Epidemiology of Hemostatic Transfusions in Children Supported by Extracorporeal Membrane Oxygenation

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Objective: To evaluate the epidemiology of hemostatic transfusions (plasma, platelet, and cryoprecipitate) in children supported by extracorporeal membrane oxygenation.

Design: Secondary analysis of a large observational cohort study.

Setting: Eight pediatric institutions within the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development's Collaborative Pediatric Critical Care Research Network.

Patients: Critically ill children supported by extracorporeal membrane oxygenation.

Interventions: None.

Measurements and Main Results: Extracorporeal membrane oxygenation was used in the care of 514 consecutive children. Platelets were transfused on 68% of extracorporeal membrane oxygenation days, plasma on 34% of the days on extracorporeal membrane oxygenation, and cryoprecipitate on 14%. Only 24% of the days on extracorporeal membrane oxygenation were free of any hemostatic transfusions. Daily platelet transfusion dose was independently associated with chest tube output ($p < 0.001$), other bleeding requiring RBC transfusion ($p = 0.03$), and daily set platelet goal ($p = 0.009$), but not with total platelet count ($p = 0.75$). Daily plasma transfusion dose was independently associated with chest tube output ($p < 0.001$), other bleeding requiring RBC transfusion ($p = 0.01$), activated clotting time ($p = 0.001$), and antithrombin levels ($p = 0.02$), but not with international normalized ratio ($p = 0.99$) or activated partial thromboplastin time ($p = 0.29$). Daily cryoprecipitate transfusion dose was independently associated with younger age ($p = 0.009$), but not with chest tube bleeding ($p = 0.18$), other bleeding requiring RBC transfusion ($p = 0.75$), fibrinogen level ($p = 0.67$), or daily fibrinogen goal ($p = 0.81$).

Conclusions: Platelets were transfused on two third of the days on extracorporeal membrane oxygenation, plasma on one third, and cryoprecipitate on one sixth of the days. Although most hemostatic transfusions were independently associated with bleeding, they were not independently associated with the majority of hemostatic testing. Further studies are warranted to evaluate the appropriateness of these transfusion strategies. (*Crit Care Med* 2020; 48:e698–e705)

Key Words: blood transfusion; children; extracorporeal membrane oxygenation; hemostasis; patient blood management

Bleeding is a frequent complication of extracorporeal membrane oxygenation (ECMO) and is independently associated with mortality (1–3). Hemostatic transfusions (plasma, platelet, and cryoprecipitate) are frequently prescribed to prevent (prophylactic transfusions) or treat bleeding (therapeutic transfusions). In two large observational cohorts of critically ill children who were administered plasma or platelet transfusions, 11% of all plasma (4) and 16% of all platelet (5) were administered to children on ECMO. Among those patients, prophylactic transfusions were more common and accounted for 60% and 78% of plasma and platelet transfusions, respectively (6).

Despite their possible therapeutic benefits, hemostatic transfusions are associated with worse clinical outcomes. Both plasma and platelet transfusions are associated with increased organ failure and mortality in critically ill children (5, 7). Furthermore, specifically in children supported by ECMO, platelet transfusions are independently associated with an increased risk of mortality (8, 9).

Currently, it is not known how frequently these blood products are administered over the course of the ECMO run and in which combination, nor are there data on the use of cryoprecipitate in children on ECMO. The factors predicting utilization of these hemostatic transfusions are unclear, such as the type of ECMO, the bleeding status, the hemostatic tests, or the daily hemostatic goals set by the attending physician. This lack of epidemiologic information prevents the design of trials to investigate hemostatic transfusion strategies in critically ill children supported by ECMO (10).

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The primary objective of this study was to describe the epidemiology of hemostatic transfusions in children supported by ECMO. The secondary objective was to identify risk factors associated with the receipt of hemostatic transfusions.

MATERIALS AND METHODS

This is a secondary analysis of a large observational study. This analysis was approved by the Institutional Review Board at Virginia Commonwealth University. A detailed methodology of the parent study has been published previously (2). In summary, consecutive patients under 19 years old treated with ECMO initiated in a PICU, cardiac ICU (CICU), or neonatal ICU (NICU) of eight *Eunice Kennedy Shriver* National Institute of Child Health and Human Development's Collaborative Pediatric Critical Care Research Network institutions between December 2012 and September 2014 were included in the study. The study was limited only to the initial ECMO course for patients who might have required multiple runs of ECMO support.

Demographic data (age, weight, primary diagnosis, and presence of comorbidities), indication for ECMO (cardiac, respiratory, extracorporeal cardiopulmonary resuscitation), need for ECMO after cardiac surgery, and ECMO characteristics (venovenous vs venoarterial mode) were collected. Clinical data collected on a daily basis included all administered blood product transfusions and laboratory results closest to 7:00 AM. We defined hemostatic tests as those that might lead to plasma, platelet, or cryoprecipitate transfusions on that day, that is, platelet count ($\times 10^9$/L), activated clotting time (ACT, in seconds), prothrombin time (PT, in seconds), activated partial thromboplastin time (aPTT, in seconds), international normalized ratio (INR), fibrinogen (in mg/dL), and antithrombin (in percentage). In addition, the daily hemostatic goals which included platelet count goals, PT or aPTT goals, fibrinogen goals, and antithrombin goals were collected. The daily hemostatic goals were set at the attending physician's discretion and not standardized across institutions. We evaluated whether these goals had changed from the previous day. Likewise, the decision to transfuse hemostatic blood products was at the discretion of the attending physician, and no algorithms were applied across institutions.

Bleeding outcomes were defined as either chest tube bleeding (as previously described [11]), intracranial hemorrhage, or any bleeding requiring RBC transfusion, which included bleeding from the surgical or cannula sites, pulmonary hemorrhage, gastrointestinal, or genitourinary bleeding. Changes in bleeding in response to hemostatic blood products were not recorded in the database. Anticoagulation was maintained with heparin infusions dosed at the attending physician's discretion.

Survival status was recorded at hospital discharge, and therefore, mortality was defined as "in-hospital" mortality. We also measured ECMO duration as well as length of stay.

Results are expressed as median and interquartile range (IQR) or frequencies and proportions. We reported the frequency of hemostatic transfusions over the course of the first 28 ECMO days, using histograms (which were censored at 28 d, for clarity). We also reported the number of ECMO days with hemostatic transfusions using a Venn diagram, the daily dose of hemostatic transfusions (in milliliters per kilogram), as well as the overall proportion of patients having received hemostatic transfusions.

The differences in hemostatic goals according to clinical variables (age, type of ECMO, bleeding status, and patient location) were assessed using the Mann-Whitney *U* test. Similar analyses were performed to describe the differences in hemostatic tests according to clinical variables, as well as transfusion doses according to clinical variables.

A one-way analysis of variance test was used to assess the association between hemostatic transfusion doses and ECMO days.

Multivariable linear models were developed to assess risk factors associated with plasma, platelet, and cryoprecipitate transfusion doses, reporting β coefficients. Variables were considered potential predictors if they were associated with the outcome in univariate analysis ($p < 0.10$). The final model was selected using a bidirectional stepwise selection on the potential predictors with a significance criterion of p value less than 0.05 to enter in the model and p value greater than 0.1 to be removed. No variables other than bleeding, hemostatic tests, and hemostatic daily goals were forced into the model.

Differences were considered statistically significant when a two-sided α level was less than 0.05. We did not adjust for repeat measures within subjects. All statistical analyses were performed with SPSS version 26 for Mac (SPSS, Chicago, IL).

RESULTS

Demographics and Clinical Outcome

Five hundred-fourteen patients were enrolled, of whom 302 of 514 (59%) were male. The median age was 0.23 months (IQR, 0–11.1), and the median weight was 3.65 kg (IQR, 3.00–8.50). Fifty-four percent of the patients (280/514) were neonates (< 28 d). The admitting diagnoses and comorbidities have been published previously (2). Fifteen percent (78/514) of the ECMO runs were venovenous, 97% (76/78) of which were for respiratory indications. Of the 436 venoarterial ECMO runs, 47% (205/436) were primarily for cardiac support, 37% (161/436) were for respiratory support, and 16% (70/436) were for ECMO-cardiopulmonary resuscitation.

The median duration of ECMO support was 5 days (IQR, 3–9 d). In total, there were 4,660 ECMO days. The median PICU length of stay was 28 days (IQR, 14–52 d). The overall survival to hospital discharge was 55% (282/514).

Daily Hemostatic Goals

Platelet goals were set on 93% (4,336/4,660) of ECMO days, ACT on 89% (4,137/4,660), fibrinogen on 68% (3,149/4,660), antithrombin on 24% (1,109/4,660), aPTT on 20% (940/4,660), and PT on 0.3% (13/4,660). **Table S1** (Supplemental Digital Content 1, http://links.lww.com/CCM/F533) demonstrates the proportions of set daily hemostatic goals according to the patient location and the type of ECMO. The median values of the defined hemostatic goals are presented in **Table 1**.

TABLE 1. Daily Hemostatic Daily Goals, According to Bleeding Status, Extracorporeal Membrane Oxygenation Type (Venoarterial vs Venevenous), and Age (≤ 28 vs > 28 d)

	Low Platelet Count	High Activated Clotting Time (s)	High Activated Partial Thromboplastin Time (s)	Low Fibrinogen	Low Antithrombin (%)
Bleeding status					
Bleeding	100 (100–100)	200 (200–220)	70 (70–80)	150 (100–150)	80 (60–80)
Nonbleeding	100 (80–100)	220 (200–220)	80 (70–90)	150 (100–150)	75 (50–85)
p	< 0.001	< 0.001	< 0.001	< 0.001	0.79
Type of extracorporeal membrane oxygenator					
Venovenous	100 (100–100)	210 (200–220)	70 (60–80)	150 (100–150)	80 (60–80)
Venoarterial	100 (80–100)	210 (200–220)	80 (70–90)	150 (100–150)	70 (50–85)
p	0.009	0.68	< 0.001	0.21	0.68
Age					
≤ 28 d	100 (100–100)	210 (200–220)	90 (70–100)	150 (100–150)	80 (50–90)
> 28 d	100 (80–100)	200 (200–220)	80 (70–90)	150 (100–150)	75 (60–80)
p	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

Daily hemostatic goals were set by the attending physician. They usually included a lowest and highest targeted value for the day. Results are expressed as median and interquartile range. Prothrombin time goals were set for only three patients (median, 15 s; IQR, 15–15) and are, therefore, not reported in the table.

Excluding the initial goals defined on the first day of the ECMO course, daily hemostatic goals were changed in 29% (1,193/4,146) of ECMO days (**Fig. S1**, Supplemental Digital Content 1, http://links.lww.com/CCM/F533). Changes in hemostatic goals were associated with the day of ECMO ($p < 0.001$): 22% (258/1,193) of the changes occurred on the day following ECMO initiation, and 50% (600/1,193) within the first 3 days after initiation. Platelet goals were changed on 5% (227/4,146) of the ECMO days, ACT on 12% (491/4,146), PT on less than 0.1% (1/4,146), aPTT on 0.9% (37/4,146), fibrinogen on 1.6% (68/4,146), and antithrombin on 1.0% (44/4,146). Bleeding was associated with changes in platelet goals ($p = 0.002$) and ACT goals ($p < 0.001$), but not with PT goals ($p = 0.99$), aPTT ($p = 0.25$), fibrinogen ($p = 0.11$), and antithrombin ($p = 0.65$).

Daily Hemostatic Tests

The median values of the hemostatic tests are presented in **Table S2** (Supplemental Digital Content 1, http://links.lww.com/CCM/F533). Regarding the use of PT and/or INR, on the majority of ECMO days, both PT and INR were measured. Specifically, both PT and INR were measured on 78% of ECMO days (3,635/4,660). Neither PT nor INR were measured on 22% of ECMO days (1,012/4,660). INR but not PT was measured on 0.1% of days (4/4,660), and PT but not INR was measured on 0.2% of days (9/4,660).

When comparing bleeding with nonbleeding patients, there were statistically significant differences in ACT ($p < 0.001$), aPTT ($p = 0.004$), fibrinogen ($p < 0.001$), and antithrombin levels ($p < 0.001$), but there were no significant differences in platelet count ($p = 0.52$), PT ($p = 0.21$), and INR ($p = 0.65$).

Hemostatic Transfusions

Platelets were transfused on 67.8% (3,160/4,660) of the ECMO days. The median daily platelet transfusion dose was 17.3 mL/kg (IQR, 10.9–28.3 mL/kg). The platelet transfusion daily dose differed according to the patients age, type of ECMO, and bleeding status (all $p < 0.001$) (**Fig. 1**). The proportion of patients who received platelets did not vary over the course of ECMO ($p = 0.47$) (**Fig. 2**).

Plasma was transfused on 33.6% (1,568/4,660) of the ECMO days. The median daily plasma transfusion dose was 16.4 mL/kg (IQR, 10.8–30.4 mL/kg). The plasma transfusion daily dose differed according to the patients age, type of ECMO, and bleeding status (all $p < 0.001$) (Fig. 1). The proportion of patients who received plasma varied significantly over the course of ECMO ($p < 0.001$) (Fig. 2).

Cryoprecipitate was transfused on 14.1% (655/4,660) of the ECMO days. The median daily cryoprecipitate transfusion dose was 5.3 mL/kg (IQR, 3.1–9.8 mL/kg). The cryoprecipitate transfusion daily dose was higher in neonates than in older children (6.8 mL/kg [IQR, 4.4–11.3 mL/kg] vs 3.6 mL/kg [IQR, 1.8–6.7 mL/kg]; $p < 0.001$). However, cryoprecipitate transfusion daily doses were not associated with the type of ECMO ($p = 0.34$) or the bleeding status ($p = 0.81$). The proportion of patients who received cryoprecipitate did not vary over the course of ECMO ($p = 0.20$) (**Fig. S2**, Supplemental Digital Content 1, http://links.lww.com/CCM/F533). Cryoprecipitate transfusion doses had a stronger correlation with platelet transfusions ($R = 0.29$; $p < 0.001$) than with plasma transfusions ($R = 0.11$; $p = 0.006$).

Both platelets and plasma were transfused in combination on 21.4% (996/4,660) of the ECMO days, plasma and cryoprecipitate on 0.9% days (44/4,660 d), platelet and cryoprecipitate

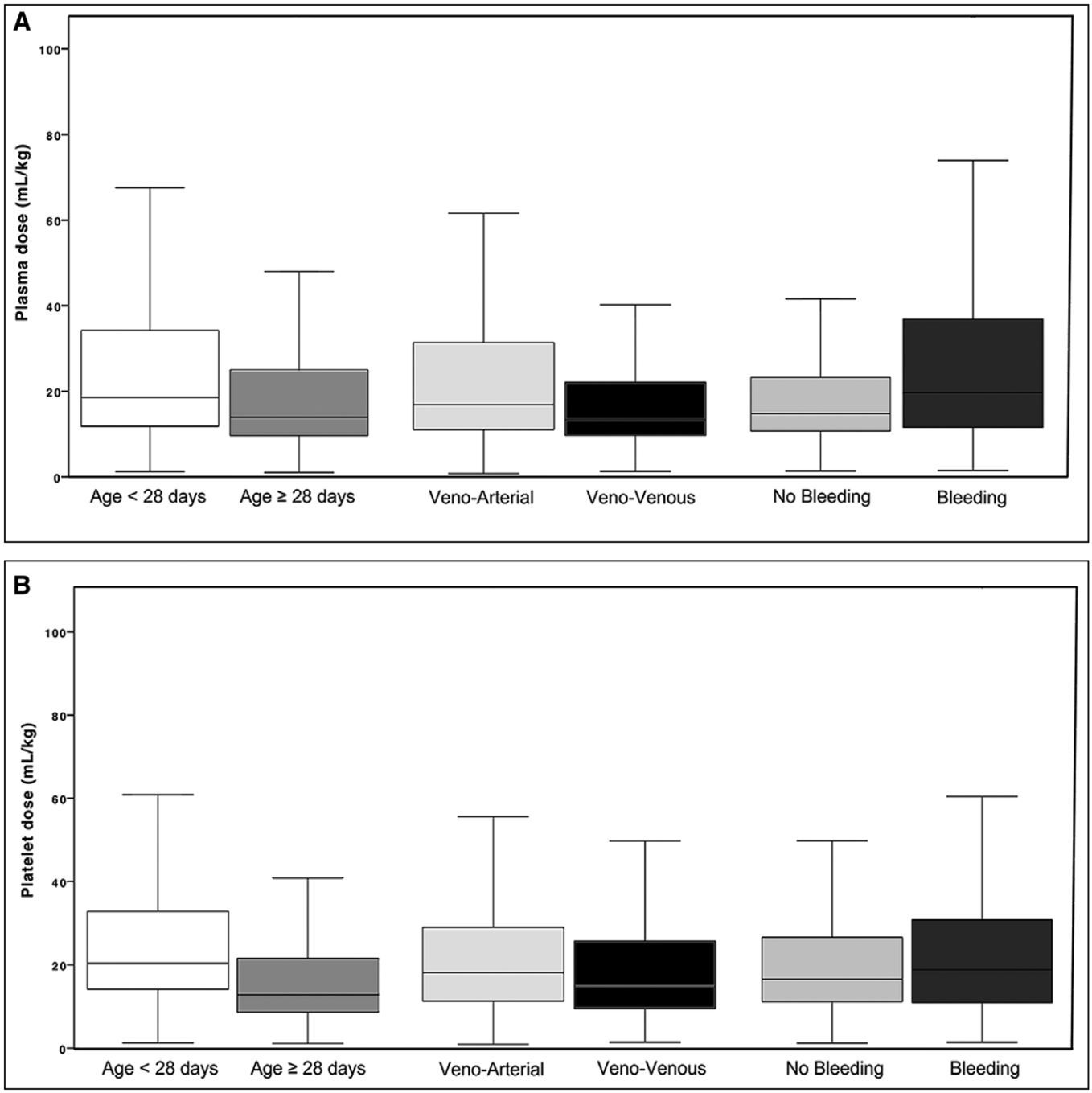

Figure 1. Plasma (**A**) and platelet (**B**) transfusion daily dose (in mL/kg) according to the patients' age (< 28 vs ≥ 28 d), type of extracorporeal membrane oxygenation (venovenous vs venoarterial), and bleeding status (bleeding vs no bleeding). The differences in transfusion doses between the various categories were all statistically significant (all $p < 0.001$).

on 4.3% (201/4,660) of the ECMO days, and all three hemostatic products on 6.5% (305/4,660) of the ECMO days. Twenty-four percent (1,170/4,660) of the ECMO days were free of any hemostatic transfusions (**Fig. 3**).

Factors Predictive of Hemostatic Transfusions

Our regression model adjusted for age, type of ECMO (venovenous vs venoarterial), location of ECMO (PICU, NICU, CICU), ECMO indication (respiratory, cardiac, extracorporeal cardiopulmonary resuscitation), chest tube output, bleeding status, other bleeding events requiring RBC transfusion, hemostatic tests (platelet count, ACT, PT, aPTT, INR, ACT, fibrinogen, and antithrombin), other hemostatic transfusions, and daily hemostatic goals. The daily plasma transfusion dose (per milliliters per kilogram) was independently associated with chest tube bleeding ($p < 0.001$), other bleeding requiring RBC transfusion ($p = 0.01$), daily ACT ($p < 0.001$) and antithrombin level ($p = 0.02$), daily platelet

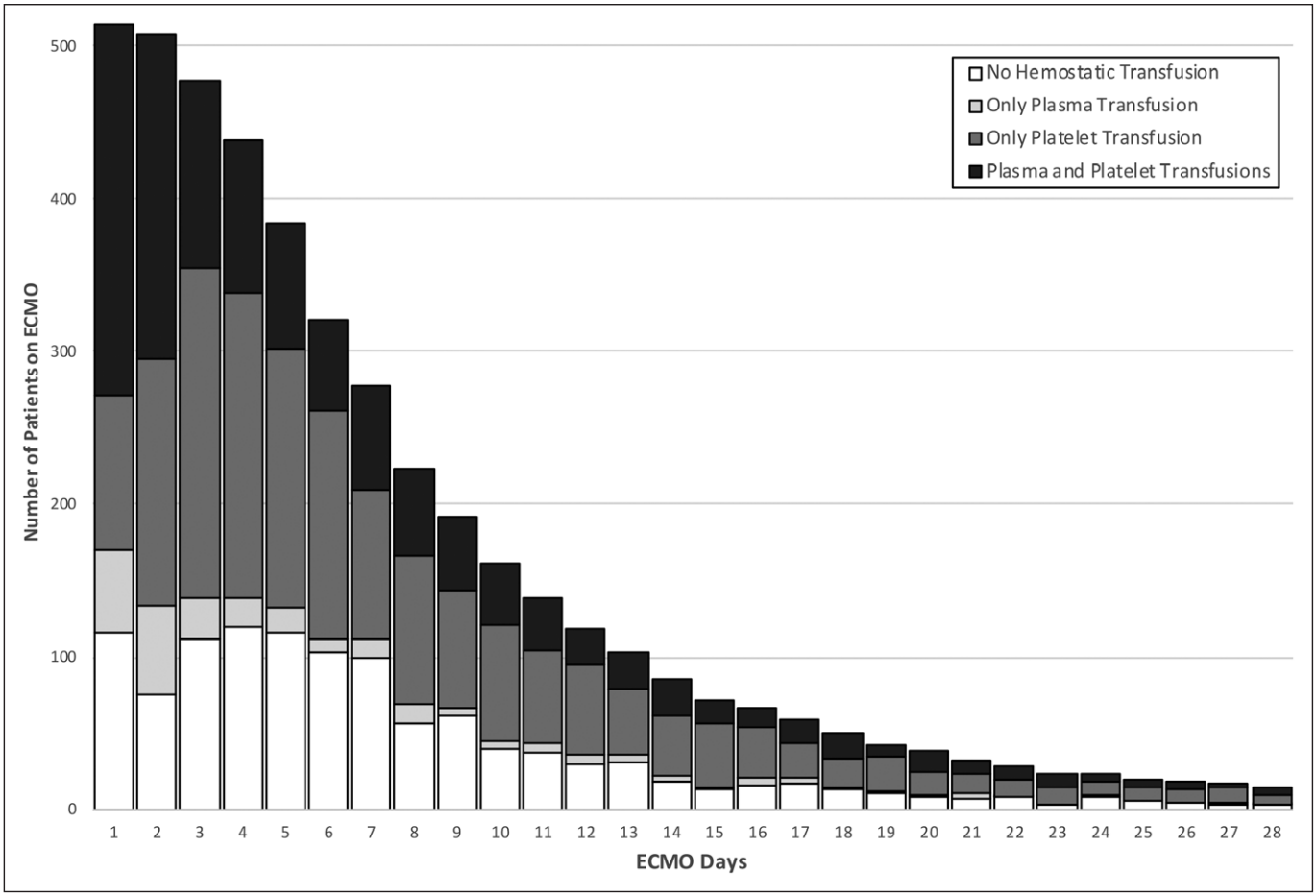

Figure 2. Histogram of the proportion of patients who received plasma, platelet, and both plasma and platelet, over the course of extracorporeal membrane oxygenation (ECMO) days.

goal ($p = 0.006$), and inversely associated with platelet transfusion ($p = 0.049$) and daily antithrombin goal ($p = 0.002$). Plasma transfusion doses were not independently associated with platelet count ($p = 0.62$), INR ($p = 0.99$), aPTT ($p = 0.29$), or daily aPTT goal ($p = 0.09$) (**Table 2**).

Adjusting for the same variables, the daily platelet transfusion dose was independently associated with chest tube output ($p < 0.001$), other bleeding requiring RBC transfusion ($p = 0.03$), plasma transfusion ($p = 0.049$), and daily set platelet goal ($p = 0.009$), but not platelet count ($p = 0.75$), INR ($p = 0.70$), ACT (0.58), or fibrinogen ($p = 0.50$) (Table 2).

Adjusting for the same variables, cryoprecipitate transfusion was independently associated with age ($p = 0.009$), but not with chest tube bleeding ($p = 0.18$), other bleeding requiring RBC transfusion ($p = 0.75$), fibrinogen level ($p = 0.67$), or daily fibrinogen goal ($p = 0.39$) (Table 2).

Hemostatic Transfusions Over the Entire Course of ECMO

Only 2% (11/514) of the patients did not receive any hemostatic transfusions "over the entire course of ECMO." The patients who did not receive any hemostatic transfusions had similar proportion of VA ECMO ($p = 0.75$) and survival ($p = 0.23$), but the duration of ECMO was shorter (2 d [IQR, 2–3 d] vs 5 d [IQR, 3–5 d]; $p = 0.005$) and chest tube bleeding was numerically, but not significantly, lower (2 mL/kg [IQR, 0–23 mL/kg] vs 25 mL/kg [IQR, 0–192 mL/kg]; $p = 0.07$).

Among those transfused, the median plasma, platelet, and cryoprecipitate dose for the entire ECMO run were 52 mL/kg (IQR, 24–111 mL/kg), 82 mL/kg (IQR, 39–176 mL/kg), and 10 mL/kg (6–22 mL/kg), respectively.

DISCUSSION

Hemostatic transfusions are frequently administered to critically ill children supported by ECMO. Plasma is transfused on one third of the days on ECMO, platelets on two thirds, and cryoprecipitate on one sixth of the days. Only a quarter of the days on ECMO were free of any hemostatic transfusions, and only 2% of the patients on ECMO did not receive any hemostatic transfusions.

Epidemiology of Hemostatic Transfusions

Virtually all critically ill children supported by ECMO receive at least one hemostatic transfusion. The frequency of plasma transfusion was higher during the first days, whereas there was no significant difference for platelet and cryoprecipitate transfusions. This might be due to the initial adjustments in anticoagulation (with a progressive increase in heparin) because the risk

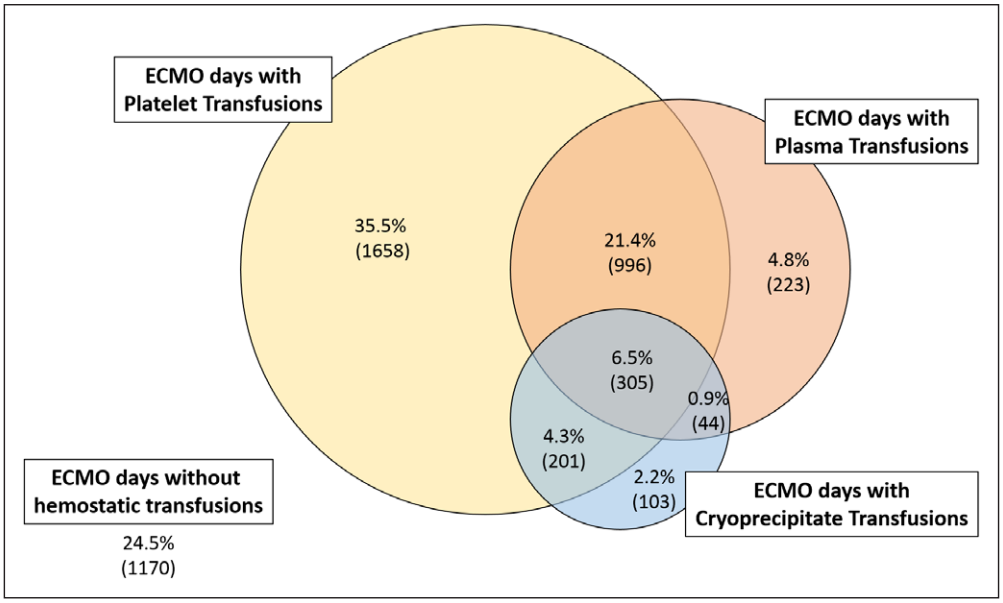

Figure 3. Venn diagram of the extracorporeal membrane oxygenation (ECMO) days with plasma, platelet, and cryoprecipitate transfusions.

of bleeding seems to be continuous over the duration of ECMO (11).

In our population, the median daily dose of hemostatic transfusions was high (16.4 mL/kg/d for plasma and 17.3 mL/kg/d for platelets). Previous reports have noted that both plasma and platelet transfusions are associated with worse outcomes in critically ill children, with each 10 mL/kg of platelets being independently associated with a 2% increase in mortality (5, 7). And as, specifically in children supported by ECMO, platelet transfusions are associated with increased risk of mortality, bleeding, and thrombosis (8), it is important to evaluate the appropriateness of these transfusion strategies.

Hemostatic Daily Goals

It is interesting to observe that defined hemostatic goals did not change based on the bleeding status of the patient. Although there are statistically significant differences in the distribution of the variables as represented by the *p* values, the medians for each hemostatic goal are similar and likely not clinically significant. The median platelet goals for both bleeding and nonbleeding patients were 100×10^9/L, the median aPTT goal was 70 seconds in bleeding patients and 80 seconds in nonbleeding patients, and the median ACT goal was 200 seconds in bleeding patients and 220 seconds in nonbleeding patients. Similar results have already been reported (6), although in a smaller sample size. These results suggest that the bleeding status of a patient does not modify the hemostatic goals defined by the medical team.

Hemostatic Tests and Transfusions

Apart from aPTT, there were very few differences in morning hemostatic tests between bleeding and nonbleeding patients. This correlates to previous published results (6). Furthermore, in adjusted models, plasma transfusion doses were not associated with aPTT or INR levels, platelet transfusion doses were not associated with platelet count, and cryoprecipitate doses were not associated with fibrinogen level. It is noteworthy that hemostatic transfusions seem not to be guided by hemostatic tests, considering most of international guidelines recommend using these tests to guide hemostatic transfusions (12–14).

This analysis provides the first large epidemiologic report of combined hemostatic transfusions in children requiring ECMO, showing that virtually all these patients received at least one hemostatic transfusion. Using regression models adjusting for numerous potential confounding variables, our results also show an association between bleeding and hemostatic transfusions, but no independent association with most hemostatic tests. These findings may be used to design future interventional trials, to provide evidence of the best balance of the risks of hemostatic transfusions with their potential therapeutic benefits.

Several limitations must be recognized. First, hemostatic transfusions were recorded on a daily basis. It was, therefore, not possible to evaluate the timing and the number of transfusions, or the timing of transfusions in relation to the laboratory tests. The exact indication for each transfusion was not noted in the database and was assumed to be given for either treatment or prevention of bleeding. We used the total daily transfusion dose in the analysis and did not adjust for repeated measures. Second, we did not assess the association between hemostatic transfusions and clinical outcomes because it was not possible to assess the temporality between the transfusion and the clinical situation leading to worse clinical outcome. Similarly, the laboratory results were only recorded in the morning. Therefore, they may not, for example, reflect the patient's worst value for that measurement over the entire day. In addition, there is a possibility that a laboratory drawn just after midnight might have prompted a hemostatic transfusion, which would have normalized the morning laboratory. Although there is yet to be sufficient evidence in children, it is also possible that providers are extrapolating from adult studies (15, 16) and are using viscoelastic testing to guide transfusion decisions. Therefore, this might explain, in part, the absence of association between hemostatic tests and hemostatic transfusions. Additionally, although INR was collected, the daily INR goals were not recorded. Whereas INR was developed with the intention of monitoring patients on vitamin K antagonist therapy, its use has been extrapolated to children supported by ECMO. It is possible that PT goals were only recorded on 1% of the ECMO days if it was perhaps set as an INR goal, as

TABLE 2. Factors Associated With Plasma, Platelet, and Cryoprecipitate Daily Transfusion Doses, Using a Linear Regression Model

	Plasma Transfusion (mL/kg/d)		Platelet Transfusion (mL/kg/d)		Cryoprecipitate Transfusion (mL/kg/d)	
Variables	**β Coefficient**	***p***	**β Coefficient**	***p***	**β Coefficient**	***p***
Age	−0.06	0.20	0.003	0.95	−0.04	**0.009**
ECMO type	−4.8	0.64	0.77	0.94	0.87	0.81
ECMO location	−2.25	0.59	−4.76	0.21	−2.00	0.18
ECMO indication	3.29	0.40	5.53	0.16	0.01	0.99
Chest tube bleeding	0.32	**< 0.001**	0.25	**< 0.001**	0.03	0.18
Other bleeding requiring RBC transfusion	9.38	**0.01**	7.99	**0.03**	−0.42	0.75
Platelet count	0.02	0.62	0.01	0.75	−0.01	0.49
Prothrombin time	0.01	0.99	0.72	0.70	−0.14	0.83
aPTT	−0.04	0.29	0.01	0.69	−0.01	0.30
International normalized ratio	0.04	0.99	−6.51	0.70	0.10	0.99
Fibrinogen	−0.01	0.54	−0.01	0.50	0.00	0.67
ACT	0.16	**< 0.001**	0.03	0.58	0.01	0.75
AT	0.17	**0.02**	0.10	0.02	0.02	0.43
Plasma transfusion	–	–	−0.25	**0.049**	−0.09	0.052
Platelet transfusion	−0.23	**0.049**	–	–	0.07	0.11
Cryoprecipitate transfusion	−0.67	0.052	0.57	0.10	–	–
Platelet minimal goal	0.29	**0.006**	0.28	**0.009**	0.03	0.34
aPTT maximal goal	−0.41	0.09	−0.14	0.58	−0.02	0.81
Fibrinogen minimal goal	0.16	0.12	0.11	0.32	0.03	0.39
AT minimal goal	−0.98	**0.002**	−0.64	0.06	−0.14	0.25
ACT maximum goal	0.13	0.46	0.25	0.16	−0.04	0.56

ACT = activated clotting time, aPTT = activated partial thromboplastin time, AT = antithrombin, ECMO = extracorporeal membrane oxygenator.

The β coefficient is the degree of change in the outcome variable (i.e., mL/kg/d of plasma, platelet, or cryoprecipitate transfusion) for every 1 unit of change in the predictor variable. The *t* test assesses whether the β coefficient is significantly different from zero.

Boldface values represent those which are statistically significant. Dashes represent those associated factors that are the same as the outcomes.

a recent study reports that INR is used to guide plasma transfusion in 67% of ECMO protocols, whereas aPTT in only 33% of ECMO protocols (6). Other parameters, such as D-dimer, plasma-free hemoglobin and von Willebrand activity levels that may influence the hemostatic management of the patient, were not collected at all sites and, therefore, not included in the analysis. The nonuniform use of these assays in all sites may have introduced bias. Other hemostatic therapies, such as tranexamic acid, aminocaproic acid, fibrinogen concentrate, factor VIIa, or antithrombin, may have been administered but are not captured in this analysis. Therefore, not all factors that may predict hemostatic transfusions are not included in the analytic models. All output from the chest tube(s), if present, was considered bleeding, and not pleural effusions. Finally, one must acknowledge that the statistical significance should not be interpreted as clinically significant differences.

CONCLUSIONS

In conclusion, hemostatic transfusions are administered to virtually all critically ill children supported by ECMO. Plasma is transfused on one third of the days on ECMO, platelets on two third of the days, and cryoprecipitate on one sixth of the days. Further studies are warranted to evaluate the appropriateness of these transfusion strategies. The epidemiologic data from this analysis can be used to plan interventional trials to examine the efficacy of transfusion thresholds in this patient population.

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