


ORIGINAL



# Mortality and costs following extracorporeal membrane oxygenation in critically ill adults: a population-based cohort study

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## Abstract

**Purpose:** Extracorporeal membrane oxygenation (ECMO) is used as temporary cardiorespiratory support in critically ill patients. Little is known about population-level short- and long-term outcomes following ECMO, including health-care use and health system cost across a wide range of sectors.

**Methods:** Population-based cohort study in Ontario, Canada (October 1, 2009–March 31, 2017) of adult patients ( $\geq 18$  years) receiving ECMO for cardiorespiratory support. We captured outcomes through linkage to health administrative databases. Primary outcome was mortality during hospitalization, as well as at 7 days, 30 days, 1 year, 2 years, and 5 years following ECMO initiation. We analyzed health system costs (in Canadian dollars) in the 1 year following the date of the index admission.

**Results:** A total of 692 patients were included. Mean (standard deviation [SD]) age was 51.3 (16.0) years. Median (interquartile range [IQR]) time to ECMO initiation from date of admission was 2 (0–9) days. In-hospital mortality was 40.0%. Mortality at 1 year, 2 years, and 5 years was 45.1%, 49.0%, and 57.4%, respectively. Among survivors, 78.4% were discharged home, while 21.2% were discharged to continuing care. Median (IQR) total costs in the 1 year following admission among all patients were Canadian \$130,157 (Canadian \$58,645–Canadian \$240,763), of which Canadian \$91,192 (Canadian \$38,507–Canadian \$184,728) were attributed to inpatient care.

**Conclusions:** Hospital mortality among critically ill adults receiving ECMO for advanced cardiopulmonary support is relatively high, but does not markedly increase in the years following discharge. Survivors are more likely to be discharged home than to continuing care. Median costs are high, but largely reflect inpatient hospital costs, and not costs incurred following discharge.

**Keywords:** Extracorporeal membrane oxygenation, ECMO, Health services, Acute respiratory distress syndrome, Cardiogenic shock, Cardiac arrest

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## Introduction

Extracorporeal membrane oxygenation (ECMO) provides temporary respiratory and/or cardiac support to critically ill patients, and is often considered in patients who have failed initial, conventional treatment [1–3]. ECMO may be considered in patients with medically refractory respiratory failure, cardiac failure, or as an adjunct to cardiopulmonary resuscitation during cardiac arrest [4–7]. While major recent advances in extracorporeal technology have improved the risk–benefit profile of ECMO [3], not all patients may be deemed candidates for therapy, including patients with advanced age and multi-organ failure [8].

With the increasing use of ECMO [9], there is a growing need to understand its impact on short- and long-term outcomes. Short-term mortality following ECMO has been estimated to range between 30 and 70%, depending upon the indication for therapy [8]. The largest trial enrolling patients with acute respiratory distress syndrome (ARDS) demonstrated a 60-day mortality of 35%, associated with venovenous ECMO (VV-ECMO) [5]. In patients with cardiogenic shock receiving venoarterial ECMO (VA-ECMO), in-hospital mortality has been estimated to range between 50 and 70%, with many survivors experiencing significant long-term disability [10, 11]. Given the paucity of data, measuring long-term survival has been identified as an area of focus for future investigation in extracorporeal life support [12, 13].

Importantly, use of ECMO requires considerable resources, and is associated with high costs [14]. Although there have been some estimates of the high expense of ECMO, there is little information on long-term costs following discharge for survivors, including no information of costs outside of the acute care sectors. To investigate these questions, we conducted a population-based cohort study to evaluate the short- and long-term health outcomes and costs of critically ill adults receiving ECMO for cardiorespiratory support.

## Methods

This study was approved by The Ottawa Health Science Network Research Ethics Board.

### Data sources and setting

We conducted a population-based, retrospective cohort study using health administrative databases in Ontario, Canada. Ontario is Canada's most populous province with approximately 13 million inhabitants. In Ontario's single-payer healthcare system, all medically necessary health care services, physician, hospital, and demographic information for residents are recorded in these

## Take-home message

Patients surviving to discharge following ECMO have low mortality up to 5 years later. While ECMO costs are significant, they largely reflect inpatient costs and not costs incurred following discharge.

databases. These data are held and linked at ICES, an independent, non-profit custodian of health data. ICES is funded by an annual grant from the Ontario Ministry of Health and Long-term Care.

The following databases are linked, then de-anonymized, at the individual level at ICES: (1) The Ontario Health Insurance Plan (OHIP) Claims Database, to capture data on physician fee-for-service claims for inpatient and outpatient services; (2) The Canadian Institute for Health Information Discharge Abstract Database, to capture information on all acute care hospitalizations, including detailed diagnostic and procedural information; (3) The Registered Persons Database, for capturing all demographic information; (4) The Home Care Database, to capture publicly funded homecare services; (5) The National Ambulatory Care Reporting System, to capture information on Emergency Department use; (6) The National Rehabilitation Reporting System for inpatient rehabilitation programs; (7) The Continuing Care Reporting System, for data on continuing care and complex continuing care use; (8) Statistics Canada Census data, for income quintile and rurality through postal codes; and (9) The Ontario Drug Benefit Claims database, for tracking data on prescription medications dispensed among patients  $\geq 65$  years of age eligible for coverage.

## Patients

We identified adult patients ( $\geq 18$  years of age) receiving ECMO in Ontario between October 1, 2009, and March 31, 2017. We identified patients whose hospitalization records indicated the presence of an inpatient ECMO intervention code by searching through the Discharge Abstract Database (all codes displayed in Supplemental Table 1). This ECMO procedural code may also be applied to a select group of cardiac surgery patients undergoing particular elective procedures, to indicate the use of percutaneous or open cardiopulmonary bypass. For this reason, we also used the OHIP Claims Database to identify all individuals who had a code for ECMO billed (OHIP code Z788) by a physician caring for them. We first included patients who had both of the above codes (Cohort A).

To further capture relevant patients who may not have had an OHIP code applied, we utilized the International Classification of Diseases, 10th Revision (ICD-10) "most responsible diagnosis" from Cohort A, and included

patients with these ICD-10 diagnoses, but who only had an ECMO inpatient code from the Discharge Abstract Database (Cohort B). As above, we again ensured these patients did not undergo elective cardiac surgery procedures.

For each subject, we calculated the Charlson Comorbidity Index (CCI) [15] using hospitalization data up to 2 years prior to the date of admission. Subjects who had not been hospitalized in the previous 2 years had their CCI score set to zero. We further identified the presence of complex chronic diseases among our cohort, using previously described methods (Supplemental Table 2) [16]. Where applicable, we used validated algorithms to ascertain cases. All other conditions were based on the presence of any one inpatient hospital diagnostic code, or two or more outpatient physician billing codes within a 2-year period, using relevant ICD, Version 9 (ICD-9) and ICD-10 codes.

As outcomes following ECMO initiation are strongly linked to indication (i.e., respiratory versus cardiac failure) [8], we conducted a secondary subgroup analysis based upon this variable. Since data related to ECMO configuration (e.g., VV-ECMO vs. VA-ECMO) were unavailable, patients were categorized as either 'Respiratory Failure' or 'Cardiac Failure', based upon the ICD-10 most responsible diagnosis (see Supplemental Table 1 for categorization). Patients whose most responsible diagnosis did not allow for clear delineation between these subgroups were categorized as 'Other'. To identify factors associated with survival, we compared characteristics of ECMO patients who died during hospitalization against those who survived to hospital discharge.

### Outcomes

The primary outcome was survival to hospital discharge. Secondary outcomes included survival at 7 days, 30 days, 1 year, 2 years, and 5 years following ECMO initiation. Time to ECMO initiation was determined by calculating the difference between the hospital admission date, and the date associated with the ECMO intervention code. Length of stay for the hospitalization was reported from the date of hospital admission to the date of discharge or in-hospital death. Discharge disposition was determined using a hierarchy approach (Supplemental Table 3). Ventricular assist device (VAD) implantation and transplant were determined using the relevant procedural codes in the Discharge Abstract Database.

For patients with available costing data (October 1, 2009–March 31, 2016), we examined the total and sector-specific direct healthcare costs accumulated in the 1 year following the date of the index hospital admission (including the admission itself). We obtained all records of health care use paid for by the Ministry of Health and

Long-term care (MOHLTC) following hospital admission. We estimated the costs associated with each record using previously described methods developed for health administrative data [17]. For sectors that use global budgets (e.g., hospital, complex continuing care, rehabilitation), we used a top-down approach through case-mix methodology. Sectors where each use has an associated fee payment (e.g., drug costs, physician remuneration) had costs estimated directly. Further details regarding cost data acquisition are included in Supplemental Fig. 1. Private patient expenses are not included. All costs were expressed in 2016 Canadian dollars, and past costs were inflated using the healthcare-specific yearly Consumer Price Index reported by Statistics Canada.

Cell sizes with  $\leq 5$  patients are suppressed, as per ICES regulations, to protect patient confidentiality.

### Statistical analyses

We conducted all statistical analyses using SAS Enterprise Guide 7.1 (SAS Institute Inc., Cary, NC). We present data as mean values, with standard deviation (SD), or medians, with interquartile range (IQR), where appropriate. The Student's *t* test (parametric values), Mann–Whitney test (non-parametric values), and  $\chi^2$  (for categorical values), were performed to determine between-group differences. We used Kaplan–Meier survival curves to describe 1-year survival. We assessed variation in total hospital costs using a multivariable generalized linear model with gamma distribution and log link.

### Results

Study flow is depicted in Supplemental Fig. 2. In total, we included 692 patients in the primary analyses. Patient characteristics are displayed in Table 1. Mean age was 51.3 years (SD=16.0), and 62.0% of patients were male. The median time to ECMO initiation from hospital admission was 2 days (IQR 0–9 days). In terms of primary indication, 321 (46.4%) patients receiving ECMO had a primary diagnosis of respiratory failure, 303 (43.8%) patients receiving ECMO had a primary diagnosis of cardiac failure, and 68 (9.8%) were categorized as 'Other'. The CCI score was  $\leq 2$  in 76.7% of patients. Patient and institution Local Health Integration Networks (LHINs) (i.e., health funding regions) are displayed in Supplemental Table 4.

A total of 277 (40.0%) patients died in-hospital, while 176 (25.4%) and 252 (36.4%) died within 7 days and 30 days of ECMO initiation, respectively (Table 2). Mortality at 1 year, 2 years, and 5 years was 45.1%, 49.0%, and 57.4%, respectively. Median hospital length of stay was 22 days (IQR 9–45). In-hospital mortality was 30.5% in patients receiving ECMO with a primary respiratory diagnosis, and 50.5% in patients receiving ECMO with a

**Table 1 Characteristics of adult patients requiring extra corporeal membrane oxygenation in Ontario, Canada (2009–2017) (n = 692)**

Variable	Value
Sex, n (%)	
Male	429 (62.0)
Female	263 (38.0)
Age, years, mean (SD)	51.3 (16.0)
Income, n (%)	
Lowest	129 (18.6)
Low	142 (20.5)
Middle	139 (20.1)
High	138 (19.9)
Highest	142 (20.5)
Unknown	<sup>a</sup>
Rurality, n (%)	
Urban	612 (88.4)
Rural	80 (11.6)
Indication for ECMO	
Respiratory failure	321 (46.4)
Cardiac failure	303 (43.8)
Other	68 (9.8)
Time to ECMO from admission, days, median (IQR)	2 (0–9)
Charlson Comorbidity Index, n (%)	
≤ 2	531 (76.7)
3–4	119 (17.2)
≥ 5	42 (6.1)
Comorbidities, n (%)	
Arrhythmia	113 (16.3)
Malignancy	127 (18.4)
Congestive heart failure	229 (33.1)
Chronic obstructive pulmonary disease	130 (18.8)
Coronary artery disease	187 (27.0)
Dementia	<sup>a</sup>
Diabetes mellitus	197 (28.5)
Hypertension	350 (50.6)
Chronic kidney disease	116 (16.8)
Cerebrovascular disease	24 (3.5)

ECMO extracorporeal membrane oxygenation

<sup>a</sup> Denotes ≤ 5 patients

primary cardiac diagnosis. Mortality after hospital discharge was higher among patients who initially required ECMO for cardiac failure than those with respiratory failure (53.8% vs. 37.1% at 1-year post-ECMO initiation). Kaplan–Meier survival curves are displayed in Fig. 1 and demonstrate a decline in survival over the first 40 days following ECMO initiation, followed by a relative plateauing of mortality rates.

During the index hospitalization, ECMO was followed by lung transplant in 193 (27.9%) patients, and heart transplant in 46 (6.6%) patients (Table 2). Of patients

receiving lung transplant, 163 (84.5%) survived to hospital discharge, while 30 patients (65.2%) receiving heart transplant survived to discharge. ECMO was followed by VAD in 92 (13.3%) patients. Among survivors to hospital discharge, 174 (41.9%) patients were discharged home with no government-sponsored homecare services, 153 (36.8%) patients were discharged home with government-sponsored homecare services, and 88 (21.2%) were discharged to a continuing care facility. Within 1 year of discharge, 270 survivors (65.1%) had at least one Emergency Department visit, with 208 (50.1%) requiring at least one hospital admission.

As compared to those who died in-hospital, patients with respiratory failure who survived to discharge had a lower CCI, shorter time to ECMO initiation, and more commonly received ECMO followed by lung transplant (Table 3). Among those with cardiac failure, survival to discharge was associated with heart transplant following ECMO, and a longer time to ECMO initiation. Outcomes stratified by patient age are displayed in Supplemental Fig. 3.

Costs in the year following the index hospital admission for ECMO were available for 550 patients and are shown in Table 4. Median cost (IQR) was Canadian \$130,157 (Canadian \$58,645–Canadian \$240,763). Following discharge, median costs for continuing care (complex continuing care, long-term care, rehabilitation, and homecare) were Canadian \$0 (Canadian \$0–Canadian \$679). Median costs for outpatient clinics and physician billings were Canadian \$2321 (Canadian \$731–Canadian \$5852) and Canadian \$22,191 (Canadian \$12,665–Canadian \$33,656), respectively. Median outpatient laboratory and drug costs were Canadian \$0 (Canadian \$0–Canadian \$314) and Canadian \$0 (Canadian \$0–Canadian \$3953), respectively. Factors associated with increased costs include younger age, respiratory failure, increased length of stay, and transplant (Supplemental Table 5). Patients receiving heart or lung transplant had significantly higher costs than patients who were not transplanted (Supplemental Tables 6 and 7). Mean and median costs of patients, based upon the region in Ontario where they received care, are shown in Supplemental Tables 8 and 9.

## Discussion

In our population-based cohort analysis of critically ill adult patients receiving ECMO for cardiorespiratory support, we found that in-hospital mortality was 40.0%, but did not substantially increase 1, 2 or 5 years following ECMO initiation. Mortality was higher among patients receiving ECMO for cardiac failure, as compared to respiratory failure. Over a third of patients received heart or lung transplant following ECMO, and the large majority of patients (78.5%) surviving to discharge were able to

**Table 2 Short- and long-term outcomes of adult patients requiring extra corporeal membrane oxygenation in Ontario, Canada (2009–2017), overall and by indication**

Variable	Overall (n = 692)	Respiratory failure (n = 321)	Cardiac failure (n = 303)	Other (n = 72)
Mortality following ECMO initiation, n (%)				
In-hospital	277 (40.0)	98 (30.5)	153 (50.5)	26 (38.2)
7-day	176 (25.4)	44 (13.7)	117 (38.6)	15 (22.1)
30-day	252 (36.4)	82 (25.5)	149 (49.2)	21 (30.9)
1-year	312 (45.1)	119 (37.1)	163 (53.8)	30 (44.1)
2-year	339 (49.0)	138 (43.0)	168 (55.4)	33 (48.5)
5-year <sup>a</sup>	147 (57.4)	62 (53.4)	69 (62.2)	16 (55.2)
Hospital length of stay, days, median (IQR)	22 (9–45)	26 (15–54)	15 (5–35)	22 (9–45)
Ventricular assist device during hospitalization, n (%)	92 (13.3)	*	75 (24.8)	*
Transplant during hospitalization, n (%)				
Heart transplant	46 (6.6)	*	42 (13.9)	*
Lung transplant	193 (27.9)	173 (53.9)	13 (4.3)	7 (9.7)
Transplant patients surviving to discharge, n (%)				
Heart transplant	30 (65.2)	0 (0)	28 (66.7)	2 (50.0)
Lung transplant	163 (84.5)	150 (92.0)	7 (53.8)	6 (85.7)
Discharge disposition among survivors, n (%) <sup>b</sup>				
Home (without homecare)	174 (41.9)	106 (47.5)	60 (40.0)	8 (17.4)
Home (with homecare)	153 (36.8)	72 (32.3)	61 (40.1)	20 (43.5)
Long-term care facility <sup>c</sup>	88 (21.2)	45 (20.2)	29 (19.3)	14 (30.4)
Emergency department visit following discharge, n (%) <sup>b</sup>				
Within 30 days	82 (19.7)	43 (19.3)	26 (17.3)	13 (28.2)
Within 90 days	157 (37.8)	90 (40.4)	48 (32.0)	19 (41.3)
Within 1 year	270 (65.1)	153 (68.6)	91 (60.1)	26 (60.5)
Hospital readmissions following discharge, n (%) <sup>b</sup>				
Within 30 days	67 (16.1)	41 (18.4)	19 (12.7)	7 (15.2)
Within 90 days	125 (30.1)	75 (33.6)	38 (25.3)	12 (26.1)
Within 1 year	208 (50.1)	121 (54.3)	70 (46.7)	17 (37.0)

ECMO extracorporeal membrane oxygenation, IQR interquartile range

\*Denotes ≤ 5 patients

<sup>a</sup> Only includes patients between 2009 and 2014 (n = 256 for 'Overall', n = 116 for 'Respiratory Failure', n = 111 for 'Cardiac Failure', n = 29 for 'Other')

<sup>b</sup> Only includes patients who survived to hospital discharge (n = 415 for 'Overall', n = 223 for 'Respiratory Failure', n = 150 for 'Cardiac Failure', n = 46 for 'Other')

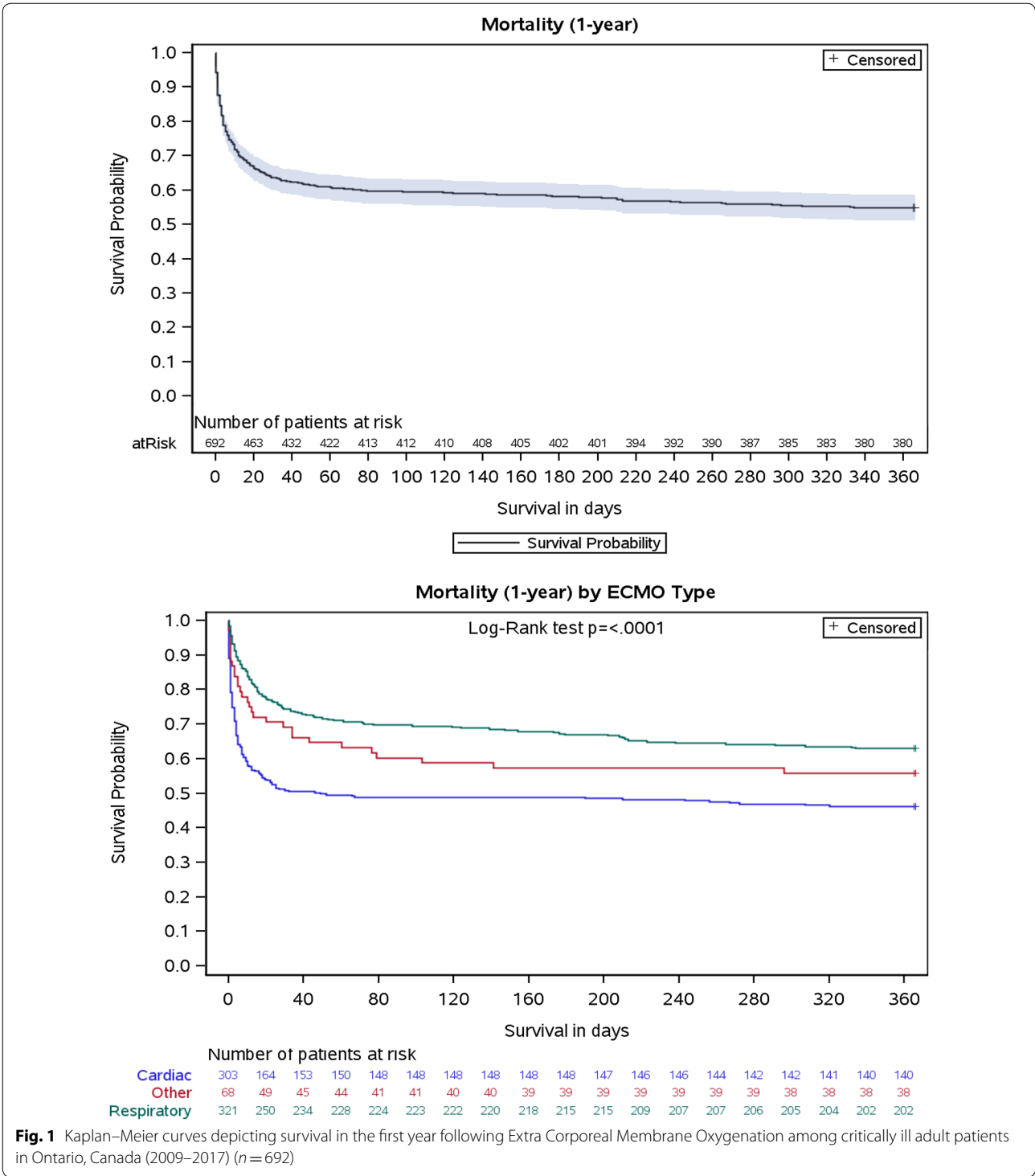
<sup>c</sup> Includes inpatient rehabilitation and complex care facilities

be discharged home. Finally, median total costs among patients in our cohort were significant at Canadian \$130,157 in the 1 year following admission for ECMO, with the large majority attributed to inpatient costs during admission. This study provides important information regarding short- and long-term outcomes following the use of this novel therapy in the care of critically ill adults.

Worldwide utilization of ECMO for cardiorespiratory support is growing [9], but the use of this technology is outpacing the existing evidence. Several important questions have been identified with regard to the use of ECMO [12], and our study sought to provide insight into many of them. The first is the importance of patient

selection. There are several patient factors that have been associated with worse outcomes, including advanced age and significant chronic comorbidities [8, 18]. The mean age of patients included in our cohort was 51.3 years, and 76.7% of patients had a CCI ≤ 2, suggesting few chronic conditions. We found that patients who died in hospital had higher CCI scores than those surviving to discharge. We also found that, among patients with respiratory failure, those who survived to discharge had earlier initiation of ECMO, while patients with cardiac failure showed the opposite relationship. The importance of these associations is unclear and may be due to unmeasured confounders. Finally, patients receiving heart and lung transplant following ECMO had higher survival, possibly





reflecting a more meticulous selection process, given the additional need to fulfill candidacy for transplantation. Further research is required to determine the optimal patient population for ECMO, and the appropriate time for initiation.

We also investigated the long-term outcomes of patients receiving ECMO, since existing evidence on this topic is largely based upon single-center experience [19]. Chang et al. previously investigated long-term outcomes in a population-based cohort of patients receiving ECMO

**Table 3 Comparison of patients receiving extra corporeal membrane oxygenation who survive to hospital discharge against those who died in-hospital, by indication for ECMO**

Variable	Respiratory failure			Cardiac failure		
	Surviving to discharge (n = 223)	Died in-hospital (n = 98)	P value	Surviving to discharge (n = 150)	Died in-hospital (n = 153)	P value
Sex, n (%)			0.06			0.81
Male	145 (65.0)	53 (54.1)		99 (66.0)	99 (64.7)	
Female	78 (35.0)	45 (45.9)		51 (34.0)	54 (35.3)	
Age, years, mean (SD)	49.3 (14.9)	47.6 (14.5)	0.35	52.8 (17.5)	54.7 (16.0)	0.33
Income, n (%)			0.11			0.04
Lowest	40 (17.9)	22 (22.4)		26 (17.3)	30 (19.6)	
Low	39 (17.5)	28 (28.6)		28 (18.7)	35 (22.9)	
Middle	46 (20.6)	16 (16.3)		41 (27.3)	23 (15.0)	
High	51 (22.9)	16 (16.3)		22 (14.7)	38 (24.8)	
Highest	47 (21.1)	16 (16.3)		32 (21.3)	27 (17.6)	
Unknown	0 (0.0)	0 (0.0)		*	0 (0.0)	
Rurality, n (%)			0.24			0.64
Urban	192 (86.1)	89 (90.8)		134 (89.3)	134 (87.6)	
Rural	31 (13.9)	9 (9.2)		16 (10.7)	19 (12.4)	
Charlson Comorbidity Index, n (%)			0.01			0.65
≤ 2	200 (89.7)	77 (78.6)		100 (66.7)	105 (68.6)	
≥ 3	23 (10.3)	21 (21.4)		50 (33.3)	48 (31.4)	
Comorbidities, n (%)						
Arrhythmia	14 (6.3)	6 (6.1)	0.96	45 (30.0)	36 (23.5)	0.20
Malignancy	49 (22.0)	28 (28.6)	0.20	19 (12.7)	16 (10.5)	0.55
Congestive heart failure	37 (16.6)	27 (27.6)	0.02	70 (46.7)	81 (52.9)	0.28
COPD	73 (32.7)	22 (22.4)	0.06	13 (8.7)	12 (7.8)	0.79
Coronary artery disease	27 (12.1)	11 (11.2)	0.82	66 (44.0)	68 (44.4)	0.94
Diabetes mellitus	66 (29.6)	21 (21.4)	0.13	36 (24.0)	54 (35.3)	0.03
Hypertension	92 (41.3)	39 (39.8)	0.81	90 (60.0)	100 (65.4)	0.36
Chronic kidney disease	23 (10.3)	24 (24.5)	<0.001	25 (16.7)	30 (19.6)	0.51
Cerebrovascular disease	*	*	0.91	9 (6.0)	8 (5.2)	0.77
Time to ECMO from admission, days, median (IQR)	1 (0–9)	2 (1–13)	0.04	5 (1–11)	2 (0–7)	<0.01
Transplant during hospitalization, n (%)						
Heart transplant	0 (0.0)	0 (0.0)	–	28 (18.7)	14 (9.2)	0.02
Lung transplant	150 (67.3)	23 (23.5)	<0.001	7 (4.7)	6 (3.9)	0.75

ECMO extracorporeal membrane oxygenation, SD standard deviation, COPD chronic obstructive pulmonary disease, IQR interquartile range

\*Denotes ≤ 5 patients

in Taiwan, and found a 30-day mortality of 59.8%, and 1-year mortality of 76.5% [20]. This study was limited by a variety of factors, including indication for ECMO (a large proportion of included patients had cardiac failure, and presumably received VA-ECMO for cardiac support) and patient selection (older cohort with a greater proportion of comorbidities). One-year mortality in our cohort was lower at 40.0%. While this value may seem high, the utilization of ECMO is often in patients who have been deemed to be refractory to medical therapy,

and mortality without the use of ECMO would likely be higher, as was demonstrated in patients with ARDS [5, 21]. Furthermore, the large majority of deaths occurred during the index hospitalization, suggesting that patients in our cohort who survived to hospital discharge were likely to survive to 1 year. We show that mortality did not substantially increase from year 1 to year 2, or even year 5, suggesting fairly stable survival curves among patients surviving their ECMO hospitalization.

**Table 4 1-year costs following admission of adult patients requiring extra corporeal membrane oxygenation in Ontario, Canada (2009–2016) (n = 550)**

	Mean costs (SD)	Median costs (IQR)
Acute care sectors		
Inpatient	137,339 (145,203)	91,192 (38,507–184,728)
Emergency department	647 (892)	421 (0–946)
Continuing care sectors		
Complex continuing care	1395 (11,462)	0 (0–0)
Long-term care	21 (454)	0 (0–0)
Rehabilitation	4518 (14,462)	0 (0–0)
Homecare	1130 (3028)	0 (0–679)
Outpatient care sectors		
Outpatient clinics	3643 (3867)	2321 (731–5852)
Laboratory (OHIP)	216 (355)	0 (0–314)
Drugs (Ontario Drug Benefit Program)	4324 (9155)	0 (0–3953)
Physician billings <sup>a</sup>	25,401 (17,447)	22,191 (12,665–33,656)
Total costs	181,248 (170,180)	130,157 (58,645–240,763)

All values in Canadian dollars

SD standard deviations, IQR interquartile range, OHIP Ontario Health Insurance Plan

<sup>a</sup> Includes both inpatient and outpatient physician billings

Disability following critical illness is a significant concern, with survivors often left with long-term impairment and reduced independence [22, 23]. This is frequently manifested by increased resource utilization following hospital discharge [24]. While we were unable to evaluate functional ability at the time of hospital discharge, the large majority of survivors in our cohort were discharged home. The proportion of patients in our cohort requiring discharge to continuing care facilities (e.g., nursing homes) was lower than what has been seen in other critical care populations [25, 26]. Though it is possible that survivors may still experience significant morbidity, the higher likelihood of disposition to home suggests at least an acceptable level of functioning at the time of hospital discharge in a high percentage of patients. Despite functional independence, existing evidence among ECMO survivors notes difficulties in important patient-oriented functional abilities, such as return to work [27], and increased incidence of neuropsychiatric comorbidities [28].

Finally, given the resource-intensive nature of ECMO [29], we evaluated its impact on total patient costs, both during hospitalization, as well as following discharge. We found that the median total cost in the year following hospital admission was Canadian \$130,157. Of these costs, the large majority were accumulated during the inpatient stay. Importantly, very little cost was accrued due to continuing care (namely long-term care, rehabilitation, and homecare) post-discharge. These findings are in particular contrast to continuing care costs

seen among other critical care populations in Ontario [24, 30]. The median total costs of patients in our cohort were high, but their inpatient costs are less than what has been found in the 90th percentile of high-cost ICU users in Ontario (median cost of Canadian \$148,328 during hospital admission [31]). Other ICU patient populations (e.g., patients with subarachnoid hemorrhage) have been shown to accrue markedly higher median inpatient costs than what was seen in our ECMO cohort [32]. More importantly, such patient populations have also been shown to incur high costs following hospital discharge [24], which was not the case in our cohort. Therefore, while the inpatient costs of patients receiving ECMO are high, they are less than some other high-cost ICU populations, and survivors incur few costs following hospital discharge.

We utilized robust population-level data to identify long-term outcomes and costs among critically ill adults receiving ECMO in Ontario, Canada. To our knowledge, this study provides some of the first data related to long-term outcomes and costs in these high-risk patients. However, there are limitations to our study. Importantly, outcomes of patients receiving ECMO are largely dependent upon the indication, and the subsequent required configuration (i.e., VV- vs. VA-ECMO) [8]. We did not have sufficient granularity in data to determine the configuration, and instead used the most responsible diagnosis to make assumptions regarding the indication



and configuration. Additionally, our cost data were not able to differentiate the specific cost of ECMO administration, (including the cost of the relevant components, e.g., cannulation, filters) from a patient's total inpatient costs. Second, the patients in our cohort reflect a highly selected group, as indicated by the relatively younger age and low CCI. Caution should be exercised in extending our findings to all critically ill patients. Third, ECMO is not a benign treatment, and is associated with important complications, including hemorrhage, thrombosis, and infection [2, 3]. We did not have data related to these complications, and, therefore, are unable to comment on incidence and impact in our population. Fourth, in Ontario, ECMO is largely centralized and conducted at a few, specialized centers. Outcomes from ECMO are associated with center-specific frequency of use and volume [33], and, therefore, our results should be interpreted in that context. Finally, while ICES databases are robust and have been used extensively for large population-based studies [16, 34], there are inherent limitations, including data related to illness severity, quality-adjusted life years associated with cost, as well as costs and resources that are funded privately by patients.

## Conclusion

In our population-based cohort, in-hospital mortality among critically ill adult patients receiving ECMO was 40.0%, and incremental increase in 1-year, 2-year, or 5-year mortality was minimal. The majority of ECMO patients who survived to hospital discharge were discharged home. Finally, while ECMO patients accrued significant inpatient costs, these costs were less than typical high-cost populations, and these patients had little healthcare-associated costs in the 1 year following ECMO initiation. This work provides novel data regarding the long-term outcomes and costs of critically ill patients receiving ECMO for cardiorespiratory support.

## Electronic supplementary material

The online version of this article (<https://doi.org/10.1007/s00134-019-05766-z>) contains supplementary material, which is available to authorized users.

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## Author contributions

SMF, PT, and KK conceived the study idea. SMF, DQ, PT, EF, LM, BR, and KK participated in study design. DQ and RT gathered the data and performed data analyses. All the authors interpreted the data analyses. All the authors co-wrote and revised the manuscript for intellectual content. All the authors provided their final approval for manuscript submission. All the authors agree to be accountable for all aspects of the work.

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## Compliance with ethical standards

## Conflicts of interest

Dr. Eddy Fan is supported by a New Investigator Award from the Canadian Institutes of Health Research. Dr. Fan reports receiving personal fees from ALung Technologies, Abbot, and MC3 Cardiopulmonary, outside of the submitted work. Dr. Daniel Brodie reports providing expert advice to Hemovent, Baxter, BREETHE, and ALung Technologies. Dr. Brodie reports receiving grants from ALung Technologies, receiving personal fees from Baxter, and anticipated personal fees from BREETHE, outside of the submitted work. None of the other authors report any conflict of interest.

## Ethical approval

The Ottawa Health Science Network Research Ethics Board.

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