Platelet Transfusion Practice and Related Outcomes in Pediatric Extracorporeal Membrane Oxygenation*

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Objective: To describe factors associated with platelet transfusion during pediatric extracorporeal membrane oxygenation and the relationships among platelet transfusion, complications, and mortality.

Design: Secondary analysis of data collected prospectively by the Collaborative Pediatric Critical Care Research Network between December 2012 and September 2014.

Setting: Eight Collaborative Pediatric Critical Care Research Network–affiliated hospitals.

Patients: Age less than 19 years old and treated with extracorporeal membrane oxygenation.

Interventions: None.

Measurements and Main Results: Of 511 children, 496 (97.1%) received at least one platelet transfusion during extracorporeal membrane oxygenation. Neonatal age, venoarterial extracorporeal membrane oxygenation, and various acute and chronic diagnoses were associated with increased average daily platelet transfusion volume (milliliters per kilogram body weight). On multivariable analysis, average daily platelet transfusion volume was independently associated with mortality (per 1 mL/kg; odds ratio, 1.05; CI, 1.03–1.08;

$p < 0.001$), whereas average daily platelet count was not (per 1×10^9/L up to 115×10^9/L; odds ratio, 1.00; CI, 0.98–1.01; $p = 0.49$). Variables independently associated with increased daily bleeding risk included increased platelet transfusion volume on the previous extracorporeal membrane oxygenation day, a primary cardiac indication for extracorporeal membrane oxygenation, adolescent age, and an acute diagnosis of congenital cardiovascular disease. Variables independently associated with increased daily thrombotic risk included increased platelet transfusion volume on the previous extracorporeal membrane oxygenation day and venoarterial extracorporeal membrane oxygenation. Variables independently associated with decreased daily thrombotic risk included full-term neonatal age and an acute diagnosis of airway abnormality.

Conclusions: Platelet transfusion was common in this multisite pediatric extracorporeal membrane oxygenation cohort. Platelet transfusion volume was associated with increased risk of mortality, bleeding, and thrombosis. (*Pediatr Crit Care Med* 2020; 21:178–185)

Key Words: child; extracorporeal membrane oxygenation; infant; neonate; platelets

Platelet transfusions are common among critically ill children receiving extracorporeal membrane oxygenation (ECMO). Optimal transfusion thresholds are not well established, and the clinical factors, complications, and mortality associated with platelet transfusion during ECMO are uncertain. A recent multicenter study in a general population of critically ill children found that most platelet transfusions were prescribed prophylactically to those who were not bleeding (1). The same study also found an association between platelet dose and mortality. A single-center study in a similar cohort of children reported that the most common indication for platelet transfusion was prophylaxis for thrombocytopenia, and that mortality was high among those transfused and associated with disease severity (2). Many of these platelet transfusions, at least 30%, were given to children on ECMO.

Quantitative and qualitative platelet dysfunction have been described during ECMO and are associated with bleeding and mortality (3, 4). Platelet transfusion also has risks including febrile reactions, transfusion-related acute lung injury, infection, thromboembolism, and multiple organ dysfunctions (5–8). The association between platelet transfusion and poor outcome in critically ill children may be related to the multiple pathologic processes that result in thrombocytopenia and lead to platelet replenishment (1, 9, 10). During ECMO, platelet consumption triggered by the ECMO circuit may lead to platelet transfusion resulting in multiple organ dysfunctions from microthrombi formation and immune dysregulation (9, 10).

Guidelines to direct platelet transfusion are mostly not evidence based but rather rely on expert opinion (11, 12). Clinical decisions regarding platelet transfusion during ECMO are likely multifactorial with various child and ECMO characteristics playing a role. Prospective, multicenter data are needed to gain more generalizable knowledge about platelet transfusion during ECMO. Our objectives are to describe factors associated with platelet transfusion during pediatric ECMO and to determine the relationship among platelet transfusion, complications, and mortality.

METHODS

Design and Setting

This study was a secondary analysis of the Bleeding and Thrombosis during ECMO (BATE) study (13) which described the occurrence of bleeding and thrombosis during neonatal and pediatric ECMO. The BATE study collected prospective observational data at eight Collaborative Pediatric Critical Care Research Network–affiliated hospitals between December 2012 and September 2014. The Institutional Review Boards for each hospital and the Data Coordinating Center at the University of Utah approved the study with waiver of parental permission. All treatments provided were dependent on the clinical team and not dictated by study protocol.

Study Subjects

All children less than 19 years old treated with ECMO in a neonatal ICU, PICU, or cardiac ICU were included in the BATE study (13). Only the initial ECMO course was included for children who required multiple courses of ECMO. Of 514 children enrolled in BATE, three had missing data for body weight and were excluded from this analysis due to inability to determine transfusion volume in milliliters per kilogram. Thus, 511 children are included in this report.

Data Collection

Pre-ECMO data included age, history of prematurity, acute and chronic diagnoses, Pediatric Risk of Mortality (PRISM) III score (14), and clinical site. Age was categorized as neonate 30 days old or younger, infant more than 30 days to 12 months old or younger, child more than 1 year old to 12 years old or younger, and adolescent more than 12 years old to less than 19 years old. Prematurity was less than 37 weeks gestational age at birth and collected for neonates only.

ECMO data included primary indication for ECMO, placement on ECMO directly from cardiopulmonary bypass, mode of ECMO, location of ECMO within the hospital, average daily heparin dose, and average daily platelet and red cell transfusion volumes per kilogram body weight. Primary indication for ECMO was categorized as respiratory, cardiac, or extracorporeal cardiopulmonary resuscitation (ECPR). Mode of ECMO was venoarterial or venovenous. Venovenous ECMO that was converted to venoarterial was categorized as venoarterial ECMO. Location of ECMO was categorized as neonatal ICU, PICU, or cardiac ICU.

Laboratory data included arterial blood gases, blood lactate, and complete blood count with platelet count. Baseline laboratory values were obtained closest and prior to ECMO initiation; daily laboratory values were obtained closest to 7 AM

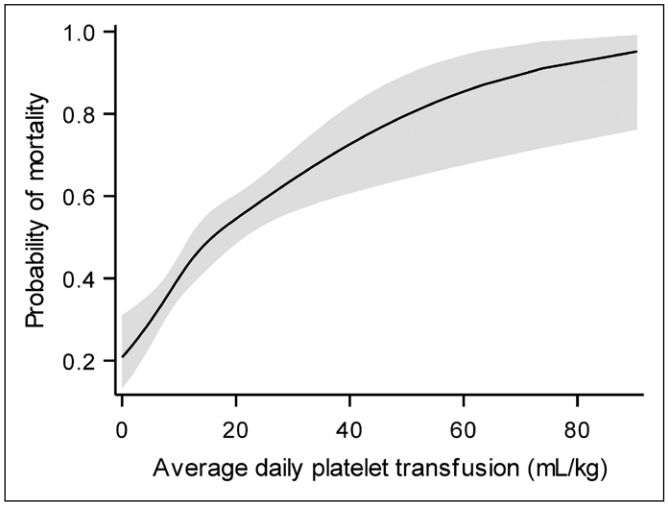

Figure 1. Unadjusted effect of average daily platelet transfusion volume on mortality risk.

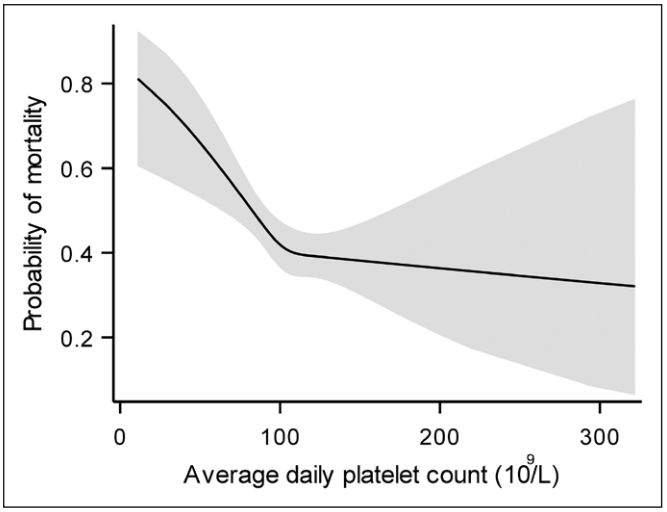

Figure 2. Unadjusted effect of average daily platelet count on mortality risk.

on each ECMO day. Outcomes included complications during ECMO and hospital mortality. Complications included bleeding events, thrombotic events, neurologic events, hepatic dysfunction, and renal failure. Bleeding events were defined as blood loss requiring a red cell transfusion or intracranial hemorrhage. Thrombotic events included intracranial infarction, limb ischemia, pulmonary embolus, intracardiac thrombus, aortopulmonary shunt thrombus, other sites of thrombosis, and circuit thrombosis requiring replacement of a circuit component. Neurologic events included seizures, intracranial hemorrhage or infarction, and brain death. Hepatic dysfunction was defined as international normalized ratio greater than 2. Renal failure was defined as creatinine greater than 2 mg/dL (> 176.8 μmol/L) or use of in-line hemofiltration or other form of continuous renal replacement therapy (CRRT).

Statistical Analysis

Clinical data were summarized by average daily platelet transfusion volume using counts and percentages for categorical variables and medians and first and third quartiles for continuous variables. Associations between clinical variables and average daily platelet transfusion volume were evaluated with the Cochran-Armitage trend test for binary variables, the Kruskal-Wallis test for other nominal variables, and the Jonckheere-Terpstra test for ordinal variables. These tests were chosen to account for the ordinal nature of average daily platelet transfusion volume.

The unadjusted association of average daily platelet transfusion volume and average daily platelet count with mortality was assessed with univariable logistic regression and natural cubic splines. Average daily platelet transfusion volume was determined to have a roughly linear association with the log odds of mortality and was therefore considered appropriate for inclusion in subsequent models as a linear (continuous) predictor (**Fig. 1**). Average daily platelet count, however, was determined to have a roughly linear association with the log odds of mortality up to a platelet count of approximately 115×10^9/L, after which there was little evidence of any change in the risk of mortality with increasing platelet count (**Fig. 2**). Subsequent modeling of mortality treated average daily platelet count as a linear (continuous) predictor only up to 115×10^9/L, after which further increases did not affect the modeled risk of mortality. This was accomplished by truncating the measurement of average daily platelet count to 115×10^9/L.

The association between average daily platelet count and in-hospital mortality was assessed with univariable and multivariable logistic regression models. Variables at least marginally associated with mortality in univariable modeling ($p < 0.10$) that were known for at least 90% of the cohort were considered candidate predictors for a multivariable model. The final multivariable model was created using a bidirectional stepwise selection process with criteria of p values less than 0.10 and 0.05 to enter and stay in the model, respectively.

The association between platelet count on the previous day with daily risk of bleeding was similarly assessed with day-level univariable and multivariable logistic regression models analogous to the models of mortality. An autoregressive covariance structure of order 1 and robust error estimates were used to account for correlation between different study days on the same subject. In particular, this accounts for a higher correlation between study days that are close together but relatively lower correlation between study days that are far apart. The association between platelet transfusion volume on the previous day with daily risk of thrombosis was similarly assessed with day-level univariable and multivariable logistic regression models analogous to the models of daily bleeding.

The decrease in platelet count after ECMO initiation was characterized by whether a platelet transfusion was administered on the day of ECMO initiation and by age. Only transfusions provided after ECMO initiation were recorded in the study, and platelet counts were only collected as obtained by standard of care. The decrease in platelets is summarized based on the last pre-ECMO and first on ECMO platelet counts, and only subjects with measurements within a 12-hour period on the first day of ECMO are included in this summary. Platelet goals are summarized

by institution, unit, and mode of ECMO using means and SDs. Analyses were performed using SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

Of 511 children, 496 (97.1%) received at least one platelet transfusion during ECMO. Neonatal age group, venoarterial ECMO, location of ECMO care in the neonatal ICU, acute diagnosis of congenital diaphragmatic hernia or persistent pulmonary hypertension of the newborn, and chronic diagnosis of congenital anomaly or chromosomal defect were associated with increased average daily platelet transfusion volume (**Table 1**). Acute diagnosis of acquired cardiovascular disease, pneumonia, or bronchiolitis; respiratory distress/failure; and chronic diagnosis of neurologic condition were associated with decreased average daily platelet transfusion volume.

Univariable and multivariable logistic models of hospital mortality are shown in **Supplemental Digital Content 1** (http://links.lww.com/PCC/B84) and **Table 2**, respectively. On multivariable analysis, variables independently associated with increased mortality included increased average daily platelet transfusion volume, higher minimum lactate within 48 hours of ECMO initiation, ECPR, renal failure, new neurologic event on ECMO, preterm neonatal age, and a diagnosis of congenital diaphragmatic hernia. Variables independently associated with decreased mortality included diagnosis of meconium aspiration syndrome and average daily heparin dose.

Univariable and multivariable logistic models of daily bleeding are shown in **Supplemental Digital Content 2** (http://links.lww.com/PCC/B85) and **Table 3**, respectively. On multivariable analysis, variables independently associated with increased daily bleeding risk included increased platelet transfusion volume on the previous ECMO day, a primary cardiac indication for ECMO, adolescent age, and an acute diagnosis of congenital cardiovascular disease. Platelet count on the previous day was not associated with daily bleeding risk.

Univariable and multivariable logistic models of daily thrombosis are shown in **Supplemental Digital Content 3** (http://links.lww.com/PCC/B86) and **Table 4**, respectively. On multivariable analysis, variables independently associated with increased daily thrombotic risk included platelet transfusion volume on the previous ECMO day and venoarterial ECMO. Variables independently associated with decreased daily thrombotic risk included full-term neonatal age and having an acute diagnosis of airway abnormality.

Of the 511 children in the study, 287 (56%) had a platelet count recorded on the first day within 12 hours after ECMO initiation. Children who received platelet transfusion on the day of ECMO initiation had lower pre-ECMO platelet counts and lower first post-ECMO platelet counts than those who did not receive platelet transfusion on the day of ECMO initiation (**Supplemental Digital Content 4**, http://links.lww.com/PCC/B87). Neonates had a larger decline in platelet count on ECMO initiation than nonneonates (**Supplemental Digital Content 5**, http://links.lww.com/PCC/B88). Platelet goals ranged across centers from $67 \pm 23 \times 10^9$/L to $113 \pm 22 \times 10^9$/L for venoarterial ECMO and 50×10^9/L to $100 \pm 0 \times 10^9$/L for venovenous ECMO (**Supplemental Digital Content 6**, http://links.lww.com/PCC/B89).

DISCUSSION

Nearly all children in our multicenter ECMO cohort received platelet transfusions. Factors related to increased average daily platelet transfusion volume included age, mode and location of ECMO, and various acute and chronic diagnoses. Average daily platelet transfusion volume was independently associated with mortality. Platelet transfusion volume on the previous ECMO day was independently associated with daily risk of bleeding and thrombosis; however, platelet count on the previous day was not.

In our ECMO cohort, neonates received a higher average daily platelet transfusion volume than older children. Thrombocytopenia is well described in the general neonatal ICU population (15–19). Additionally, neonatal platelets are hyporeactive in vitro in response to multiple agonists. Both low platelet count and hyporeactivity are more pronounced in preterm than in full-term neonates. Due to these concerns, early research suggested targeting a higher platelet count to prevent bleeding in neonates receiving ECMO (20). However, more recent work has shown that healthy full-term neonates display no clinical evidence of abnormal hemostasis and suggests that neonatal platelet hyporeactivity is part of balanced neonatal hemostatic system. Target platelet count was about 100×10^9/L in the neonatal ICUs included in our ECMO cohort, slightly higher than targets set in some of our pediatric and cardiac ICUs (Supplemental Digital Content 6, http://links.lww.com/PCC/B89). Previous studies have shown that most platelet transfusions administered to critically ill children are given prophylactically to meet a predefined threshold (1, 2); however, the reasons clinicians transfused platelets were not captured in the BATE study. Location of ECMO in a neonatal ICU and diagnoses such as congenital diaphragmatic hernia and persistent pulmonary hypertension of the newborn were also associated with increased average daily platelet transfusion volume likely due to their common occurrence in neonates. Venoarterial ECMO was associated with increased average daily platelet transfusion volume. In a prior study, neonates on venoarterial ECMO received more platelet transfusions that those on venovenous ECMO (21). Mechanical flow differences between venoarterial and venovenous ECMO, differences in disease severity and diagnosis, and other unmeasured factors were suggested explanations for the difference in platelet transfusions.

Interestingly, although average daily platelet transfusion volume was an independent predictor of mortality, average daily platelet count was not. Our findings suggest that platelet transfusion practice should not be based on a specific target level alone but should also consider the potential harms associated with platelet transfusion including immune, inflammatory, and hemodynamic consequences. A recent randomized trial in premature neonates with severe thrombocytopenia compared target platelet transfusion thresholds of 50×10^9/L versus 25×10^9/L and found a greater proportion of neonates exposed to platelet transfusion

TABLE 1. Clinical Characteristics by Average Daily Platelet Transfusion Volume

Characteristic	Average Daily Platelet Transfusion Volume (mL/kg Body Weight)[a]			p
	< 9 (*n* = 187)	9 to < 17 (*n* = 158)	≥ 17 (*n* = 166)	
Age, *n* (%)				< 0.001[b]
Preterm neonate	4 (2.1)	18 (11.4)	28 (16.9)	
Full-term neonate	50 (26.7)	81 (51.3)	86 (51.8)	
Infant	55 (29.4)	29 (18.4)	38 (22.9)	
Child	44 (23.5)	23 (14.6)	12 (7.2)	
Adolescent	34 (18.2)	7 (4.4)	2 (1.2)	
Primary ECMO indication, *n* (%)				0.811[c]
Respiratory	84 (44.9)	75 (47.5)	77 (46.4)	
Cardiac	76 (40.6)	61 (38.6)	69 (41.6)	
Extracorporeal cardiopulmonary resuscitation	27 (14.4)	22 (13.9)	20 (12.0)	
Mode of ECMO, *n* (%)				0.048[d]
Venoarterial	148 (79.1)	137 (86.7)	144 (86.7)	
Venovenous	39 (20.9)	21 (13.3)	22 (13.3)	
Location of ECMO care, *n* (%)				< 0.001[c]
PICU	54 (28.9)	27 (17.1)	21 (12.7)	
Neonatal ICU	23 (12.3)	65 (41.1)	68 (41.0)	
Cardiac ICU	110 (58.8)	66 (41.8)	77 (46.4)	
Baseline Pediatric Risk of Mortality III	8.0 (3.0–12.0)	9.0 (5.0–13.0)	9.0 (4.0–14.0)	0.117[b]
Acute diagnoses, *n* (%)				
Airway abnormality	4 (2.1)	2 (1.3)	6 (3.6)	0.380[d]
Immune dysfunction	17 (9.1)	11 (7.0)	8 (4.8)	0.117[d]
Cardiac arrest	21 (11.2)	17 (10.8)	10 (6.0)	0.099[d]
Cardiovascular disease (acquired)	35 (18.7)	15 (9.5)	14 (8.4)	0.003[d]
Cardiovascular disease (arrhythmia)	5 (2.7)	3 (1.9)	10 (6.0)	0.097[d]
Cardiovascular disease (congenital)	70 (37.4)	54 (34.2)	69 (41.6)	0.446[d]
Hypoxic/anoxic injury	3 (1.6)	7 (4.4)	7 (4.2)	0.163[d]
Gastrointestinal disorder	8 (4.3)	4 (2.5)	11 (6.6)	0.311[d]
Pertussis or sepsis	29 (15.5)	33 (20.9)	29 (17.5)	0.602[d]
Pneumonia or bronchiolitis	14 (7.5)	6 (3.8)	4 (2.4)	0.023[d]
Shock (nonseptic)	5 (2.7)	4 (2.5)	5 (3.0)	0.851[d]
Respiratory distress/failure	79 (42.2)	44 (27.8)	47 (28.3)	0.005[d]
Neurologic condition	9 (4.8)	4 (2.5)	3 (1.8)	0.102[d]
Meconium aspiration syndrome	11 (5.9)	17 (10.8)	19 (11.4)	0.067[d]
Congenital diaphragmatic hernia	3 (1.6)	24 (15.2)	29 (17.5)	< 0.001[d]
Persistent pulmonary hypertension of the newborn	16 (8.6)	42 (26.6)	32 (19.3)	0.006[d]
Chronic diagnoses, *n* (%)				
Chronic lung disease	8 (4.3)	4 (2.5)	5 (3.0)	0.494[d]
Immune dysfunction	8 (4.3)	5 (3.2)	3 (1.8)	0.184[d]
Congenital anomaly or chromosomal defect	29 (15.5)	38 (24.1)	51 (30.7)	< 0.001[d]
Neurologic condition	18 (9.6)	4 (2.5)	4 (2.4)	0.002[d]
Cardiovascular disease (congenital)	31 (16.6)	36 (22.8)	29 (17.5)	0.791[d]

ECMO = extracorporeal membrane oxygenation.

[a]Categories of average daily platelet transfusion volume are based on tertiles of platelet transfusion volume within this study cohort.

[b]Jonckheere-Terpstra test.

[c]Kruskal-Wallis test.

[d]Cochran-Armitage trend test.

TABLE 2. Multivariable Logistic Model of Mortality

Characteristic	In-Hospital Mortality OR (95% CI)	*p*
Average daily platelet count (per 10^9/L up to 115×10^9/L)	1.00 (0.98–1.01)	0.487
Average daily platelet transfusion volume (1 mL/kg)	1.05 (1.03–1.08)	< 0.001
Lowest lactate in 48 hr post-ECMO initiation (mmol/L)	1.38 (1.19–1.66)	< 0.001
Average daily heparin dose (U/kg/min)	0.26 (0.07–0.91)	0.032
Meconium aspiration syndrome	0.15 (0.02–0.63)	0.007
Renal failure	1.92 (1.15–3.21)	0.012
New neurologic event	4.05 (2.48–6.73)	< 0.001
Primary ECMO indication		0.027
Respiratory	Reference	
Cardiac	2.08 (1.17–3.76)	
Extracorporeal cardiopulmonary resuscitation	2.34 (1.06–5.24)	
Age		0.002
Preterm neonate	3.97 (1.72–9.53)	
Full-term neonate	Reference	
Infant	2.50 (1.36–4.68)	
Child	2.22 (1.08–4.60)	
Adolescent	2.60 (1.06–6.35)	
Congenital diaphragmatic hernia	3.63 (1.56–8.63)	0.003

ECMO = extracorporeal membrane oxygenation, OR = odds ratio.

The reported effect of average daily platelet count on mortality is for each additional 1×10^9 cells/L up to a count of 115×10^9/L, beyond which the odds of mortality is assumed constant.

TABLE 3. Multivariable Logistic Model of Daily Bleeding

Characteristic	Bleeding Event OR (95% CI)	*p*
Platelet transfusion volume on the previous day (1 mL/kg)	1.01 (1.00–1.01)	< 0.001
Primary extracorporeal membrane oxygenation indication		0.033
Respiratory	Reference	
Cardiac	1.72 (1.15–2.58)	
Extracorporeal cardiopulmonary resuscitation	1.42 (0.84–2.38)	
Age		0.003
Preterm neonate	1.39 (0.91–2.13)	
Full-term neonate	Reference	
Infant	1.18 (0.81–1.73)	
Child	1.74 (1.11–2.71)	
Adolescent	3.58 (2.17–5.92)	
Cardiovascular disease (congenital)	1.54 (1.04–2.28)	0.037

OR = odds ratio.

and higher rate of death or major bleeding in the 50×10^9/L target group (22). In our study, both average daily platelet transfusion volume and average daily red cell transfusion volume were associated with mortality on univariable analysis. However, on multivariable analysis, average daily platelet transfusion volume remained a significant predictor of mortality, whereas average daily red cell transfusion volume did not.

Our findings suggest that platelet transfusion volume is associated with complications during ECMO. As noted in the BATE study, although the cumulative rates of bleeding and thrombosis were related to the duration of ECMO, the daily occurrence rates remained steady for the duration of ECMO (13). Consequently, it is unlikely that the duration of ECMO was a major contributor to daily complication rates. Platelet transfusion volume on the previous ECMO day was independently associated with daily bleeding events suggesting that children receiving platelets had ongoing bleeding and/or platelet consumption. Children with a primary cardiac indication for ECMO, an acute diagnosis of congenital cardiovascular disease, or adolescent age had increased bleeding risk. Postoperative cardiac surgical patients have increased bleeding risk due to surgical incisions and platelet dysfunction from cardiopulmonary bypass (23, 24) which is amplified with systemic anticoagulation on ECMO. Bleeding during ECMO is multifactorial and related to increased fibrinolysis, loss of large von Willebrand factor multimers, and decreased platelet count and function (25–27). Although platelets have a key role in normal hemostasis, transfusing platelets to increase the platelet count during ECMO may not lead to the desired clinical outcome.

In our study, platelet transfusion volume on the previous day was independently associated with daily thrombotic events. Platelet activation occurs when blood is exposed to the ECMO circuit leading to increased clot burden (3, 28). Recent studies have shown that activated platelets promote thrombosis by release of platelet-derived microparticles (PMPs) and that PMPs are generated by ECMO systems (29, 30). Due to the observational nature of our study, we cannot differentiate whether ongoing thrombus formation and its associated platelet consumption led to decreased platelet count and subsequent transfusion, or whether platelet transfusion led to thrombus formation. Both processes are feasible and may occur

TABLE 4. Multivariable Logistic Model of Daily Thrombosis

Characteristic	Thrombotic Event	
	OR (95% CI)	*p*
Platelet transfusion volume on the previous day (1 mL/kg)	1.01 (1.00–1.02)	0.010
Mode of extracorporeal membrane oxygenation		< 0.001
Venoarterial	Reference	
Venovenous	0.40 (0.26–0.64)	
Age		0.032
Preterm neonate	1.08 (0.64–1.81)	
Full-term neonate	Reference	
Infant	2.09 (1.39–3.13)	
Child	1.62 (0.94–2.78)	
Adolescent	1.37 (0.78–2.40)	
Airway abnormality	0.24 (0.09–0.67)	0.007

OR = odds ratio.

simultaneously. We know from the BATE study that 37.5% of children had a thrombotic event. Of these, 12.8% were patient related and 31.1% were circuit related. Unfortunately, the relationship between platelet transfusion volume and site/type of thrombosis was not evaluated (13).

The mechanisms driving platelet consumption and activation are important to define in order to target therapies on ECMO. Children with ventricular assist devices routinely receive antiplatelet agents, but children on ECMO do not; such agents may increase bleeding risk during ECMO without substantially reducing thrombosis (31). Others report using modified surfaces that create local release of nitric oxide to inhibit platelets that directly interface with the biomaterial surface, whereas the remaining platelets maintain normal functionality (32–34). Further research regarding mechanisms of platelet dysfunction including activation, consumption, and oxidative stress may help guide therapeutic interventions to reduce rates of thrombosis during ECMO (35).

Our findings demonstrate that most children had a substantial reduction in platelet count after ECMO initiation. Children transfused platelets on the day of ECMO initiation had lower platelet counts pre-ECMO and after ECMO initiation. Although neonates had higher platelet counts pre-ECMO, they also had a greater decline in platelets after ECMO initiation than older children. The decline in platelets observed in our neonates (56%) was even larger than a previous report (42%) (36). These findings may help bedside clinicians anticipate the magnitude of decline in platelet count prior to laboratory sampling. Anecdotal data suggest that including platelets in the ECMO prime for neonates prevents the large decline in platelet count seen on initiation. Whether this practice prevents bleeding, thrombosis, or less platelet transfusion requires further study.

Strengths of this study include the multicenter design and daily prospective collection of data. Limitations include recording platelet counts obtained closest to 7 AM rather than all values. We used platelet counts and transfusion volumes from the previous day to evaluate associations with daily bleeding and thrombosis events. We did this because the exact timing of platelet counts and transfusions, and bleeding and thrombosis events, were not recorded in the BATE study. Only the day of the bleeding or thrombosis event was recorded, not the time. Platelet counts and transfusion volumes from the same day as the bleeding or thrombosis event could potentially have occurred after the event. This was avoided by using the platelet count and transfusion volume from the previous day in our analyses. Indications for transfusing platelets were not recorded in the BATE study. Thus, the number of children who received a platelet transfusion for bleeding or solely because their count was below a predefined threshold is unknown, as is the extent that predefined thresholds may have influenced our results. The lack of data on the reason for platelet transfusion is a major limitation of our study. Information regarding platelet function was also not available. Platelet transfusion volume may be a surrogate marker for severity of illness. Although we found no association between baseline PRISM scores and bleeding or thrombotic events, severity of illness could potentially be an explanatory factor in the relationship between transfusion volume and outcomes. Concomitant CRRT may cause thrombocytopenia, unfortunately the various forms of CRRT used in this study were not collected and their associations with outcome could not be assessed. Renal failure, which included the use of CRRT in its definition, was associated with mortality. Importantly, this is an observational study and the associations observed do not infer causation.

CONCLUSIONS

Our findings suggest that nearly all children undergoing ECMO receive platelet transfusion. Platelet transfusion volume is associated with increased mortality and daily bleeding and thrombotic risk. Future investigations should include measures of platelet function to determine whether platelet count is the optimal parameter to follow clinically or whether other indices should be used in decision-making for platelet transfusion.

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