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Research Article

Evaluating the predictive effect of comorbidities on hemolysis in extracorporeal membrane oxygenation

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Introduction

Extracorporeal Membrane Oxygenation (ECMO) is a valuable support system that can treat severe cardiopulmonary disease.

ECMO support comes in two types: Veno-Venous (VV) and Veno-Arterial (VA). VV ECMO is typically indicated when cardiac function is sufficient, but the patient requires additional respiratory support. VV ECMO serves to provide additional oxygenation to supplement a patient's lungs, and is commonly used in severe Acute Respiratory Distress Syndrome (ARDS) caused by aspiration, pneumonia, barotrauma, pneumonitis, etc [1]. It can also be used as a bridge therapy in patients awaiting lung transplant. In contrast, VA ECMO is typically used in patients with both cardiac and respiratory failure, as it can provide both oxygenation and circulatory support. Common indications for VA ECMO include cardiogenic shock, acute myocardial infarction, chromic heart failure and cardiac arrest [1].

However, ECMO is associated with several complications, such as hemolysis. Intravascular hemolysis can occur due to blood flow through the mechanical components of ECMO or due to underlying patient complications [2]. Hemolysis can be measured with markers such as Plasma Free Hemoglobin (PFH) and is associated with complications such as renal failure and multiorgan failure [3]. Much research has been done evaluating how ECMO's mechanical support can cause hemolysis. Damage to red blood cells is thought to be due to pressure drop or shear stress caused by the ECMO circuit [4].

ECMO hemolysis has also been linked to an increase in mortality risk. Previous research has shown that PFH values over 50 mg/dL 24 hours after ECMO initiation can serve as an independent marker of mortality [5]. In VV ECMO, it has also been shown that non-survivors tended to have higher incidence of hemolysis and a higher average peak PFH compared to survivors [6].

While much research has been done on links between ECMO hemolysis and mortality as well as the mechanical causes of hemolysis, there is limited data on whether the presence of certain comorbidities in patients is linked to hemolysis while on ECMO support. While we know that ECMO hemolysis is primarily believed to be due to mechanical characteristics, we believe that underlying comorbidities can play a potentiating factor as well. We aim to evaluate whether presence of past Myocardial Infarction (MI), Heart Failure (HF) and Hypertension (HTN) is linked with increased rates of hemolysis while on ECMO. This will help inform future studies to further investigate this due to the lack of literature on the topic.

Methods

Patient information and data collection: We conducted a retrospective study of patients receiving ECMO support at Tampa General Hospital from 2020 to 2023. This study was approved by the Institutional Review Board at the University of South Florida (IRB 005536). Patients who were over the age of 18 and remained on ECMO support for less than 30 days in the specified time period were included. Patients were categorized into the type of ECMO support received (VA or VV). We then collected patient data such as Age, Sex, Body Mass Index (BMI), duration of ECMO support, use of Impala in VA ECMO, survival

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outcome (defined as expiration during ECMO or within 30 days post ECMO decannulation), PFH levels per day, history of past MI, history of past HF (HF that occurred directly prior to ECMO cannulation was not included) and history of past HTN.

At our institution, ECMO decisions follow a structured organizational framework for all patients with cardiopulmonary failure.

For cardiogenic shock, a Cardiac Shock Alert activates a conference call with a multidisciplinary team that typically includes the primary cardiologist, cardiac surgeon (when indicated), intensivist, and sometimes an emergency physician. During this call, the team evaluates the patient's rapid clinical deterioration and requests urgent heart failure consultation. The collective discussion determines whether to proceed with ECMO. A coordinator then assembles the ECMO team through text messages, managing personnel allocation and scheduling for VA-ECMO placement in either the operating room or ICU.

Following the COVID-19 pandemic, a parallel structure was established for respiratory failure through a Respiratory Shock Team comprising an ICU physician, admitting pulmonologist, and potentially lung transplant surgeons. After completing consultations, this pathway leads to VV-ECMO when appropriate.

Regarding anticoagulation practices, all VA-ECMO patients receive moderate-intensity anticoagulation, whereas VV-ECMO patients rarely require it. For both modalities, ECMO pump aspiration pressure is maintained below 100 mmHg.

Classification of hemolysis: Hemolysis was defined according to the 2024 ELSO Registry Data Definitions that described hemolysis as PFH over 50 mg/dL for at least two consecutive days. Using this definition, patients were sorted into either hemolysis present or hemolysis absent groups.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation and compared using Wilcoxon rank sum. Categorical variables were expressed by counts and percentages. Comparisons were done by utilizing Chi-squared tests or Fisher's Exact Test if expected counts were less than 5. Univariate analysis was used to see if any variables had a significant association with hemolysis. Variables with a p-value of less than 0.15 were included in a multivariable logistic regression. P-values less than 0.05 were considered significant.

Results

Patient characteristics between VA and VV ECMO: A total of 182 patients received ECMO with 74 patients receiving VA ECMO and 108 patients receiving VV ECMO. VA patients tended to suffer greater hemolysis compared to patients receiving VV ECMO, though the difference was not statistically significant (p=0.078). VA patients tended to be older (p=0.002) and spent less days on ECMO (p<0.001) compared to VV patients. Additionally, among VA patients, there was a higher incidence of a positive history for past MI (p<0.001), past HF (p<0.001) and HTN (p=0.020). There was no statistically significant difference in BMI and mortality rates between patients receiving either VA or VV ECMO.

Table 1: VA ECMO indications.

Indications	Sample Size (N)
Cardiogenic Shock	51
Cardiac Arrest	5
Respiratory Failure	4
Cardiomyopathy	3
Cardiac Surgery	7
Transplant Related	4

Table 2: VV ECMO indications.

Indications	Sample Size (N)
Covid Pneumonia	55
Transplant Related	15
Respiratory Failure	25
ARDS (Non-COVIDP)	7
Cardiac Arrest	4
Aspiration	2

Table 3: Characteristics of patients receiving VA and VV ECMO.

Variables	VA (N=74)	VV ECMO (N=108)	P Value
Body Mass Index (Kg/M^2)	28.6 ± 7.15	28.82 ± 7.91	0.948
Age (Years)	56.3 ± 14.5	49.79 ± 14.03	0.002
Duration of ECMO (Days)	6.91 ± 5.45	10.94 ± 7.65	P < 0.001
History of Past Mi	31 (41.9%)	6 (5.6%)	P < 0.001
History Of Past Hf	32 (43.2%)	16 (14.8%)	P < 0.001
History of Hypertension	52 (70.3%)	56 (51.9%)	0.020
Presence of Hemolysis	38 (51.4%)	40 (37.0%)	0.078
Mortality	50 (67.6%)	66 (61.1%)	0.464

Note: Variables with P<0.05 are displayed in bold.

Univariate analysis of risk factors for hemolysis in patients receiving VA ECMO: Among patients receiving VA ECMO, patients who suffered hemolysis had a lower BMI (p=0.044). Additionally, there was a higher incidence of hemolysis in patients who had a history of MI compared to those without (p=0.031). While the difference was not statistically significant (p=0.072), patients with hemolysis tended to spend more days on ECMO than those without hemolysis. There was no statistically significant difference in age between patients with and without hemolysis. History of HF and history of HTN was also not significantly associated with hemolysis in patients. There was also no statistically significant association between use of an impala and hemolysis.

Table 4: Risk factors for hemolysis in VA ECMO (Univariate Analysis).

Variables	Hemolysis (N=38)	No Hemolysis (N=36)	P Value
Body Mass Index (Kg/M^2)	27.22 ± 7.17	30.06 ± 6.91	0.044
Age (Years)	56.56 ± 14.01	56.05 ± 15.12	0.697
Duration of ECMO (Days)	7.68 ± 5.26	6.08 ± 5.58	0.072
History of Past Mi	21 (55.3%)	10 (27.8%)	0.031
History of Past Hf	15 (39.5%)	17 (47.2%)	0.585
History of Hypertension	27 (71.1%)	25 (69.4%)	1.0
Use of Impala	13 (34.2%)	15 (41.7%)	0.674

Note: Variables with P<0.05 are Displayed in Bold While Variables with 0.05<P<0.15 Are Italicized

Multivariable analysis of risk factors for hemolysis in patients receiving VA ECMO: After conducting multivariable analysis, the association between BMI and hemolysis did not show significance. However, history of past MI was independently associated with hemolysis (OR=2.91, 95% confidence level = 1.07-8.87, p=0.036).

Table 5: Risk factors for hemolysis in VA ECMO (Multivariable Analysis).

Variables	Odds Ratio	95% Ci	P Value
Body Mass Index (Kg/M²)	0.97	0.90-1.04	0.362
Age (Years)	-	-	-
Duration of ECMO (Days)	1.04	0.94-1.14	0.457
History of Past Mi	2.91	1.07-8.87	0.036
History of Past Hf	-	-	-
History of Hypertension	-	-	-
Use of Impala	-	-	-

Note: Variables with P<0.05 are displayed in bold.

Univariate analysis of risk factors for hemolysis in patients receiving VV ECMO: In patients receiving VV ECMO, patients with hemolysis spent more days on ECMO than those without hemolysis (p = 0.012). Additionally, there was lower incidence of hemolysis in patients with a history of HTN compared to higher incidence of hemolysis in patients without HTN (p=0.048).

Table 6: Risk factors for hemolysis in VV ECMO (Univariate Analysis).

Variables	Hemolysis (N=40)	No Hemolysis (N=68)	P Value
Body Mass Index (Kg/M²)	29.11 ± 8.53	28.65 ± 7.6	0.627
Age (Years)	47.08 ± 14.85	51.38 ± 13.38	0.142
Duration of ECMO (Days)	13.12 ± 7.35	9.65 ± 7.59	0.012
History of Past Mi	0 (0.0%)	6 (8.8%)	0.084
History of Past Hf	4 (10.0%)	12 (17.6%)	0.563
History of Hypertension	15 (37.5%)	41 (60.3%)	0.048

Note: Variables with P<0.05 are displayed in bold while variables with 0.05<P<0.15 are Italicized.

Multivariate analysis of risk factors for hemolysis in patients receiving VV ECMO: After conducting multivariable analysis, no variables remained significant and thus were not independently associated with hemolysis.

Table 7: Risk factors for hemolysis in VV ECMO (Multivariable Analysis).

Variables	Odds Ratio	95% CI	P value
Body Mass Index (Kg/M²)	-	-	-
Age (Years)	1.00	0.97-1.03	0.831
Duration of ECMO (Days)	1.04	0.99-1.11	0.127
History of Past Mi	0.00	0.00-Inf	1.000
History of Past Hf	-	-	-
History of Hypertension	0.50	0.20-1.22	0.127

Note: Variables with P<0.05 are displayed in bold.

Discussion/Conclusion

Our study found that a history of MI is significantly associated with increased risk of hemolysis while on VA ECMO in both univariate and multivariate analysis. While atherosclerosis is the main pathophysiology behind MI, it is unlikely that underlying atherosclerosis is the cause of increased risk of hemolysis in the MI cohort within VA ECMO. However, those with a history of MI tend to have other comorbid conditions such as an increased risk of coagulopathy due to underlying thrombophilia disorders [7]. Literature suggests that pre-existing coagulopathy increases hemolysis risk. Patients with elevated INR at cannulation (greater than 3.5) have a sevenfold risk of hemolysis [8]. ECMO is also known to cause complement activation, which can contribute to hemolysis potentiate the effect [9]. Patients with history of MI also demonstrate sustained complement activation beyond the acute phase which may also potentiate increased hemolysis [10]. While hemolysis that occurs during hemolysis is primarily due to mechanical and technical factors, these results may suggest that underlying cardiac history can also affect hemolysis. This can allow clinicians to monitor these patients more closely if they know their patient has had an MI in the past and may be at increased risk for hemolysis while on a VA ECMO circuit.

Patients receiving VA ECMO had a significantly higher incidence of past MI (5.6% of VV patients vs. 41.9% of VA patients) as well as significantly higher incidences of past HTN and past HF. These findings align with expected trends, as VA ECMO is typically indicated for patients with cardiopulmonary insufficiency, while VV ECMO is reserved for isolated respiratory failure. However, past MI did not increase hemolysis in VV ECMO patients. With only 6 patients in the VV cohort presenting with history of MI, power is limited in this cohort.

We also found that VV ECMO patients tended to spend significantly more days on ECMO than VA ECMO patients, which is consistent with previous research [11]. Additionally, our study showed that patients on VA ECMO tended to be significantly older compared to patients on VV ECMO, which is also consistent with previous research [12]. We found certain trends that were significant in univariate analysis but not significant in multivariate analysis. In the VA patient cohort, for example, patients with higher BMI showed less hemolysis. In the VV cohort, patients with past HTN had lower incidence of hemolysis while patients with hemolysis spent more days on ECMO. The loss of significance in the multivariate analysis suggests that relationships observed in univariate analysis may have confounded by other factors.

While not significant, VA ECMO did seem to show more hemolysis than VV ECMO. Previous research has shown that VA ECMO has significantly more hemolysis than VV ECMO, with Applet et al. finding than hemolysis (defined as PFH>50 mg/dL) was found in 4% of patients in VA ECMO compared to 2% of patients in VV ECMO (p<0.001) [12]. Reasons for the increased hemolysis include higher shear stress and flow rates, different cannulation techniques, increased afterload and left ventricular stress as well as pre-existing conditions [12-14]. While our study did not show this trend significantly, our p-value of 0.07 suggests a possible correlation that may demonstrate significance at higher sample sizes.

Additionally, use of an impala alongside VA ECMO has been associated with a higher risk of hemolysis when compared to VA ECMO alone [9]. However, our data did not demonstrate a significant association between Impala use and hemolysis (p=0.674). We hypothesize that this may be due to different definitions of hemolysis being used. In the meta-analysis by Bhatia et al. [9], four studies were included. Papalardo et al. [15], defined hemolysis as an "increase in Lactate Dehydrogenase (LDH) > 1000 U/L and increase in plasma free hemoglobin in

at least two consecutive blood samples within 24 hours". The second study used the definition "serum LDH 2.5 x upper limits of the normal range at the implanting center (normal LDH range at the center: 115-221 u/l) post device implant and an absence of elevated Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) levels over three times their normal ranges" [16]. Patel et al. [17], used the definition of "LDH ≥ 1,000 U/L associated with appropriate elevations in schistocytes, reticulocytes, or plasma-free hemoglobin in at least two consecutive blood samples" while Schrage et al. [18], defined hemolysis as "Lactate dehydrogenase ≥1000 U/L and haptoglobin <0.3 g/L in 2 consecutive samples within 24 hours". As seen, the definition of hemolysis was not constant and seemed to focus on LDH as the main marker of hemolysis. This differs from our approach, which defined hemolysis as PFH greater than 50 mg/dL for at least two consecutive days. This difference in definition can explain why we did not find a significant association. PFH is a direct marker of intravascular hemolysis while LDH is more a general marker of cell turnover and tissue damage, making it not as specific for hemolysis. While the other studies did use other clinical signs in conjunction with an elevation in LDH, our definition may have been more stringent resulting in there appearing to be no association between impala use and hemolysis.

Limitations

There are several limitations to this study. The study design was a single-center retrospective chart review with a moderate sample size. Additionally, this study used an updated definition of hemolysis which was PFH greater than 50 mg/dL for at least two consecutive days. Previous research defined hemolysis as PFH greater than 50 mg/dL for only one day, making it difficult to compare results with past studies. Another limitation is that the machine to measure PFH at Tampa General Hospital is not precise at PFL levels less than 30 mg/dL. Thus, any values less than 30 mg/dL were recorded as 30 mg/dL. However, considering that our cutoff for hemolysis was greater than 50 mg/dL, this limitation should have no impact on our findings.

We also did not collect data regarding rate of AKI, urinary output and creatinine. We acknowledge that AKIs can decrease renal clearance of PFH, thus elevate plasma levels of PFH. Future research should evaluate these factors to gain a more comprehensive understanding of our findings. As the role of PFH monitoring during ECMO remains under investigation, our institution does not routinely measure pre-ECMO PFH levels. Additionally, oxygenator clotting risk was managed clinically rather than through systematic documentation; consequently, parameters such as pre- and post-oxygenator pressures and coagulation values were not consistently recorded in the electronic medical record. Furthermore, ECMO pump settings, including flow rate and RPM, were not systematically documented, precluding analysis of these variables. We acknowledge these limitations on our data analysis and future research should evaluate these factors for a comprehensive analysis. We also acknowledge limitations in our sample size and hope to include more patients in future explorations.

Future directions

Our study was primarily to establish framework regarding the impact of comorbidities on ECMO hemolysis. There is limited research in this area and further exploration can allow for clinicians to monitor certain patients closely for hemolysis and prevent associated complications. Future research should include larger sample sizes with additional variables that our study did not include. Additionally, our study focused on cardiac related co-morbidities, which tend to have higher prevalence in VA ECMO populations. In the future, it might be of use to examine comorbidities more prevalent in VV ECMO patients that can lead to hemolysis. We hope that this study can inform further research and exploration into this topic.

References

1. Niroomand A, Olm F, Lindstedt S. Extracorporeal Membrane Oxygenation: Set-up, Indications, and Complications. Adv Exp Med Biol. 2023; 1413: 291-312. doi:10.1007/978-3-031-26625-6-15

2. Murphy DA, Hockings LE, Andrews RK, et al. Extracorporeal Membrane Oxygenation-Hemostatic Complications. Transfus Med Rev. 2015; 29(2): 90-101. doi:10.1016/j.tmrv.2014.12.001

3. Borasino S, Kalra Y, Elam AR, et al. Impact of Hemolysis on Acute Kidney Injury and Mortality in Children Supported with Cardiac Extracorporeal Membrane Oxygenation. J Extra Corpor Technol. 2018; 50(4): 217-224.

4. Naito N, Cook K, Toyoda Y, Shigemura N. Artificial Lungs for Lung Failure: JACC Technology Corner. J Am Coll Cardiol. 2018; 72(14): 1640-1652. doi: 10.1016/j.jacc.2018.07.049

5. Omar HR, Mirsaeidi M, Socias S, et al. Plasma Free Hemoglobin Is an Independent Predictor of Mortality among Patients on Extracorporeal Membrane Oxygenation Support. PLOS ONE. 2015; 10(4): 0124034. doi: 10.1371/journal.pone.0124034

6. Kutleša M, Novokmet A, Josipovic Mraovic R, Filar B, Mardešic P, et al. Extracorporeal membrane oxygenation treatment for H1N1-induced acute respiratory distress syndrome (ARDS): Results of the Croatian Referral Center for Respiratory ECMO. Int J Artif Organs. 2014; 37(10): 748-752. doi:10.5301/ijao.5000356

7. Camaj A, Fuster V, Giustino G, et al. Left Ventricular Thrombus Following Acute Myocardial Infarction: JACC State-of-the-Art Review. J Am Coll Cardiol. 2022; 79(10): 1010-1022. doi: 10.1016/j.jacc.2022.01.011

8. Okochi S, Cheung EW, Barton S, et al. An Analysis of Risk Factors for Hemolysis in Children on Extracorporeal Membrane Oxygenation. Pediatr Crit Care Med J Soc Crit Care Med World Fed Pediatr Intensive Crit Care Soc. 2018; 19(11): 1059-1066. doi:10.1097/PCC.0000000000001699

9. Bhatia K, Jain V, Hendrickson MJ, et al. Meta-Analysis Comparing Venoarterial Extracorporeal Membrane Oxygenation with or Without Impella in Patients with Cardiogenic Shock. Am J Cardiol. 2022; 181: 94-101. doi: 10.1016/j.amjcard.2022.06.059

10. Yasojima K, Schwab C, McGeer EG, McGeer PL. Human heart generates complement proteins that are upregulated and activated after myocardial infarction. Circ Res. 1998; 83(8): 860-869. doi:10.1161/01.res.83.8.860

11. Kon ZN, Bittle GJ, Pasrija C, et al. Venovenous Versus Venoarterial Extracorporeal Membrane Oxygenation for Adult Patients With Acute Respiratory Distress Syndrome Requiring Precannulation Hemodynamic Support: A Review of the ELSO Registry. Ann Thorac Surg. 2017; 104(2): 645-649. doi:10.1016/j.athoracsur.2016.11.006

12. Appelt H, Philipp A, Mueller T, et al. Factors associated with hemolysis during extracorporeal membrane oxygenation (ECMO)-Comparison of VA- versus VV ECMO. PLOS ONE. 2020; 15(1): 0227793. doi: 10.1371/journal.pone.0227793

13. Li Y, Liu X, Sun A, Deng X, Chen Z, et al. Multi-Method Investigation of Blood Damage Induced by Blood Pumps in Different Clinical

Support Modes. ASAIO J Am Soc Artif Intern Organs 1992. 2024; 70(4): 280-292. doi:10.1097/MAT.0000000000002116

14. Roumy A, Liaudet L, Rusca M, Marcucci C, Kirsch M. Pulmonary complications associated with veno-arterial extra-corporeal membrane oxygenation: A comprehensive review. Crit Care Lond Engl. 2020; 24(1): 212. doi:10.1186/s13054-020-02937-z

15. Pappalardo F, Schulte C, Pieri M, et al. Concomitant implantation of Impella® on top of veno-arterial extracorporeal membrane oxygenation may improve survival of patients with cardiogenic shock. Eur J Heart Fail. 2017; 19(3): 404-412. doi:10.1002/ejhf.668

16. Akanni OJ, Takeda K, Truby LK, et al. EC-VAD: Combined Use of Extracorporeal Membrane Oxygenation and Percutaneous Microaxial Pump Left Ventricular Assist Device. ASAIO J Am Soc Artif Intern Organs 1992. 2019; 65(3): 219-226. doi:10.1097/MAT.0000000000000804

17. Patel SM, Lipinski J, Al-Kindi SG, et al. Simultaneous Venoarterial Extracorporeal Membrane Oxygenation and Percutaneous Left Ventricular Decompression Therapy with Impella Is Associated with Improved Outcomes in Refractory Cardiogenic Shock. ASAIO J Am Soc Artif Intern Organs 1992. 2019; 65(1): 21-28. doi:10.1097/MAT.0000000000000767

18. Schrage B, Becher PM, Bernhardt A, et al. Left Ventricular Unloading Is Associated with Lower Mortality in Patients with Cardiogenic Shock Treated with Venoarterial Extracorporeal Membrane Oxygenation: Results From an International, Multicenter Cohort Study. Circulation. 2020; 142(22): 2095-2106. doi:10.1161/Circulationaha.120.048792.