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Blood Product Utilization in Patients With COVID-19 on ECMO

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ABSTRACT

Introduction: Although extracorporeal membrane oxygenation (ECMO) has been associated with improved outcomes in COVID patients with respiratory failure, data regarding the need for blood product utilization in this population is inadequate.

Methods: We conducted a retrospective review of all COVID patients requiring ECMO support at our facility. Patient demographics, co-morbidities, measures of acuity, and blood product utilization were identified. Patients were stratified by the presence of a major bleed and the need for dialysis. The primary outcome was blood product utilization. Linear regression models were used to assess predictors of the need for blood products.

Results: From 2020 to 2021, 41 patients with COVID-19 were included in our study. Overall 1601 d of support, COVID ECMO patients received 755 units of packed red blood cells (PRBC), 51 units of fresh frozen plasma (FFP), 326 platelets, and 1702 cryoprecipitate, amounting to 18.4 units PRBC per patient or 3.30 units per week of ECMO support. Both major bleeding and the need for dialysis were associated with higher rates of transfusion of PRBC, FFP, and platelets. The average non-bleeding COVID ECMO patient who did not need dialysis required 2.17 units of PRBC, 0.12 units of FFP, 0.76 platelets, and 8.36 of cryoprecipitate per week of ECMO support. On multivariable linear regression analysis, each day on ECMO was associated with 0.30 [0.19-0.42, $P < 0.01$] units of PRBC.

Conclusions: In conclusion, COVID ECMO is associated with a significant need for blood and blood products. Major bleeding and dialysis are important drivers of blood product requirements.

Introduction

The severe acute respiratory syndrome coronavirus two virus (SARS-CoV-2) can cause refractory respiratory failure and death.[1] Extracorporeal membrane oxygenation (ECMO) support has been shown to improve survival rate in carefully selected patients who cannot be adequately supported with a ventilator.[2-4] Unfortunately, ECMO support can be associated with a number of complications including, bleeding and the need for blood product transfusion.[5] Although Coronarvirus-19 (COVID-19) infection is well-known to cause hypercoaguability, it can also cause coagulopathy, leading to

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significant bleeding.[6-8] Thus, COVID-19 patients may suffer from an infection-related coagulopathy which further exacerbates the already high risk of bleeding associated with ECMO support leading to a considerable utilization of blood products.

Although, ECMO is known to improve survival in severe COVID-19 respiratory failure, data evaluating blood product utilization in this population is limited. Therefore, we undertook this study to evaluate the use of blood products in COVID ECMO patients. We hypothesized that, COVID ECMO support is associated with a significant need for blood and blood products, particularly in patients who suffer a major bleeding complication.

Methods

Data collection

We conducted a retrospective review of all patients requiring ECMO for respiratory failure at Baylor Scott and White, The Heart Hospital, Plano, from March 2020 to October 2021. Patients with polymerase chain reaction (PCR) confirmed SARS-CoV-2 infection were included. Patients with primarily respiratory failure were included. Patients with primarily cardiogenic shock in the absence of respiratory failure were excluded. The Baylor Scott and White institutional review board approved this study. Informed consent was waived by our institutional review board. The manuscript was prepared by the first author, but all co-authors were involved in the design of the study, the analysis of the data, and the synthesis of the manuscript. The authors have no conflicts of interest.

Patient inclusion

All patients had refractory hypoxic and/or hypercarbic respiratory failure and met EOLIA criteria for ECMO cannulation.[9] Briefly, EOLIA patients have a PaO_2:FiO_2 ratio $<$50 mmHg for $>$3 h or a PaO_2:FiO_2 $<$ 80 for 6 h, or an arterial blood pH $<$ 7.25 with a $PaCO_2$ $\geq$ 60 for $>$6 h despite maximum ventilatory support. After ECMO cannulation, lung protective ventilatory strategies were utilized. Patient care was multidisciplinary. Throughout the study period, various COVID-specific therapeutics were temporally dependent and included approved therapies, re-purposed therapies, and treatments with emergency use authorizations. An expert in infectious disease and an expert in critical care, reviewed each case and administered COVID-specific therapies in accordance with the dominant paradigm at that time. As many of these therapies were administered at other facilities, patient-specific data is unobtainable.

Although we use standard ECMO inclusion and exclusion criteria as described in the EOLIA study, several COVID-specific exclusion criteria are notable. First, building on our early experience, we declined to support anyone over the age of 60 as we have not found these patients to achieve a survival benefit. Second, we do not initiate ECMO in anyone who has already been intubated for 7 d because we believe that they have already sustained irrecoverable ventilatory induced lung injury at that point. Third, we generally only offer ECMO to patients with single organ system failure although we have made exceptions for both acute and chronic renal failure on a case-by-case basis.

Anticoagulation and blood transfusion thresholds

Our center's anticoagulation strategy is standardized. Each patient receives a bolus dose of heparin before cannulation. Those weighing less than 100 kg, get 5000 units of heparin, while those greater than 100 kg get 8000 units of heparin. The patients are then maintained on either a heparin or an argatroban drip at the discretion of the surgeon for a goal partial thromboplastin time of 40-60 s. Anticoagulation is titrated by protocol but can be held if there is suspected or confirmed bleeding or if a procedure is planned. Argatroban is mostly utilized for patients who are known to be positive for heparin induced thrombocytopenia (HIT), or for those who require high doses of heparin anticoagulation to become therapeutic; however, argatroban was intermittently used as the primary anticoagulant for exploratory purposes.

In the non-bleeding COVID ECMO patients, blood product transfusions are protocolized. We transfuse packed red blood cells (PRBC) for a hematocrit less than 24%; fresh frozen plasma (FFP) for an international normalized ratio (INR) greater than 2.0; platelets for a platelet count less than 50 per L; and cryoprecipitate for a fibrinogen less than 100 mg/dL. FFP is also given if we believe the patient is antithrombin III deficient to help achieve therapeutic anticoagulation. Although protocolized, blood transfusion thresholds can be raised and lowered by the clinical scenario, particularly in the setting of significant bleeding.

Equipment

All patients were supported with centrifugal pumps and heparin coated circuits. All patients were initially supported with dual lumen single venous cannulae through the right internal jugular vein. Two cannulae were used in the study: the Avalon (Getinge, Goteborg, Sweden) and the Crescent (Medtronic, Minneapolis, Minnesota). Several patients suffered right ventricular dysfunction or failure as their course progressed. For these patients we recannulated them in a right atrial to pulmonary artery fashion using a dual lumen cannula the Protek Duo cannula (LivaNova, London, United Kingdom).

For patients in renal failure, continuous renal replacement therapy (CRRT) was utilized. Our practice is to use separate venous access for CRRT rather than connecting the CRRT device to the circuit because the ECMO flow rates can interfere with the consistency of CRRT. Our anticoagulation protocol is not affected by the need for CRRT.

Variables and outcomes

Patient demographics, co-morbidities, laboratory values, and measures of acuity data were readily available in the medical record. All ECMO patients have some bleeding from access sites including their ECMO cannulae, endotracheal tubes, central lines, chest tubes, nasogastric tubes, rectal tubes, and operative sites. Most of these constitute occasional oozing

that stops over time. However, some had more significant bleeding requiring intervention. Therefore, major bleeding was defined as bleeding requiring both blood product transfusion and an operative intervention. Possible operative interventions included, exploratory surgery, endoscopic clipping or other intervention, arterial embolization in interventional radiology, and bronchoscopic intervention beyond diagnostic bronchoscopy with or without bronchoalveolar lavage (packing, topical hemostasis, etc). All cannulation sites had some limited oozing but none had significant bleeding. Blood product utilization was extracted from the electronic medical record and confirmed with the blood bank record.

The primary outcome measured was blood product utilization. Secondary outcomes included survival. Since both bleeding and dialysis are thought to increase the need for blood products, blood product utilization was stratified by the presence of a major bleed and by the need for CRRT.

Statistical analysis

Demographics, co-morbidities, laboratory values, and measures of acuity were normally distributed. These continuous variables are presented as mean values with standard deviations while categorical variables are presented as whole numbers with percentages. When stratified, these variables were compared using the *t*-test for continuous variables and the chi squared test for categorical variables.

Blood product utilization and duration of ECMO support were both non-normally distributed. These non-parametric variables are presented as medians with interquartile ranges (IQR) and compared using the Kruskal–Wallis test.

Predictors of blood product utilization were determined using linear regression. Preliminary analysis was conducted using simple univariate linear regression. Variables with a *P*-value < 0.20, biologic plausibility, or previous literature support were considered for inclusion in the final multivariable model. These variables were incorporated in forward and backward step-wise fashion to achieve the maximal explanatory power. The model with the most explanatory power was different for each blood product. The final multivariable linear regression model for PRBC transfusion included the need for vasopressors pre-cannulation, ECMO duration, the presence of a major bleed, the use of CRRT, and the use of argatroban. The model for FFP contained duration of ECMO support, baseline creatinine, baseline total bilirubin, the need for pre-cannulation vasopressors, the use of CRRT, and the presence of a major bleed. The model for platelet transfusion included duration of ECMO support, diabetes, the presence of a major bleed, and the use of CRRT. Finally, the model for cryoprecipitate transfusion included duration of ECMO support, the presence of a major bleed, and the use of CRRT.

Survival to discharge was assessed using a chi squared analysis and predictors of mortality were evaluated using logistic regression. For all statistical measures including *t*-test, chi squared test, and the Kruskal–Wallis test, a two-tailed $P < 0.05$ was considered significant. Statistical analysis was performed using Stata/SE 17.0 (College Station, TX).

Results

Patient demographics

From May 2020 to November 2021, 48 patients were placed on ECMO support at our hospital for refractory respiratory failure secondary to COVID-19 pneumonia. Four patients remain on support and were excluded. In addition, because of changes in the electronic medical record, blood product data on three patients were missing and these patients were excluded as well. Therefore, 41 patients were evaluated. Of the 41 patients, 37 (90.24%) were placed on venovenous ECMO through the right internal jugular vein. One patient was placed on femoral venoarterial ECMO before being converted to a right atrial to pulmonary artery strategy for primarily respiratory failure with mild concomitant right ventricular dysfunction within 24 h. Three other patients were initially placed on venovenous ECMO but were converted to venoarterial, venoarterial venous, or right atrial to pulmonary artery cannulation because of hemodynamic deterioration.

The average age of the cohort was 47.1 ± 8.0 y (Table 1). Most were male (31, 75.61%) and the plurality were Hispanic (18, 43.90%). In this cohort, while hypertension was common (20, 48.78%), diabetes mellitus was not. Most of the patients had normal renal function (0.79 ± 0.32) but two (4.88%) had dialysis-dependent renal failure. Most patients had a leukocytosis, the majority required vasopressor support before

Table 1 – Baseline demographics, laboratory values, and measures of acuity.

Variable	Data
Demographics	
Age (y)	47.1 ± 8.0
Male gender (%)	31 (75.61%)
Ethnicity	
Hispanic (%)	18 (43.90%)
White (%)	16 (39.02%)
Black (%)	6 (14.63%)
Other (%)	1 (2.44%)
Comorbidities	
Hypertension (%)	20 (48.78%)
Diabetes mellitus (%)	9 (21.95%)
End-stage renal disease (%)	2 (4.88%)
Body mass index (kg/m^2)	33.60 ± 5.42
Laboratory values	
Creatinine (mg/dL)	0.79 ± 0.32
Total bilirubin (md/dL)	0.60 ± 0.26
White blood cell count (K/uL)	17.47 ± 7.96
Measures of acuity	
Need for vasopressors (%)	24 (58.54%)
Need for inhaled epoprostenol (%)	32 (78.05%)

mg/dL = milligram per deciliter; K/uL = thousand per microliter; kg/m^2 = kilograms per meter squared.

cannulation, and the overwhelming majority were receiving inhaled epoprostenol at the time of ECMO initiation.

Anticoagulation and bleeding

All patients were anticoagulated. Thirty patients (73.2%) were primarily anticoagulated with heparin while 11 (26.8%) were anticoagulated with argatroban. Only two of the patients anticoagulated with argatroban were positive for heparin induced thrombocytopenia HIT.

Of the total cohort, 15 patients (36.6%) had major bleeds. The major bleeds included seven patients (46.7%) with gastrointestinal bleeding requiring endoscopic intervention; four patients (26.7%) with percutaneous gastrostomy related bleeding requiring exploratory laparotomy; two (13.3%) patients with nasal and mouth bleeds, one requiring operative intervention and the other requiring arterial embolization; one exploratory laparotomy for a spontaneous splenic rupture; and one pulmonary hemorrhage requiring bronchoscopic intervention with topical hemostatic packing. In addition, 11 patients (26.8%) developed renal failure requiring CRRT.

Outcomes and blood product utilization

Of the 41 patients, 25 (61.0%) survived to discharge. The median time of support was 23 [13-56] d for a total support time of 1601 d or approximately 228.7 wk. Over this time period, the 41 COVID ECMO patients required 755 units of PRBC, 51 units of FFP, 326 platelets, and 1702 cryoprecipitate (Table 2). For PRBC specifically, this amounts to 18.4 units per patient and approximately 3.30 units per week of ECMO support.

When stratified by the presence of bleeding, 7 (46.7%) with a major bleed and 18 (69.2%) without a major bleed survived to discharge ($P = 0.15$). The presence of a major bleed was associated with a significantly higher use of PRBC, FFP, and platelets (Table 3). There was no difference in the need for cryoprecipitate.

When stratified by renal failure, those requiring CRRT were less likely to survive to discharge than those who did not (21 [70.0%] *versus* 4 [36.4%], $P = 0.05$). The need for CRRT was also associated with a significantly higher use of PRBC, FFP, and platelets (Table 4). There was no difference in the need for cryoprecipitate.

Table 2 – Overall blood product utilization.

Blood product	Total	Median [IQR]	Per patient per week
PRBC (units)	755	14 [3-26]	3.30
FFP (units)	51	0 [0-1]	0.22
Platelets (dose)	326	2 [0-9]	1.43
Cryoprecipitate (units)	1702	0 [0-50]	7.44

IQR = interquartile range; PRBC = packed red blood cell; FFP = fresh frozen plasma.

Table 3 – Blood product utilization per patient stratified by major bleed.

Blood product	No major bleed	Major bleed	P-value*
PRBC (units)	7.5 [2-16]	26 [8-39]	<0.01
FFP (units)	0 [0-0]	1 [0-4]	<0.01
Platelets (dose)	1 [0-3]	8 [2-19]	0.01
Cryoprecipitate (units)	0 [0-30]	0 [0-75]	0.51

PRBC = packed red blood cell; FFP = fresh frozen plasma.
*P-value determined by Kruskal–Wallis test.

Comparing patients primarily anticoagulated with heparin to those anticoagulated with argatroban, there was no difference in the need for PRBC ($P = 0.17$), FFP ($P = 0.56$), platelets ($P = 0.34$), or cryoprecipitate ($P = 0.11$). Cannulation strategy was not associated with blood product transfusions.

After excluding patients experiencing a major bleed and those requiring CRRT, 21 patients remained. These patients required a median of 9 [2-16] units PRBC, 0 [0-0] FFP, 0 [1-3] units of platelets, and 0 [0-50] units of cryoprecipitate. These patients were supported for a total of 683 d or 97.57 wk. Thus the average non-bleeding COVID ECMO patient not requiring CRRT requires 2.17 units of PRBC, 0.12 units of FFP, 0.76 platelets, and 8.36 of cryoprecipitate per week of ECMO support.

Multivariable analysis

On linear regression analysis, duration of ECMO support, the presence of a major bleed, the need for CRRT, and the need for vasopressors pre-cannulation were strongly associated with PRBC transfusions (Table 5). Primary use of argatroban also showed a strong trend toward more PRBC transfusion. On adjusted analysis, each day of ECMO was associated with a need for 0.30 [0.19-0.42, $P < 0.01$] units of PRBC. Major bleeds and the need for pre-cannulation vasopressors were also associated with a statistically significantly increased need for PRBC transfusions. The type of anticoagulation was not associated with the need for blood transfusion.

Multivariable linear regression analysis did not reveal statistically significant predictors of FFP or cryoprecipitate transfusion. However, on adjusted analysis, the need for CRRT

Table 4 – Blood product utilization per patient stratified by CRRT.

Blood product	No CRRT	CRRT	P-value*
PRBC (units)	9.5 [3-19]	33 [6-49]	0.02
FFP (units)	0 [0-1]	1 [0-3]	0.046
Platelets (dose)	1.5 [0-7]	11 [1-29]	0.03
Cryoprecipitate (units)	0 [0-60]	15 [0-50]	0.59

CRRT = continuous renal replacement therapy; PRBC = packed red blood cell; FFP = fresh frozen plasma.
*P-value determined by Kruskal–Wallis test.

Table 5 – Predictors of the need for packed red blood cell transfusions.

Variable	Univariate		Multivariable	
	Coefficient [95% CI]	P-value*	Coefficient [95% CI]	P-value†
Age, per year	0.30 [−0.51 to 1.12]	0.46		
Male gender	4.26 [−11.26 to 19.78]	0.56		
Hypertension	2.80 [−10.14 to 15.74]	0.66		
Diabetes	7.58 [−7.89 to 23.05]	0.33		
BMI, per kg/m^2	−0.22 [−1.43 to 0.99]	0.71		
Cr, per mg/dL	5.82 [−14.77 to 26.41]	0.57		
Bili, per mg/dL	11.08 [−13.56 to 35.72]	0.37		
WBC, per K/uL	0.42 [−0.40 to 1.23]	0.31		
Vasopressors	13.77 [1.39 to 26.15]	0.03	7.87 [0.51 to 15.23]	0.04
Epoprostenol	−7.16 [−22.65 to 8.34]	0.36		
ECMO duration, per day	0.39 [0.27 to 0.50]	<0.01	0.30 [0.19 to 0.42]	<0.01
Major bleed	20.69 [9.01 to 32.36]	<0.01	14.95 [7.54 to 22.67]	<0.01
CRRT	18.19 [4.80 to 31.59]	<0.01	6.28 [−2.20 to 14.76]	0.14
Argatroban	13.35 [0.63 to 27.32]	0.06	3.99 [−5.68 to 13.66]	0.41

CI = confidence interval; BMI = body mass index; kg/m^2 = kilogram per meter squared; Cr = creatinine; mg/dL = milligram per decliter; Bili = bilirubin; WBC = white blood cell count; K/uL = thousand per microliter; CRRT = continuous renal replacement therapy.
* Linear regression.
† Multivariable linear regression model. Final model contains need for pre-cannulation vasopressors, ECMO duration, presence of a major bleed, CRRT, and primary use of argatroban.

was associated with a significantly increased need for platelet transfusion (10.99 [0.38-21.61], $P = 0.04$).

Logistic regression analysis demonstrated that neither increased transfusion of PRBC (0.98 [0.95-1.02], $P = 0.34$), nor FFP (0.89 [0.68-1.17], $P = 0.41$), nor platelets (0.95 [0.88-1.02], $P = 0.13$), nor cryoprecipitate (1.00 [0.99-1.01], $P = 0.41$) were associated with an increased odds of mortality. There were insufficient outcomes to make multivariable assessments of survival.

Discussion

COVID-19 pneumonia can progress to respiratory failure refractory to mechanical ventilatory support. In select patients, ECMO support can lead to increased survival; however, ECMO support in general and COVID ECMO support in particular are associated with significant resource utilization. Both the coronavirus pandemic itself and the worldwide response have combined to stress and intermittently exhaust local, regional, and international healthcare resources. Before the pandemic, the blood product supply was limited and occasionally in dire shortage. The increased utilization of blood products associated with COVID hospitalizations combined with the decreased donor pool because of COVID mitigation efforts have severely exacerbated this shortage. Therefore, it is incumbent upon healthcare providers to better understand and further delineate the resources involved in providing ECMO support for patients suffering from COVID pneumonia.

In this study, we found that COVID ECMO is associated with a tremendous need for blood and blood products. In total, our series of 41 patients who were supported for 1601 d required 755 units of PRBCs, 51 units of FFP, 326 platelets, and 1702 cryoprecipitate. This represents a median of 14 units of PRBCs per patient or roughly 3.30 units per week. Although such blood product usage is significant, there are several factors that determine how much blood a given patient will need.

ECMO support in general can be associated with significant bleeding. A recent systemic review found that 28% of patients supported with venovenous ECMO had significant bleeding.[5] Moreover, COVID itself can be associated with a significant coagulopathy, similar to disseminated intravascular coagulation, known as COVID-Associated Coagulopathy (CAC).[10] Such coagulopathy can affect as many as 20%-55% of critically ill COVID patients regardless of the need for anticoagulation or ECMO support. This coagulopathy may exacerbate the bleeding already associated with ECMO, increasing blood loss and associated blood transfusions. In our series, 37% of patients experienced a major bleed. This compares favorably with the extant literature in which significant COVID ECMO bleeding has been reported in 40%-60% of patients.[7,10] Not surprisingly, major bleeding is associated with a significantly increased use of blood and blood products.

Another common risk factor for blood product utilization is the need for CRRT. Renal failure can be common in COVID ECMO cases. The need for CRRT can increase the risk of blood transfusion as blood can be lost in the circuit and renal failure itself can result in decreased red blood cell (RBC) production and dilutional consumption of blood products. Thus, it is again not surprising that our series found patients who underwent CRRT required more blood and blood products than those who did not.

However, exclusive of major bleeds and dialysis, ECMO patients have an ongoing need for blood products. The circuit itself is traumatic and intermittent oozying around cannulae can consume red blood cells (RBC) and platelets. Moreover, the resuscitation needed for critically ill patients, combined with the vasodilatory effects of the blood/ECMO interface, fluid shifts, and frequent blood draws for laboratory evaluation can all contribute to dilution of intravascular blood cells. Finally, excessive fibrinolysis,[11] disseminated intravascular coagulation,[11] severe vascular endothelial injury,[12] and sheer stress[13] may all further contribute to bleeding and blood product requirements.[14] Thus, exclusive of overt bleeding, COVID ECMO patients may require a maintenance transfusion of blood and blood products. In our series, the average non-bleeding COVID ECMO patient not requiring CRRT required 2.17 units of PRBC, 0.12 units of FFP, 0.76 platelets, and 8.36 of cryoprecipitate per week of ECMO support. These results compare favorably with previously reported results in which non-bleeding COVID ECMO patients required 0.76 units per day compared to bleeding patients who required 1.64 units per day.

Given the maintenance need for blood transfusions, it is not surprising that on multivariable linear regression, we found time on ECMO to be strongly associated with the need for PRBC transfusion, at a rate of 0.30 units per day. As expected, major bleeding was also strongly associated with the need for blood products. After adjusting for other covariates, the need for CRRT was not statistically associated with the need for PRBC transfusion although it was strongly associated with the need for platelet transfusion. We suspect that the lack of association between CRRT and PRBC transfusion is explained by some collinearity between both length of time on ECMO and major bleeds. Moreover, it is our experience in non-ECMO patients that CRRT circuits result in significant platelet consumption, thus this association is expected.

Perhaps most interesting is the strong association between the pre-cannulation need for vasopressors and PRBC transfusion. Our experience has been that most patients transferred to us for ECMO support are intravascularly dry, likely reflecting the limited critical care treatment options available to the COVID patient requiring mechanical ventilation other than diuresis and supportive care. We would speculate that such hypovolemic patients are predisposed to needing vasopressor support after intubation. Since the ECMO circuit is strongly preload dependent, these hypovolemic patients often require significant volume resuscitation after cannulation. It is likely they subsequently undergo dilution of their hemoglobin and hematocrit necessitating transfusion.

Although the need for and appropriate transfusion threshold for PRBCs has been extensively studied, the appropriate use of other blood components is less well understood. In our study, we find that significant amounts of FFP, platelets, and cryoprecipitate are all used in support COVID ECMO patients. While, PRBC transfusion triggers are readily available, thresholds for transfusing other products are unknown and standing thresholds for transfusion of blood products may lead to excessive and potentially unnecessary utilization. However, the possibility of unnecessary transfusion must be balanced against the risk of allow clotting factors to drift too low resulting in spontaneous or other bleeding complications; moreover, once these bleeding complications start, correcting the clotting deficiency alone may not stop the hemorrhage. Furthermore, arresting the hemorrhage alone may not be enough to avoid significant morbidity and mortality for example, as in the case of an intracranial bleed. Thus at our institution we have standing transfusion thresholds for hematocrit, platelet count, international normalized ratio (INR), PTT, and fibrinogen. We recognize this may result in unnecessary transfusions but think the benefit outweighs the risk.

Finally, in this series, we report a survival of 61%. This compares favorably with the published literature.[2-6,15] Although multiple reports in various clinical situations have previously shown blood transfusions to be associated with poorer outcomes, we did not find evidence of that in the present study. We suspect that the presents study is underpowered to detect this different. Further investigation is warranted.

Limitations

First, this study is a single-center, retrospective study and thus susceptible to selection bias. In addition, the relative sample size is small, limiting the ability to compensate for selection bias with multivariable analysis. This study is best viewed as descriptive and exploratory. Further investigation is necessary to better understand the need for blood products in COVID ECMO patients.

Second, this study represents the transfusion practices at one institution, with an institution specific set of transfusion thresholds, type of ECMO circuits, and a specific subset of ECMO patients, namely those with COVID-19 pneumonia. Although we have made every effort to make our center's guidelines data driven, we recognize they may differ from other centers' practices. Moreover, we lack a local control group to which to compare these COVID patients. Thus, it remains unclear if COVID ECMO blood product requirements are different from other VV ECMO patients with refractory respiratory failure.

Third, although we note that blood product transfusion is not associated with mortality in this cohort, we recognize that the sample size is inadequate to definitively draw this conclusion and thus have not emphasized it in our report. Most of the extant literature would suggest that blood transfusion in most clinical situations can be associated with adverse outcomes. We do not contest this assertion and believe a larger sample size is needed to more fully investigate this question.

This study lacks the granularity to examine risk factors for bleeding, appropriate anticoagulation goals, and transfusion thresholds; however, such information may help decrease blood product utilization. Therefore, further investigation of blood product use in COVID ECMO patients is warranted.

Conclusion

In conclusion, COVID ECMO support is associated with a significant need for blood and blood product transfusion. Although major bleeds and the need for dialysis account for a significant portion of the needed transfusions, non-bleeding COVID ECMO patients have a meaningful maintenance requirement of blood and blood products for ongoing support.

Author Contributions

Design of study: Drs George, Shih, Lilly, Harness-Brumley, Taylor, Curry, Erwin, Vaquera, Myers, and DiMaio and Ms Sheasby. Data collection: Dr George and Ms Sheasby. Data analysis and interpretation: Dr George. Drafting of the article: Drs George and DiMaio and Ms Sheasby. Critical revision of the article: Drs George, Shih, Lilly, Harness-Brumley, Taylor, Curry, Erwin, Vaquera, Myers, and DiMaio and Ms Sheasby. Final approval of the version to be published: Drs George, Shih, Lilly, Harness-Brumley, Taylor, Curry, Erwin, Vaquera, Myers, and DiMaio and Ms Sheasby.

Disclosure

The authors have no known conflicts of interest.

Dr. DiMaio is a member of the Editorial Board of the Journal of Surgical Research; as such, he was excluded from the entire peer-review and editorial process for this manuscript.

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