Abstract The development of paediatric intensive care has contributed to the improved survival of critically ill children. Physical and psychological sequelae and consequences for quality of life (QoL) in survivors might be significant, as has been determined in adult intensive care unit (ICU) survivors. Awareness of sequelae due to the original illness and its treatment may result in changes in treatment and support during and after the acute phase. To determine the current knowledge on physical and psychological sequelae and the quality of life in survivors of paediatric intensive care, we undertook a computerised comprehensive search of online databases for studies reporting sequelae in survivors of paediatric intensive care. Studies reporting sequelae in paediatric survivors of cardiothoracic surgery and trauma were excluded, as were studies reporting only mortality. All other studies reporting aspects of physical and psychological sequelae were analysed. Twenty-seven studies consisting of 3,444 survivors met the selection criteria. Distinct physical and psychological sequelae in patients have been determined and seemed to interfere with quality of life. Psychological sequelae in parents seem to be common. Small numbers, methodological limitations and quantitative and qualitative heterogeneity hamper the interpretation of data. We conclude that paediatric intensive care survivors and their parents have physical and psychological sequelae affecting quality of life. Further well-designed prospective studies evaluating sequelae of the original illness and its treatment are warranted.

Keywords Paediatric intensive care unit · Outcome assessment (health care) · Quality of life · Post-traumatic stress disorder · Health status

Abbreviations ARDS adult respiratory distress syndrome CPCCRN Collaborative Pediatric Critical Care Research Network CPR cardio-respiratory arrest HRQoL health-related quality of life HUI health utilities index MAHSC multi-attribute health status classification MOF multi-organ failure PELOD paediatric logistic organ dysfunction PICU paediatric intensive care unit PTSD post-traumatic stress disorder RAHC Royal Alexandra Hospital for Children QoL quality of life

Introduction

The development of paediatric intensive care has contributed to improved survival rates in children with critical illnesses [68, 69]. Consequently, new disease patterns have emerged due to long-term complications and effects of the original illness and its treatment. In addition to survival and morbidity, physical and psychological sequelae, as well as
the quality of life (QoL) in survivors and in their families are important outcome measures.

Historically, outcome research in paediatrics is either based on an age-specific approach, such as follow-up studies of premature infants [41, 72, 73], or on a more disease-oriented approach, such as follow-up studies in survivors of cardiothoracic surgery or trauma [15, 55, 64, 70]. These studies have shown substantial physical, psychological and neurocognitive sequelae, interfering with daily life and normal development. In addition, effects on parents and siblings have been shown [26]. Evaluative research of adult intensive care survivors showed the effect of intensive care treatment per se. Irrespective of the underlying illnesses, sequelae on all domains with effects on QoL were found [2, 19, 58, 75]. In multi-disciplinary paediatric intensive care unit (PICU) populations, reports on outcome are scarce [24, 25].

Based on these observations, we believe that follow-up research of paediatric intensive care survivors and their families is needed to evaluate: (1) physical sequelae and their impact during growth and development; (2) psychological sequelae in patients and their families and their impact on the QoL of patients and family members; and (3) the need for treatment and support after discharge.

The aim of this article is to provide an overview of the available literature concerning the different domains of QoL (i.e. physical, psychological and social functioning) in children surviving paediatric intensive care, including the effect on parents, and to suggest directions for future follow-up research.

Methods

To identify studies eligible for this review, we searched Medline (1966–2006), EMBASE (1974–2006), CINAHL (1982–2006), pre-CINAHL and the Cochrane Library (2006) in March 2006. In the search strategy, all terms mapped to the appropriate MeSH/EMTREE subject headings and “exploded” were used; among them were: paediatric intensive care unit (PICU), septic shock, respiratory insufficiency, meningococcal disease, central venous catheterisation, intubation, physical and psychological sequelae, post-traumatic stress disorder (PTSD), QoL, health status and long-term outcome.

Definitions

Functional health is defined as an individual’s ability to perform normal daily activities, to fulfil usual roles and to maintain health and well-being.

QoL is defined as an individual’s perception of their position in life, in the context of the culture and value systems and in relation to their goals, expectations, standards and concerns [1].

Health-related QoL (HRQoL) is defined as QoL in which a dimension of personal judgement over one’s health and disease is added [21].

Study selection

Studies were selected for review if they met two inclusion criteria: (1) study of a representative population of PICU survivors (defined as a population consisting of medical and/or surgical PICU patients <18 years old) and (2) evaluation of physical sequelae, measurement of QoL or functional health >30 days after PICU discharge. Because of the limited number of studies, the measurement tools did not need to be standardised. Studies with a retrospective and prospective design were included.

Excluded were: (1) studies in homogeneous PICU populations (e.g. survivors of cardiothoracic surgery and trauma) reporting diagnosis-related outcome in particular but not intensive care treatment as such, and (2) studies evaluating mortality only.

Results

Eligible studies and quality of the studies

Twenty-seven studies were found in which one or more aspects of long-term sequelae in PICU survivors and/or their families were described. The patient characteristics, populations, measurement tools and outcomes are described in Tables 1 and 2. The quality criteria are described in Table 3. None of the studies met all of the quality criteria. In studies describing the same outcome aspect, differences in study population, follow-up time and measurement tools make the comparison and synthesis of results difficult.

Physical and neuro-cognitive sequelae (Table 1)

In 12 studies that included in total 340 patients, aspects of physical and neuro-cognitive sequelae were evaluated.

Neurological evaluation was conducted in five studies including 275 survivors. The majority of the children were neurologically normal. In the remaining children, disabilities such as hearing loss, coordination, cognition and developmental problems turned out to be severe [23, 35, 43, 53, 59].

Pulmonary evaluation was conducted in six studies including 65 patients [6, 14, 22, 30, 48, 74]. Restrictive and obstructive disease and hypoxaemia during exercise was found.
| Reference | Population\(^a\), \(n\)^\(b\) | Age\(^c\) (yrs) | Follow-up time\(^d\) (yrs) | Severity of illness\(^e\) | LOS\(^f\) (days) | Measurement tool | Outcome (\(n\)^\(g\)) | Interpretation of outcome |
|-----------|-----------------------------|----------------|-----------------------------|--------------------------|----------------|----------------|--------------------------|--------------------------------|
| 23        | Meningococcal disease \(n=115\) (139) | 0.1–15.3 | 8–12 | GMSPS Median 5 | NA | Neurological examination, Cognitive tests, Audiological test | 1 spastic quadriplegia | Majority of children surviving meningococcal disease neurologically normal. |
| 35        | Cardiopulmonary resuscitation (CPR) \(n=44\) (48) | 0–16 | 1 | NA | NA | PCPC\(^h\) | 60% of survivors of CPR neurologically normal. Location, underlying cause and duration of CPR determinants of outcome. |
| 43        | CPR \(n=65\) (94) | 0–17 | 1 | NA | NA | PCPC\(^h\), POPC\(^i\) | 54 normal or mild disability, 6 moderate, 5 severe disability | 80% of survivors of CPR neurologically normal. Location, underlying cause and duration of CPR not determinants of outcome. |
| 53        | Acquired brain injury \(n=38\) (53) | <3 | >0.5 | GCS<9 | NA | GOS\(^j\), BSID-II\(_k\), Neuro-developmental examination | GOS: 23 good recovery, 7 moderate, 5 severe disability BSID-II: 8 normal, 12 cerebral palsy, 11 cognitive delay | Majority of children with acquired brain injury dead or disabled. |
| 59        | CPR \(n=13\) | 0–18 | 1 | NA | PICU Median 5 | PCPC\(^h\), POPC\(^i\) | 5 normal, 1 mild, 4 moderate, 1 severe disability, 2 persistent vegetative state | 38% of survivors of CPR neurologically normal. Underlying cause and duration of CPR determinants of outcome. |
| 6         | ARDS \(n=7\) (15) | 2–13 | 5.6±4.3 | NA | NA | Chest radiography, Pulmonary function | \(\text{SaO}_2\) 94% during exercise 1 reduced diffusion capacity | ARDS survivors at risk for hypoxaemia during exercise. |
| 14        | Meningococcal disease with ARDS \(n=12\) | 0.3–3.7 | 0.5–2.1 | PRISM 12-53% | NA | Pulmonary function | 1 wheezing for which salbutamol 2 obstructive disease | ARDS survivors possibly at risk for mild obstructive lung disease. |
| 22        | ARDS \(n=9\) (12) | 4.6–15.9 | 0.9–4.2 | NA | NA | Pulmonary function, Electrocardiography, Echocardiography | 3 restrictive or obstructive disease Cardiac function normal in all | ARDS survivors at risk for restrictive and obstructive lung disease. |
| 30        | ARDS \(n=5\) | 5–14 | 4.4 | NA | NA | Pulmonary function | 1 limitations in activity 4 restrictive disease | ARDS survivors at risk for restrictive and obstructive lung disease. |
| Reference | Populationa, nb | Agec (yrs) | Follow-up time (yrs) | Severity of illnesse | LOSf (days) | Measurement tool | Outcome (n)g | Interpretation of outcome |
|-----------|-----------------|------------|---------------------|---------------------|-------------|------------------|-------------|--------------------------|
| 48        | Meningococcal septic shock n=18 | 1.6–15.4 | 2.2–4.9 | NA | NA | Pulmonary function | 18 normal lung function 6 SaO2≤95% during exercise | Meningococcal septic shock survivors at risk for hypoxaemia during exercise. |
| 74        | ARDS n=14 (20) | 0.5–16 | 0.3–5.5 | PRISM 18±14% | NA | Chest radiography Pulse oximetry Pulmonary function Electrocardiography Echocardiography | 7 (11) restrictive or obstructive disease 4 (7) decreased diffusion capacity | ARDS survivors at risk for restrictive and obstructive lung disease. |
| 62        | Meningococcal sepsis with renal replacement therapy n=12 (15) | 0.5–15 | 2.7–7.1 | NA | PICU Median 12 | Glomerular filtration rate (GFR) | 2 decreased GFR, proteinuria, hypertension 1 parenchymal defect 1 proteinuria | Children surviving acute renal failure due to septic shock at risk for long-term renal dysfunction. |
| 9         | Near drowning admitted to PICU n=25 (27) | 0.7–14 | ≥0.5 | PRISM 71% GCS≤5 | NA | Functional health: Contact primary physician or examination by study facility | 8 severe neurological impairment 17 normal or mildly impaired | Majority of near-drowning survivors lead a normal life. |
| 12        | PICU n=775 | 0–18 | 2.5–3 | NA | PICU Mean 2.8 | Functional health: Written questionnaire or telephone contact with the specialist physician or parents | 7% moderate or severe handicap 12% mild handicap 91% will lead independent life | Majority of PICU survivors seem to lead a normal life. |
| 44        | Bacterial meningitis with respiratory insufficiency n=21 (22) | 0–12 | 0.6–6.4 | PRISM Mean 22% Range 1–47% | NA | Functional health: Telephone interview | 12 normal 1 independent 6 dependent 2 partially dependent | Half of children surviving severe bacterial meningitis seem to lead a normal life. |

a Studied population. b n=studied patients (eligible patients). c Age of patients at admission to PICU (mean±SD or range). d Follow-up time (mean±SD or range). e Severity of Illness (PRISM, Glasgow Coma Score (GCS), Glasgow Meningococcal Septicaemia Prognostic Score (GMSPS) and/or parent rating). f Length of stay (LOS) in PICU and/or hospital (mean±SD or range). g n=examined patients (eligible patients) h PCPC=Paediatric Cerebral Performance Category. i POPC=Paediatric Overall Performance Category. j GOS=Glasgow Outcome Scale. k BSID-II=Bayley Scales of Infant Development-II
| Reference | Population, n | Age (yrs) | Follow-up time (yrs) | Severity of illness (% of risk) | LOS (days) | Measurement tool | Outcome (n) | Interpretation of outcome |
|-----------|---------------|-----------|---------------------|--------------------------------|------------|------------------|------------|--------------------------|
| 40        | PICU children and mothers n=29 (33) | 2.1–15.9 | 0.3–1 | PRISM 0.4–76% | PICU 1–30 | Psychological outcome: Child: Behaviour Check List, SDQ, IES, CHLOC | Children: Behaviour high 3 (8), SDQ high 3 (21), IES PTSD 3 (29) | PICU survivors and their mothers at risk for psychological distress and PTSD. |
| 50        | PICU n=35 (46) General ward n=33 (41) | 5–18 | Median 0.6 | Parent rating 10 | Hospital 4–14 | Psychological outcome: Child: PTSD, SDQ, IES, depression, anxiety, CST, Parent: GHQ, IES | Children: PTSD 4 (19) PICU, 0 (27) ward IES high 4 (21) PICU, 2 (17) ward | PICU survivors and their parents at risk for psychological distress and PTSD. |
| 51        | PICU n=60 (69) General ward n=60 (69) | 11.3±3.2 | 0.5 | PRISM 25±3% | Hospital 13.0 | Psychological outcome: Children: IES, CMFS, CHLOC | IES and CMFS dependent on invasive procedures, CMFS and CHLOC on age | Stress symptoms in children possibly dependent on number of invasive procedures. |
| 52        | PICU n=60 | Mean Low risk 11.5 | 0.5 | PRISM Low risk<34% | NA | Psychological outcome: Children: IES, CMFS, CHLOC | IES higher in high risk, not decreasing over time, IES related with invasive procedures | Stress symptoms possibly dependent on invasive procedures. Stress symptoms not decreasing over time. |
| 61        | Meningococcal disease PICU and ward Children and parents n=78 (118) | Median 6.8 | 0.3 | GMSPS 6.9±3.3 | PICU LOS 0–62 | Psychological outcome: Child: SDQ, IES, Parent: GHQ, IES | Child: PTSD 4 (26) Mothers: PTSD 22 (58) Fathers: PTSD 8 (43) | PICU survivors and their parents at risk for psychological distress and PTSD. |
| 4         | PICU parents n=272 (291) | 25% <1, 25% 1–4, 25% 5–11, 25% >11 | 0.2–0.9 | PRISM 0–26% | PICU 1–200 | Psychological outcome: Parents: Acute Stress Disease symptoms PTSD symptoms | ASD 87 PTSD 33 | Parents of PICU survivors with ASD more at risk for PTSD. |
| Reference | Population<sup>a, b</sup> | Age<sup>c</sup> (yrs) | Follow-up time<sup>d</sup> (yrs) | Severity of illness<sup>e</sup> | LOS<sup>f</sup> (days) | Measurement tool | Outcome (<i>n</i>)<sup>g</sup> | Interpretation of outcome |
|-----------|--------------------------|----------------------|-------------------------------|-----------------------------|----------------------|-----------------|---------------------|-----------------------------|
| 8         | PICU 1.2±1.3             | <0.5                 | PRISM 12±7%                   | PICU 10.5±11.5               | Psychological outcome mothers: Parental Stress Scale SCL-90-R<sup>h</sup> | Mothers PICU more stress. Stress decreases over time in all groups | Mothers of PICU survivors at risk for psychological distress; families at risk for dysfunctioning. |
| 20        | Meningococcal Disease Parents 1.8–18 0.25–7 NA NA | Psychological outcome parents: GHQ<sup>i</sup> | High psychological distress in mothers and fathers, not decreasing over time | Mothers and fathers of PICU survivors at risk for psychological distress. |
| 27        | PICU 4.6                 | 1                    | PRISM 223 <5%                 | NA                           | QoL: MAHSC<sup>c</sup> | 106 equal to before PICU 58 improved 62 deteriorated | 50% of PICU survivors seem to have the same QoL as before admission; 10% normal QoL. |
| 38        | PICU 5.7±3.6             | 1                    | PRISM 79 <5%                  | PICU 5.7±5.5                  | QoL: MAHSC<sup>c</sup> | 26 normal 52 improved 29 deteriorated | 50% of PICU survivors seem to have good QoL. |
| 47        | PICU Median 2.3          | 0.3–2                | PRISM Mean 5.5                | NA                           | QoL: RAHC<sup>o</sup> measure of function | 65 normal after PICU 256 normal QoL 140 fair QoL 9 poor QoL | 60% of PICU survivors seem to have normal QoL. |
| 65        | PICU 0–29.3              | 2.3–6                | PRISM 554 <5%                 | PICU 0–57.4                   | QoL: HSUI GOS<sup>α</sup> | HSUI (727): 608 normal, 29 (very) poor QoL GOS (727): 515 normal, 137 mild disability, 75 moderate/severe disability | 70% of PICU survivors seem to have good QoL. 60% seem to have normal functional health. |

<sup>a Studied population. b</sup> <i>n</i>=studied patients (eligible patients). <sup>c</sup> Age of patients at admission to PICU (mean±SD or range). <sup>d</sup> Follow-up time (mean±SD or range). <sup>e</sup> Severity of illness (PRISM, Glasgow Coma Score, GMSPS and/or parent rating). <sup>f</sup> Length of stay (LOS) in PICU and/or hospital (mean±SD or range). <sup>g</sup> <i>n</i>=examined patients (eligible patients).<sup>h</sup> SDQ=Strength and Difficulties Questionnaire. <sup>i</sup> IES=Impact of Event Scale. <sup>j</sup> GHQ=General Health Questionnaire. <sup>k</sup> PTSD=Post-traumatic stress disorder. <sup>l</sup> CSI=Child Somatization Inventory. <sup>m</sup> CMFS=Child Medical Fears Scale. <sup>n</sup> CHLOC=Child Health Locus Control Scale. <sup>o</sup> SCL-90-R=Symptom Checklist-90 Revised. <sup>p</sup> FAM III=Family Assessment Measure III. <sup>q</sup> FILE=Family Inventory of Life Events and Change. <sup>r</sup> MAHSC=Multi-attribute health status classification. <sup>s</sup> RAHC=Royal Alexandra Hospital for Children. <sup>t</sup> HSUI=Health State Utility index. <sup>u</sup> GOS=Glasgow Outcome Score.
Cardiac evaluation was conducted in two studies including 23 survivors [22, 74]. No abnormalities were found, except for left ventricular hypertrophy in one child.

Renal evaluation was conducted in one study including 12 survivors [62]. In two children, glomerular filtration was impaired, one had hypertension and one had proteinuria.

Psychological sequelae (Table 2)

Various questionnaires were used. Cut-off points for the diagnosis of PTSD differed between studies but all of them showed high scores for PTSD in children and parents.

Psychological evaluation of children was conducted in five studies including 202 children [40, 50–52, 61]. Symptoms of PTSD were found in 11 of 74 evaluated children. In one study, a relation was found between invasive procedures and high scores [52].

Psychological evaluation of parents was conducted in six studies including parents of 547 children [4, 8, 20, 40, 50, 61]. Symptoms of PTSD were found in 72 of 295 evaluated parents. In some studies, a relation was found between high scores and illness severity as perceived by parents [4, 50, 61]. In one study, these high scores decreased over time [8].

Functional health and QoL (Tables 1 and 2)

Evaluation of functional health was conducted in three studies including 821 children [9, 12, 44]. The majority of the children seemed to have normal functional health; the remainder was found to be seriously impaired.

Evaluation of QoL was conducted in four studies including 1,664 children [27, 38, 47, 65]. QoL was evaluated using three different questionnaires. In the majority of children, the QoL was normal or equal to the QoL before PICU admission. In all studies, some of the children had poor QoL.

Discussion

Only 27 studies consisting of 3,444 PICU survivors met our inclusion criteria. The small numbers, heterogeneity of the
studied populations and the used measurement tools, the frequent use of non-validated measurement tools and the various aspects of outcomes studied make aggregation of the data and, therefore, strong conclusive statements difficult.

Physical sequelae

The reviewed studies report distinct physical sequelae, including neurological abnormalities in PICU survivors. Standardised neurological examination of PICU survivors was validated in 1994 but very few studies have been carried out since [24, 25]. As neurological problems have a great impact on daily life, standardised evaluation and adequate support and rehabilitation seem to be relevant, similar to in NICU survivors [11, 46, 56].

Follow-up studies evaluating lung function in children are hampered by the small incidence of severe respiratory insufficiency in children [49]. In adult respiratory distress syndrome (ARDS), the recovery of lung function is shown during the first year and physical limitations seem to be partly dependent on lung function [34, 58]. In infants and children, post-natal lung growth may contribute to the improvement of lung function after critical illness. In addition to lung function, the long-term effect of small airway disease should be evaluated, for instance, in children with respiratory syncitial virus infection.

Data on the structured evaluation of cardiac and renal function in paediatric and adult ICU survivors is not available. In young children, septic shock and the need for vasoactive support of the circulation may interact with the developing myocardium and may have persistent effects on cardiac growth and function [10, 67, 77].

Complications of intensive care procedures per se, (e.g. vascular complications due to intra-vascular catheters and side-effects of ototoxic drugs and sedatives) are not evaluated [5, 18, 32, 33, 45, 54, 57, 63]. One can assume the exact incidence of physical sequelae to be higher than has been reported so far.

Psychological sequelae and functional health and QoL

In the reviewed studies, psychological sequelae have been established in 10–14% of survivors and their parents. The comparison of findings is hampered due to different measurement tools and cut-off points for the diagnosis of PTSD and various follow-up intervals. Risk factors accounting for hampered psychological outcome could be diverse (severity of illness, being removed from one’s child, having been witness to the accident, mental health, family functioning, social support, coping strategies and lack of information from the medical team) [17, 26, 29, 31]. Psychological support to improve coping strategies and prevent over-protection might improve psychological outcome in children and parents [3, 28]. Further research is essential to establish the appropriate time and extent of the psychological support needed.

Cognitive sequelae have rarely been studied in the reviewed studies. Adequate neuro-cognitive evaluation is both expensive and time-consuming. Studies in neonatal ICU survivors show substantial cognitive dysfunction with great impact on daily life [7]. Consequently, early intervention, education and rehabilitation are expected to improve daily life [11, 46].

A majority of PICU survivors seem to have unchanged functional health and good QoL. In the reviewed studies, functional health is evaluated by telephone interviews [27, 38, 47, 65]. In most of these studies, the physician rather than the child or its parents evaluates functional health. Ideal (HR)QoL questionnaires should measure all aspects of QoL and preferably be filled in by the children themselves. Proxy investigation of functional health and (HR) QoL (in children <6–8 years of age) is second best [36, 37, 39, 66]. Besides, the pre-morbid state is probably an important factor which is difficult to assess [16].

Suggestions for future follow-up research

The reviewed studies have a number of methodological limitations. Heterogeneity is the most important one. Consensus on all aspects of follow-up research is essential for well-founded conclusions. For example, structured and standardised evaluation of: (1) organ system function with a validated tool such as the Paediatric Logistic Organ Dysfunction (PELOD) score [13, 42, 60, 71]; (2) neuro-cognitive function; (3) complications of PICU treatment; and (4) (HR)QoL are warranted. Multi-centre studies as proposed by the Collaborative Pediatric Critical Care Research Network (CPCCRN) with a uniform approach will provide answers either in general PICU cohorts or in disease-oriented study groups [76].

In conclusion, this review indicates that PICU survivors and their parents may have substantial physical and psychological sequelae interacting with QoL. Because of longer life expectancy, longer follow-up time is warranted, emphasising the consequences for health care in children. We believe that paediatric intensivists and psychologists should be involved as core members of follow-up teams.

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