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Outcomes of Patients Undergoing Interfacility Extracorporeal Membrane Oxygenation Transfer Based on Cannulation Location and Mode of Transport

OBJECTIVES: As the use of extracorporeal membrane oxygenation (ECMO) expands, so has the need for interfacility transfer to ECMO centers. However, the impact of these transfers has not been fully studied. This study evaluates complications and inhospital mortality in adult patients treated with venovenous (V-V) ECMO based on institutional location of cannulation and mode of transport.

DESIGN: Retrospective cohort study.

SETTING: Large midwestern ECMO center. **PATIENTS:** Adult patients receiving VV-ECMO.

INTERVENTIONS: Need for transfer to ECMO center following VV-ECMO

cannulation.

MEASUREMENTS AND MAIN RESULTS: The study included 102 adult patients, 57% of which were cannulated at an outside institution prior to transfer. Of these, 60% were transported by ground, and the remainder were transported by air. Risk-adjusted logistic regression did not reveal any significant increase in odds for any complication or inhospital mortality between the groups based on location of cannulation or mode of transport.

CONCLUSIONS: This study supports the practice of interfacility ECMO transfer with no difference in outcomes or inhospital mortality based on institutional location of cannulation or mode of transport.

KEY WORDS: aircraft, extracorporeal membrane oxygenation, interfacility transfer

irst introduced in the 1960s, advanced organ support through extracorporeal membrane oxygenation (ECMO) is a lifesaving measure for critical cardiac and respiratory failure (1). The volume of adult patients who require ECMO support continues to increase, expanding the network of regional ECMO centers (2). The development of ECMO transport protocols has increased the accessibility of this resource to critically ill patients who may not otherwise survive transport to their regional ECMO center (3). Several studies have reported overall survival rates of 62–68% in patients transported on ECMO, equivalent to patients cannulated inhouse (4, 5). However, fewer studies have examined complication rates following interfacility ECMO transport, and the results have been variable, with some studies suggesting complication rates as high as 30% (6–8). Furthermore, studies comparing mode of transport such as ground versus air are even more limited.

A systematic review by Kim et al demonstrated that commonly reported venovenous (VV)-ECMO complications include renal failure, multiple organ failure, sepsis, stroke, and intracranial hemorrhage (9). Cannulation-related injuries are also prevalent and estimated to occur in around 7% of cases (9).

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Cannulation itself can lead to numerous complications including hemostatic dysfunction, cannula or surgical site bleed, thromboembolic events, clotting in the circuit, and trauma to the heart leading to cardiac tamponade or arrest (10, 11). Once cannulated, the patient is at risk for arrhythmias, blood stream or wound infections, and bleeding from ongoing systemic anticoagulation (9, 12, 13). Understandably, there is concern that transport of ECMO patients between facilities could heighten the risk for patient complications, cannulation-related injury, and circuit system malfunction due to influences of transport time, equipment and resource limitations, and vehicle malfunction. As ECMO becomes increasingly used and available, there is a need for up-to-date information on complication and mortality rates for patients transported on ECMO, as well as any potential effects from mode of transport.

In this study, we compare the complication rates and inhospital mortality of patients cannulated at an outside facility and transported on VV ECMO with those who are cannulated at our ECMO center. We also examine the effect of different modes of transport including ground and air travels on complication rates and mortality in VV ECMO patients.

MATERIALS AND METHODS

Participants

This is a retrospective study of adult patients treated with VV ECMO at our institution, University of Minnesota, an Extracorporeal Life Support Organization Center of Excellence, from 2013 to 2020. Patients were analyzed based on institutional location of cannulation (i.e., our hospital vs outside hospital). There was a subanalysis performed on the patients transported on ECMO comparing the mode of transportation (i.e., ground vs air). Patients were excluded if they had any form of arterial ECMO support or ventricular assist device. The study was approved by the institutional review board at our institution (study 00001170).

Transport Protocol

Prior to transferring a patient to our facility for ECMO, the patient's case is first discussed by phone by the admitting and referring physicians. We do not apply different eligibility criteria for ECMO for patients who are transferred. On occasion, a physician from our institution will

travel to the referring facility and cannulate the patient. Most often, however, this is done by a surgeon at the referring facility and according to their protocols. Once the patient is cannulated, a transport team consisting of a flight or ground crew and a perfusionist travel to the referring hospital and transport the patient.

Study Variables

We collected patient characteristics, indications for ECMO, complications, cannulation information, transport details, discharge disposition, and mortality from our electronic medical record. Length of stay was defined as time from admission to time of discharge and included time spent at an outside facility prior to transfer. To assess anticoagulation status, we also collected the highest activated partial thromboplastin time and heparin 10a level within 24 hours of cannulation. The medical complications were combined into groups. The cardiac complications group includes cardiac arrest, cardiac arrhythmia, pericardial effusion, and cardiac tamponade. The pulmonary complications group includes pulmonary hemorrhage, pneumothorax, pulmonary embolism, and pulmonary effusion. The thrombosis group includes pulmonary embolism, deep vein thrombosis, other thrombus/embolism, ischemic stroke, gastrointestinal ischemia, and limb ischemia. The bleeding group includes pulmonary hemorrhage, hemothorax, hemorrhagic stroke, gastrointestinal hemorrhage, other hemorrhage, and hematoma. We also report prevalence of shock liver and hemorrhagic stroke alone. For equipment complications, cannula problem was defined as requiring repositioning or exchange of the cannula due to incorrect position, clots, or other failure. Oxygenator failure and pump failure were included if there was an issue that required exchange of those components. Clots in circuit was included if the clot was severe enough to require change of one of the circuit components. Clot in hemofilter was included if the clot was severe enough to require exchange of the hemofilter. Air in circuit was included if it required intervention or clamping of the circuit. Circuit change was included if the entire circuit except for the cannula was changed.

Statistical Analysis

All data were stored in a Research Electronic Data Capture tool provided by the University of Minnesota (14). Using Stata 16 (StataCorp LLC, College Station,

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TX) (15), we analyzed basic descriptive statistics and reported them as a mean with sp if normally distributed or median with interquartile range otherwise. Two-tailed t tests, Wilcoxon rank-sum test, and chisquare tests were used as appropriate to determine if there were significant differences in demographics and pre-ECMO clinical variables between the groups. A p value of less than or equal to 0.05 was deemed significant. Complications and inhospital mortality were evaluated using logistic regression with results reported using odds ratios with CIs. The adjusted analysis was performed based on variables that were significantly different between groups, which included body mass index (BMI) for cannulation institutional location analysis, and race, asthma, chronic obstructive pulmonary disease (COPD), tobacco use, pre-ECMO proning, and vasopressor use for the mode of transport analysis.

RESULTS

Patient Characteristics Based on Institutional Location of Cannulation

There were 102 patients included in the study, 58 were cannulated at an outside facility and transported to our ECMO center, with 35 transported by ground and 23 aircraft (**Fig. 1**). **Table 1** summarizes the patient

characteristics and comorbidities based on cannulation site. The only characteristic that was significantly different between the groups was BMI (p = 0.04).

Patient Outcomes Based on Institutional Location of Cannulation

Table 2 summarizes complications, length of stay, mortality, and other outcomes based on institutional location of cannulation. Time on ECMO was similar between groups, but hospital length of stay was longer in the patients cannulated at our ECMO center (p = 0.004) as was ICU length of stay (p = 0.04). There was no significant difference in disposition at discharge. No patients died during transport. As shown in **Figure 2**, risk-adjusted logistic regression did not reveal any significant increase in odds for any complication or outcome between the groups.

Patient Characteristics Based on Mode of Transport

Table 3 summarizes patient characteristics and comorbidities of patients who were cannulated at an outside hospital based on whether they were transported by air or ground. There were significant differences in the race and ethnicity of the patients, with a high proportion

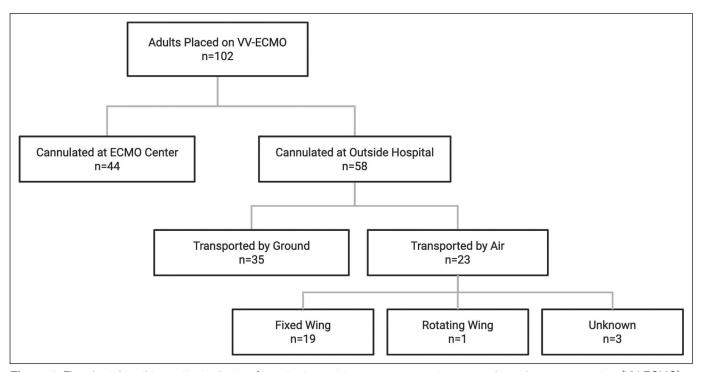


Figure 1. Flowchart describing patient selection for patients receiving venovenous extracorporeal membrane oxygenation (VV-ECMO) based on institutional location of cannulation and mode of transport.

TABLE 1.

Demographics, Comorbidities, and Preextracorporeal Membrane Oxygenation
Characteristics of Patients Treated With Venovenous Extracorporeal Membrane Oxygenation
Based on Whether They Were Cannulated at Our Institution or an Outside Facility

Characteristic	Outside Institution, $n = 58$	Our Institution, $n = 44$	p
Age, median (IQR)	46 (38–56)	41 (31–56)	0.13
Sex, n (%)			
Male	37 (64)	32 (73)	0.34
Race/Ethnicity			
White, <i>n</i> (%)	32 (55)	34 (77)	0.16
Black/African American, n (%)	8 (14)	6 (14)	
Hispanic, n (%)	6 (10)	2 (5)	
Asian, n (%)	5 (9)	1 (2)	
Unknown, n (%)	4 (7)	0 (0)	
Native American, n (%)	2 (3)	0 (0)	
Other, n (%)	1 (2)	1 (2)	
Body mass index, median (IQR)	31 (28–38)	29 (25–34)	0.04ª
Comorbidity, n (%)			
Obesity	31 (53)	20 (45)	0.42
Hypertension	19 (33)	11 (25)	0.39
Hyperlipidemia	15 (26)	8 (18)	0.36
Diabetes mellitus	11 (19)	10 (23)	0.64
Asthma	10 (17)	4 (9)	0.24
Chronic obstructive pulmonary disease	7 (12)	4 (9)	0.63
Coronary artery disease	6 (10)	1 (2)	0.11
Chronic kidney disease, n (%)	4 (7)	1 (2)	0.28
Tobacco use	28 (48)	22 (50)	0.86
Positive for COVID-19	9 (17)	4 (10)	0.34
Indication for ECMO, n (%)			
Pneumonia	47 (81)	32 (73)	0.25
Trauma/burn	3 (5)	0 (0)	
Acute respiratory distress syndrome 2 to sepsis	3 (5)	3 (7)	
Bridge to transplant	2 (3)	7 (16)	
Acute airway obstruction	1 (2)	1 (2)	
Pulmonary fibrosis	1 (2)	1 (2)	
Asthma	1 (2)	0 (0)	
Pre-ECMO Pao ₂ /Fio ₂ ratio, mean (sD)	65 (22)	67 (27)	0.66
Pre-ECMO interventions, n (%)			
Prone positioning	36 (62)	22 (50)	0.22
Vasopressors	39 (67)	22 (50)	0.08
Respiratory ECMO survival prediction, median (IQR)	3 (2-5)	3 (0-4)	0.073
Highest activated partial thromboplastin time within 24 hr of cannulation, median (IQR)	103 (50–186)	134 (71–240)	0.24
Highest heparin 10a within 24hr of cannulation, median (IQR)	0.24 (0.1-0.74)	0.49 (0.16-0.93)	0.09

ECMO = extracorporeal membrane oxygenation, IQR = interquartile range. $^{\rm a}p$ < 0.05

TABLE 2.

Complications, Length of Stay, Mortality, and Discharge Disposition in Patients Treated With Venovenous Extracorporeal Oxygenation Based on Whether They Were Cannulated at Our Hospital or an Outside Facility

Characteristic	Outside Hospital, $n = 58$	Our Hospital, <i>n</i> = 44	p
Cardiac complications, n (%)	24 (41)	13 (30)	a
Respiratory complications, n (%)	17 (29)	12 (27)	a
Thrombosis, n (%)	14 (24)	11 (25)	a
Bleeding, n (%)	28 (48)	16 (36)	a
Shock liver, n (%)	2 (3)	3 (7)	a
Hemorrhagic stroke, n (%)	13 (22)	4 (9)	a
Equipment complications, n (%)			
Oxygenator failure	6 (11)	5 (11)	a
Circuit change	14 (24)	6 (14)	a
Cannula problems	29 (50)	19 (43)	a
Circuit clot	0 (0)	1 (2)	a
Hemofilter failure	0 (0)	0 (0)	a
Pump failure	0 (0)	0 (0)	a
Air in circuit	0 (0)	0 (0)	a
Inhospital mortality, n (%)	22 (38)	17 (39)	a
Time on extracorporeal membrane oxygenation (d), median (IQR)	9 (5–18)	11 (5–17)	0.97
ICU LOS (d), median (IQR)	18 (9–37)	23 (18–38)	0.04 ^b
Hospital LOS (d), median (IQR)	21 (14–39)	32 (23–56)	0.004 ^b
Discharge disposition, n (%)			
Home	7 (12)	11 (25)	0.17
Another hospital	6 (10)	1 (2)	
Transitional care unit/rehab	23 (40)	15 (34)	
Deceased	22 (38)	17 (39)	

IQR = interquartile range, LOS = length of stay.

of Asian, Black, and Hispanic White patients being transported by ground compared with air (p = 0.048). There was also increased prevalence of tobacco use (p = 0.009) and COPD (p = 0.008) in patients transported by air. Patients transported by ground were more likely to be proned prior to cannulation (p = 0.018), whereas patients transported by air were more likely to be on vasopressors prior to cannulation (p = 0.043).

Patient Outcomes Based on Mode of Transport

Supplemental Table 1 (http://links.lww.com/CCX/A951) summarizes complications, length of stay,

mortality, and other outcomes in patients cannulated for ECMO at an outside hospital based on whether they were transported by ground or air. Time on ECMO, ICU length of stay, and hospital length of stay were comparable. There was no difference in discharge disposition. The median number of miles traveled by ground was 7.8 compared with 155 by air. Median hours of transport was longer in patients who traveled by air, 2.5 compared with 0.6 hours in those transported by ground. As shown in **Figure 3**, risk-adjusted logistic regression did not reveal any significant increase in odds for any complication or outcome between the groups.

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 $^{^{}b}p < 0.05.$

^ap is not listed due to having risk adjusted odds ratio.

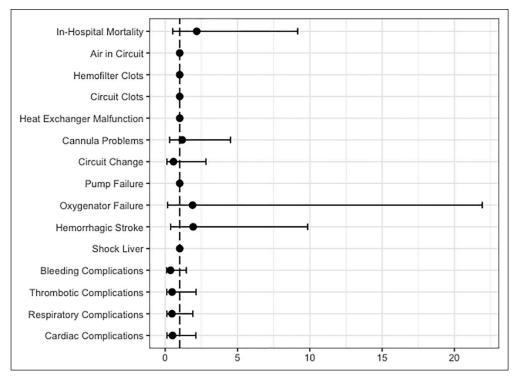


Figure 2. Forest plot depicting risk adjusted odds ratios for complications occurring after extracorporeal membrane oxygenation cannulation based on whether the patient was cannulated at our institution or an outside facility.

DISCUSSION

In this retrospective, cohort study, we found that interfacility ECMO transfers are not associated with complications based on institutional location of cannulation or mode of transportation. We did find increased ICU and hospital length of stay in patients cannulated at our facility. Ultimately, there were no significant differences in time on ECMO, mortality, or discharge disposition based on institutional location of cannulation. Mode of transport had even less of an effect, with no significant differences found in outcomes for patients who were cannulated at an outside hospital and transported via ground versus air.

Our equipment complication rates were consistent with existing literature. One large study of 452 transfers reported less than 1% rate of ECMO circuit clotting, pump change, oxygenator clot, cannula clot, and air in circuit; findings that are very similar to our own (16). Another study of 908 transfers found 7% air in circuit, 3% cannula clot, 7% oxygenator clot, and 3% poor cannula position (6). Due to differing systems of classification, we are unable to compare our medical complication rates with existing literature. Hospital and ICU length of stays were found to be higher in the

group cannulated at our ECMO center. This finding is likely related to more of the patients at our center being transplant patients and having long pre-ECMO stays. Notably, time on ECMO was equivalent between the groups suggesting that the differences in hospital and ICU length of stays may be related to underlying disease rather than ECMO itself. Survival to discharge for patients transported on ECMO from an outside facility was 62%. This is consistent with existing literature including systematic review including 643 patients transported on ECMO, which reported that 61% survived to discharge (4,

17). Ultimately, there were no differences in discharge disposition between these groups, suggesting that institutional location of cannulation does not increase the likelihood for needing rehabilitative services.

In those patients cannulated at outside institutions, we did not detect any significant differences in outcomes of patients transported by air versus ground. We found equivalent rates of thrombosis, bleeding, stroke, cardiac and respiratory complications, and ECMO equipment-related complications. Inhospital mortality, length of stay, length of ECMO run, and discharge disposition were also comparable. These results differ from a recent study by Read et al (18), which found lower survival to discharge in patients who were transported by air and higher acute renal failure in patient transported by ground. However, our results do concur with small studies done in the pediatric population, which have reported comparable complications and mortality in children transported by aircraft on ECMO (19, 20). Our results suggest that transfer by air does not increase the risk of medical or ECMO equipment complications nor does it increase mortality or length of stay. This adds to the extremely limited literature on interfacility transfer by aircraft for patients

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TABLE 3.Demographics, Comorbidities, and Severity Scores of Patients Transported on Venovenous Extracorporeal Membrane Oxygenation Based on Mode of Transportation

Characteristic	Ground Transport, n = 35	Air Transport, n = 23	p
Age, median (IQR)	45 (34–56)	50 (39–58)	0.31
Sex, (%)			
Male	24 (69)	13 (57)	0.35
Race/Ethnicity			
White	18 (51%)	14 (61%)	0.048ª
Black/African American	7 (20%)	1 (4%)	
Hispanic	4 (11%)	2 (9%)	
Asian	5 (14%)	0 (0%)	
Unknown	1 (3%)	3 (13%)	
Native American	0 (0%)	2 (9%)	
Other	0 (0%)	1 (4%)	
Body mass index, median (IQR)	31 (27–35)	31 (28-40)	0.29
Comorbidity, n (%)			
Obesity	17 (49)	14 (61)	0.36
Hypertension	11 (31)	8 (35)	0.79
Hyperlipidemia	9 (26)	6 (26)	0.97
Diabetes mellitus	4 (11)	7 (30)	0.07
Asthma	7 (20)	3 (13)	0.49
Chronic obstructive pulmonary disease	1 (3)	6 (26)	0.008a
Coronary artery disease	2 (6)	4 (17)	0.15
Chronic kidney disease	2 (6)	2 (9)	0.66
Tobacco use, n (%)	12 (34)	16 (70)	0.009ª
Indication for ECMO, n (%)			
Pneumonia	31 (89)	16 (70)	0.17
Trauma/burn	0 (0)	3 (13)	
Acute respiratory distress syndrome 2 to sepsis	1 (3)	2 (9)	
Bridge to transplant	1 (3)	1 (4)	
Acute airway obstruction	0 (0)	1 (4)	
Pulmonary fibrosis	1 (3)	0 (0)	
Asthma	1 (3)	0 (0)	
Pre-ECMO Pao ₂ /Fio ₂ ratio, mean (sp)	62 (22)	70 (23)	0.25
Pre-ECMO interventions, n (%)			
Prone positioning	26 (74)	10 (43)	0.018ª
Vasopressors	20 (57)	19 (83)	0.043ª
Respiratory ECMO Survival Prediction, median (IQR)	4 (2-5)	3 (2-4)	0.42
Highest activated partial thromboplastin time within 24 hr of cannulation, median (IQR)	119 (72–221)	93 (57–178)	0.43
Highest heparin 10a within 24 hr of cannulation, median (IQR)	0.24 (0.1-0.92)	0.24 (0.1-0.43)	0.76

ECMO = extracorporeal membrane oxygenation, IQR = interquartile range. $^{\rm a}p$ < 0.05.

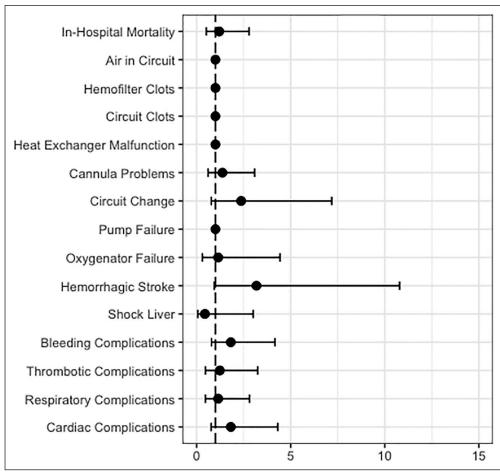


Figure 3. Forest plot depicting risk adjusted odds ratios for complications occurring after extracorporeal membrane oxygenation (ECMO) cannulation based on whether the patient was transported on ECMO via ground or air.

evaluate these questions using a larger patient population from a national database.

CONCLUSIONS

Our study shows that interfacility ECMO transport is not associated common medical and equipment complications, regardless of mode of transportation. Overall, mortality, length of time on ECMO, and discharge disposition were not significantly different based on institutional location of cannulation or mode of transport. We believe this supports the ongoing use of transport protocols for patients on VV ECMO to support the geographic expansion of referral networks to maximize access for patients.

receiving ECMO and supports continuing use of this mode of transport in larger referral networks.

Our study has several limitations. First, the small overall and group sample sizes reduced statistical power. ECMO is an intensive and relatively uncommon procedure, and despite including over 7 years of data, the study population was limited to 102 patients. Furthermore, this was a single-center study, and therefore, our results may be confounded by institutional practices that are not present elsewhere. Similarly, some of our patients who were transported were cannulated by physicians at the referring facility, so the protocol used for cannulation may differ. It is also worth noting that this study occurred in the United States and may not be generalizable to countries with more integrated healthcare systems or who have different configurations of their transport teams. Finally, this is a retrospective cohort study, and thus, we can only report associations. Moving forward, we hope to

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Ms. Wothe and Dr. Bergman are cofirst authors.

Dr. Brunsvold is the guarantor of this article. Ms. Wothe, Dr. Bergman, Dr. Lusczek, and Dr. Brunsvold contributed to the study concept and design. Ms. Wothe and Ms. Kalland performed the data collection. Drs. Bergman and Lusczek conducted statistical analysis. Ms. Wothe, Ms. Kalland, and Mr. Peter wrote the initial draft of the article. Ms. Wothe, Dr. Bergman, Ms. Kalland, Mr. Peter, Dr. Lusczek, and Dr. Brunsvold performed critical revisions of the article. All authors approved the final article.

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