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Outcomes of Patients Transported in the Prone Position to a Regional Extracorporeal Membrane Oxygenation Center: A Retrospective Cohort Study

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IMPORTANCE: Prone positioning is associated with improved mortality in patients with moderate/severe acute respiratory distress syndrome (ARDS) and has been increasingly used throughout the COVID-19 pandemic. In patients with refractory hypoxemia, transfer to an extracorporeal membrane oxygenation (ECMO) center may improve outcome but may be challenging due to severely compromised gas exchange. Transport of these patients in prone position may be advantageous; however, there is a paucity of data on their outcomes.

OBJECTIVES: The primary objective of this retrospective cohort study was to describe the early outcomes of ARDS patients transported in prone position for evaluation at a regional ECMO center. A secondary objective was to examine the safety of their transport in the prone position.

DESIGN: Retrospective cohort study.

SETTING: This study used patient charts from Ornge and Toronto General Hospital in Ontario, Canada, between February 1, 2020, and November 31, 2021.

PARTICIPANTS: Patient with ARDS transported in the prone position for ECMO evaluation to Toronto General Hospital.

MAIN OUTCOMES AND MEASURES: Descriptive analysis of patients transported in the prone position and their outcomes.

RESULTS: One hundred fifteen patients were included. Seventy-two received ECMO (63%) and 51 died (44%) with ARDS and sepsis as the most common listed causes of death. Patients were transported primarily for COVID-related indications (93%). Few patients required additional analgesia (8%), vasopressors (4%), or experienced clinically relevant desaturation during transport (2%).

CONCLUSIONS AND RELEVANCE: This cohort of patients with severe ARDS transported in prone position had outcomes ranging from similar to better compared with existing literature. Prone transport was performed safely with few complications or escalation in treatments. Prone transport to an ECMO center should be regarded as safe and potentially beneficial for patients with ARDS and refractory hypoxemia.

KEY WORDS: acute respiratory distress syndrome; COVID-19; critical care transport; extracorporeal membrane oxygenation; prone transport; safety

Acute respiratory distress syndrome (ARDS) accounts for approximately 10% of all ICU admissions with a mortality ranging between 35% and 46% (1, 2). Although transporting patients with ARDS carries inherent risks, transferring patients with severe ARDS to an extracorporeal membrane oxygenation (ECMO) center is associated with better outcomes regardless of if they ultimately receive ECMO (3–5). In patients with moderate/severe ARDS

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KEY POINTS

Question: Single-center, retrospective study in Ontario, Canada, assessing outcomes of patients with acute respiratory distress syndrome (ARDS) transported prone for extracorporeal membrane oxygenation (ECMO) consideration.

Findings: In this cohort study, ARDS patients transported prone to an ECMO referral center had outcomes similar or improved when compared with existing literature. Prone transport of these patients was able to be performed safely with minimal complications.

Meanings: More collaboration should be undertaken between critical care centers and local transport organizations to develop protocols for identification and safe prone transport of ARDS patients to ECMO referral centers as this is a safe and potentially beneficial practice.

(defined as $Pa{O_2}/F{IO_2}$ [P/F] ratio below 150 mm Hg) prone positioning is associated with improved survival independent of effects on oxygenation (6, 7). As such, it may be advantageous for patients already in the prone positioning to remain in the prone position during transport.

Interfacility transport of patients with ARDS carries risks for worsening hypoxemia, hemodynamic instability, and cardiac arrest (8, 9). Prone transport carries its own concerns that are unique to the transport environment due to confined spaces in the aircraft or land ambulance. These include impeded IV and airway access, and difficulties performing standard cardiopulmonary resuscitation (CPR) (9). While there have been small numbers of case reports discussing adverse events related to prone transport (9–13), there is also evidence that CPR and defibrillation can be reasonably performed in the prone position (14, 15). Since there is a relative paucity of data on the safety of prone positioning in patient transport compared with its in-hospital use, it has been difficult to determine the relative risk and benefits to prone transport. With the COVID-19 pandemic, prone positioning was increasingly used in peripheral hospitals increasing the number of patients already in prone position prior to transport (16, 17). Combined with the increase in the number of patients with ARDS due to COVID-19, this has provided us the opportunity to evaluate our experience in transporting these patients in prone position to a regional ECMO referral center.

In this retrospective cohort study, we describe the characteristics and outcomes of patients transported prone to a regional ECMO center for treatment consideration, and report safety events during prone transportation of patients with ARDS.

MATERIALS AND METHODS

Study Setting

The Toronto General Hospital (TGH) is a regional ECMO referral center that accepts patients across Ontario, Canada. TGH is a quaternary care hospital in Toronto, Ontario, with 463 beds and 35 ICU beds.

Ornge is the sole provider of critical care transport for interfacility transfers in Ontario. It operates 12 bases across Ontario with 12 Leonardo AW-139 helicopters, eight Pilatus Next Generation PC-12 airplanes and has five dedicated critical care land bases for urban critical care transport. All prone transports in the study cohort were performed by specially trained Critical Care Paramedics (CCPs) through Ornge.

Critical care transport paramedic crews are comprised of two paramedics who are either both trained as CCPs or one CCP and one Advanced Care Paramedic (ACP). CCPs are initially trained as ACPs and receive an additional 2 years of training for their critical care certification. They work under base hospital medical directives and perform a delegated medical acts which includes titration of drug infusions, mechanical ventilation, and monitoring of invasive devices.

All transported patients were placed on cardiac and end-tidal carbon dioxide monitoring. Invasive blood pressure monitoring was also used if initiated at the sending hospital. Previous in-hospital ventilatory settings were used upon transfer and paramedics employed ARDS medical directives to titrate ventilation afterwards. Paramedics were trained to deal with most complications and were able to communicate with a base hospital physician at any point. Shared decision-making was done with the paramedic crew, patient family, and sending facility in regard to transport risks. A protocol for prone CPR was available and paramedics were given the option to divert to the nearest emergency department if necessary. A copy of Ornge paramedic protocols is available as a **Supplemental File** (http://links.lww.com/CCX/B225).

Study Design

We retrospectively reviewed the electronic health records from TGH and Ornge between February 1, 2020, and November 30, 2021, and included all adult patients (18 yr old or greater) with ARDS who were transported prone by Ornge to TGH for consideration of ECMO cannulation.

Data Sources

Ornge ambulance call reports were reviewed for information including age, sex, arrival/departure times, chief complaint, reason for transfer, treatment prior to Ornge arrival, current hospital medications, existing injuries/comorbidities, vitals at start of transport, required interventions during transport, and ventilator settings. Patient matching was then done by searching physical records held at the ICU at TGH to identify each transported patient's respective hospital medical record number. A probabilistic match between paramedic and hospital records was determined if a patient was successfully matched on age, sex, chief complaint, and time of arrival. Subsequently, each patient's electronic health record was accessed to retrieve additional information including ventilator settings upon arrival, arterial blood gas upon arrival, ECMO treatment, timeframe of other interventions (e.g., dialysis, tracheostomy), hospital complications, and final outcome (e.g., discharge, death).

Research Ethics

We obtained a waiver for informed consent from the Research Ethics Board of the University Health Network since only retrospective, de-identified patient data was used (University Health Network, REB No. 21-5315).

Data Analysis

All study data analysis was performed with Excel (Microsoft, Redmond, WA, 2016). Descriptive statistics and counts were generated for findings of interest. Quantitative data was represented with mean and SD or median with interquartile range (IQR) depending on data distribution.

ICU length of stay was calculated with the date the patient arrived at TGH as the starting day and discharge from TGH ICU as the last day. For patients who were cannulated for ECMO and later died, if an ECMO end date was not explicitly stated, it was assumed to be their date of death. Patients were stratified by their P/F ratio as a representation of the severity of their respiratory status, calculated based on available data immediately prior to transport to TGH. The severe category was defined as having a P/F ratio below 100, with the nonsevere category being a P/F greater than or equal to 100. Patients in which a pre-transport P/F could not be calculated due to missing data were assigned into the "P/F Not Available (N/A)" category.

Management of Missing Data

We did not substitute data or perform a sensitivity analysis for missing data in this study. We have commented upon any results which were affected by missing data points in the Results section.

RESULTS

Cohort Characteristics

During the study period, 115 patients were transported by Ornge to TGH for ECMO consideration. The majority of patients had severe ARDS (n = 69, 60%) and as well as COVID-19 (n = 107, 93%). Most patients were transported by land ambulance (n = 107, 93%) (**Supplemental Material 1**, http://links.lww.com/CCX/B223). Median (IQR) patient age in the severe and nonsevere groups were 47 (21–65) and 49 (19–61), respectively. Most patients received neuromuscular blocking medication (n = 82, 71.3%) and dexamethasone (n = 809, 69.6%) while use of inhaled pulmonary vasodilators such as epoprostenol (n = 19, 16.5%) and nitric oxide (n = 5, 4.3%) were less frequently used.

Excluding transfer delays after arriving at the receiving hospital, median prone transport time was 32 minutes (23–41 min), ranging from 11 to 143 minutes. Most patients had no adverse events while being transported prone (n = 83, 72.2%). Reported events included ventilator adjustments (severe n = 13, 18.8%; nonsevere n = 4, 14.3%), additional analgesia (severe n = 5, 7.2%; nonsevere n = 3, 10.7%), and additional vasopressor support (severe n = 3, 4.3%; nonsevere n = 1, 3.6%). Within the severe group, two patients experienced desaturation during vehicle-to-hospital transfer, and another two experienced desaturation during transport. It is unknown if a specific threshold was used by paramedics to define these desaturation events when documented as adverse events within the ambulance call report. No patients experienced other major adverse events, including endotracheal tube dislodgement and cardiac arrest.

Ventilation Requirements

The median (IQR) P/F ratio prior to transport was 96 (71–103) and following arrival at TGH was 96.0 (IQR, 80.0–120.0) (**Table 1**). Within the severe group, the P/F ratio was 71.0 (IQR, 59.0–82.1) during transport and 91.0 (76.87–112.9) upon arrival at TGH while in the nonsevere, this was 118.48 (IQR, 109.8–126.4) and 102.5 (IQR, 89.0–126.4), respectively. A number of ventilatory settings were decreased upon arrival to the ECMO center. The average inspiratory pressure decreased from 20 cm/H_2O (± 5 cm H_2O) to 16 cm/H_2O (± 4 cm H_2O), as well average patient tidal volumes decreased from 369 mL (± 76 mL) prior to transport and 346 mL (± 105 mL) upon arrival. Similarly pH improved from 7.28 (IQR, 7.21–7.35) prior to transport to 7.31 (IQR, 7.25–7.36) upon arrival, with median $Paco_2$ values decreasing from 64 mm Hg (IQR, 53–74 mm Hg) to 58 mm Hg (IQR, 50–66 mm Hg).

Hospital Course

ECMO therapy was initiated for 72 patients (63%) with the majority being placed on venovenous configuration (**Table 2**). Less than half of our cohort was ultimately weaned from ECMO. Similar proportions of patients received ECMO therapy with 44 severe ARDS patients (63.8%) and 17 nonsevere (60.7%). Of the three patients who ultimately received venoarterial ECMO, two were first cannulated with a venovenous configuration. These two patients had an unknown P/F, and the third had severe ARDS.

Patients were in hospital for an overall median (IQR) of 9 days (5–11 d) prior to transfer to TGH. Severe ARDS patients had a median (IQR) ECMO treatment duration of 25 days (15–41 d) and ICU stay of 29.5 days (IQR, 17–48 d), compared with nonsevere patients who had respective medians of 20 days (IQR, 14–35 d) and 20 days (IQR, 16.5–40 d).

The hospital mortality of our cohort was 44.3% (n = 51), with a lower proportion of the severe group (42%) in comparison to our nonsevere cohort (53.6%). Across the entire cohort, the three most common listed causes of death were ARDS (n = 14, 26.9%), sepsis (n = 11, 21.6%), and intracranial hemorrhage (n = 10, 19.6%). In severe patients, ARDS and intracranial hemorrhage were the most common causes of death (n = 10, 34.5% and n = 8, 27.6%, respectively), and in the nonsevere group, sepsis was the most common (n = 8, 53.5%).

A total of 40 patients were repatriated, 26 patients with severe ARDS, eight nonsevere and six with unknown P/F ratios. We were unable to collect further hospital stay data on patients repatriated to other hospitals and therefore have missing data pertaining to final hospital length of stay, survival, and discharge home.

ICU Complications

Table 3 shows a full list of complications patients encountered during their ICU stay. Ventilator-associated pneumonia (n = 40, 34.8%), acute kidney injury (n = 36, 31.3%), bacteremia (n = 30, 26.1%), and sepsis (n = 29, 25.2%) were the most common listed complications. In regard to thrombotic events, 10 patients (8.7%) had a pulmonary embolism, 9 (7.8%) developed deep vein thrombosis, and 15 (13.0%) experienced other types of thrombotic events which included right ventricle, internal jugular, and inferior vena cava thrombi.

DISCUSSION

Herein, we describe the outcomes of patients with ARDS transported prone to a regional ECMO center in Toronto, Ontario, Canada. We also describe the safety profile of prone transportation of mechanically ventilated patients. Our study represents one of the largest cohorts currently reported and includes in hospital outcomes often not reported in previous studies (8, 18). This cohort demonstrates that prone transport of severe ARDS patients is not only safe, but these patients have similar outcomes and complications according to previous literature.

Prone Transport Safety

Existing cohort studies on adverse events in prone transport have reported rates of manageable complications including mild desaturation events and transient hypotension at comparable rates to patients

TABLE 1.
Ventilator Settings

Parameter	Mean (SD) or Median (IQR)					
	All Patients		Severe		Nonsevere	
	Prior to Transport	Arrival to ECMO Center	Prior to Transport	Arrival to ECMO Center	Prior to Transport	Arrival to ECMO Center
F_{IO_2}	0.95 (0.10)	0.92 (0.15)	0.98 (0.21)	0.95 (0.20)	0.88 (0.15)	0.87 (0.16)
Pa_{O_2}/F_{IO_2} ratio	96.2 (71.0–103.3)	96.0 (80.0–118.0)	71.0 (59.0–82.1)	91.0 (76.8–112.9)	118.5 (109.8–145.6)	102.5 (89.0–126.4)
Frequency (resps/min)	30 (26–32)	30 (28–33)	28 (26–32)	30 (28–32)	32 (28–34)	32 (28–34)
Positive end-expiratory pressure (cm/H_2O)	13 (4)	14 (4)	13 (4)	14 (4)	13 (3)	14 (3)
Peak inspiratory pressure (cm/H_2O)	34 (7)	N/A	35 (13)	N/A	33 (5)	N/A
Inspiratory pressure (cm/H_2O)	20 (5)[a]	16 (4)[b]	22 (9)	17 (7)	20 (9)	17 (8)
Tidal volume (mL)	369 (76)	346 (105)	376 (124)	354 (125)	353 (118)	332 (65)
VE total (L/min)	10.6 (2.2)	10.1 (2.2)	10.7 (3.6)	10.2 (2.7)	10.6 (3.5)	10.1 (1.8)
pH	7.28 (7.21–7.35)	7.31 (7.26–7.36)	7.28 (7.17–7.34)	7.32 (7.26–7.36)	7.28 (7.19–7.38)	7.3 (7.26–7.37)
P_{CO_2}	64 (53–74)	58 (50–66)	60 (43–70)	58 (49–64)	70 (56–78)	57 (50–68)

ECMO = extracorporeal membrane oxygenation, IQR = interquartile range, N/A = not available, resps = respirations, VE = Minute Ventilation.

[a]Twenty-five patients received pressure control ventilation during transport.

[b]Thirty-four patients received pressure control ventilation at the ECMO center.

TABLE 2.
Patient ICU Stay Lengths and Outcomes

Characteristic/Outcome	Median (IQR) or *n* (%)			
	All Patients	Severe	Nonsevere	Pao_2/Fio_2 Not Available
Total patients	115	69 (60.0)	28 (24.3)	18 (15.7)
No. of patients placed on ECMO	72 (62.2)	44 (63.8)	17 (60.7)	11 (61.1)
No. of patients weaned from ECMO	30 (41.7)	19 (43.2)	6 (35.3)	5 (45.5)
ECMO configuration (% of ECMO patients)				
Venous-venous	62 (86.1)	39 (88.6)	15 (88.2)	8 (72.7)
Venous-arterial	3 (4.2)	1 (2.3)	0 (0.0)	2 (18.2)
NR	7 (9.7)	4 (9.1)	2 (11.8)	1 (9.1)
Length of stay/treatment (d)[a]				
Length of stay prior to Toronto General Hospital	9 (5–11)	8 (4–11.5)	9 (6.8–10.3)	7 (3.3–10)
ECMO treatment duration	23.5 (14–41)	25 (5–41)	20 (14–35)	31 (21.5–58.5)
ICU length of stay–overall[b]	26 (17–45)	29.5 (17–48)	20 (16.5–40)	37 (21.5–65)
ICU length of stay to discharge[b]	18 (10.5–37)	24 (10–45)	17.5 (11.5–19)	19 (18–37)
ICU length of stay to death[b]	21.5 (9.5–36)	22.5 (10.5–35.5)	19.5 (10–35)	29 (14–52)
Total deaths (% of group)	51 (44.3)	29 (42.0)	15 (53.6)	7 (38.9)
Causes of death (% of deaths in group)				
Acute respiratory distress syndrome	14 (26.9)	10 (34.5)	3 (20.0)	1 (14.3)
Sepsis	11 (21.6)	3 (10.3)	8 (53.3)	–
Intracranial hemorrhage	10 (19.6)	8 (27.6)	1 (6.7)	1 (14.3)
Multiple organ failure	8 (15.7)	3 (10.3)	2 (13.3)	3 (42.9)
Pneumonia	2 (3.9)	1 (3.5)	–	1 (14.3)
Cardiac arrest	1 (2.0)	1 (3.5)	–	–
Ischemic stroke	1 (2.0)	–	–	1 (14.3)
Anoxic brain injury	1 (2.0)	–	1 (6.7)	–
Idiopathic interstitial lung disease	1 (2.0)	1 (3.5)	–	–
Liver hemorrhage	1 (2.0)	1 (3.5)	–	–
Unspecified COVID-19	1 (2.0)	1 (3.5)	–	–

ECMO = extracorporeal membrane oxygenation, IQR = interquartile range, NR = not reported.
[a]Excludes two patients who were transported for organ retrieval.
[b]Excludes two patients who were transported for organ retrieval and one patient with missing value for ICU discharge date.
Dashes represent null value or 0.

transported supine (8). Similarly, nearly two-thirds of our cohort of patients was transported without adverse events. Although ventilator settings were adjusted in 18 patients, only two of these cases had desaturation events, and both resolved with no further complications. Overall, all patients were safely transported prone, and any events were fully resolved in-route by paramedics. No patients experienced arrhythmias, mechanical airway issues, cardiac arrests, or deaths, and none of the transports required diversion to a nearby emergency department while en-route.

It is important to highlight that in this study and others which demonstrate safe prone transport, transport of the patient was performed by specialized staff who operate with robust protocols (3, 18, 19). It is not likely that local emergency service agencies are

TABLE 3.
ICU Complications

Complication	Severe	Nonsevere	Pao_2/Fio_2 Not Available	Total *n* (% of All Patients)
Ventilator-associated pneumonia	23	10	7	40 (34.8)
Acute kidney injury	16	14	6	36 (31.3)
Bacteremia	22	4	4	30 (26.1)
Sepsis	16	9	4	29 (25.2)
Thrombus	10	3	2	15 (13.0)
Pneumothorax	12	1	1	14 (12.2)
Multiple organ dysfunction	6	3	3	12 (10.4)
Right ventricle failure	5	3	2	10 (8.7)
Pulmonary embolism	6	3	1	10 (8.7)
Deep vein thrombosis	7	–	2	9 (7.8)
Intracranial hemorrhage	5	1	1	7 (6.1)
Tracheal bleeding	4	1	–	5 (4.3)
Cardiac arrest	3	2	–	5 (4.3)
Gastrointestinal bleed	2	2	1	5 (4.3)
Line infection	3	1	1	5 (4.3)
Hemothorax	2	–	–	2 (1.7)
Limb extremity ischemia	–	1	1	2 (1.7)

Dashes represent null value or 0.

equipped, from both human and physical resource standpoints, to handle prone transport of mechanically ventilated patients, particularly in jurisdictions where prone positioning emerged as a relatively new practice alongside the COVID-19 pandemic. Additionally, the scope of practice for CCPs in Ontario includes use of sedation, analgesia, paralytics, vasopressors, and ventilator management, allowing them to perform these transports independently without the need for any additional healthcare staff. Future use of prone transport should be carried out only in the context of extensive initial and ongoing training as well as appropriate resource infrastructure, which may limit its practice. This necessitates a need for the development of programs to train critical transport crews and best-practice operational protocols to further disseminate the availability of prone transport.

Outcomes of Prone-Transported Patients

Due to previous studies demonstrating improved outcomes in patients treated at centralized, high-volume ECMO centers, establishment of regional ECMO centers has been largely favored over widespread implementation in community hospitals (4, 20–23). This benefit to survival has previously been shown to apply to all patients treated at an ECMO center for ARDS, regardless of if they received ECMO therapy (4, 22, 23). While the exact patient selection criteria may vary between ECMO centers for transport from a referring hospital and cannulation consideration, all patients included in our cohort had severe ARDS and were receiving prone positioning. Upon arrival to the ECMO center, over a third of the patients in our cohort were managed without ECMO. While in-hospital mortality rates for severe ARDS have been observed to be nearly 50% (2), the mortality rate in our patient population who did not receive ECMO was 21%, and the overall cohort mortality rate was 44%. Patients who received ECMO had a 58% mortality rate; comparable to existing literature during the COVID pandemic (8, 24, 25).

While ECMO treatment can improve outcomes of patients with severe ARDS, hemorrhagic and thrombotic complications are common. Hemorrhagic complications occurred in nearly a quarter of our cohort.

Patient ventilator setting differences were noted both between patient subsets based on P/F ratio, as well as when comparing settings during transport and upon ECMO center arrival. As expected, patients who had severe ARDS necessitated increased ventilatory support. Regardless of disease severity, peak pressures and tidal volumes were lower after arrival to the ECMO center. This may reflect the increased experience of teams operating at an ECMO center and likely contributes to the improved survival of patients when transported to ECMO centers (26). It would be difficult to perform any additional nuanced analysis of these ventilator settings as ventilator settings were modified in-route in 16% of our transports.

Strengths and Limitations

First, the nature of retrospective chart reviews, missing data and inconsistencies in the level of information prevented us obtaining a full dataset from some of the cohort and may have biased our analysis. The prevailing decision-making behind transporting each patient prone was also not reported. The nature of our study also precluded us from demonstrating the potential benefit of prone transportation in these patient populations. Overall, this study was based at a single regional ECMO center. While this may limit the generalizability of our results, as they may be amenable to differently trained staff and regional differences, a single-site analysis allowed for greater internal validity for our study as organizational practices were controlled and standardized. Finally, nearly all patients included in this study developed ARDS secondary to COVID-19, and special considerations regarding ARDS of other etiologies were not examined in this study.

CONCLUSIONS

In this study, we described the experience of patients with ARDS transported prone to a large ECMO referral center during the COVID-19 pandemic. Despite the severity of illness in our patients which necessitated their prone transport, their overall outcome was similar or improved when compared with existing literature. These results both add to the literature on the safety and feasibility of transporting mechanically ventilated patients in the prone position and demonstrates the value of prone transportation of ARDS patients. Based on our findings, critical care centers should work with their local critical care transport organizations to develop protocols for the identification and transport of ARDS patients in the prone position.

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Timothy Zhang was involved in data curation, formal analysis, investigation, writing the original draft, and reviewing and editing the writing. Dr. Nikouline was involved in conceptualization, data curation, formal analysis, investigation, methodology, project administration, supervision, writing the original draft, and reviewing and editing the writing. Dr. Riggs was involved in data curation, investigation, methodology, project administration, supervision, writing the original draft, and reviewing and editing the writing. Drs. Nolan and Granton were involved in conceptualization, methodology, resources, supervision, and reviewing and editing the writing. Drs. Pan, Peddle, and Fan were involved in reviewing and editing the writing. Dr. Del Sorbo was involved in conceptualization, methodology, and reviewing and editing the writing.

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