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Extracorporeal membrane oxygenation in children with COVID-19 and PIMS-TS during the second and third wave

During the first wave of the COVID-19 pandemic, the European Extracorporeal Life Support Organization (ELSO) established a prospective survey[1] including 52 European neonatal and paediatric centres and reported the use of extracorporeal membrane oxygenation (ECMO) in seven children with acute respiratory distress syndrome (ARDS) related to COVID-19 and paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 (PIMS-TS; also known as multisystem inflammatory syndrome in children). All European neonatal and paediatric ECMO centres affiliated with ELSO were included in the survey. Non-ELSO centres were also invited and included as representation for neonatal and paediatric ECMO centres in their respective country. The study was approved by the Maastricht University Ethical Committee (the coordinating centre) and registered at ClinicalTrials.gov (NCT04366921). Data were collected once per week and were reported as anonymised and deidentified using password-protected datasheets, and hence individual parent and patient consent was waived.

This survey[1] highlighted the low use of ECMO in children compared with adults[2,3] (seven children *vs* 1531 adults), with similar survival to hospital discharge rates (57% in children *vs* 55% in adults).[2,3] The survey continued to capture contemporaneous data on ECMO use during the second and third waves of the pandemic, which we report now. Between July, 2020 and December, 2021, 24 children (<18 years) from nine countries (appendix p 1) were supported with ECMO for COVID-19. The predominant indication for ECMO was severe ARDS (n=18, 75%) followed by shock associated with PIMS-TS (n=5, 21%) and COVID-19 myocarditis (n=1, 4%). The median age was 9 years (range 11 days to 17 years) and 13 children (54%) had comorbidities. Comorbidities were more prevalent in children with ARDS than with PIMS-TS (appendix p2). The median time from the onset of symptoms to ECMO was 8·5 days (IQR 6·3–16·3, range 2–49) and it was not significantly different between children with ARDS and PIMS-TS (9·5 [6·5–17·3] in ARDS *vs* 7·0 [6·5–14·5] in PIMS-TS; Mann-Whitney U test p=0·59).

In the 18 children with ARDS, the median oxygenation index was 30 (range 22–48), similar to the one reported during the first wave.[1] Several adjunctive respiratory therapies were attempted in patients with ARDS before the initiation of ECMO: prone positioning (n=14, 78%), inhaled nitric oxide (n=13, 72%), high-frequency oscillatory ventilation (n=8, 44%), and surfactant therapy (n=1, 5%). In the five children with PIMS-TS and in the one child with COVID-19 myocarditis supported for cardiogenic shock, the median vaso-active inotropic score was 66·5 (range 17–270) and the median lactate concentration was 12 mmol/L (range 9–16). Children with PIMS-TS had high concentrations of inflammatory proteins pre-ECMO: C-reactive protein, 26·9 mg/dL (range 22–60); ferritin, 912 ng/mL (range 501–5264); and fibrinogen, 350 mg/dL (range 320–929), consistent with previous reports.[4,5] COVID-19 myocarditis was confirmed with a cardiac biopsy. In contrast with adult COVID-19-related ARDS, the median concentrations of D-dimer (2 µg/mL [0·90–32]) were not consistently high in all children with ARDS.[6]

The ECMO method was veno-arterial ECMO in 11 of 24 children (46%), veno-venous ECMO in 12 children (50%), and venoveno-arterial in one child (4%; appendix p 3). Surgical cannulation was done in 19 children (79%), and percutaneous cannulation in only five children (21%). Most patients with COVID-19 ARDS were managed with veno-venous ECMO (single site cannulation with a dual lumen cannula or multisite cannulation with two single cannulas); veno-arterial ECMO for COVID-19 ARDS was used only when the jugular or femoral veins were considered too small to accommodate a venous cannula or in the case of concomitant cardiac dysfunction. Of 11 patients with veno-arterial ECMO, two (18%) required left heart decompression with atrial septostomy and one (9%) was converted to veno-venous after an improvement in cardiac function. All children were managed with lung rest settings in a pressure-controlled mode and variables ranged from a median tidal volume of 3 mL/kg (range 1–6), a respiratory rate of 15 breaths per min (range 13–20), a positive end-expiratory pressure of 10 cmH_2O (range 5–15), and a FiO_2 of 0·40 (range 0·30–0·55). All children were anticoagulated with unfractionated heparin with standard targets.

All children received steroids; and other anti-inflammatory therapies were used variably (appendix p 3). Renal replacement therapy was used in eight of 24 children (33%).

The median ECMO duration was 10 days (range 4–51) and median intensive care unit stay was 55 days (range 20–120). Patients with PIMS-TS had a shorter ECMO duration (15·0 [7·7–22·5] for ARDS *vs* 4·0 [4·0–6·5] for PIMS-TS; Mann-Whitney U p=0·004) and a shorter intensive care unit stay (20·5 [15·8–30·5] for ARDS *vs* 9·0 [8·5–14·0] for PIMS-TS; Mann-Whitney U p=0·003) than did patients with ARDS. Complications reported during ECMO included: pneumothorax, pulmonary haemorrhage, gastrointestinal or multisite bleeding, and brain infarction. 23 patients (96%) survived and were discharged from hospital. The only death

Published Online
March 3, 2022
https://doi.org/10.1016/S2352-4642(22)00065-7

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See Online for appendix

(from multiorgan failure) was in a patient with a SARS-CoV-2 infection after haematopoietic stem cell transplantation for severe combined immunodeficiency.

This survey has several limitations. Despite reaching out to all European ECMO providers, we might not have captured all centres in Europe. The data are observational, with a low number of patients and no control group. There was no standardised criteria for initiating and managing ECMO in children with COVID-19 and no data on long-term outcomes.

Nevertheless, we found that the use of ECMO in children with COVID-19 in Europe is still low, but survival after hospital discharge increased compared with the first wave (96% in the second and third waves *vs* 57% in the first wave),[1] which might be explained by a better patient selection and understanding of the management of critical illness in children with COVID-19. Patients with PIMS-TS had a higher inflammatory profile compared with patients with ARDS, and children with COVID-19 critical illness had a higher rate of ECMO survival to hospital discharge than adults (96% in children *vs* 55% in adults).[2,3]

MDN and RL are advisers for Eurosets. LMB is an adviser for Eurosets and Xenios. RL is also a consultant for Medtronic, Getinge, LivaNova, and Abiomed. All other authors declare no competing interests. We thank the EuroELSO Steering Committee and all centres who participated in this survey (list included in the appendix).

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