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Surfactant administration during pediatric extracorporeal membrane oxygenation

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Abstract

Administering surfactant during pediatric extracorporeal membrane oxygenation (ECMO) may influence important clinical variables, but has been insufficiently described. Ninety-six courses of ECMO from our center were retrospectively assessed and 89 surfactant doses were identified during 37 ECMO courses. Surfactant administration was associated with a respiratory indication for ECMO, and increased durations of ECMO and positive pressure ventilation. Hospital survival was 64.9% (24/37) in surfactant-treated ECMO courses and 72.9% (43/59) otherwise ($p = 0.41$). Dynamic compliance of the respiratory system (C_{dyn}) (shown as least squares mean [standard error] in mL/cm-H₂O/kg by mixed effects modeling) increased significantly from 0.34 (0.03) before surfactant to 0.40 (0.03) within 12 hours ($p = 0.023$) and to 0.45 (0.03) within 24 hours ($p < 0.001$) of surfactant administration. Other mechanical ventilator parameters, ECMO settings and arterial blood gas results did not differ significantly following surfactant administration. Among surfactant recipients, significantly increased C_{dyn} was observed in the non-surgical group ($n=20$) but not in the cardiac surgery group ($n=17$). In conclusion, respiratory system compliance is increased following surfactant administration and non-cardiac surgical patients may preferentially benefit from this therapy. Surfactant administration was associated with longer durations of mechanical support, but not with unfavorable mortality.

Keywords

pediatrics; Extracorporeal Membrane Oxygenation; pulmonary surfactants

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Introduction

Extracorporeal membrane oxygenation (ECMO) is employed in children with severe cardiac and/or respiratory failure. Although outcomes vary based upon underlying diagnosis, and despite advances in equipment, surgical technique and critical care, only half of all children treated with ECMO survive to hospital discharge.^{1–4} Longer duration of ECMO is significantly associated with poorer survival.^{5–7} Prolonged duration of ECMO is also associated with increased rates of adverse events, with 95% of children who survive > 21 days of ECMO having at least one complication.^{5, 8} Interventions aimed at decreasing ECMO duration may therefore improve patient outcomes. Successful ECMO decannulation necessitates sufficient improvement in cardiac and/or respiratory function. Underlying causes of organ dysfunction must be addressed, and organ function may also be supported pharmacologically or mechanically. Innovative, aggressive organ support strategies may hasten ECMO decannulation and further improve patient outcome. Administering pulmonary surfactant during ECMO may be such a therapy.

Surfactant is a naturally occurring lipoprotein that decreases alveolar surface tension, which reduces atelectasis and improves lung compliance. Surfactant abnormalities have been described in neonates on ECMO and in many pediatric conditions that may require ECMO, including pneumonia, the acute respiratory distress syndrome (ARDS) and convalescence from cardio-pulmonary bypass (CPB) surgery.^{9–13} Surfactant administration often improves oxygenation and may improve survival in children with respiratory failure not on ECMO, though data are heterogeneous and do not support routine use.^{14–17} Administration of surfactant has been shown to decrease duration of neonatal ECMO in a single study from 1993.¹⁸ However, there are scant data describing the administration of surfactant during pediatric ECMO outside the neonatal period.¹⁹ To that end we retrospectively reviewed surfactant administration during pediatric ECMO at our institution, including pertinent outcome variables such as respiratory system compliance, ECMO duration and patient survival. This paper describes 96 courses of ECMO and 89 doses of surfactant administered during 37 of those courses.

Materials and Methods

This study was approved by the Institutional Review Boards of the Children's Hospital of Pittsburgh (CHP) of UPMC and of Rainbow Babies and Children's Hospital (University Hospitals of Cleveland). Patients treated with ECMO in the Pediatric Intensive Care Unit (ICU) or Cardiac ICU at CHP between January 2010 and March 2013 were included in the study. Multiple courses of ECMO for the same child were considered as separate events. Exclusion criteria were patient age < 18 years and initiation or termination of ECMO at another center. Data were retrospectively extracted from the electronic health record and from an institutional ECMO database for each course of ECMO, including demographics, performance of cardiac surgery during the hospitalization, type of cannulation (veno-venous or veno-arterial), and primary indication for ECMO, dichotomized as "respiratory failure" or "cardiac failure" (including eCPR, which is ECMO as an extension of cardiopulmonary resuscitation).

All patient care, including all aspects of surfactant prescription (indication, dose, delivery technique, timing, etc.), was at the discretion of the clinical team. The dose and timing of all surfactant administrations during ECMO were collected. Arterial blood gas (ABG) results, mechanical ventilator parameters and ECMO settings within one calendar day of any surfactant administration were extracted for patients treated with surfactant. Median values of these variables were calculated for the six hours preceding (baseline) and for three epochs following surfactant administration: 0–6 hours, 0–12 hours and 0–24 hours. Dynamic compliance of the respiratory system (C_{dyn}) was calculated using exhaled tidal volume (TV), peak inspiratory pressure (PIP) and positive end expiratory pressure (PEEP) using the equation: $C_{dyn} = TV/(PIP-PEEP)$. Maximum C_{dyn} was calculated for the six hours preceding surfactant administration (baseline) and for the three epochs described above. The end of positive pressure ventilation (PPV) was defined as the onset of 24 hours without invasive or non-invasive PPV.

All analyses were performed using SAS version 9.3 (SAS Inc., NC). Patient demographics, clinical characteristics and outcome variables were compared between groups using Wilcoxon two-sample test for continuous variables and Chi square or Fisher exact test for categorical variables. Overall changes from baseline to each above-mentioned epoch in ECMO settings, ABG results and ventilator parameters were explored using mixed effects models. Since surfactant prescription was not standardized (i.e. dosing, brand, indications, etc.), we treated administration as a random factor in the analysis. Patients were divided based on performance or absence of cardiac surgery during the hospitalization. Mixed effects modeling was used to compare C_{dyn} between these groups at baseline, in the 0–24hr epoch and as absolute change from baseline to 0–24hrs, and analysis was adjusted for factors that differed significantly between groups. All p values presented are two-sided, and $p < 0.05$ is considered as statistically significant. Variables are presented as least squares mean (standard error), n (%) or median (interquartile range) unless otherwise noted.

Results

Ninety-six courses of ECMO met study criteria (Table I). Most patients were less than 12 months old and approximately half underwent cardiac surgery during their hospital stay (n = 49). The recorded indication for ECMO was respiratory support in 26 courses (27.1%), mostly secondary to ARDS or respiratory tract infection (21 courses). Veno-arterial cannulation was employed 88 times (91.7%) and median duration of ECMO was 69 (28.5–129) hours. Survival to hospital discharge approached 70%. Eighty-nine doses of surfactant were administered during 37 courses (1–8 doses/course; median = 2 doses). Calfactant was administered 61 times (mean dose [standard deviation]: 101.9 [18.6] mg phospholipids/kg) and poractant was administered 28 times (156.2 [48.6] mg phospholipids/kg). Gender, age, weight, race and need for cardiac surgery were similar between children treated with surfactant and the remainder of the study population. A respiratory indication for ECMO was more common in surfactant-treated children vs. others (48.6% vs. 13.6%, $p < 0.001$). Despite increased durations of ECMO (115 [58–154] vs. 51 [24–94] hours, $p < 0.001$) and PPV (14 [8–27] vs. 7 [4–16] days, $p = 0.004$) in treated patients, there was no significant decrease in survival to hospital discharge associated with surfactant administration (64.9% vs. 72.9%, $p = 0.41$).

ECMO parameters and ABG results did not differ significantly following surfactant administration (Table II). Exhaled tidal volume was increased following surfactant administration, but no other mechanical ventilator parameters differed significantly. C_{dyn} was increased from baseline (0.34 [0.03] mL/cm-H₂O/kg) within 12 hours (0.40 [0.03] mL/cm-H₂O/kg, $p = 0.023$) and within 24 hours (0.45 [0.03] mL/cm-H₂O/kg, $p < 0.001$) following surfactant administration (Figure 1). Compared to non-surgical patients treated with surfactant, cardiac surgery patients given surfactant had higher baseline C_{dyn} (0.423 [0.035] vs. 0.240 [0.029] mL/cm-H₂O/kg, $p < 0.001$), were younger (1.0 [0.5–3.0] vs. 10.5 [1.5–27.0] months, $p = 0.02$), had shorter ECMO duration (58 [23–115] vs. 142.5 [103.5–395] hours, $p < 0.001$) and were less likely to have a respiratory indication for ECMO (17.6% vs. 75%, $p < 0.001$) (Table III). C_{dyn} increased following surfactant administration in both surgical and non-surgical patients (Figure 2), but only reached statistical significance in the non-cardiac surgery cohort (surgical: $p = 0.177$; non-surgical: $p < 0.001$). Results were similar after controlling for baseline C_{dyn} , age, ECMO duration and ECMO indication, with C_{dyn} increased significantly uniquely in the non-surgical group (surgical group: C_{dyn} increased by 0.07 ± 0.04 mL/cm-H₂O/kg, $p = 0.119$; non-surgical group: C_{dyn} increased by 0.16 ± 0.03 mL/cm-H₂O/kg, $p < 0.001$).

Among the entire study population, survival to hospital discharge did not differ between cardiac surgery and non-cardiac surgery patients (75.5% vs. 63.8%, $p = 0.306$). Surfactant administration was associated with decreased survival in cardiac surgery patients (52.9% vs. 87.5%, $p = 0.013$) but not in non-surgical patients (75.0% vs. 55.6%, $p = 0.226$) (Table III). In the non-surgical group, surfactant administration was associated with younger age; lower weight; a respiratory ECMO indication; and longer durations of ECMO, PPV, ICU care and hospitalization. There were no associations between surfactant use and available patient characteristics in the surgical cohort.

Twenty-seven children were treated with multiple doses of surfactant. There were no significant differences in demographics or outcomes vs. the 10 children treated with a single dose (Table IV). After controlling for both surfactant type and number of doses, we again found a significant increase in C_{dyn} that was unique to the non-cardiac surgery group ($p=0.008$) and not observed in the cardiac surgery group ($p=0.654$).

Discussion

This single-center, retrospective description of our recent pediatric ECMO experience supports that surfactant administration is associated with improved respiratory system compliance and may impact patient outcome. To our knowledge, this is the largest published cohort of pediatric patients given surfactant during ECMO. Among 37 courses of ECMO in which 89 doses of surfactant were administered, our data demonstrate that C_{dyn} increased significantly from 0.340 to 0.450 mL/cm-H₂O/kg ($p < 0.001$). This 32% increase in compliance is less than the 76.1% increase after surfactant reported by Hermon et al.¹⁹ Our findings are derived from a larger population and multiple measurements of C_{dyn} per epoch, as opposed to three singular measurements (baseline, 4 hours and 10 hours) of C_{dyn} per patient. Both studies support that surfactant may increase C_{dyn} , which may in turn improve outcome. Increased C_{dyn} often precedes successful ECMO discontinuation and is associated

with improved survival in children on ECMO not treated with exogenous surfactant.²⁰ A prospective study could test if the surfactant-induced increases in C_{dyn} seen in our cohort improve patient outcome.

In our cohort, ABG results, ECMO parameters and mechanical ventilator settings (other than increased tidal volume and C_{dyn}) were similar before and after surfactant, suggesting that patients tolerated surfactant administration well. Complications of surfactant include transient bradycardia and/or desaturation due to airway obstruction and vagal stimulation by the viscous material, and also pneumothorax, pulmonary hemorrhage and hypotension.^{14–16, 21, 22} Desaturation/bradycardia events may have occurred in our cohort but not be reflected in our analysis due to their transient nature, or may have been mitigated by sufficient oxygen delivery from the ECMO system. Transient airway obstruction was likely in our cohort as evidenced by the lack of increase in C_{dyn} observed within 6 hours of surfactant, though the typical practice of limiting endotracheal tube suctioning acutely following surfactant administration may also have influenced this finding. Overall, although our study was not designed to thoroughly evaluate the safety of administering surfactant to children on ECMO, our data suggest that this practice was well tolerated by patients. Further safety data are needed, especially in patients supported by veno-venous ECMO, who compromised a very small part of our treated cohort ($n=2$) and in whom adverse effects of surfactant may be more prevalent and severe.

The biologic plausibility of surfactant administration improving C_{dyn} is based on these children having insufficient surfactant quantity and/or function. Prior literature has reported surfactant abnormalities in children following CPB and in children with ARDS or acute respiratory infections, which were the diagnoses in most of our subjects.^{9, 10, 13} Similar to CPB, the ECMO circuit may elicit a systemic inflammatory response that alters surfactant, and abnormal surfactant composition has been reported in neonates on ECMO.^{11, 12, 23} Thus, even those children in our cohort with conditions not typically associated with surfactant dysfunction (e.g. cardiac arrest) may have had some degree of surfactant abnormality secondary to ECMO itself. Surfactant prescription was likely influenced by understanding of these risks of surfactant insufficiency, but patient-level factors of respiratory dysfunction, such as abnormal lung mechanics or radiographic findings, likely also impacted the decision to treat with surfactant. Additionally, some practitioners may avoid surfactant use when lung disease is related to inflammation and edema, such as in ARDS.

In subgroup analysis, surfactant administration was not associated with significant improvements in C_{dyn} among cardiac surgery patients. C_{dyn} did increase by nearly 15% from 0.423 to 0.486 mL/cm-H₂O/kg ($p = 0.177$) after surfactant in this group, so our study may have been simply underpowered for this analysis. Alternatively, the higher baseline C_{dyn} in our cardiac surgery patients (vs. non-surgical patients) suggests that surfactant function in this subgroup may have been sufficient as to render exogenous treatment ineffective. While several authors have previously described abnormalities in surfactant composition following CPB, some prior evidence shows that surface tension is maintained despite abnormal surfactant composition.^{9, 24} Identification of C_{dyn} thresholds or other

patient-level factors associated with surfactant efficacy could improve clinical care for surgical and non-surgical patients, as only select patients are likely to benefit from therapy.

The overall survival of our ECMO cohort (69.8%) compares favorably with prior reports, in which overall pediatric ECMO survival is often ~50%.^{2–4} Surfactant administration was associated with increased durations of PPV and ECMO, but no change in survival in our observational study. One could interpret this to either support surfactant administration (it mitigated worsened mortality in the “sicker” patients who received it) or refute it (it prolonged mechanical support and did not improve survival), but only a controlled, prospective study can determine the effects of surfactant administration on ECMO outcomes.

Survival in our cardiac surgery subgroup was 75.6%. This also compares favorably with prior reports of children treated with ECMO after cardiac surgery.^{25–28} This likely reflects advances that we have made as an international ECMO community, though institution-specific practices may contribute as well.^{29, 30} Surprisingly, there was a significant association between surfactant administration and unfavorable mortality in cardiac surgery patients (52.9% vs. 87.5%, $p = 0.013$). This may reflect preferential administration to more severely ill patients, premature ECMO discontinuation following transiently increased C_{dyn} or inflammatory modulation by exogenous surfactant protein B.³¹ In the non-surgical cohort, associations between surfactant administration and increased durations of ECMO, PPV and ICU care could be interpreted that surfactant was administered to sicker patients and perhaps had a positive influence on survival. Prospective study of the impact of surfactant on ECMO survival is needed.

Our study has several limitations beyond those previously mentioned. While this is the largest reported cohort of children on ECMO treated with surfactant, it is still a limited sample size from a single institution. The administration of surfactant was not standardized in regards to indication, dose, formulation or delivery technique. Surfactant may have been administered based on patient-level variables not included in our database. Granular details about the drug administration, such as patient positioning and the number of aliquots used, are not available. Surfactant quantity and function were not measured prior to exogenous administration. Imprecision in C_{dyn} measurements were minimized by measuring pressure and volume at the endotracheal tube (not the ventilator) and by using median values (as opposed to individual values) and mixed effect models. More over, increased C_{dyn} does is not necessarily equivalent to improved lung function, which is difficult to ascertain during ECMO support. Atrial decompression during ECMO may influence pulmonary mechanics, but data pertaining to its use were not available in the dataset. Surfactant is costly to administer, which should influence its prescription; however, financial data were not included in our database. Most importantly, like all retrospective clinical studies, we are only able to show association, not causation. Any conclusion about effects on survival from our study should be interpreted cautiously, due to the observational study design, the large number of confounding variables and the absence of illness-severity variables from our data (e.g. PRISM, RACHS-1, etc.).

Conclusions

In conclusion, in the largest reported cohort of surfactant administration during pediatric ECMO, surfactant treatment was associated with a significant improvement in respiratory system compliance. Further study is needed to better inform clinicians regarding which patient-level variables are associated with improved C_{dyn} and the effects of surfactant administration on ECMO outcome.

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Figure 1.

Maximum dynamic compliance during each of 4 epochs (6hrs preceding surfactant; 0–6, 0–12 and 0–24hrs following surfactant). All values calculated using mixed effects modeling and shown as least squares mean. Error bars represent standard error and asterisks denote $p < 0.05$ by mixed effects modeling vs. baseline.

Figure 2.

Maximum dynamic compliance for the 6hrs preceding surfactant and 0–24hrs following surfactant for cardiac surgery patients and other patients. All values calculated using mixed effects modeling and shown as least squares mean. Error bars represent standard error. Caret denotes $p < 0.05$ by mixed effects modeling vs. Cardiac surgery before surfactant. Asterisk denotes $p < 0.05$ by mixed effects modeling vs. Other patients before surfactant.

Table I

Demographics, patient variables and outcomes of all subjects.

	All	Surfactant	No Surfactant	p value
Courses of ECMO	96	37	59	
Female (%)	38 (39.6%)	13 (35.1%)	25 (42.4%)	0.48
Age in months	3.0 (1.0–33.0)	3.0 (0.9–15.0)	3.0 (1.0–48)	0.29
Weight (kg)	4.2 (3.1–11.0)	3.9 (3.0–9.2)	4.2 (3.1–13.0)	0.4
Caucasian (%)	81 (84.4%)	31 (83.8%)	50 (84.7%)	0.9
Cardiac surgery patients	49 (51.0%)	17 (45.9%)	32 (54.2%)	0.43
ECMO support type				< 0.001
<i>Respiratory</i>	26 (27.1%)	18 (48.6%)	8 (13.6%)	
<i>Cardiac/eCPR</i>	70 (72.9%)	19 (51.4%)	51 (86.4%)	
Hours on ECMO	69.0 (28.5–129.0)	115.0 (58.0–154.0)	51.0 (24.0–94.0)	< 0.001
Duration of PPV, days	9.0 (5.0–19.0)	14.0 (8.0–27.0)	7.0 (4.0–16.0)	0.004
Length of stay, days				0.05
<i>ICU</i>	18.0 (12.5–32.0)	21.0 (15.0–34.0)	16.0 (11.0–29.0)	
<i>Hospital</i>	28.0 (20.0–52.0)	33.0 (22.0–53.0)	27.0 (18.0–50.0)	
Survival to hospital discharge	67 (69.8%)	24 (64.9%)	43 (72.9%)	0.41

Variables are compared between children treated with surfactant during ECMO vs. those not treated using chi squared or Wilcoxon rank-sum. Data shows as median (IQR) or n (%).

ECMO = extracorporeal membrane oxygenation, eCPR = extracorporeal cardio-pulmonary resuscitation; PPV = positive pressure ventilation; ICU = intensive care unit.

Table II

ECMO settings, ABG results and mechanical ventilator parameters preceding and following surfactant administration

	Before surfactant (6hrs)	After surfactant (24hrs)	p value
ECMO Settings			
Sweep Gas (L/min)	1.09 ± 0.24	0.89 ± 0.23	0.39
Oxygenator FiO₂	0.63 ± 0.03	0.64 ± 0.03	0.29
Flow (L/min)	0.13 ± 0.01	0.12 ± 0.01	0.12
ABG Results			
pH	7.45 ± 0.01	7.44 ± 0.01	0.32
PaCO₂ (mm Hg)	45.17 ± 0.86	45.05 ± 0.86	0.9
PaO₂ (mm Hg)	138.95 ± 11.69	139.86 ± 11.65	0.91
Bicarbonate (mEq/L)	32.03 ± 0.99	31.57 ± 0.99	0.48
Ventilator Parameters			
Rate (breaths/min)	13.41 ± 0.81	14.16 ± 0.81	0.18
PIP (cm H₂O)	25.72 ± 0.68	25.98 ± 0.68	0.53
PEEP (cm H₂O)	8.25 ± 0.33	8.38 ± 0.33	0.55
TV (mL/kg)	4.92 ± 0.45	5.74 ± 0.45	0.002
FiO₂	0.47 ± 0.03	0.49 ± 0.03	0.43

Values for the 6hrs preceding and the 24hrs following administration calculated using mixed effects modeling and reported as least squares mean ± standard error.

ECMO = extracorporeal membrane oxygenation, PIP = peak inspiratory pressure, PEEP = positive end-expiratory pressure, TV = exhaled tidal volume.

Table III

Demographics, patient variables and outcomes by treatment groups

	Cardiac surgery patients			Non-surgical patients		
	Surfactant (n=17)	No Surfactant (n=32)	p value	Surfactant (n=20)	No Surfactant (n=27)	p value
Female (%)	5 (29.4%)	11 (34.4%)	1.000	8 (40%)	14 (51.9%)	0.556
Age in months	1.0 (0.5–3.0)	1.0 (0.3–2.0)	0.307	10.5 (1.5–27.0)*	42.0 (17.0–165.0)**	0.003
Weight (kg)	3.0 (2.7–3.9)	3.4 (2.8–4.0)	0.621	7.3 (3.8–11.0)*	12.3 (7.5–43.8)**	0.036
Caucasian (%)	15 (88.2%)	26 (81.3%)	0.696	16 (80%)	24 (88.9%)	0.438
ECMO support type			0.116			0.017
Respiratory	3 (17.6%)	1 (3.1%)		15 (75%)*	7 (25.9%)*	
Cardiac/eCPR	14 (82.4%)	31 (96.9%)		5 (25%)	20 (74.1%)	
Surfactant doses on ECMO	2 (1.25–2.0)	n/a	n/a	2 (1.5–3.0)	n/a	n/a
Hours on ECMO	58.0 (23.0–115.0)	38.0 (21.0–72.0)	0.182	142.5 (103.5–395.0)*	67.0 (35.0–119.0)**	<0.001
Duration of PPV, days	8.0 (6.0–17.0)	7.0 (5.0–11.0)	0.302	19.5 (11.5–39.5)	6.0 (3.0–18.0)	0.011
Length of stay, days						
ICU	19.0 (13.0–28.0)	16.5 (13.0–28.5)	0.941	26.5 (17.0–50.5)	14.0 (3.0–30.0)	0.011
Hospital	28.0 (19.0–49.0)	29.5 (25.0–60.0)	0.350	43.0 (26.0–60.5)	21.0 (4.0–44.0)**	0.012
Hospital survival	9 (52.9%)	28 (87.5%)	0.013	15 (75.0%)	15 (55.6%)*	0.226

Variables are compared using Fischer's exact or Wilcoxon rank-sum. Reported p values are for Surfactant vs. No Surfactant. Single asterisks denote $p < 0.05$ vs. cardiac surgery patients treated with surfactant. Double asterisks denote $p < 0.05$ vs. cardiac surgery patients not treated with surfactant. Data shows as median (IQR) or n (%).

ECMO = extracorporeal membrane oxygenation, eCPR = extracorporeal cardio-pulmonary resuscitation; PPV = positive pressure ventilation; ICU = intensive care unit.

Table IV

Demographics, patient variables and outcomes by number of surfactant doses administered during ECMO

	Multiple Doses of Surfactant	Single Dose of Surfactant	p value
Courses of ECMO	27	10	
Female (%)	8 (29.6%)	5 (50.0%)	0.27
Age in months	2.0 (0.5–8.0)	8.0 (1.0–50.0)	0.39
Weight (kg)	3.8 (3.0–8.0)	6.0 (3.0–13.8)	0.48
Caucasian (%)	23 (85.2%)	8 (80.0%)	0.65
Cardiac surgery patients	12 (44.4%)	5 (50.0%)	1.00
ECMO support type			1.00
<i>Respiratory</i>	13 (48.1%)	5 (50.0%)	
<i>Cardiac/eCPR</i>	14 (51.9%)	5 (50.0%)	
Hours on ECMO	126.0 (78.0–154.0)	42.5 (20.0–202.0)	0.18
Duration of PPV, days	17.0 (8.0–29.0)	10.0 (4.0–26.0)	0.16
Length of stay, days			
<i>ICU</i>	25.0 (14.0–44.0)	19.0 (15.0–32.0)	0.61
<i>Hospital</i>	39.0 (25.0–62.0)	26.5 (21.0–53.0)	0.36
Survival to hospital discharge	19 (70.4%)	5 (50.0%)	0.27

Variables are compared between children treated with multiple doses of surfactant during ECMO vs. those treated with a single dose using Fischer's exact or Wilcoxon rank-sum. Data shows as median (IQR) or n (%).

ECMO = extracorporeal membrane oxygenation, eCPR = extracorporeal cardio-pulmonary resuscitation; PPV = positive pressure ventilation; ICU = intensive care unit.