follow-up studies in PICU patients had similar response rates, this may have biased our results [4, 7]. We probably missed a number of patients of whom parents were experiencing psychological problems, such as posttraumatic stress disorder [28–30]. Furthermore, the distinct subgroups of participants were not equally distributed; relatively more trauma patients and children with cardiac disorders are evaluated and fewer children with septic shock. Second, structured history taking by one observer involved in PICU care may have biased our results. Third, participants had significantly longer length of stay and more ventilation days than nonparticipants. This might be associated with an increased number of complications and severity of sequelae. Fourth, follow-up time was only 3 months; therefore conclusions on sequelae over an extended period cannot be drawn. Finally, PCPC and POPC scores have been validated for PICU populations; it remains questionable whether these scores can be used to predict problems in the individual patient.

Despite these limitations we believe that these outcome data of a mixed pediatric and surgical PICU population are important. Our findings are comparable to the few existing studies on physical sequelae in PICU survivors. In an Australian study of 974 children 42% of survivors were normal and 17% functionally normal but required medical supervision. Of the remaining 41% functionally nonnormal survivors 32% will probably be able to lead an independent life [3]. The Health Utilities Index 2 used in four studies showed 27–37% of survivors in full health 1 year after discharge [5–7].

Suggestions for future research

Cohort studies of PICU survivors evaluating patient outcome (physical and neurocognitive sequelae, functional status, and quality of life) are essential. Awareness of long-term sequelae may result in changes in treatment during the acute phase and in supportive programs after discharge [17, 18, 31–33]. Long-term follow-up clinics of PICU survivors and rehabilitation programs in exactly the same manner as in neonatal and trauma patients should be developed to detect, support, and treat children with neurocognitive, developmental, and psychological problems. These programs are expected to improve daily life [34, 35]. Pediatric intensivists should be core-members of the multidisciplinary follow-up team as they are familiar with possible risks and complications of PICU treatment. In addition, notifying complications of PICU procedures may serve as a valuable tool of providing feedback on procedures in the acute phase. Proper cohort studies in a pediatric population should be multidisciplinary, multicenter long-term follow-up studies applying specific measurement tools to evaluate sequelae in different age groups.
Conclusion

PICU survival leads to substantial physical sequelae related to underlying illnesses, complications from PICU procedures, or both. We believe that preferably multicenter, long-term follow-up research in a structured and validated way is warranted in PICU survivors. This should include (a) multidisciplinary evaluation of physical and neurocognitive sequelae of the underlying illness and the intensive care treatment per se and subsequently their impact during growth and development, (b) evaluation of risk factors for sequelae, and (c) support after discharge if needed. To guarantee all this, follow-up is needed for a sufficient and extended period of time after discharge.

Acknowledgements. The authors thank J. H. van der Lee, MD, PhD, Department of Pediatric Clinical Epidemiology, Emma Children’s Hospital, AMC Amsterdam, for advice and statistical expertise.

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