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Research paper

Thirty-day readmissions among patients with cardiogenic shock who underwent extracorporeal membrane oxygenation support in the United States: Insights from the nationwide readmissions database

Abdulelah Nuqali [a,1], Amandeep Goyal [a,1], Prakash Acharya [a], Ioannis Mastoris [a], Tarun Dalia [a], Wan-Chi Chan [a], Andrew Sauer [a], Nicholas Haglund [a], Andrija Vidic [a], Travis Abicht [b], Matthew Danter [b], Kamal Gupta [a], Joseph E. Tonna [c,d], Zubair Shah [a,*]

[a] Department of Cardiovascular Medicine, The University of Kansas Health System, University of Kansas School of Medicine, Kansas City, KS, United States of America
[b] Department of Cardiothoracic Surgery, The University of Kansas Health System, University of Kansas School of Medicine, Kansas City, KS, United States of America
[c] Division of Cardiothoracic Surgery, Department of Surgery, University of Utah Health, Salt Lake City, UT, United States of America
[d] Division of Emergency Medicine, Department of Surgery, University of Utah Health, Salt Lake City, UT, United States of America

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ABSTRACT

Background: There is a paucity of data on readmission rates and predictors of readmissions in cardiogenic shock patients after contemporary Extracorporeal Membrane Oxygenation (ECMO) use.
Methods: Using the Nationwide Readmission Database, we included adult patients (≥18 years old) hospitalized between January to November 2016–2018 for cardiogenic shock requiring ECMO support. Thirty-day readmission rates, associated variables, and predictors of readmission were assessed.
Results: A total of 10,723 patients underwent ECMO for cardiogenic shock. After excluding patients who died (*n* = 5602; 52%) and who underwent LVAD or OHT during index admission (*n* = 892; 8%), 4229 patients discharged alive were included. Of those, 694 (16.4%) were readmitted within 30 days. The median time to readmission was 10 days. Diabetes mellitus (OR = 1.77; 95% CI 1.32–2.37), chronic liver disease (OR = 1.35; 95% CI 1.03–1.77), and prolonged LOS (≥30 days; OR = 1.38; 95% CI 1.05–1.81) were associated with increased risk of 30-day readmissions while heart failure diagnosis (OR = 0.69; 95% CI 0.50–0.95) and short-term hospital post-discharge care (OR = 0.53; 95% CI 0.28–0.99) conferred a lower risk. Sepsis, followed by congestive heart failure, was the most common readmission diagnoses.
Conclusions: Patients with CS requiring ECMO support have high mortality and high 30-day readmission rates, with sepsis being the leading cause of readmissions followed by heart failure.

1. Introduction

Cardiogenic shock (CS) is characterized by significant morbidity and mortality ranging between 38 and 75% despite continued improvement in therapeutics, including mechanical circulatory support (MCS) [1,2]. Extracorporeal membrane oxygenation (ECMO) is a high output MCS modality that has been increasingly used in patients with profound CS as a bridge to either recovery or advanced heart failure therapies [3,4]. It has been reported to improve outcomes in CS patients in some retrospective studies, although results have been mixed [5–7]. ECMO remains a complex and resource intensive therapy associated with high rates of complications [2].

Thirty-day risk-standardized readmission rates for specific diagnoses, including heart failure and acute myocardial infarction, are an important, publicly reported metric by the Center for Medicare and Medicaid Services (CMS) as part of the national strategy to provide

Abbreviations: ACS, acute coronary syndrome; CHF, congestive heart failure; CS, cardiogenic shock; ECMO, extracorporeal membrane oxygenation; LOS, length of stay; LVAD, left ventricular assist device; MCS, mechanical circulatory support; OHT, orthotopic heart transplant.

* Corresponding author at: Department of Cardiovascular Medicine, The University of Kansas School of Medicine, 3901 Rainbow Blvd, Kansas City, KS 66160, United States of America.

E-mail address: zhah2@kumc.edu (Z. Shah).

[1] Drs Nuqali and Goyal have equally contributed to the manuscript.

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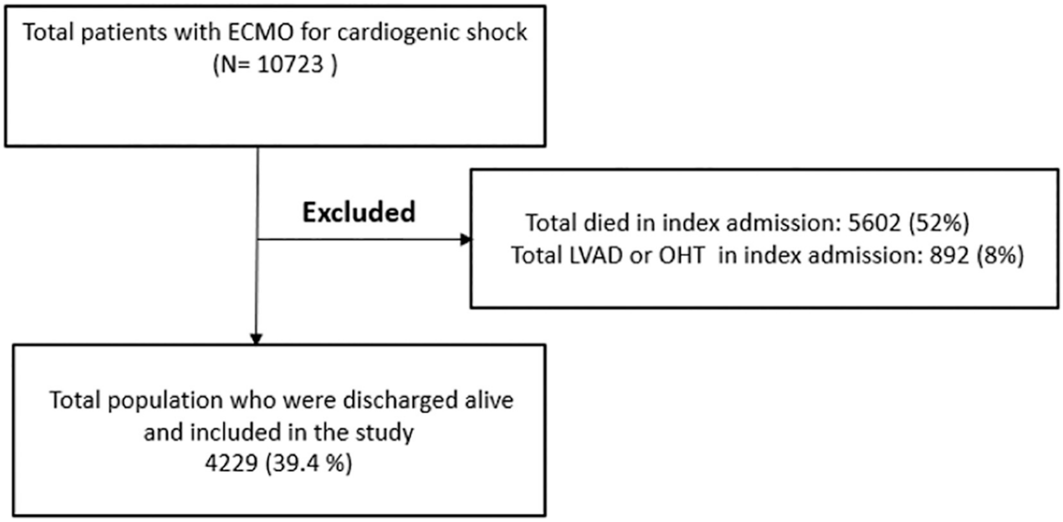

Flow chart 1. Study population.

incentives to improve the quality of care and prevent readmissions [8,9]. Hospitals have implemented various measures to decrease readmissions, including care coordination and discharge transition planning, medication reconciliation, addressing social determinants of health, and leveraging data to identify high-risk populations [10]. Given the rapid contemporary increased use of ECMO [11,12], especially for CS, there is a need to explore readmission rates and predictors of readmissions that could inform targeted hospital interventions. To address this gap, we sought to assess 30-day readmission rates, predictors of readmission, and outcomes among patients receiving ECMO for CS.

2. Methods

2.1. Data source

Data were obtained using the National Readmission Database (NRD), maintained by the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project (HCUP). NRD is a database compiled from the HCUP State Inpatient database from twenty-seven states and accounts for about 57% of all US hospitalizations. The NRD contains information about the index admission and a verified patient linkage number that can be used to track subsequent patient readmission across hospitals within a state. Available data include diagnoses and procedures reported using the International Classification of Diseases, tenth revision (ICD-10), and current procedural classification (CPT) codes. Patient-related outcomes include mortality, length of hospitalization (LOS), and readmissions. The database is publicly available and contains de-identified patient information. Hence, this study was deemed exempt by the institutional review board.

2.2. Patient population

Using pertinent ICD-10 codes, we included adult patients (≥18 years old) who were hospitalized between January to November from 2016 to 2018 for CS (ICD code R57.0) requiring ECMO support (ICD-10-PCS 5A15223) [13]. Patients who died before their discharge or received advanced heart failure therapies [left ventricular assist device (LVAD) or heart transplant (OHT)] during the index admission were excluded from the study as they were to be a distinct patient cohort with different rates of readmission (Flowchart 1). All readmissions within a period of thirty-day from patient hospital discharge were recorded. Comorbidities were mapped by AHRQ-HCUP using billing codes. Elixhauser comorbidity index was used to quantify the chronic comorbidity burden for the cohort.

2.3. Outcomes

The outcomes of interest included all-cause readmission rates and predictors of readmission within 30 days. Additional outcomes of interest included readmission diagnosis, in-hospital mortality, and LOS.

2.4. Statistical analysis

NRD database provides weights in the variable "DISCWT" used in weighting and stratification methods to produce national estimates. Weights were applied to the unweighted NRD data using "SURVEY" procedures in STATA, producing a nationwide discharge-level estimate for discharges from all hospitals in the USA. Comorbidity burden was assessed by computing the Elixhauser comorbidity measure. It is a set of thirty comorbidities that impact patient outcomes, including mortality. A scoring system developed by van Walraven assigns a score to each comorbidity group that reflects the strength of association of each comorbidity with hospital death. The composite of all these scores forms the Elixhauser score [14]. The Elixhauser score can be further classified into five categories (<0, 0, 1–5, 6–13, and >14) according to the comorbidity burden [15].

Categorical and continuous variables were reported as percentages and mean ± SD, respectively. Differences in mean and percentage were assessed using the Student's *t*-test, Pearson chi-squared test, and two-way ANOVA test. We performed univariate logistic regression to compare the differences in baseline characteristics between the patients who did and did not have readmission within 30 days of discharge. Subsequently, the variables with $P < 0.2$ were considered for multivariable analysis. These variables included hospital size, median household income, comorbidities (diabetes mellitus, congestive heart failure, coronary artery disease, chronic liver disease), comorbidity burden (Elixhauser >14), length of stay during index hospitalization of >30 days, and discharge disposition (short term hospital stay, skilled nursing facility, and home health care). Multivariable logistic regression was performed to delineate the predictors of 30-day readmission. A two-sided *p*-value of <0.05 was chosen as a level of statistical significance. Statistical analysis was performed using STATA 13.1 (Stata Corp, College Station, TX).

3. Results

3.1. Study population

A total of 10,723 patients underwent ECMO for cardiogenic shock

Table 1
Baseline characteristics of patients with cardiogenic shock requiring ECMO support discharged alive after index hospitalization.

Patient characteristics	Total population $N = 4229$	30 day readmissions		p-Value
		No $N = 3535$	Yes $N = 694$	
Demographics				
Mean age (years) (SD)	47.62 (21.51)	47.63 (21.74)	47.54 (20.33)	0.96
Age ≥ 55 years (%)	45.9	46.16	44.59	0.63
Female gender (%)	37.24	37.41	36.34	0.73
Median household income percentile (%)				
0–25	23.97	23.27	27.54	
26–50	26.10	26.08	26.23	
51–70	225.72	25.57	26.45	
76–100	24.21	25.08	19.77	
Primary payer (%)				0.06
Medicare	29.18	28.49	32.68	
Medicaid	21.28	21.11	22.12	
Private insurance	41.44	41.76	39.84	
Other	4.77	4.96	3.85	
Type of admission (%)				
Elective	13.84	13.97	13.19	0.76
Weekend admission	22.06	21.69	23.94	0.36
Hospital characteristics				
Teaching status				
Teaching	94.45	93.94	97.06	0.03
Bed-size				0.09
Small	4.64	5.03	2.65	
Medium	8.96	8.36	8.36	
Large	86.40	85.89	88.9	
Comorbidities (%)				
Hypertension	53.07	53.73	49.69	0.24
Dyslipidemia	29.06	29.13	28.74	0.91
Diabetes mellitus	25.25	23.93	31.94	0.02
Obesity	16.39	16.32	16.76	0.85
Chronic lung disease	17.93	17.51	20.09	0.31
Peripheral vascular disease	14.52	14.65	13.87	0.73
Stroke	3.48	3.24	4.67	0.31
Tobacco use (current or former)	12.06	12.39	10.35	0.27
Coronary artery disease	35.56	36.46	30.98	0.09
Congestive heart failure	71.43	72.16	67.75	0.19
Atrial fibrillation	16.51	16.26	17.76	0.54
Chronic kidney disease/ESRD	19.95	19.97	19.88	0.97
Anemia	4.95	4.84	5.56	0.70
Coagulopathy	51.84	52.12	50.43	0.61
Chronic liver disease	31.78	30.60	37.79	0.01
Mean Elixhauser score (SD)	23.10 (10.63)	22.65 (11.18)	23.44 (10.65)	0.30
Elixhauser score ≥ 14	78.85	78.08	82.78	0.09
High risk of mortality[a]	95.59	95.29	97.09	0.25
High severity of illness[a]	96.98	96.73	98.23	0.27
Index admission				
Indication for ECMO				0.49
ACS	28.28	28.59	26.72	
Non-ACS	71.72	71.41	73.28	
Mean time to ECMO (SD)	3.49 (7.09)	3.2 (6.76)	7.80 (8.47)	<0.001
Concomitant diagnoses during index admission				
Acute respiratory failure/mechanical ventilator use	89.38	88.99	91.31	0.18
Median length of stay during index admission (25–75 percentile) days	25 (14–42)	24 (13–41)	32 (18–50)	<0.001
Length of stay >30 days	42.54	40.66	52.09	0.001
Discharge disposition				0.89
Home (self-care)	25.09	25.33	23.88	
Short term hospital	16.49	17.88	9.47	
Skilled nursing facility	34.81	34.07	38.57	
Home health care	22.89	21.98	27.57	

[a] Based on APR-DRG coding (All patient refined diagnosis related groups).

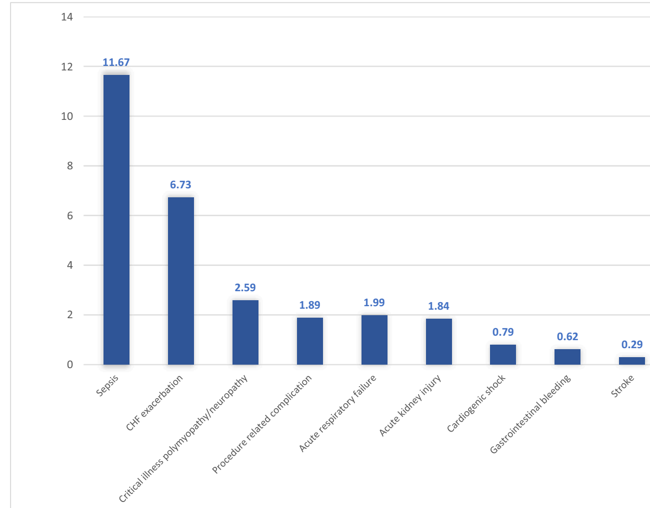

Fig. 1. Common primary diagnoses on readmissions.

from 2016 to 2018. After excluding patients who died ($n = 5602$; 52%) and those who underwent LVAD or OHT during index admission ($n = 892$; 8%), 4229 patients discharged alive were included in our analysis (Flowchart 1). The most common primary diagnosis on the index admission for the patients with CS and ECMO use was ST-elevation myocardial infarction (52.2%). Baseline demographics, comorbidities, hospital characteristics, and length of stay are summarized in Table 1. The mean age of the study cohort was 47.6 ± 21.5 years, and 62.8% were males. Past medical conditions including heart failure, hypertension, coronary artery disease, and chronic liver disease were the most common comorbidities. The mean time to ECMO was 3.49 days (SD: 7.09 days), and the median LOS during index hospitalization was 25 (IQR:14–42 days). Most patients required post-acute inpatient care after discharge. ECMO use occurred almost exclusively in large teaching centers.

3.2. Incidence and causes of 30-day readmission

Among the study population who survived the index hospitalization, 694 patients (16.4%) were readmitted within 30 days. When compared to patients without readmission, patients who were readmitted were more likely to have diabetes mellitus (31.9% vs. 23.9%; $p = 0.02$), chronic liver disease (37.8% vs. 30.6%; $p = 0.01$), and longer LOS (32 days vs. 24 days; $p < 0.001$). Most readmissions occurred within the first ten days after discharge (Supplement 1). The in-hospital mortality rate for readmitted patients was 9.7% ($n = 67$), and the median length of stay during readmission was seven days. Very few patients underwent advanced therapies on readmission (LVAD only in 1.08% and OHT in 0.68%). The most common indication for 30-day readmission was sepsis, followed by acute heart failure exacerbation and critical illness myopathy/neuropathy, as illustrated in Fig. 1.

3.3. Predictors of 30-day readmission

On multivariate analysis, diabetes mellitus (OR = 1.77; 95% CI 1.32–2.37), chronic liver disease (OR = 1.35; 95% CI 1.03–1.77), and prolonged LOS (≥30 days; OR = 1.38; 95% CI 1.05–1.81) were found to be independent predictors of 30-day readmissions (Table 2). Heart failure (OR = 0.69; 95% CI 0.50–0.95) and short-term hospital post-discharge care (OR = 0.53; 95% CI 0.28–0.99) conferred a lower risk of 30-day readmission. To further explore the finding of heart failure conferring a lower risk, we plotted the mortality associated with common comorbid conditions (Fig. 2). A diagnosis of HF did not appear to confer an increased in-hospital mortality risk compared to diabetes, liver

Table 2
Predictors of 30-day readmission after index admission for cardiogenic shock with ECMO use.

	Univariate analysis	Multivariate analysis
Age (>55) years	0.94 (0.73–1.21); $p = 0.63$	
Female gender	0.96 (0.74–1.24); $p = 0.73$	
Mean household income percentile (compared to 0–25 percentile)		
26–50	0.85 (0.5801.25); $p = 0.41$	
51–70	0.87 (0.59–1.28); $p = 0.49$	
76–100	0.67 (0.46–0.97); $p = 0.04$	0.68 (0.47–1.01); $p = 0.06$
Insurance (compared to medicare)		
Medicaid	0.91 (066–1.26); $p = 0.58$	
Private insurance	0.83 (0.62–1.12); $p = 0.22$	
Elective admission	0.94 (0.65–1.36); p = 0.73	
Weekend admission	1.14 (0.87–1.48); $p = 0.35$	
Hospital size (compared to small bed size)		
Medium	1.75 (0.74–4.16); p-0.21	
Large	1.97 (0.92–4.21); $p = 0.08$	1.59 (0.73–3.45); $p = 0.24$
Hypertension	0.85 (0.65–1.12); p = 0.24	
Dyslipidemia	0.98 (0.71–1.35); $p = 0.91$	
Diabetes mellitus	1.49 (1.08–2.04); $p = 0.013$	1.77 (1.32–2.37); $p \leq 0.001$
Obesity	1.03 (0.74–1.45); $p = 0.85$	
Carotid artery disease	1.14 (0.26–4.95); $p = 0.86$	
Chronic lung disease	1.18 (0.86–1.63); $p = 0.29$	
Peripheral vascular disease	0.94 (0.65–1.35); p = 0.73	
Stroke	1.46 (0.75–2.87); $p = 0.27$	
Tobacco use (current or former)	0.82 (0.56–1.19); p = 0.29	
Coronary artery disease	0.78 (0.59–1.04); $p = 0.09$	0.79 (0.58–1.08); $p = 0.14$
Congestive heart failure	0.81 (0.59–1.11); $p = 0.19$	0.69 (0.50–0.95); p = 0.02
Atrial fibrillation	1.11 (0.79–1.55); $p = 0.53$	
Chronic kidney disease/ESRD	0.99 (0.74–1.35); $p = 0.97$	
Anemia	1.16 (0.56–2.38); $p = 0.69$	
Coagulopathy	0.93 (0.72–1.21); $p = 0.61$	
Chronic liver disease	1.38 (1.08–1.76); p = 0.01	1.35 (1.03–1.77); $p = 0.03$
Elixhauser score ≥ 14	1.35 (0.96–1.92); p = 0.09	1.27 (0.85–1.91); $p = 0.25$
High risk of mortality*	1.64 (0.65–4.18); p = 0.29	
High severity of illness*	1.88 (0.57–6.02); $p = 0.30$	
ACS as primary cause of index admission	0.91 (0.69–1.19); $p = 0.50$	
Acute respiratory failure or mechanical ventilator use during index admission	1.29 (0.87–1.95); $p = 0.21$	
Length of stay >30 days	1.59 (1.22–2.06); $p = 0.001$	1.38 (1.05–1.81); p = 0.02
Discharge disposition (compared to home (self-care))		
Short term hospital	0.56 (0.31–1.01); p = 0.06	0.53 (0.28–0.99); $p = 0.05$
Skilled nursing facility	1.20 (0.83–1.73); $p = 0.32$	
Home health care	1.33 (0.93–1.90); $p = 0.12$	1.23 (085–1.77); p = 0.27

* Based on APR-DRG coding (All patient refined diagnosis related groups).

failure, and coronary artery disease. A forest plot is illustrated in Fig. 3.

4. Discussion

In this contemporary analysis of 4229 patients who survived to discharge after ECMO for CS, we sought to identify risk factors associated with all-cause 30-day readmission in a nationwide and contemporary cohort of patients undergoing ECMO for CS. We report multiple novel findings: i) Of patients who survived to discharge, 16.4% were readmitted within 30 days with a median time to readmission of 10 days post-discharge, ii) Diabetes mellitus, chronic liver disease, and prolonged LOS (>30 days) conferred a higher risk for 30-day readmissions while heart failure diagnosis and being discharged to a short term hospital conferred a lower risk for readmission, and iii) Sepsis, heart failure and critical illness polymyopathy/neuropathy were the most common indications for 30-day readmission.

The observed thirty-day readmission rate of 16.4% is somewhat lower than previous literature. Two studies conducted by Shah et al. analyzing patients with AMI and non-AMI-related cardiogenic shock have found a 30-day readmission rate of 20.2% and 22.6%, respectively [16,17]. These findings were derived using 2013–2014 NRD data in a population not restricted to ECMO use. Furthermore, in a more recent study of ECMO use in CS, using NRD data from 2016, the readmission rate was reported at 23.9% [18]. Among patients receiving ECMO for all indications (including venovenous and venoarterial ECMO), readmission rates are higher at 21.1% and 43.8% [19,20]. The observed lower rate in our study may be explained in two ways. It is plausible that the increased ECMO use for cardiac reasons has led to improved management, experience, and familiarity with this modality, eventually resulting in improved outcomes. Alternatively, this may represent bias due to increased out-of-hospital mortality post-discharge.

Another iterative observation in our cohort was that more than 50% of the readmissions occurred within the first ten days after discharge. This observation has been reproduced in previous analyses [16,17]. It appears that the first days post-discharge represent a vulnerable period where gaps in the transition of in- to out-of-hospital care may occur in addition to lack of social and emotional support. This is further supported by the lower readmission risk seen in patients discharged to a short-term hospital facility where care lapses are less likely to occur. Therefore, an accurate assessment of patients' frailty before discharge may help identify high-risk individuals, decrease readmission rates and implement a multipoint strategy for close post-discharge monitoring.

History of diabetes mellitus, chronic liver disease, and prolonged LOS are associated with increased risk of readmission, which could be explained by these patients' poor overall functional status. Although previously reported by Sanaiha et al., a history of heart failure was surprisingly associated with a lower risk of readmission [19]. The observed decrease in readmission with baseline heart failure was unexpected owing to the large body of literature supporting high readmission rates for patients with various etiologies of cardiomyopathy [21–23]. Compared to other comorbidities (like CAD, DM, and chronic liver disease), heart failure patients did not have higher mortality during the index admission to explain this finding (shown in Fig. 3). The reason

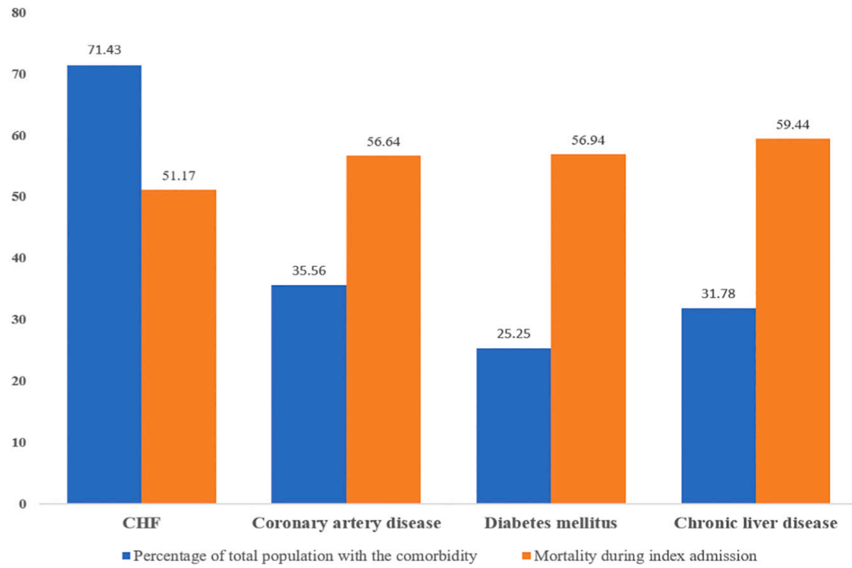

Fig. 2. Total population (%) with comorbidity and mortality during index admission.

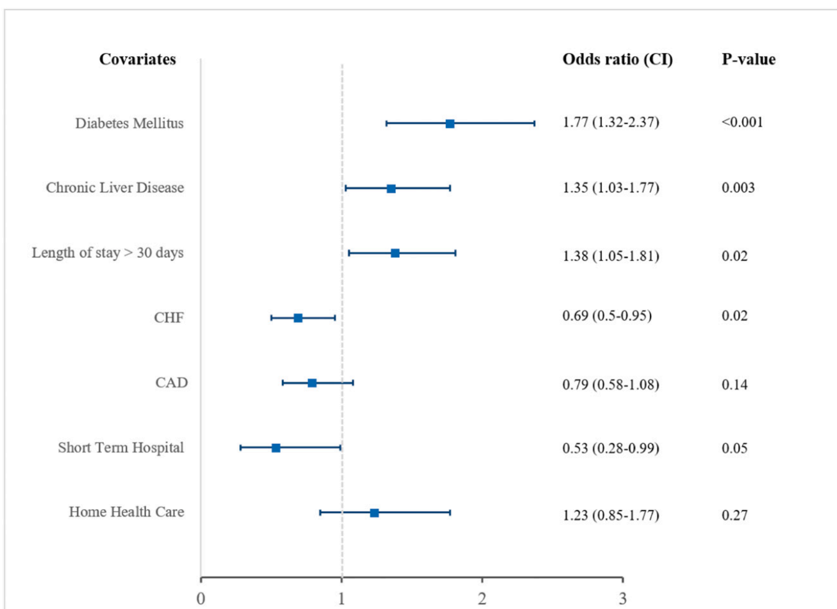

Fig. 3. Forest plot showing independent predictors of 30-day readmission after index admission for cardiogenic shock requiring ECMO.

for low readmission in heart failure patients could be secondary to higher out-of-hospital mortality after discharge versus a paradox finding. This is a limitation of the NRD as it lacks information on out-of-hospital mortality, which could affect the 30-day readmission rate. Independent predictors of 30-day readmission after index admission for cardiogenic shock requiring ECMO has shown in the forest plot (Fig. 3).

ECMO use in patients with CS was associated with 52.2% mortality in our study, consistent with previous studies. Sanaiha et al. reported an overall mortality of 50.2% in an analysis of adult patients who underwent ECMO using the NRD from 2010 to 2015 [19]. Another study showed 59.2% in an analysis of the National Inpatient Sample (NIS) database from 2000 to 2014 in a cohort of AMI utilizing ECMO [1]. Truby et al. reported a lower mortality rate of 38.6% in patients with refractory CS who underwent ECMO support in a single tertiary center experience [25]. Our high mortality rate could be attributed to our cohort's heterogeneity that included all payers and a wide variety of hospitals.

Sepsis was the most common cause of 30-day readmission (11.7%) in our study, followed by cardiac causes, heart failure being the most common. Previous studies have shown cardiac causes for most of the rehospitalizations, heart failure being the most common (20–24%) and infections being the third most common cause (9–11%) that is consistent with our findings [17,18]. Patients who underwent ECMO cannulation usually require invasive procedures such as pulmonary artery catheter placement and frequently require prolonged use of central lines, urinary catheters, and endotracheal tubes. This will expose them to various healthcare-associated infections, such as ventilator-associated pneumonia, central line-associated bloodstream infections, and surgical site infections [24]. The risk of infection and cardiac decompensation among these sick patients should be identified early. Strategies to minimize the risk of infections should result in significantly lower 30-day rehospitalization rate. Close follow-up by the multidisciplinary team approach as an outpatient should be implemented to reduce the readmissions rate.

4.1. Limitations

This study has several limitations. This retrospective study uses the NRD, which relies on the ICD-10 codes with no hemodynamics, clinical, or laboratory data. Data regarding readmission beyond 30 days was not available in this database, and this database lacks information regarding out-of-hospital mortality, which could affect the 30-day readmission rate.

5. Conclusion

In conclusion, patients with CS requiring ECMO support have high mortality and high 30-day readmission rates, with sepsis being the leading cause of readmissions followed by heart failure. Prolonged hospitalization, diabetes mellitus, and chronic liver disease were identified as the independent predictors of 30-day readmission.

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-Rest of the authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Declaration of competing interest

Joseph E. Tonna, MD reports a relationship with LivaNova and Philips Healthcare that includes: speaking and lecture fees and travel reimbursement. Joseph E. Tonna, MD reports a relationship with The National Institutes of Health, The National Heart, Lung, And Blood Institute that includes: funding grants.

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