

LETTER



Research priorities in pediatric onco-critical care: an international Delphi consensus study

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Dear Editor,

Up to 40% of pediatric cancer patients require admission to PICU during the course of their disease, with acute respiratory failure and sepsis as the main admission reasons [1–3]. Further intensification, as well as development of novel strategies such as immunotherapy, may potentially increase the need for intensive-care admission and support. A recent review on current standard of care for critical care delivery to adult cancer patients and major recent advances in this field has shown the importance of new clinical perspectives such as time-limitation in PICU treatment trials, the value of using surveillance strategies for earlier admission to ICU, and the value of starting chemotherapy in high-risk patients while providing advanced supportive care on the ICU [4]. However, scarce data are available on the optimal standard of critical care delivered to the pediatric cancer patient group, nor are systematic multi-center outcome data available.

Recognizing the need for international collaboration on this issue, the European Society for Paediatric and Neonatal Intensive Care (ESPNIC) established, in collaboration with pediatric oncologists, the PICU Oncology Kids in Europe Research group (POKER), with the aim to design international optimal common harmonized care and a research agenda for the next decade, to ultimately improve the outcomes of children with cancer admitted to PICU.

As a first step, we conducted a three-round modified Delphi consensus process among pediatric intensivists

and pediatric oncologists in Europe from October 2018 to April 2019 [5]. Detailed information on the Delphi methodology is provided in the electronic supplementary material (ESM_1). An anonymous questionnaire was distributed online via SurveyMonkey. One hundred and seventy-two (59% intensivists and 34% oncologists) and one hundred and fifty-seven physicians (53% intensivists and 38% oncologists) from 13 different countries participated in rounds 1 and 2, respectively (Table S1, ESM_3). POKER consortium members drafted ten candidate research topics (Questionnaire round 1, ESM_2). Participants rated these topics using a 4-point scale (Table S2, ESM_3). Research topics meeting the a priori consensus thresholds for >80% high priority were included in round 2, complemented with additional research topics suggested by participants, resulting in a total of 15 topics (Questionnaire round 2 ESM_2). Round 2 yielded consensus on high priority topics (Table S3, ESM_3), which were ranked based on the mean of each item's ranking by POKER members in round 3 to create a final top five (Table 1). The following research topics were identified as top priorities: (1) optimal timing of the use of life-sustaining therapies; (2) development of specific oncological early warning scores; (3) role of non-invasive ventilation in acute respiratory insufficiency; (4) end-of-life care and ethical issues; and (5) sepsis. Rational, current knowledge, and existing areas of uncertainties of these topics are provided in the ESM_4.

The results of this Delphi study indicate a broad consensus among providers from different subspecialties and across Europe on the research priorities for pediatric onco-critical care. In the context of limited published evidence, these results create a framework for the top research priorities in the field

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Table 1 Consensus research priorities in pediatric onco-critical care

Top five research priorities ranked in order	Suggestions for future studies	Suggested future endpoints
1. Determine the optimal timing of the use of life-sustaining therapies (mechanical ventilation, use of vasopressors, CRRT, and ECMO) and identify agreements and controversies between the different clinicians (intensivists and oncologists) and parents at the PICU on the futility or non-futility of these therapies in critically ill pediatric cancer patients	Prospective, observational studies to stratify life-sustaining therapies by days of PICU treatment and outcome to determine the optimal time for a time-limited "PICU-Trial" of therapy	PICU mortality Degree of organ dysfunction measured by daily Pediatric Logistic Organ Dysfunction (PELOD) score Length of PICU stay
2. Development of specific early warning scores to timely recognize critically ill pediatric cancer patients on the non-ICU ward requiring intensive care support	Prospective, multi-center study to develop specific oncological pediatric early warning score consisting of the clinical signs most predictive for critical deterioration requiring PICU admission and treatment	Transfer to PICU Use of life-sustaining therapies such as mechanical ventilation, vasopressors, renal replacement therapy, and ECMO PICU- and hospital mortality Length of PICU stay
3. Determine the role of non-invasive ventilation in acute respiratory insufficiency in critically ill pediatric cancer patients	A multicenter randomized-controlled trial of the (early) use of non-invasive ventilation or high-flow nasal cannula versus standard care in acute hypoxemic respiratory failure	Need for intubation PICU mortality
4. Exploring end-of-life care and ethical issues for children with cancer at the PICU, i.e., change to end-of-life care, ethical considerations regarding decision making, communication with patients and parents, 'suffering' in pediatric cancer patients and their families on PICU, young people decision making in oncology	Qualitative studies to examine the quality of collaborative decision making from the perspective of physicians, nurses, and families	Qualitative measurement of parents, oncologist and PICU physicians' feelings and acceptance of the discussion and eventual decision (e.g. moral distress in PICU teams) Formalization of time limited trials of therapy and innovative and experimental therapy use in PICU End-of-life choices in PICU (parent and child)
5. Sepsis in critically ill pediatric cancer patients at the PIC: management, outcomes, and costs	Multicenter, clinical trials with prospectively collected data to delineate those factors that predispose pediatric cancer patients to sepsis, and to identify factors that stratify their outcome	PICU admission PICU- and hospital mortality Factors predicting sepsis development Requirement of life sustaining therapies (MV, vasopressors, CRRT) Length of PICU stay

CRRT continuous renal replacement therapy, ECMO extracorporeal membrane oxygenation, MV mechanical ventilation, PICU pediatric intensive-care unit

of pediatric cancer patients at PICU for the next 10 years.

Electronic supplementary material

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Compliance with ethical standards

Conflicts of interest

The authors declare that they have no competing interests.

Ethical approval

The study was approved by the Institutional Ethical Review Board of the University Medical Center Utrecht (METC reference number 19-223/C). Consent of participants was implied when they responded to the survey via the survey portal and checked a box on the survey instrument indicating consent to participate.

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