

Extracorporeal carbon dioxide removal integrated into continuous renal replacement therapy for pediatric patients with ARDS and AKI: a retrospective single-center analysis

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Abstract

Objective: To evaluate the feasibility, physiological effects, and safety of integrating extracorporeal carbon dioxide removal (ECCO₂R) into an already indicated continuous renal replacement therapy (CRRT) circuit in pediatric patients with acute respiratory distress syndrome (pARDS) and acute kidney injury (AKI), with the aim of facilitating lung-protective ventilation.

Design: Retrospective single-center observational study.

Setting: Tertiary pediatric intensive care unit.

Patients: Eight pediatric patients with pARDS and AKI requiring CRRT who underwent ECCO₂R between November 2023 and November 2025. ECCO₂R was added to the existing CRRT circuit as a pragmatic adjunct to optimize ventilatory management and was not intended as an alternative to venovenous extracorporeal membrane oxygenation (vvECMO), which was considered independently according to multidisciplinary clinical assessment.

Interventions: None.

Measurements and Main Results: A total of 11 ECCO₂R-CRRT runs were performed over 141 treatment days. Median age was 12 years (interquartile range [IQR] 6.3–14.8), and median baseline oxygenation index was 29 (IQR 5–49). ECCO₂R was delivered at a median blood flow of 300 ml/min (IQR 200–300), corresponding to 10% (IQR 8–19) of estimated cardiac output. Within 24 hours, significant reductions were observed in peak inspiratory pressure (36 to 26 mbar, $p = 0.001$), driving pressure (28 to 17 mbar, $p = 0.001$), tidal volume (4.7 to 2.9 mL/kg ABW, $p = 0.027$), paCO_2 (75 to 61 mmHg, $p = 0.019$), and ventilation index (71 to 44, $p = 0.01$). Oxygenation parameters and vasoactive support did not significantly change. Four patients (50%) were successfully weaned from ECCO₂R-CRRT. No major adverse events, especially clinically significant bleeding or hemolysis, were observed; membrane clotting requiring circuit change occurred in three of eleven runs.

Conclusions: In this single-center cohort, ECCO₂R integrated into a CRRT circuit was feasible in carefully selected pediatric patients with ARDS and AKI. This approach may be particularly relevant in patients already requiring CRRT, enabling carbon dioxide removal without additional vascular access and facilitating lung-protective ventilation. ECCO₂R integrated into CRRT represents a pragmatic adjunct to an already indicated extracorporeal therapy rather than a substitute for vvECMO, for which patient selection should continue to be based on multidisciplinary clinical assessment. ECCO₂R-CRRT was associated with consistent improvements in ventilatory parameters without major safety signals. These findings provide preliminary evidence supporting this integrated strategy; prospective multicenter studies are needed to further define its safety, efficacy, and optimal patient selection.

Introduction

Acute respiratory distress syndrome (ARDS) and acute kidney injury (AKI) frequently coexist in critically ill children and are independently associated with increased morbidity and mortality, especially in the case of fluid overload, which independently increases mortality (1–3). Their concurrence reflects shared pathophysiological mechanisms, including systemic inflammation, endothelial dysfunction, capillary leak, and hemodynamic instability, resulting in bidirectional lung–kidney crosstalk and progression toward multiorgan failure. Mechanical ventilation itself contributes to renal injury through alterations in intrathoracic pressure, neurohormonal activation, and inflammatory mediator release, while AKI exacerbates pulmonary edema and acid–base disturbances, further complicating ventilatory management (4–6). Hence, the combination of respiratory and renal support is a common challenge in pediatric intensive care.

Lung-protective ventilation using low tidal volumes and limitation of plateau, peak inspiratory and driving pressures remains the cornerstone of ARDS management and the only intervention consistently associated with improved survival (7, 8). However, escalation toward ultraprojective ventilation is frequently limited by hypercapnia and respiratory acidosis. Extracorporeal carbon dioxide removal (ECCO₂R) selectively removes CO₂ from the blood, thereby decoupling carbon dioxide clearance from mechanical ventilation and enabling reductions in tidal volume, driving pressure, and minute ventilation without compromising gas exchange (9).

In adult patients, ECCO₂R has been evaluated in observational studies, randomized trials, and meta-analyses. A recent systematic review and meta-analysis by Stommel et al. demonstrated consistent reductions in PaCO₂, tidal volume, plateau pressure, and driving pressure across heterogeneous populations with acute respiratory failure, including ARDS, although no mortality benefit was observed and complication rates varied by device type and blood-flow strategy (10). Earlier analyses similarly reported reliable physiological effects but raised concerns regarding bleeding and device-related adverse events (11). The REST trial, the largest randomized controlled trial to date, showed no mortality benefit of ECCO₂R-facilitated ultraprojective ventilation and reported increased rates of serious adverse events, particularly bleeding, highlighting the importance of careful patient selection (12).

Patients with combined ARDS and AKI represent a distinct subgroup in whom ECCO₂R may be particularly advantageous. In contrast to venovenous extracorporeal membrane oxygenation (vvECMO), which requires high extracorporeal blood flows, large-bore cannulation, and a dedicated extracorporeal circuit to provide full gas-exchange support, ECCO₂R operates at substantially lower blood flows and provides partial respiratory support focused on CO₂ removal (13, 14). When integrated into a continuous renal replacement therapy (CRRT) platform, ECCO₂R can be delivered using an already existing extracorporeal circuit, avoiding additional vascular access and minimizing extracorporeal blood volume and circuit complexity. This combined ECCO₂R-CRRT approach is particularly attractive in patients who already require renal support (9, 15).

Importantly, certain pediatric populations are poor candidates for vvECMO despite severe respiratory failure. Children following hematopoietic stem cell transplantation and/or with invasive fungal

pulmonary infections are at high risk for bleeding, infection, and poor outcomes on ECMO, often rendering full extracorporeal life support contraindicated. The same applies to patients with a highly likely life-limiting conditions. In these circumstances low-flow venovenous ECCO₂R may offer meaningful physiological benefit by facilitating lung-protective ventilation while avoiding the risks associated with high-flow ECMO circuits, particularly when CRRT is already indicated (16–19).

Despite growing adult experience, pediatric data on ECCO₂R remain extremely limited and are restricted to case reports and small case series, precluding robust conclusions regarding safety, efficacy, and patient selection (20–22). Moreover, the multiECCO₂R gas-exchange membrane is approved for use in adult patients above a body weight of 40 kg only; its application in smaller pediatric patients represents a use outside the device's approved labeling (23). Given these knowledge gaps, systematic reporting of pediatric ECCO₂R experience is urgently needed.

The present study reports our single-center experience with venovenous ECCO₂R using the multiECCO₂R device integrated into a CRRT circuit in pediatric patients with ARDS and AKI, focusing on feasibility, ventilatory effects, and safety. We hypothesized that this integrated approach represents a pragmatic adjunct to an already indicated CRRT therapy that facilitates lung-protective ventilation by improving carbon dioxide clearance, rather than serving as an alternative to vvECMO, for which patient selection should remain based on multidisciplinary clinical assessment.

Methods

Study design: This is a retrospective study that included all patients treated with ECCO₂R-CRRT (Fresenius multiECCO₂R blood gas exchanger) between November 2023 and November 2025 at our tertiary pediatric intensive care unit (PICU).

The multiECCO₂R blood gas exchanger is intended for use in adults (> 18 years with body weight > 40 kg) in combination with renal replacement therapy using a CRRT platform. The described therapy in pediatric patients was performed following interdisciplinary consensus and in accordance with institutional guidelines for emergency use. The patients and/or their legal guardians were informed and approved this use outside the currently approved indication.

All patients suffered from ARDS (diagnosis according to the second Pediatric Acute Lung Injury Consensus Conference guidelines) (24) and AKI requiring dialysis. The indication for CRRT was based on clinical judgement and usually because of relevant fluid overload, to reduce ventilator requirements.

ECCO₂R was considered in pediatric patients with ARDS and hypercapnic respiratory failure despite optimized conventional ventilatory management who also required CRRT for acute kidney injury and/or fluid management. In these patients, ECCO₂R was integrated into the existing CRRT circuit as a pragmatic strategy to facilitate lung-protective ventilation without the need for additional vascular access or a separate extracorporeal support platform. Eligibility for vvECMO was determined independently according to institutional multidisciplinary assessment. In all patients, vvECMO was not

pursued because the anticipated risks were considered to outweigh the potential benefits in the context of underlying comorbidities, overall prognosis, and/or irreversible pulmonary injury.

Intervention: The multiECCO₂R blood gas exchanger features a membrane lung surface area of 1.35 m² and the priming volume is 100 ml. It can be integrated into a CRRT platform downstream of the hemofilter, facilitating the simultaneous treatment of patients with ARDS and acute kidney injury (ECCO₂R-CRRT) (Fig. 1).

This licensed medical device is intended for extracorporeal carbon dioxide removal and is designed for supporting the management of patients with respiratory dysfunction in combination with CRRT using a single extracorporeal circuit thereby limiting invasiveness (ECCO₂R-CRRT). According to our local practice CRRT was started after establishing a double lumen vascular dialysis cannula (Shaldon catheter). Anticoagulation for CRRT was either performed systemically with unfractionated heparin or regional by using a trisodium citrate solution. Patients were treated in the continuous venovenous hemodialysis (CVVHD) setting using the multiFiltrate device (Fresenius Medical Care, Bad Homburg, Germany).

During CRRT, the following laboratory parameters with corresponding therapy thresholds were regularly monitored and therapy adjusted accordingly: hemoglobin > 8 g/dl, platelet count > 50 G/l, fibrinogen > 100 mg/dl, Anti-Xa-activity 0.3–0.5 U/l.

Data collection: We gathered demographic data, disease history and admission diagnosis of all patients.

The Pediatric Risk of Mortality (PRISM) III was calculated using an online calculator (<https://www.cpccrn.org/calculators/prismiiicalculator/>) (25).

ECCO₂R data were collected, including indications, configuration (blood flow, gas flow, anticoagulation), and arterial blood gases as well as mechanical ventilation settings, Oxygenation Index (OI), Ventilation Index (VI) and Vasoactive Inotropic score (VIS) at the beginning of the therapy and at 1, 6 ($\pm$ 1), 12 ($\pm$ 2), and 24 ($\pm$ 2) hours after initiation. We also included an analysis of the blood gases and ventilation settings at a later time point than 24 hours of therapy (Δ T) to show the effectiveness beyond this time period. Therefore, we analyzed the parameters 7 days after initiation of ECCO₂R or 24 hours before discontinuation of ECCO₂R, if therapy was shorter than 7 days.

Furthermore, we documented the occurrence of adverse events associated with the extracorporeal CRRT circuit and ECCO₂R device, including device failure (clotting of the blood gas exchanger with a need for replacement), hemolysis (increase in LDH and/or bilirubin), thrombembolic events, bleeding events as well as infectious complications.

Platelet and red blood cell (RBC) transfusion requirements were assessed by comparing the mean number of transfusions per day before and after initiation of ECCO₂R-CRRT. To ensure comparable observation periods, the duration of each ECCO₂R-CRRT run was used to define the pre-treatment

observation period. Thus, transfusion requirements during ECCO₂R-CRRT were compared with those during an equally long period immediately preceding ECCO₂R initiation. For treatment runs lasting longer than 7 days, transfusion requirements during the first 7 days of ECCO₂R-CRRT were compared with those during the 7 days before ECCO₂R initiation.

The calculation of OI, VI, and VIS was performed as follows:

$OI = [FiO_2 * P_{aw} \text{ (mean airway pressure)} * 100] / PaO_2$ and

$VI = [PaCO_2 * PIP \text{ (peak inspiratory pressure)} * RR \text{ (respiratory rate)}] / 1000$

$VIS = [Dopamine \text{ dose } (\mu g/kg/min)] + [Dobutamine \text{ dose } (\mu g/kg/min)] + [100 * Noradrenaline \text{ dose } (\mu g/kg/min)] + [100 * Adrenaline \text{ dose } (\mu g/kg/min)] + [10000 * Vasopressin \text{ dose } (U/kg/min)] + [10 * Milrinone \text{ dose } (\mu g/kg/min)]$

For the estimation of the cardiac output, we used the aimed full ECMO flow as described in (26) (Suppl. Table 1), although this represents just an approximation of the resting cardiac output.

Statistical analysis: Since this is a retrospective study, no sample size calculation was performed. Patient characteristics are summarized as medians with ranges to reflect the heterogeneity of the study population. All other measured variables are presented as the median and interquartile ranges (IQR) or count in %. For comparison of the repeated pairwise measurements the Wilcoxon matched-pairs signed rank test was used (each with reference to the baseline data). The statistical analyses were performed using GraphPad Prism Version 10.6.1 (September 8, 2025, GraphPad Software, Boston, MA, USA). The p-values were two-tailed and values < 0.05 were considered statistically significant.

Results

Study Population: Between November 2023 and November 2025, a total of 8 patients received 11 cycles of venovenous ECCO₂R using a CRRT (ECCO₂R-CRRT) circuit over a total duration of 141 days at our pediatric intensive care unit. The characteristics of the study cohort are presented in Table 1. 5 of 8 were pediatric patients after hematopoietic cell transplantation (GATA2-deficiency, severe aplastic anemia, myelodysplastic syndrome, acute myeloid leukemia, acute lymphocytic leukemia) with infectious complications (viral and/or bacterial pneumonia) or non-infectious complications (bronchiolitis obliterans, transplant-associated thrombotic microangiopathy) leading to pARDS. In one patient the ARDS was due to a diffuse alveolar hemorrhage as a result of hemophagocytic lymphohistiocytosis. The two remaining patients suffered from severe pneumonia (primary viral) with bacterial superinfections. Both patients had underlying potentially life-limiting conditions (Rett syndrome and Cornelia de Lange syndrome).

By definition, one patient in our cohort was not a pediatric patient because of his age of 42 years. However, because of his weight (17 kg) and physiognomy as well as neurocognitive impairment, this

patient rather represents a pediatric patient – and was accordingly treated at our pediatric intensive care unit.

Table 1

Characteristics of the study population. Data are reported as count (%) or median (ranges).

Characteristic	N = 11 ECCO₂R-CRRT runs (8 patients)
Age, years	12 (0,5–42)
Male sex – n (% of patients)	7 (87,5)
ABW, Kgs	24 (10–72)
PRISM III score on admission	11 (7–13)
Diagnosis/Medical History (n = 8 patients)	
HCT & infectious complication	2
HCT & non-infectious complication	3
DAH	1
Life-limiting disease* with pneumonia	2
ECCO₂R-CRRT characteristics	
Shaldon cannulation site FV/JV, n (of patients)	7/1
Systemic anticoagulation with UFH – n (% of runs)	8 (73)
ECCO ₂ R-CRRT blood flow [ml/min]	300 (100–400)
ECCO ₂ R-CRRT blood flow of estimated CO [%]	10 (2–21)
Duration of therapy, days	5 (2–58)
Adverse Events, n (% of runs)	
Bleeding complication	0 (0)
Thrombembolic complication	0 (0)
Membrane clotting requiring device replacement	3 (27)
Infection	0 (0)
Hemolysis (significant elevation of LDH, Bilirubin)	0 (0)
Outcome	
Weaned from ECCO ₂ R-CRRT, n (% of patients)	4 (50)
Survival to discharge, n (% of patients)	2 (25)
ABW = actual body weight; PRISM = pediatric risk of mortality score; HCT = hematopoietic cell transplantation; DAH = diffuse alveolar hemorrhage; FV = femoral vein; JV = jugular vein; LDH = lactate dehydrogenase; *1x Cornelia de Lange syndrome, 1x Rett syndrome	

ECCO₂R implementation: Regarding the configuration, all patients received ultrasound-guided single-site cannulation using a Shaldon catheter (GamCath/Vantive Health Germany, Unterschleißheim, Germany or Joline Medical Technology, Hechingen, Germany). In 7 patients the femoral vein (FV) was cannulated, in one patient the dual lumen dialysis catheter was placed in the right jugular vein (JV). One 8 French, six 11.5 French and one 13 French catheter were placed.

Measurements: The median age of the patients was 12 (IQR 6.25–14.75) years and the median weight 24 (IQR 14–60.25) kg. The median PRISM III Score was 11 (IQR 8.25–12.5). The median ECCO₂R duration was 5 (IQR 3–33.75) days with a median RRT blood flow of 300 (IQR 200–300) ml/min corresponding to a median portion of 10 (IQR 8–19) % of the estimated cardiac output.

The median baseline pH and PaCO₂ levels were 7.30 (IQR 7.22–7.38) and 75 (IQR 65–88) mmHg respectively. The median baseline peak inspiratory pressure was 36 (IQR 31–40) mbar and the median driving pressure was 28 (IQR 22–36) mbar, with a median baseline Ventilation Index of 71 (IQR 47–143) and a median Oxygenation Index of 29 (IQR 5–49). The median VIS at baseline was 0 (0–7.3).

Changes in ventilatory, extracorporeal and vasoactive support parameters as well as changes in laboratory values over time are shown in Table 2 and illustrated in Figs. 2 and 3. Within one hour of initiation of ECCO₂R, in all patients, we observed a marked and statistically significant decrease of the PaCO₂ (median – 19 mmHg, IQR – 26 to -8 mmHg, $p = 0.001$) and consequently of the ventilation index (median – 43.9, IQR – 45.6 to -21.2, $p = 0.001$). Accordingly, respirator settings could be reduced significantly in all patients: peak inspiratory pressure (median – 9 mbar, IQR – 11 to -6 mbar, $p = 0.002$), driving pressure (median – 10 mbar, IQR – 13 to -6 mbar, $p = 0.002$), tidal volume (-1.4 ml/kg ABW, IQR – 6.9 to -0.7 ml/kg ABW, $p = 0.008$). Importantly, ECCO₂R remained equally effective in reducing ventilatory requirements over and beyond 24 hours of therapy.

The pH increased during the first 12 hours of ECCO₂R-CRRT. The absence of a further increase in pH after 24 hours is likely multifactorial. First, our treatment strategy continued to target permissive hypercapnia rather than normocapnia, limiting the extent of paCO₂ reduction. Second, integration of ECCO₂R into a bicarbonate-based CVVHD circuit continuously corrected the metabolic component of acid-base balance, thereby buffering pH changes despite variations in PaCO₂.

Following the implementation of ECCO₂R-CRRT, markers of oxygenation (FiO₂, PEEP, OI) did not significantly change (Fig. 3). Furthermore, the VIS did not change as well (Table 2).

Table 2

Time course of main study variables (Baseline, 12 hours, 24 hours, ΔT) and laboratory values (Baseline, 24 hours). Data are presented as median (IQR).

Variable	Baseline	12-h	p Value	24-h	p Value	ΔT	p Value
pH	7.3 (7.22–7.38)	7.41 (7.36–7.47)	0.006	7.35 (7.29–7.44)	0.150	7.38 (7.33–7.43)	0.143
PaCO ₂ , mmHg	75 (65–88)	59 (47–67)	0.001	61 (55–79)	0.019	60 (51–66)	0.003
PaO ₂ , mmHg	65 (47–90)	53 (45–67)	0.239	58 (53–78)	0.849	69 (53–79)	0.831
ECCO ₂ R BF, ml/min	0	300 (200–300)	0.001	300 (200–300)	0.001	300 (200–300)	0.001
ECCO ₂ R GF, l/min	0	4.5 (3–4.5)	0.001	4.5 (3–4.5)	0.001	4.5 (3–4.5)	0.001
PIP, mbar	36 (31–40)	27 (26–33)	0.001	26 (22–29)	0.001	26 (20–40)	0.002
ΔP , mbar	28 (22–36)	18 (15–24)	0.001	17 (14–21)	0.001	15 (14–22)	0.006
Vt, ml/kg ABW	4.7 (2.8–9.6)	3.3 (2.1–5.9)	0.020	2.9 (1.4–5.2)	0.027	3.6 (1.5–5.6)	0.004
PEEP, mbar	8 (0–12)	10 (5–14)	0.117	8 (5–11)	0.848	8 (5–12)	0.824
FiO ₂ , %	70 (35–100)	65 (40–100)	0.578	65 (50–100)	0.383	60 (40–75)	0.678
Oxygenation Index	29 (5–49)	17 (13–44)	0.175	17 (12–37)	0.054	13 (6–17)	0.123
Ventilation Index	71 (47–143)	41 (29–61)	0.001	44 (33–69)	0.0098	40 (26–69)	0.002
VIS	0 (0–7.3)	0 (0–20)	0.813	0 (0–30)	> 0.999	0 (0–10.3)	> 0.999
Hemoglobin, g/dl	9.9 (9–12.5)	-	-	10.8 (8.8–13.4)	0.48	-	-

ECCO₂R = extracorporeal CO₂ removal; BF = blood flow; GF = gas flow; PIP = peak inspiratory pressure; ΔP = driving pressure; Vt = tidal volume; ABW = actual body weight; PEEP = positive end-expiratory pressure; FiO₂ = inspiratory oxygen fraction; VIS = vasoactive inotropic score; LDH = lactate dehydrogenase

Variable	Baseline	12-h	p Value	24-h	p Value	ΔT	p Value
Platelets, G/l	96 (64–110)	-	-	76 (63–149)	0.24	-	-
Fibrinogen, mg/dl	539 (274–708)	-	-	464 (260–654)	0.38	-	-
LDH, U/l	442 (305–725)	-	-	455 (317–740)	0.49	-	-
Bilirubin, mg/dl	0.59 (0.4–1.1)	-	-	0.5 (0.4–0.9)	0.36	-	-
Creatinine, mg/dl	0.33 (0.18–0.7)	-	-	0.26 (0.18–0.51)	0.18	-	-
ECCO ₂ R = extracorporeal CO ₂ removal; BF = blood flow; GF = gas flow; PIP = peak inspiratory pressure; ΔP = driving pressure; Vt = tidal volume; ABW = actual body weight; PEEP = positive end-expiratory pressure; FiO ₂ = inspiratory oxygen fraction; VIS = vasoactive inotropic score; LDH = lactate dehydrogenase							

Regarding potential adverse events, we did not observe increased hemolysis (as measured by LDH and/or bilirubin plasma levels) as a consequence of the extracorporeal circuit. Also, we did not detect an increased thrombocyte or erythrocyte consumption during extracorporeal support in our cohort (see Tables 2 and 3). Among 11 ECCO₂R-CRRT runs a total of 3 (27%) membrane clotting events were noted. By changing the CRRT circuit including the gas exchange membrane this problem could always be promptly solved.

Table 3
Platelet and erythrocyte (RBC) transfusions per day – pre and post initiation of ECCO₂R-CRRT. Data are presented as median (IQR).

Variable	Pre ECCO ₂ R-CRRT	Post ECCO ₂ R-CRRT	p Value
Platelet transfusions/day	0.43 (0–1.00)	0.50 (0–1.00)	0.69
RBC transfusions/day	0.43 (0–0.67)	0.17 (0–0.71)	0.46

4 of 8 patients were successfully weaned from the ECCO₂R-CRRT. Unfortunately, only 2 of 8 patients survived to hospital discharge. In 2 patients, care was ultimately redirected because of progression of the underlying pathology after weaning from ECCO₂R-CRRT. In one patient, support was escalated to vvECMO following multidisciplinary reassessment and after discussion with the patient's family, reflecting their wish to pursue maximal life-sustaining therapy; however, the patient subsequently died. Three patients died from progression of the underlying pathology on ECCO₂R-CRRT, further escalation of

therapy was deemed contraindicated in these patients, mostly because of progressive multi-organ failure.

Discussion

In this retrospective single-center cohort of pediatric patients with ARDS and AKI, venovenous ECCO₂R integrated into a CRRT circuit using the multiECCO₂R device was feasible and associated with consistent improvements in ventilatory parameters, without major safety signals in this small cohort.

Accordingly, the clinical question addressed by this study is not whether ECCO₂R should replace vvECMO, but whether an already indicated CRRT circuit can be pragmatically augmented to facilitate lung-protective ventilation in selected pediatric patients.

Across 11 ECCO₂R runs, we observed consistent reductions in PaCO₂, tidal volume, peak inspiratory pressure, and ventilation index, supporting the ability of ECCO₂R-CRRT to facilitate lung-protective and ultraprotective ventilation strategies.

The magnitude and direction of these physiological effects are consistent with adult ECCO₂R data. Stommel et al. reported comparable reductions in ventilatory pressures and PaCO₂ across multiple ECCO₂R platforms (10), and similar effects were observed in the SUPERNOVA (11) and REST (12) trials. However, unlike adult randomized trials, our cohort experienced no clinically relevant bleeding events, and no patient required therapy discontinuation due to hemorrhagic complications. This contrasts with adult trials like REST (12), SUPERNOVA (11) and a study by Del Sorbo et al. (27), in which bleeding represented the predominant serious adverse event. On the other hand, adult studies using CRRT platforms likewise did not report relevant adverse events (28–30).

Several factors may explain this difference. First, ECCO₂R-CRRT in our cohort was delivered at dialysis-range blood flows, substantially lower than those used in stand-alone ECCO₂R or ECMO systems. Second, integration into an existing CRRT circuit avoided additional cannulation and minimized extracorporeal surface area. Third, anticoagulation strategies were tailored to renal replacement therapy requirements rather than high-flow extracorporeal support. Together, these factors likely contributed to the favorable safety profile observed.

The oxygenation variables (PEEP, FiO₂, Oxygenation Index) did not significantly change, as expected, since the ECCO₂R device is not designed to provide relevant oxygenation. Furthermore, when reducing the peak inspiratory pressure, the mean airway pressure is usually decreased as well. This necessitates an increase in PEEP and/or FiO₂ to stabilize oxygenation.

Comparable to other studies, we did not find a significant change in the requirement of vasoactive support (30).

The baseline creatinine was 0.33 (IQR 0.18–0.7), which does not seem to be elevated. But since the predominant indication for CVVHD in our cohort was fluid overload we have to assume that most

patients suffered from cryptic AKI. Current definitions of AKI rely on urine output and measured creatinine and therefore fail to account for confounding effects of fluid overload. Fluid overload itself changes distribution volume of creatinine and could consequently mask AKI (31). This confounding effect could also explain the insignificant decrease after implementation of ECCO₂R-CRRT (24h creatinine of 0.26 mg/dl, $p = 0.18$).

From a clinical perspective, our findings suggest that the greatest potential value of integrated ECCO₂R-CRRT lies in pediatric patients who already require CRRT because of AKI and/or fluid overload. In this setting, the existing extracorporeal circuit provides an opportunity to augment renal support with carbon dioxide removal without additional vascular access or the need for a separate extracorporeal support platform. This pragmatic approach may facilitate lung-protective ventilation by reducing hypercapnia and ventilatory pressures while utilizing an extracorporeal therapy that is already clinically indicated.

Importantly, the objective of this strategy is not to replace vvECMO in patients who meet established indications for extracorporeal life support. Rather, ECCO₂R integrated into CRRT should be viewed as a complementary approach for carefully selected patients in whom additional carbon dioxide removal is considered beneficial. In our cohort, this included several immunocompromised children and patients with severe underlying comorbidities, in whom the anticipated risks and benefits of vvECMO were evaluated independently through multidisciplinary assessment. Although our findings suggest that this integrated strategy is feasible and was associated with improved ventilatory parameters, prospective studies are required to better define its role within the spectrum of pediatric extracorporeal respiratory support.

Regarding the mortality in our small cohort, it has to be mentioned that especially for pediatric patients with hematologic or immune-related diseases with ARDS the expected mortality is about 66% (32). Notably, the expected mortality for pediatric hematopoietic stem cell transplant recipients requiring mechanical ventilation is about 47% for moderate pARDS and rises to 75% for patients with severe pARDS (33). In our cohort, 5 of 8 patients were hematopoietic cell transplant recipients, and 6 of 8 patients had a hematologic or immune-related disease. The median baseline Oxygenation Index of the cohort was 29 (IQR 5–49), illustrating the severity of lung injury at the time of ECCO₂R initiation. Consequently, the high mortality in our small cohort of severely ill children is not surprising given their risk profile.

Limitations

This study has several limitations. First, its retrospective design, small sample size, and absence of a control group limit generalizability, preclude causal inference, and prevent definitive conclusions regarding clinical outcome benefits. Second, although ECCO₂R-CRRT was associated with improvements in ventilatory parameters consistent with lung-protective ventilation, we did not assess biomarkers of ventilator-induced lung injury or evaluate regional lung mechanics using electrical impedance

tomography or computed tomography. Therefore, the physiological mechanisms underlying these observations remain speculative.

Third, exact extracorporeal carbon dioxide removal rates could not be quantified because device-specific CO_2 elimination was not routinely measured in this pragmatic clinical setting. Consequently, the physiological effect of ECCO₂R was inferred from changes in arterial PaCO_2 and ventilatory parameters rather than direct measurements of membrane lung CO_2 clearance.

Fourth, membrane clotting requiring circuit exchange occurred in three of eleven treatment runs. Although no major bleeding or hemolysis was observed, integrated ECCO₂R-CRRT systems require replacement of the entire extracorporeal circuit in the event of clotting, which may increase treatment interruptions and blood loss compared with standalone CRRT circuits. Further technical refinement and prospective evaluation of circuit performance are warranted.

Furthermore, the highly selected nature of the cohort, including a large proportion of immunocompromised patients, and the conduct of all treatments at a single tertiary pediatric center with extensive extracorporeal support experience may limit the generalizability of our findings.

Finally, use of the multiECCO₂R device in patients weighing less than 40 kg was outside the manufacturer's approved labeling. Although no device-related safety concerns beyond those reported were observed, this approach requires careful risk–benefit assessment and should be undertaken only in experienced centers with expertise in pediatric extracorporeal support until further evidence becomes available.

Conclusion

Venovenous ECCO₂R integrated into a CRRT circuit was feasible in this retrospective single-center cohort of carefully selected pediatric patients with ARDS and AKI. The greatest potential value of this approach may lie in patients who already require CRRT, in whom the existing extracorporeal circuit can be pragmatically augmented with carbon dioxide removal without additional vascular access, thereby facilitating lung-protective ventilation. This integrated strategy should be considered a complementary adjunct to an already indicated CRRT circuit rather than a substitute for vvECMO, for which patient selection should continue to be based on multidisciplinary clinical assessment.

ECCO₂R-CRRT was associated with consistent improvements in ventilatory parameters, including reductions in PaCO_2 , driving pressure, and tidal volume, without major safety signals in this cohort. Given the scarcity of pediatric data and representing, to our knowledge, one of the largest reported pediatric cohorts evaluating ECCO₂R integrated into CRRT, these findings provide preliminary evidence supporting the feasibility and physiological benefits of this integrated extracorporeal strategy. Prospective multicenter studies are warranted to better define its safety, efficacy, and optimal patient selection.

Abbreviations

ABW
Actual body weight
AKI
Acute kidney injury
BF
Blood flow
CO₂
Carbon dioxide
CRRT
Continuous renal replacement therapy
CVVHD
Continuous venovenous hemodialysis
DAH
Diffuse alveolar hemorrhage
 ΔP
Driving pressure
ECCO₂R
Extracorporeal carbon dioxide removal
ECMO
Extracorporeal membrane oxygenation
FiO₂
Inspiratory oxygen fraction
FV
Femoral vein
GF
Gas flow
HCT
Hematopoietic cell transplantation
IQR
Interquartile range
JV
Jugular vein
LDH
Lactat dehydrogenase
OI
Oxygenation index
pARDS
Pediatric acute respiratory distress syndrome
PEEP
Positive end-expiratory pressure

PIP
Peak inspiratory pressure
PRISM
Pediatric risk of mortality score
RBC
Red blood cell
VI
Ventilation index
VIS
Vasoactive inotropic score
Vt
Tidal volume
vv
Venovenous

Declarations

Ethics Approval and Consent to participate

This retrospective observational study was reviewed and approved by the Ethics Committee of the University of Freiburg, Faculty of Medicine, University of Freiburg, Germany (Reference No. 26-1030-S1-retro). The Ethics Committee raised no ethical or legal objections to the conduct of the study. The Ethics Committee determined that individual informed consent was not required because the study exclusively involved the retrospective analysis of routinely collected, anonymized clinical data without any study-specific interventions or additional patient contact. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analyzed during the current study are not publicly available due to institutional and data protection regulations but are available from the corresponding author on reasonable request.

Competing Interests:

This research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. Therefore, the authors declare that they have no competing interests.

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Author contributions

The study was conceived and designed by MK, HS and DK. HS and MK collected and analyzed the data. HS drafted the manuscript, MK and DK contributed substantially. HS takes overall responsibility for the article. All authors critically reviewed the manuscript and approved the final version for submission.

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References

1. Dixon CG, Thadani S, Fitzgerald JC, Akcan-Arikan A, Yehya N. Fluid Overload Precedes and Masks Cryptic Kidney Injury in Pediatric Acute Respiratory Distress Syndrome. *Crit Care Med*. 2023;51(6):765–74. 10.1097/CCM.0000000000005836.
2. Flori HR, Church G, Liu KD, Gildengorin G, Matthay MA. Positive fluid balance is associated with higher mortality and prolonged mechanical ventilation in pediatric patients with acute lung injury. *Crit Care Res Pract*. 2011;2011:854142. 10.1155/2011/854142.
3. Kaushik S, Villacres S, Eisenberg R, Medar SS. Acute Kidney Injury in Pediatric Acute Respiratory Distress Syndrome. *J Intensive Care Med*. 2021;36(9):1084–90. 10.1177/0885066620944042.
4. Kumar A, Epler K, DeWolf S, Barnes L, Hepokoski M. Bidirectional pressure: a mini review of ventilator-lung-kidney interactions. *Front Physiol*. 2024;15:1428177. 10.3389/fphys.2024.1428177.
5. Kusirisin P, Bagshaw SM. Kidney-ventilator interaction and kidney-protective ventilation. *Curr Opin Crit Care*. 2026;32(1):42–51. 10.1097/mcc.0000000000001342.
6. Starr MC, Gorga S, Gist KM. Interconnected Organs: Exploring the Impact of Kidney-Lung Crosstalk in Critically Ill Neonates and Children. *Compr Physiol*. 2025;15(6):e70084. 10.1002/cph4.70084.
7. de Prost N, Ricard JD, Saumon G, Dreyfuss D. Ventilator-induced lung injury: historical perspectives and clinical implications. *Ann Intensive Care*. 2011;1(1):28. 10.1186/2110-5820-1-28.
8. Koopman AA, de Jager P, Blokpoel RGT, Kneyber MCJ. Ventilator-induced lung injury in children: a reality? *Ann Transl Med*. 2019;7(19):506. 10.21037/atm.2019.09.13.
9. Cappadona F, Costa E, Mallia L, Sangregorio F, Nescis L, Zanetti V, et al. Extracorporeal Carbon Dioxide Removal: From Pathophysiology to Clinical Applications; Focus on Combined Continuous Renal Replacement Therapy. *Biomedicines*. 2023;11(1). 10.3390/biomedicines11010142.

10. Stommel AM, Herkner H, Kienbacher CL, Wildner B, Hermann A, Staudinger T. Effects of extracorporeal CO removal on gas exchange and ventilator settings: a systematic review and meta-analysis. *Crit Care*. 2024;28(1). doi: ARTN 146.
11. 1186/s13054-024-04927-x.
12. Combes A, Fanelli V, Pham T, Ranieri VM. European Society of Intensive Care Medicine Trials G, the Strategy of Ultra-Protective lung ventilation with Extracorporeal CORfN-OmtsAi. Feasibility and safety of extracorporeal CO(2) removal to enhance protective ventilation in acute respiratory distress syndrome: the SUPERNOVA study. *Intensive Care Med*. 2019;45(5):592–600. 10.1007/s00134-019-05567-4.
13. McNamee JJ, Gillies MA, Barrett NA, Perkins GD, Tunnicliffe W, Young D, et al. Effect of Lower Tidal Volume Ventilation Facilitated by Extracorporeal Carbon Dioxide Removal vs Standard Care Ventilation on 90-Day Mortality in Patients With Acute Hypoxemic Respiratory Failure: The REST Randomized Clinical Trial. *JAMA*. 2021;326(11):1013–23. 10.1001/jama.2021.13374.
14. Giraud R, Banfi C, Assouline B, De Charriere A, Cecconi M, Bendjelid K. The use of extracorporeal CO(2) removal in acute respiratory failure. *Ann Intensive Care*. 2021;11(1):43. 10.1186/s13613-021-00824-6.
15. Omecinski K, Cove M, Duggal A, Federspiel W. Extracorporeal carbon dioxide removal (ECCO R): A contemporary review. *Appl Eng Sci*. 2022;10. doi: ARTN 100095.
16. 1016/j.apples.2022.100095.
17. Parrilla-Gomez FJ, Castelli A, Colombo R, do Vale-Fernandes A, Nalesso F, Pestana-Lagunas D, et al. The role of extracorporeal CO(2) removal from pathophysiology to clinical applications with focus on potential combination with RRT: an expert opinion document. *Front Med (Lausanne)*. 2025;12:1651213. 10.3389/fmed.2025.1651213.
18. Di Nardo M, Ahmad AH, Merli P, Zinter MS, Lehman LE, Rowan CM, et al. Extracorporeal membrane oxygenation in children receiving haematopoietic cell transplantation and immune effector cell therapy: an international and multidisciplinary consensus statement. *Lancet Child Adolesc Health*. 2022;6(2):116–28. 10.1016/s2352-4642(21)00336-9.
19. Gow KW, Wulkan ML, Heiss KF, Haight AE, Heard ML, Rycus P, et al. Extracorporeal membrane oxygenation for support of children after hematopoietic stem cell transplantation: the Extracorporeal Life Support Organization experience. *J Pediatr Surg*. 2006;41(4):662–7. 10.1016/j.jpedsurg.2005.12.006.
20. Olson TL, O'Neil ER, Kurtz KJ, MacLaren G, Anders MM. Improving Outcomes for Children Requiring Extracorporeal Membrane Oxygenation Therapy Following Hematopoietic Stem Cell Transplantation. *Crit Care Med*. 2021;49(4):e381–93. 10.1097/CCM.0000000000004850.
21. Maratta C, Potera RM, van Leeuwen G, Castillo Moya A, Raman L, Annich GM. Extracorporeal Life Support Organization (ELSO): 2020 Pediatric Respiratory ELSO Guideline. *ASAIO J*. 2020;66(9):975–9. 10.1097/MAT.0000000000001223.

22. Marupudi N, Lau-Braunhut S, Bons J, Smith B, Coons R, Cohen G. 46: Single center experience with extracorporeal carbon dioxide removal in children with respiratory failure secondary to severe hypercarbia. *ASAIO J.* 2024;70(Supplement 4). doi.
23. Morris JL, Rosen DA, Calvert KS, Gustafson RA, Steelman RJ, Rosen KR, et al. Extracorporeal CO₂ removal in a child with a single ventricle by the addition of an oxygenator to a dialysis circuit. *Pediatr Crit Care Med.* 2003;4(1):104–6. 10.1097/00130478-200301000-00021.
24. Özçifçi G, Koç G, Eydurhan E, Durak F, Anıl AB. Extracorporeal carbon dioxide removal for acute hypercapnic respiratory failure in a child with cystic fibrosis. *Turk J Pediatr.* 2024;66(2):257–64. 10.24953/turkjpediatr.2024.4588.
25. Care FM. Additional Sheet to the multiFiltratePRO Instructions for Use regarding the use of the multiECCO₂R to remove CO₂ together with the multiFiltratePRO device2019. Instruction Manual for the multiECCO₂R gas exchanger p.
26. Emeriaud G, López-Fernández YM, Iyer NP, Bembea MM, Agulnik A, Barbaro RP, et al. Executive Summary of the Second International Guidelines for the Diagnosis and Management of Pediatric Acute Respiratory Distress Syndrome (PALICC-2). *Pediatr Crit Care Med.* 2023;24(2):143–68. 10.1097/pcc.0000000000003147.
27. Pollack MM, Dean JM, Butler J, Holubkov R, Doctor A, Meert KL, et al. The ideal time interval for critical care severity-of-illness assessment. *Pediatr Crit Care Med.* 2013;14(5):448–53. 10.1097/PCC.0b013e31828a7270.
28. Das S, Gupta S, Das D, Dutta N. Basics of extra corporeal membrane oxygenation: a pediatric intensivist's perspective. *Perfusion.* 2022;37(5):439–55. 10.1177/02676591211005260.
29. Del Sorbo L, Pisani L, Filippini C, Fanelli V, Fasano L, Terragni P, et al. Extracorporeal Co₂ removal in hypercapnic patients at risk of noninvasive ventilation failure: a matched cohort study with historical control. *Crit Care Med.* 2015;43(1):120–7. 10.1097/ccm.0000000000000607.
30. Combes A, Levy B, Tapponnier R, Capellier G, Mekontso Dessap A, Duburcq T, et al. A prospective clinical evaluation of new ECCO₂R technology in mild to moderate ARDS patients: assessing ultra-lung-protective ventilation with PRISMALUNG+. *Crit Care.* 2026;30(1):15. 10.1186/s13054-025-05827-4.
31. Husain-Syed F, Birk HW, Wilhelm J, Ronco C, Ranieri VM, Karle B, et al. Extracorporeal Carbon Dioxide Removal Using a Renal Replacement Therapy Platform to Enhance Lung-Protective Ventilation in Hypercapnic Patients With Coronavirus Disease 2019-Associated Acute Respiratory Distress Syndrome. *Front Med (Lausanne).* 2020;7:598379. 10.3389/fmed.2020.598379.
32. Taccone FS, Rinaldi S, Annoni F, Nobile L, Di Nardo M, Maccieri J, et al. Safety and Effectiveness of Carbon Dioxide Removal CO₂RESET Device in Critically Ill Patients. *Membr (Basel).* 2023;13(7). 10.3390/membranes13070686.
33. Liu KD, Thompson BT, Ancukiewicz M, Steingrub JS, Douglas IS, Matthay MA, et al. Acute kidney injury in patients with acute lung injury: impact of fluid accumulation on classification of acute

kidney injury and associated outcomes. Crit Care Med. 2011;39(12):2665–71. 10.1097/CCM.0b013e318228234b.

34. Wang Q, Dang H, Fu Y, Liu C, Li J, Xu F. Risk factors for mortality in children with moderate-to-severe ARDS with concurrent hematological or immune-related diseases: a retrospective analysis. BMC Pediatr. 2025;25(1):396. 10.1186/s12887-025-05734-1.
35. Rowan CM, Smith LS, Loomis A, McArthur J, Gertz SJ, Fitzgerald JC, et al. Pediatric Acute Respiratory Distress Syndrome in Pediatric Allogeneic Hematopoietic Stem Cell Transplants: A Multicenter Study. Pediatr Crit Care Med. 2017;18(4):304–9. 10.1097/PCC.0000000000001061.

Figures

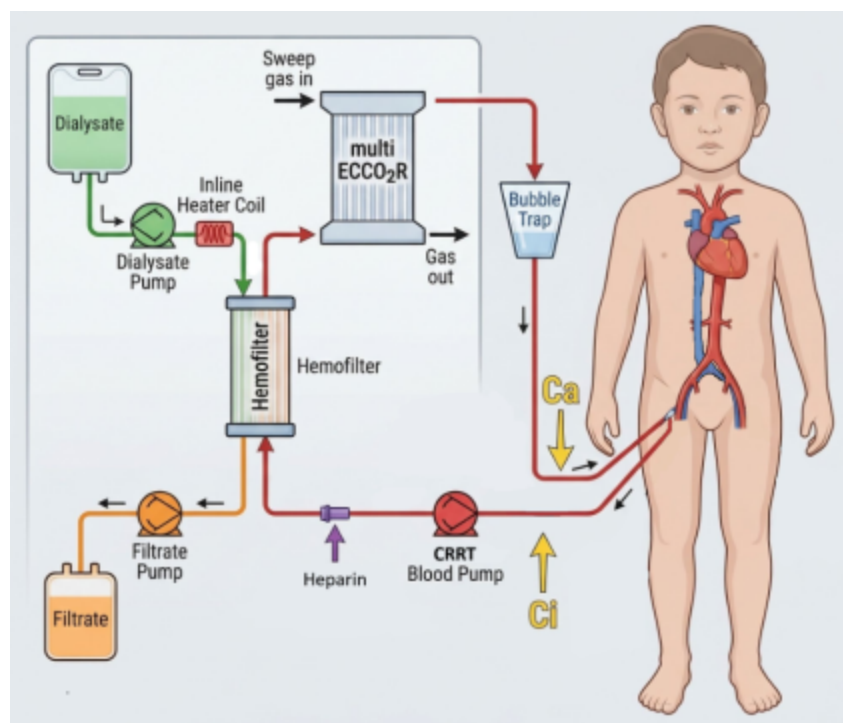


Figure 1

Schematic representation of the ECCO₂R circuit in combination with CRRT. ECCO₂R-CRRT may be performed with regional citrate anticoagulation or systemic heparinization (OpenAI. *AI-generated illustration* created with ChatGPT/DALL·E, January 2026)

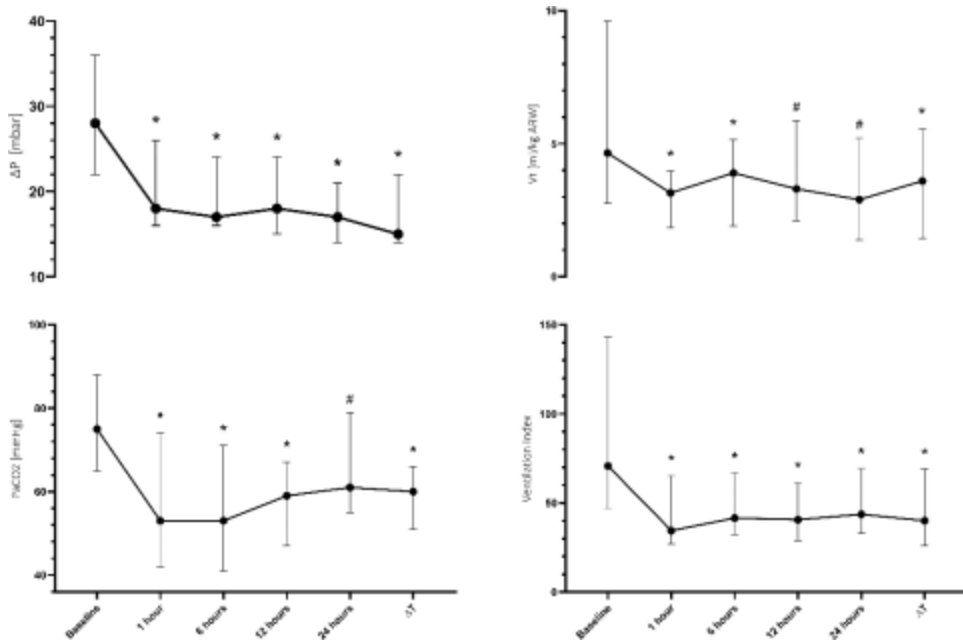


Figure 2

Time course of ΔP , V_t , $PaCO_2$ and Ventilation Index over time with median and IQR. ΔT = 24 hours before discontinuation of $ECCO_2R$, or 7 days in the case of a therapy duration longer than 1 week. # and * indicate significant differences with baseline values (# $P < 0.05$ vs baseline; * $P < 0.01$ vs baseline; ns = not significant).

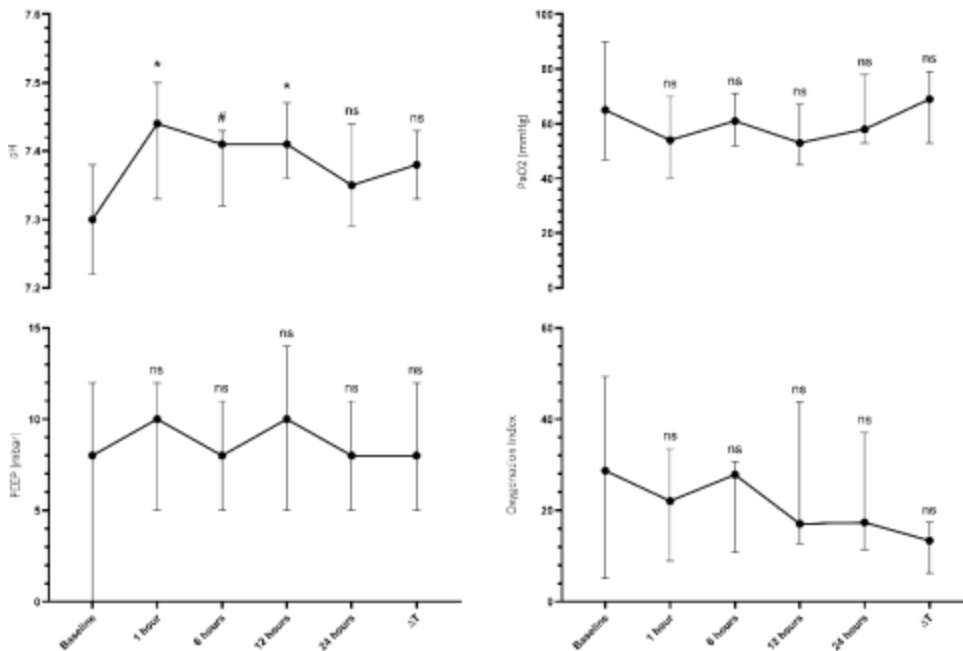


Figure 3

Time course of pH, PEEP, PaO_2 and Oxygenation Index over time with median and IQR. ΔT = 24 hours before discontinuation of $ECCO_2R$, or 7 days in the case of a therapy duration longer than 1 week. # and *

indicate significant differences with baseline values (# $P < 0.05$ vs baseline; * $P < 0.01$ vs baseline; ns = not significant).

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