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Extracorporeal Membrane Oxygenation Patient Outcomes Following Restrictive Blood Transfusion Protocol

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OBJECTIVES: To investigate the effect of a restrictive blood product utilization protocol on blood product utilization and clinical outcomes.

DESIGN: We retrospectively reviewed all adult extracorporeal membrane oxygenation (ECMO) patients from January 2019 to December 2021. The restrictive protocol, implemented in March 2020, was defined as transfusion of blood products for a hemoglobin level less than 7, platelet levels less than 50, and/or fibrinogen levels less than 100. Subgroup analysis was performed based on the mode of ECMO received: venoarterial ECMO, venovenous ECMO, and ECMO support following extracorporeal cardiopulmonary resuscitation (ECPR).

SETTING: M Health Fairview University of Minnesota Medical Center.

PATIENTS: The study included 507 patients.

INTERVENTIONS: One hundred fifty-one patients (29.9%) were placed on venoarterial ECMO, 70 (13.8%) on venovenous ECMO, and 286 (56.4%) on ECPR.

MEASUREMENTS AND MAIN RESULTS: For patients on venoarterial ECMO (48 [71.6%] vs. 52 [63.4%]; $p = 0.374$), venovenous ECMO (23 [63.9%] vs. 15 [45.5%]; $p = 0.195$), and ECPR (54 [50.0%] vs. 69 [39.2%]; $p = 0.097$), there were no significant differences in survival on ECMO. The last recorded mean hemoglobin value was also significantly decreased for venoarterial ECMO (8.10 [7.80–8.50] vs. 7.50 [7.15–8.25]; $p = 0.001$) and ECPR (8.20 [7.90–8.60] vs. 7.55 [7.10–8.88]; $p < 0.001$) following implementation of the restrictive transfusion protocol.

CONCLUSIONS: These data suggest that a restrictive transfusion protocol is noninferior to ECMO patient survival. Additional, prospective randomized trials are required for further investigation of the safety of a restrictive transfusion protocol.

KEYWORDS: blood product utilization; clinical outcomes; extracorporeal membrane oxygenation patients; hemoglobin level; platelet levels

Extracorporeal membrane oxygenation (ECMO) is an advanced form of life support that can be used to sustain patients with severe cardiac or respiratory failure. ECMO is an extremely resource intensive technology, requiring an ICU, specialized staff, and precise monitoring of physiologic metrics (1). Patients supported by ECMO will typically require multiple blood transfusions for anemia due to hemorrhage, therapeutic anticoagulation use, critical illness, and hemolysis associated with the ECMO circuit (1, 2). Despite this, guidelines on transfusion thresholds for patients on ECMO have not been well established, and there remains some controversy on the optimal transfusion strategy for ECMO patients (3, 4).

Historically, the recommendation of the Extracorporeal Life Support Organization (ELSO) was that patients on ECMO should receive blood

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KEY POINTS

Question: What is the effect of a restrictive blood product utilization protocol in adult extracorporeal membrane oxygenation (ECMO) patients on blood product utilization and clinical outcomes?

Findings: A restrictive blood product transfusion protocol does not significantly affect survival on ECMO for patients on venoarterial ECMO, venovenous ECMO, and ECMO support following extracorporeal cardiopulmonary resuscitation, and the protocol was proven to effectively reduce blood product utilization among such patients.

Meanings: These findings suggest that a restrictive transfusion protocol can be safe for ECMO patients. Further investigation through prospective randomized trials is necessary to fully evaluate the safety of this protocol.

transfusions to maintain a normal hemoglobin of approximately 12–14 g/dL (5, 6). However, this can require multiple units of packed RBCs per day, which can be challenging during a blood shortage. For this reason, some researchers have trialed more restrictive blood transfusion protocols and found similar or even improved outcomes (7). However, large studies exist primarily in the general critically ill population and not specifically patients on ECMO, which have unique challenges (8).

During the COVID-19 pandemic, widespread, critical blood shortages caused many healthcare systems to reconsider their transfusion protocols (9). As a result, our ECMO center ultimately instituted more restrictive transfusion guidelines for ECMO patients during the pandemic. The purpose of this study was to investigate the effect of a restrictive transfusion threshold on ECMO patient survival and blood product usage. We hypothesized that a more restrictive transfusion protocol would result in reduced blood product usage without increasing mortality in patients on ECMO.

METHODS

Study Population

This retrospective cohort study enrolled 507 consecutive adult patients who received ECMO for illness refractory to conventional treatment. Included were patients who received venoarterial ECMO, venovenous ECMO, and extracorporeal cardiopulmonary resuscitation (ECPR). Excluded were patients younger than 18 years old or who had opted out of research. ECPR was defined by our institution as patients who were placed on venoarterial ECMO during conventional cardiopulmonary resuscitation (CPR) after failure to obtain return to spontaneous circulation through CPR, as stated by Kumar (10). Blood product usage data was obtained from M Health Fairview Laboratory records, managed by the institutional transfusion safety officer. Patient demographic information and clinical variables were collected through review of patient charts in the electronic medical record. The study protocol was approved by the institutional review board with a waiver of informed consent (University of Minnesota Internal Review Board Study No. 00016657, approved July 22, 2022). These procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975.

Study Design

Due to the nationwide blood product shortages caused by the COVID-19 pandemic, our institution, the University of Minnesota Fairview Health System, implemented a restrictive ECMO transfusion protocol on March 18, 2020. Under the restrictive protocol, blood products were transfused for a hemoglobin level less than 7, platelet levels less than 50, and/or fibrinogen levels less than 100. Before the implementation of the restrictive transfusion protocol, packed RBCs were transfused for hemoglobin levels less than 8 for venoarterial ECMO and ECPR and less than 10 for venovenous ECMO. Fresh frozen plasma (FFP) was transfused for fibrinogen levels less than 200, and platelets for levels less than 100 for venoarterial ECMO, venovenous ECMO, and ECPR.

For this investigation, patients were differentiated into three groups based on the type of ECMO support: venoarterial ECMO, venovenous ECMO, or ECPR. For each group, we identified two cohorts of patients: a liberal transfusion cohort who received ECMO support from January 1, 2019, to March 3, 2020, corresponding with the liberal transfusion protocol, and a restrictive transfusion cohort of patients who received ECMO support from March 21, 2020, to December 28, 2021, corresponding with the restrictive transfusion

guidelines. Patients placed on a right ventricular assist device (n = 15) or hybrid veno-arterio-venous ECMO support system (n = 17) during this interval were also excluded from the study. To measure adherence to the restrictive transfusion protocol, the hemoglobin, platelets, and fibrinogen levels the day before ECMO decannulation or death were obtained. If there were no values available on the day before ECMO decannulation or death, the last available value was used.

Outcome Measures

The primary outcome measure of this investigation was mortality while on ECMO. Secondary outcomes included the length in days on ECMO and blood product usage per patient. The type and amount of RBCs, platelets, FFP, and cryoprecipitate were recorded for each patient, including the total number of each blood product given throughout ECMO cannulation, and the average number of each blood product used per day.

Statistical Analysis

Categorical patient characteristics and key outcomes between the liberal transfusion cohort and the restrictive transfusion cohort were compared using Pearson's chi-square test. The Mann-Whitney *U* test was used for non-normal continuous variables. All continuous variables did not meet criteria for normality. The statistical significance for differences in primary and secondary outcomes was defined at a p value of less than 0.05. R (R Foundation for Statistical Computing, Vienna, Austria) was used to perform all statistical analysis (11).

RESULTS

Study Population

A total of 507 patients were included in the study between January 1, 2019, and December 28, 2021. Overall, 151 patients were placed on venoarterial ECMO, 70 on venovenous ECMO, and 286 on ECPR. Two hundred twelve patients received ECMO support with a liberal transfusion strategy and 295 with restrictive transfusion strategy.

Venoarterial ECMO

There were no significant differences in demographic or comorbidity profile between the liberal transfusion and restrictive transfusion groups (**Supplemental Table 1**, http://links.lww.com/CCX/B283). There was no significant difference in survival on ECMO in the liberal transfusion group compared with the restrictive transfusion group (48 [71.6%] vs. 52 [63.4%]; p = 0.374) (**Supplemental Table 2**, http://links.lww.com/CCX/B283).

The average daily units of RBCs given was unchanged after implementation of the restrictive transfusion protocol (1.73 [0.86–2.88] vs. 1.29 [0.60–2.36]; p = 0.057). However, the total number of RBC units used per patient decreased after implementation of the restrictive transfusion protocol (9.00 [4.50–18.5] vs. 7.00 [3.00–14.5]; p = 0.076). The last recorded hemoglobin value significantly decreased in the restrictive transfusion group (8.10 [7.80–8.50] vs. 7.50 [7.15–8.25]; p = 0.001).

A significant decrease in the average daily units of administered blood products was observed for platelets (1.00 [0.51–1.71] vs. 0.50 [0.00–1.00]; $p < 0.001$), and FFP (0.67 [0.00–1.62] vs. 0.20 [0.00–1.00]; p = 0.035) after implementation of the restrictive transfusion protocol. The total number of platelets per patient (5.00 [2.00–12.50] vs. 2.00 [0.00–6.50]; p = 0.002) and the last recorded platelets value (86.00 [69.00–105.00] vs. 68.00 [46.00–103.5]; p = 0.021) both significantly decreased for the restrictive transfusion group compared with the liberal transfusion group.

Venovenous ECMO

There were no significant demographic differences between the liberal and restrictive transfusion groups (Supplemental Table 1, http://links.lww.com/CCX/B283). The liberal transfusion group was significantly more likely to be on ECMO due to COVID-19 (1 [2.9%] vs. 27 [79.4%]; p = 0.374). Furthermore, the number of days on ECMO was significantly increased for the restrictive transfusion group (10.50 [5.00–13.00] vs. 16.00 [9.00–25.50]; p = 0.043). We did not find a significant difference in survival on ECMO in the liberal transfusion group compared with the restrictive transfusion group (23 [63.9%] vs. 15 [45.5%]; p = 0.195).

For patients on venovenous ECMO, the number of RBC units used per day (0.98 [0.50–1.35] vs. 0.56 [0.33–1.00]; p = 0.091) and the total number of RBC units used per patient (8.50 [4.00–16.00] vs. 10.00 [5.25–14.75]; p = 0.883) was not statistically different after implementation of the protocol. There was also no significant difference in the last recorded hemoglobin value between

the liberal and restrictive transfusion groups (8.20 [7.80–8.65] vs. 8.10 [7.53–9.52]; $p = 0.972$).

There was a significant decrease in the average daily units of platelets given (0.34 [0.00–1.05] vs. 0.00 [0.00–0.08]; $p < 0.001$) and the total number of platelets administered per patient (3.50 [0.00–9.00] vs. 0.00 [0.00–1.00]; $p = 0.001$) between groups. No significant changes in the average daily units of FFP (0.13 [0.02–0.46] vs. 0.00 [0.00–0.41]; $p = 0.157$) and cryoprecipitate (0.00 [0.00–0.00] vs. 0.00 [0.00–0.20]; $p = 0.287$) were observed. The last recorded platelets value (91.5 [61.5–121.0] vs. 131.00 [77.5–195.75]; $p = 0.045$) significantly increased in the restrictive transfusion group compared with the liberal transfusion group.

Extracorporeal Cardiopulmonary Resuscitation

There were no significant differences in demographic or comorbidity profile between the liberal transfusion and restrictive transfusion groups (Supplemental Table 1, http://links.lww.com/CCX/B283). The number of days on ECMO was significantly decreased for the restrictive transfusion group (5.00 [4.00–7.00] vs. 4.00 [3.00–6.25]; $p = 0.033$). There was no significant difference in survival between the liberal and restrictive transfusion groups (54 [50.0%] vs. 69 [39.2%]; $p = 0.097$).

The average daily units of RBCs (1.33 [0.56–2.50] vs. 1.00 [0.29–1.96]; $p = 0.057$) and the total number of RBC units used per patient (7.00 [3.00–12.00] vs. 5.00 [1.75–10.00]; $p = 0.015$) significantly decreased after implementation of the restrictive transfusion protocol for ECPR patients. The last recorded hemoglobin value also significantly decreased (8.20 [7.90–8.60] vs. 7.55 [7.10–8.88]; $p < 0.001$) following implementation of the restrictive protocol.

We found a significant decrease in the average daily units for platelets (0.65 [0.20–1.29] vs. 0.00 [0.00–0.38]; $p < 0.001$) and total number of platelet units given per patient (3.00 [1.00–6.00] vs. 0.00 [0.00–2.00]; $p < 0.001$). However, the last recorded platelet value was statistically unchanged (91.00 [75.00–105.75] vs. 78.00 [56.75–126.50]; $p = 0.146$) following implementation of the restrictive protocol.

DISCUSSION

Previous literature has investigated the impact of transfusion thresholds on mortality in the general ICU population. However, the effects of a restrictive transfusion protocol for ECMO patients are underreported in the literature (3, 4, 8, 12). The most important finding of this study was that a restrictive transfusion threshold was not associated with decreased rates of survival for patients on venoarterial ECMO, venovenous ECMO, or ECPR. These results indicate that a restrictive transfusion protocol is nonharmful to ECMO patient survival.

The management of blood products for ECMO patients has been a subject of debate in the literature. However, no large studies have been done in this population. A randomized controlled clinical trial of non-ECMO critical care patients by the Canadian Critical Care Trials Group first reported that a RBC restrictive transfusion strategy of 7 g/dL was not associated with significantly increased patient mortality compared with a liberal transfusion strategy of 10 g/dL (8). Since this landmark study, multiple studies in the critical care patient population have also reported noninferior patient outcomes with a restrictive transfusion strategy (3, 12–16). Due to the limited clinical evidence of transfusion protocols in the ECMO population, many established transfusion protocols are currently based on extrapolated knowledge from research in critically ill patients (3).

However, the ELSO guidelines currently recommend maintenance hemoglobin levels of 12–14 g/dL and platelet counts greater than 75,000/mm^3 (3). The ELSO guidelines are based on the principle of increasing oxygen tissue delivery through maintenance of arterial oxygen saturation at a level greater than 95% and preventing the common ECMO complications of coagulopathy and hemorrhage, which require frequent transfusions to maintain normal hemoglobin levels (3). Importantly, these guidelines are not evidence-based–recent studies have reported that RBC and platelet transfusions may increase the risk of infection and thrombosis, although the mechanisms of transfusion-related organ dysfunction have not been fully elucidated (7, 17, 18). Physiologic studies have also reported that, in the setting of significant bleeding and/or hypoxemia, oxygen tissue delivery can remain stable up until a critical threshold due to tissue adaptations in oxygen extraction (19). However, it is currently unknown whether a difference exists in the critical threshold between critically ill and ECMO patients.

For ECMO patients, stratified by venoarterial, venovenous, and ECPR modes, we report that a restrictive

transfusion protocol did not result in significantly decreased survival on ECMO. These findings are broadly consistent with recent literature. A recent retrospective analysis of 763 ECMO patients from 2010 to 2019 by Ng et al (4) reported no significant changes to patient mortality following implementation of a restrictive hemoglobin transfusion threshold of 8.5 g/dL. In addition, a limited case series of predominantly venovenous ECMO patients for acute respiratory distress syndrome by Agerstrand et al (7) reported that a decreased hemoglobin transfusion threshold of 7.0 g/dL did not result in increased mortality and was associated with fewer bleeding complications. In September 2020, several months after the implementation of the restrictive transfusion protocol at our institution, the Canadian Journal of Cardiology published an expert consensus statement that reported a hemoglobin transfusion threshold of 7–7.5 g/dL for RBCs and greater than 50,000 mm^3 for platelets in nonbleeding venovenous ECMO patients (1).

We theorize that unchanged ECMO survival may be explained by the risks associated with the number of transfusions, as past studies have reported that increased blood product utilization rates were significantly associated with ECMO patient mortality (20–22). While the exact mechanism is unknown, it may be that increased blood product transfusions result in an elevated, dose-dependent risk of thrombotic events. Specifically, RBC storage has been established to affect the structural properties of the RBC through increased osmotic fragility and reduction in cell membrane deformity. These structural alterations contribute to the prothrombotic characteristic of stored RBCs and may explain the increased risk of thrombosis (3, 19, 20, 23). In addition, given the profound respiratory failure in venovenous ECMO patients and circulatory failure in venoarterial ECMO patients, increased transfusions may heighten the risk of transfusion-related complications, such as transfusion-related acute lung injury and transfusion-associated circulatory overload (4, 23, 24).

We also report significant decreases in blood product usage for venoarterial ECMO and ECPR patients. These findings are consistent with past literature, which has reported that lowering the transfusion threshold effectively reduces daily usage of blood products (7, 17, 18). Importantly, we did not find that RBC blood product usage significantly decreased for venovenous ECMO patients. This may be due to the confounding influence of COVID-19 in the restrictive transfusion group. A past study by George et al (24) reported significant blood product requirements in COVID-19 ECMO patients.

The institutional implications of a safe and effective reduction in blood product usage are also significant. As the COVID-19 pandemic decreased the global supply of blood products due to labor shortages and the implementation of new blood-collection policies, blood product stewardship was required to maintain proper care of critically ill patients, including those on ECMO. This study demonstrates that a new, institutional restrictive transfusion policy efficiently allocated blood products to patients, decreased usage of unnecessary resources and reduced healthcare costs.

This study found that an institutional restrictive transfusion protocol, which was associated with decreases in blood product usage, did not result in significantly decreased survival for patients on venoarterial ECMO, venovenous ECMO, or ECPR. One of this study's strengths is the inclusion of platelets, cryoprecipitate, and FFP utilization, which has not been reported in the literature to the authors' knowledge. Many institutions, including our own, transfuse RBCs based on hemoglobin levels without well-established transfusion thresholds for platelets, cryoprecipitate and FFP, and may result in excessive transfusion of additional blood products (24). These results underscore that a well-defined restrictive transfusion protocol for hemoglobin, platelets, and fibrinogen can effectively decrease RBC, platelets, cryoprecipitate, and FFP blood product usage.

The primary limitation of the study was the single-center, retrospective design. Because this study was nonrandomized, there may exist several biases that influence our results, including selection bias, confounding bias, and evolution in clinical management over the course of the 2-year investigation. In addition, the onset of COVID-19, which coincided with the implementation of the restrictive protocol, represents a possible source of confounding bias as COVID-19 infection has been established to increase the number of days on ECMO and blood product requirements (24). Furthermore, it is important to note that transfusion rates are inherently constrained for cardiac surgery patients, a demographic that contributes a significant portion of venoarterial ECMO

cases, potentially introducing another source of confounding bias. Therefore, we recognize the need for future randomized controlled trials that investigate the effect of a restrictive transfusion protocol in ECMO patients.

A second limitation is that our findings represent the transfusion practices at a single institution. While we strive to design evidence-based transfusion practices based on the latest literature, it is possible that our institutional policies, type of ECMO circuits, and blood product availability may limit the generalizability of these findings. Furthermore, before the implementation of the restrictive transfusion protocol, our institution did not have exact transfusion thresholds in the liberal transfusion group for platelets, cryoprecipitate, or FFP and transfusion of these blood products was left to provider preference.

We acknowledge that there may be clinical circumstances where rigid adherence to a specific hemoglobin target could potentially be detrimental given the variability in native cardiac output, metabolic rate, and oxygen consumption during ECMO. Despite this, we found significant decreases in the hemoglobin, platelet, and fibrinogen laboratory values during the ECMO run (3). Given the trends observed in our study, larger prospective investigations with expanded sample sizes are necessary to substantiate these findings and establish more robust conclusions regarding the impact of restrictive of restrictive transfusion protocols on ECMO patient outcomes.

CONCLUSIONS

These data suggest that a restrictive transfusion protocol is nonharmful to ECMO patient survival. Additional, prospective randomized trials are required for further investigation of the safety of a restrictive transfusion protocol.

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REFERENCES

1. Singh G, Nahirniak S, Arora R, et al: Transfusion thresholds for adult respiratory extracorporeal life support: An expert consensus document. *Can J Cardiol* 2020; 36:1550–1553
2. Cavarocchi NC: Introduction to extracorporeal membrane oxygenation. *Crit Care Clin* 2017; 33:763–766
3. Kim HS, Park S: Blood transfusion strategies in patients undergoing extracorporeal membrane oxygenation. *Korean J Crit Care Med* 2017; 32:22–28
4. Ng PY, Chan HCV, Ip A, et al: Restrictive and liberal transfusion strategies in extracorporeal membrane oxygenation: A retrospective observational study. *Transfusion* 2022; 63:294–304
5. Bartlett RH, Roloff DW, Custer JR, et al: Extracorporeal life support: The University of Michigan experience. *JAMA* 2000; 283:904–908
6. Barbaro RP, MacLaren G, Boonstra PS, et al; Extracorporeal Life Support Organization: Extracorporeal membrane oxygenation support in COVID-19: An international cohort study of the Extracorporeal Life Support Organization registry. *Lancet* 2020; 396:1071–1078
7. Agerstrand CL, Burkart KM, Abrams DC, et al: Blood conservation in extracorporeal membrane oxygenation for acute respiratory distress syndrome. *Ann Thorac Surg* 2015; 99:590–595
8. Hébert PC, Wells G, Blajchman MA, et al: A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. *N Engl J Med* 1999; 340:409–417
9. McGann PT, Weyand AC: Lessons learned from the COVID-19 pandemic blood supply crisis. *J Hosp Med* 2022; 17:574–576
10. Kumar KM: ECPR—extracorporeal cardiopulmonary resuscitation. *Indian J Thorac Cardiovasc Surg* 2021; 37(Suppl 2):294–302
11. R Development Core Team: *R: A Language and Environment for Statistical Computing*. Vienna, Austria, R Foundation for Statistical Computing, 2023
12. Zhang Y, Xu Z, Huang Y, et al: Restrictive vs liberal red blood cell transfusion strategy in patients with acute myocardial infarction and anemia: A systematic review and meta-analysis. *Front Cardiovasc Med* 2021; 8:736163
13. Docherty AB, O'Donnell R, Brunskill S, et al: Effect of restrictive versus liberal transfusion strategies on outcomes in patients with cardiovascular disease in a non-cardiac surgery setting: Systematic review and meta-analysis. *BMJ* 2016; 352:i1351
14. Carson JL, Terrin ML, Noveck H, et al; FOCUS Investigators: Liberal or restrictive transfusion in high-risk patients after hip surgery. *N Engl J Med* 2011; 365:2453–2462
15. Holst LB, Petersen MW, Haase N, et al: Restrictive versus liberal transfusion strategy for red blood cell transfusion: Systematic review of randomised trials with meta-analysis and trial sequential analysis. *BMJ* 2015; 350:h1354
16. Holst LB, Haase N, Wetterslev J, et al; TRISS Trial Group: Lower versus higher hemoglobin threshold for transfusion in septic shock. *N Engl J Med* 2014; 371:1381–1391
17. Lelubre C, Vincent JL: Red blood cell transfusion in the critically ill patient. *Ann Intensive Care* 2011; 1:43

18. Kiefel V: Reactions induced by platelet transfusions. *Transfus Med Hemother* 2008; 35:354–358
19. Roubinian N: TACO and TRALI: Biology, risk factors, and prevention strategies. *Hematology Am Soc Hematol Educ Program* 2018; 2018:585–594
20. Qin CX, Yesantharao LV, Merkel KR, et al: Blood utilization and clinical outcomes in extracorporeal membrane oxygenation patients. *Anesth Analg* 2020; 131:901–908
21. Smith A, Hardison D, Bridges B, et al: Red blood cell transfusion volume and mortality among patients receiving extracorporeal membrane oxygenation. *Perfusion* 2013; 28:54–60
22. De Cloedt L, Savy N, Gauvin F, et al: Transfusion-associated circulatory overload in ICUs: A scoping review of incidence, risk factors, and outcomes. *Crit Care Med* 2019; 47:849–856
23. Mazzeffi M, Greenwood J, Tanaka K, et al: Bleeding, transfusion, and mortality on extracorporeal life support: ECLS working group on thrombosis and hemostasis. *Ann Thorac Surg* 2016; 101:682–689
24. George TJ, Sheasby J, Shih E, et al: Blood product utilization in patients with COVID-19 on ECMO. *J Surg Res* 2022; 276:24–30