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Trends in mortality and resource utilization for extracorporeal membrane oxygenation in the United States: 2008–2014 ☆

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ABSTRACT

Background: Extracorporeal membrane oxygenation is used as a life-sustaining measure in patients with acute or end-stage cardiac or respiratory failure. We analyzed national trends in extracorporeal membrane oxygenation use and outcomes and assessed the influence of hospital demographics.
Methods: Adult extracorporeal membrane oxygenation patients in the 2008–2014 National Inpatient Sample were evaluated. Patient and hospital characteristics, extracorporeal membrane oxygenation indication, mortality, and hospital costs were analyzed.
Results: A total 17,020 adult extracorporeal membrane oxygenation patients were considered: 47.4% respiratory failure, 38.6% postcardiotomy, 5.5% lung transplantation, 5.5% cardiogenic shock, and 3.2% heart transplantation. Admissions rose 361% from 1,026 in 2008 to 4,815 in 2014 ($P < .0001$), and the fraction of respiratory failure increased 40.5%–49.8% ($P < .001$). Elixhauser scores rose from 3.1 to 4.1 ($P < .0001$). Mortality decreased among total admissions from 62.4% to 42.7% ($P < .0001$) associated with an observed decline in postcardiotomy mortality. Mean hospital costs and length of stay remained stable throughout the study period. Although extracorporeal membrane oxygenation occurred most frequently at large hospitals, small and medium-sized hospitals showed significant expansion ($P < .001$). The Northeast exhibited a sustained three-fold per capita increase in extracorporeal membrane oxygenation rate ($P < .0001$).
Conclusion: The past decade has seen an exponential growth of ECMO extracorporeal membrane oxygenation in the United States, with the fraction for respiratory failure displaying considerable growth. Overall extracorporeal membrane oxygenation patients experienced substantially reduced mortality, driven by improved outcomes for postcardiotomy patients, along with a trend toward an increased risk profile. Disproportionate use of extracorporeal membrane oxygenation in the Northeast warrants investigation of access to this technology across the United States.

Introduction

Modern advances in technology, surgery, and critical care have allowed extracorporeal membrane oxygenation (ECMO) to become the standard of care for selected patients with refractory cardiac and respiratory failure.[1–4] ECMO utilization for all clinical indications has experienced a dramatic surge throughout the past decade, and this modality is now commonly applied as a bridge to heart or lung transplant, organ recovery, or definitive surgery.[1,5–12]

Increased application of ECMO undoubtedly affects patient care, treatment algorithms, hospital resource allocation, and provider qualification and training requirements. However, objective consensus criteria for successful treatment with ECMO are lacking, and the ultimate decision to implement ECMO remains at the discretion of the care team. Although centers performing a high volume of ECMO are establishing techniques for maintaining quality in the face of increasing demand, there is a paucity of data examining the influence of smaller bed size and geographic location on outcomes and economic efficiency.[13]

The intent of the present study was to characterize current national trends in ECMO utilization and to systematically examine the impact of hospital-specific characteristics on outcomes with ECMO. With increasing use of ECMO, effective and judicious resource utilization is of paramount importance. Establishing current trends is essential to appropriate future resource allocation,

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decision-making, and continued improvement of ECMO outcomes in the United States.

Methods

Patient discharge information January 2008–December 2014 was obtained from the National Inpatient Sample (NIS) maintained by the Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality.[14] The NIS is the largest collection of all-payer hospital discharges in the United States and has been validated extensively in the medical literature. Before 2012, the NIS reported 100% of discharges from 20% of US hospitals. However, beginning in 2012, the NIS was built on 20% of discharges from 100% of reporting hospitals using a self-weighting design that improved the precision of national estimates by 42%–48%.[14,15] In the present study, we used the method suggested by Khera et al[16] to account for this change in sampling methodology. National estimates were calculated across various institutional strata, including small, medium, or large bed sizes and regions in the Northeast, the Midwest, the South, or the western United States. Census Bureau data were used to calculate the population density and ECMO incidence for each year independently to obtain case volumes per 100,000 individuals.

International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) procedural codes were used to identify discharge records with extracorporeal membrane oxygenation (39.65) and percutaneous extracorporeal membrane oxygenation (39.66). All adult patients receiving ECMO were categorized by ICD-9-CM diagnostic and procedure codes for the following five clinical indications: (1) postcardiotomy, (2) cardiogenic shock, (3) respiratory failure, (4) heart transplantation, and (5) lung transplantation. Details of the categorization process to ensure mutually exclusive groups are described elsewhere.[17,18] Briefly, placement into the cardiogenic shock group required the absence of cardiac surgery, respiratory failure, and heart and lung transplantation codes. Heart and lung transplant patients were excluded from the postcardiotomy group. The lung transplantation code was excluded from the heart transplant group, and, similarly, heart transplant patients were excluded from the lung transplant group. Patients who received preoperative ECMO were identified by using the PRx DAY variable provided by the NIS. Any patients who received ECMO before PRx DAY for the operation of interest were excluded. The Elixhauser Comorbidity Index, measuring 30 categories of comorbidity based on ICD-9-CM diagnosis codes, was used to describe patients' risk profile.[19] The primary outcomes of the study were temporal trends in utilization of ECMO and discharge survival with patients stratified by clinical indication. Secondary outcomes included the impact of region and hospital bed size on gross domestic product–adjusted hospital costs and length of stay (LOS). Costs were calculated after correction of charges by cost-to-charge ratio data provided by the NIS for individual hospitals. All mortality estimates were adjusted for changes in patient age throughout the study period.[20] Furthermore, mortality rates by region were adjusted by a factor of each region's mean Elixhauser index compared with the Northeast annual standard.

Data extraction and calculation were performed with STATA 14.0 software (StataCorp, College Station, TX). Trend analyses were conducted with a nonparametric test for continuous variables and Royston Ptrend for categorical outcomes.[21] Pearson χ^2 tests were used to analyze categorical variables and *t* tests were used for continuous variables. One-way ANOVA was used to compare mean differences among ECMO indications. Costs and LOS are reported as mean ± standard deviation of US $ and days, respectively. Statistical significance was defined as α less than 0.05. This study was deemed exempt by our institutional review board.

Results

Patient demographics and hospital characteristics

During the period 2008–2014, ECMO was deployed in a total of 17,020 adult patients (age = 52.8 ± 16.9 years, female = 37.6%). Patient and hospital characteristics for the overall population and for each ECMO indication are presented in the Table 1. Among those placed on ECMO, 8,062 (47.4%) were for respiratory failure, 6,583 (38.6%) were for postcardiotomy, 930 (5.5%) were for lung transplant, 903 (5.3%) were for cardiogenic shock, and 542 (3.2%) were for heart transplant. Compared with all indications, patients in the postcardiotomy group on average were older and had the highest Elixhauser Comorbidity Score. Among all patients receiving ECMO therapy, the Elixhauser Comorbidity Score increased from 3.1 to 4.1 ($P < .001$) during the 7-year study period. As expected, the heart and lung transplant cohorts were treated predominantly at large bed-size institutions.

Trends

In the overall study, annual ECMO admissions increased 369% from 1,026 in 2008 to 4,825 in 2014 ($P < .001$). The number of sampled hospitals performing ECMO also significantly expanded from 206 for the 2008–2011 period to 660 institutions 2012–2014. When stratified by indication, there was a 477% increase from 415 to 2,400 cases in the respiratory failure group, a 349% increase from 420 to 1,885 procedures in postcardiotomy patients, a 402% increase from 28 to 140 procedures in heart transplant patients, a 207% increase from 62 to 190 cases in the cardiogenic shock group, and a 100% increase from 100 to 200 cases in the lung transplant group (Fig. 1). ECMO for respiratory failure significantly increased from 40.5% to 49.8% ($P < .001$) of all admissions, and the fractions for cardiogenic shock and lung transplant decreased from 6.0% to 4.0% ($P < .001$) and 9.8% to 4.2% ($P < .001$), respectively. ECMO use for the postcardiotomy and heart transplant cohorts as fractions of total admissions did not exhibit a significant change ($P = .43$ and $P = 0.48$, respectively).

Geographically, the majority of ECMO patients (33.6%) were treated at hospitals in the southern United States (Fig. 2). In addition, ECMO use in the South and the Midwest as a fraction of total admissions displayed the largest growth, increasing from 21.3% to 36.8% ($P < 0.001$) and 13.8% to 22.1% ($P < 0.001$), respectively. The proportion of overall ECMO use in the Northeast and Western United States decreased from 41.8% to 28.3% ($P < 0.001$) and from 23.1% to 12.8% ($P < 0.001$), respectively. However, when adjusted for adult population density based on US census data for each year independently, the Northeast displayed the highest ECMO incidence and rose from 1.0 to 3.0 cases per 100,000 adults. In comparison, the incidence of ECMO per 100,000 adults increased from 0.2 to 1.6 in the South and the Midwest, and 0.34 to 0.82 in the western United States (all $P < 0.0001$; Fig. 3).

Fluctuations in ECMO admissions in small, medium, and large bed-size hospitals are presented in Fig. 4, with medium-sized facilities displaying the greatest relative growth since 2008. ECMO at medium bed-size hospitals as a fraction of all admissions increased from 4.2% to 11.9% ($P < 0.0001$) and rose from 43 to 575 cases throughout the study period. In addition, the frequency of ECMO at small hospitals grew from 16 to 170 cases and the fraction of all admissions increased from 1.6% to 3.5% ($P = 0.0003$). Although large bed-size hospitals had an increase from 967 to 4,070 cases, the fraction significantly decreased from 94.2% to 84.5% ($P < 0.0001$).

Given the change in sampling strategy of the NIS database, we compared the proportion of ECMO cases performed at small, medium, and large bed-size facilities before and after 2012. Com-

Table 1
Patient demographics excluding preprocedure ECMO.

	Postcardiotomy (N = 6,583)	Heart transplant (N = 542)	Lung transplant (N = 930)	Cardiogenic shock (N = 903)	Respiratory failure (N = 8,062)	Total (N = 17,020)
Age (y)	60.94	51.05	53.78	52.88	46.24	52.8
Female (%)	35.4	30.3	41.5	40.0	39.2	37.6
Coronary artery disease (%)	19.4	19.1	1.1	13.0	5.9	11.6
Heart failure (%)	53.8	93.7	11.3	51.9	36.9	44.6
Hypertension (%)	28.4	13.4	11.5	30.2	13.9	20.2
Diabetes (%)	16.5	8.0	9.4	19.8	11.2	13.5
Peripheral vascular disease (%)	16.5	7.2	0.5	5.5	2.6	8.1
Chronic pulmonary disease (%)	15.7	12.4	37.4	11.7	9.6	13.7
Renal failure (%)	15.9	19.0	6.1	15.2	9.1	12.2
Elixhauser score	4.3	4.0	3.6	4.0	3.6	3.9
Hospital bed size						
Small (%)	4.1	0.0	0.0	2.4	1.9	2.6
Medium (%)	11.9	2.8	2.7	10.2	10.5	10.4
Large (%)	84.0	97.2	97.3	87.4	87.6	87.0
Region						
Northeast (%)	25.5	30.7	42.4	37.1	30.2	29.5
Midwest (%)	24.2	25.8	20.1	22.4	20.2	22.0
South (%)	32.7	27.0	28.7	27.8	36.0	33.6
West (%)	17.6	16.5	8.7	12.8	13.6	14.9

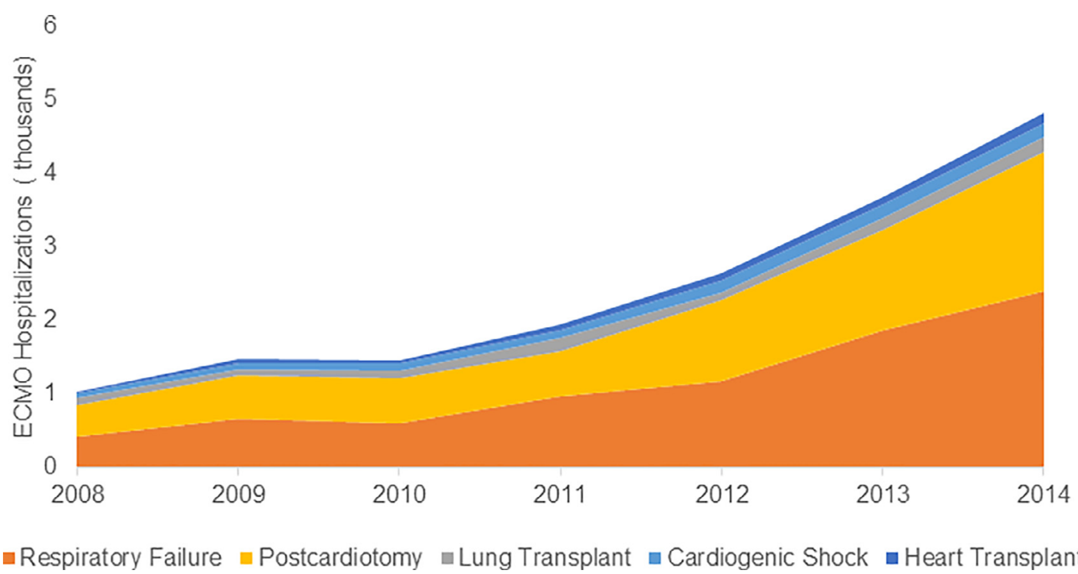

Fig. 1. Temporal trends by indication for ECMO in the United States, 2008–2014.

paring both cohorts (2008-2011 versus 2012-2014), more than 80% of all ECMO cases were performed at large bed-size institutions (86.9% versus 83.2%, $P = 0.28$) with only a slight increase in proportion performed at small bed-size hospitals in the 2012–2014 group (2.1% versus 3.7%, $P = 0.02$). Additional comparisons across teaching status demonstrated that a majority of ECMO is performed at urban-teaching institutions, with a minor increase in the proportion of urban-teaching institutions in the 2012-2014 era (88.8% versus 94.2%, $P = 0.007$).

Clinical outcomes

The overall average mortality rate for the study population was 53.5%, with cardiogenic shock patients incurring the highest mortality (65.3%) and lung transplant patients the lowest (36.3%). Despite the dramatic rise in annual ECMO admissions, inhospital age-adjusted mortality decreased from 62.4% to 42.7% ($P < 0.0001$) throughout the study period (Fig. 5). The observed decrease in mortality rates was predominantly attributable to significant improvements in the postcardiotomy group (60.3%–31.2%, $P < 0.0001$). In contrast, mortality among lung transplant (35.7%–82.4%, $P < 0.001$), cardiogenic shock (17.5%–45.9%, $P < 0.0001$), heart transplant (50.9%–75.3 %, $P < 0.0001$), and respiratory failure (36.4%–50.9%, $P < 0.0001$) cohorts increased significantly.

Given the discrepancies of ECMO utilization by hospital bed size and region, mortality analysis by hospital characteristics was also performed. Age-adjusted mortality revealed a significantly higher mortality at large bed-size hospitals compared with small bed-size institutions (54.6% versus 36.1%, $P = 0.002$). However, the difference in mortality between small and medium bed-size institutions was not statistically significant (48.4% versus 36.1%, $P = .05$). Although in-hospital mortality was highest in the South, this difference was not statistically significant across the nation (Northeast 52.8%, Midwest 52.8%, South 55.3%, and the US western region 51.6%, $P = .75$). Despite statistically similar overall mortality, the Midwest (20.5%–44.8%, $P = 0.04$) was the only region with increased mortality throughout the study period, and all other regions exhibited decreased in-hospital ECMO mortality (Northeast

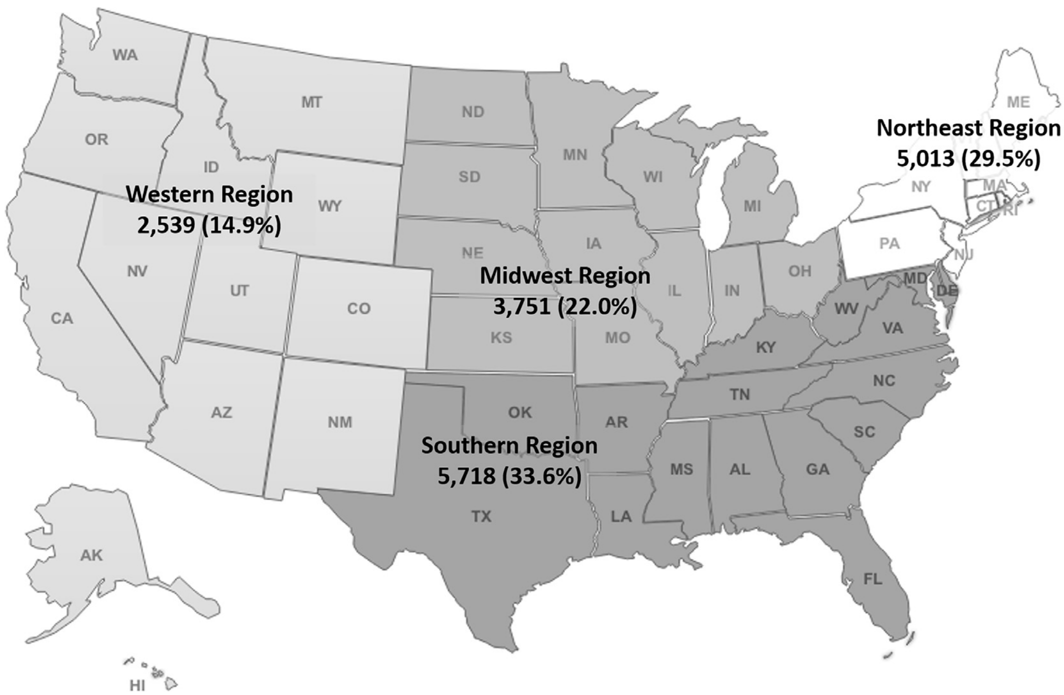

Fig. 2. Regional variation of ECMO hospitalizations in the United States, 2008–2014.

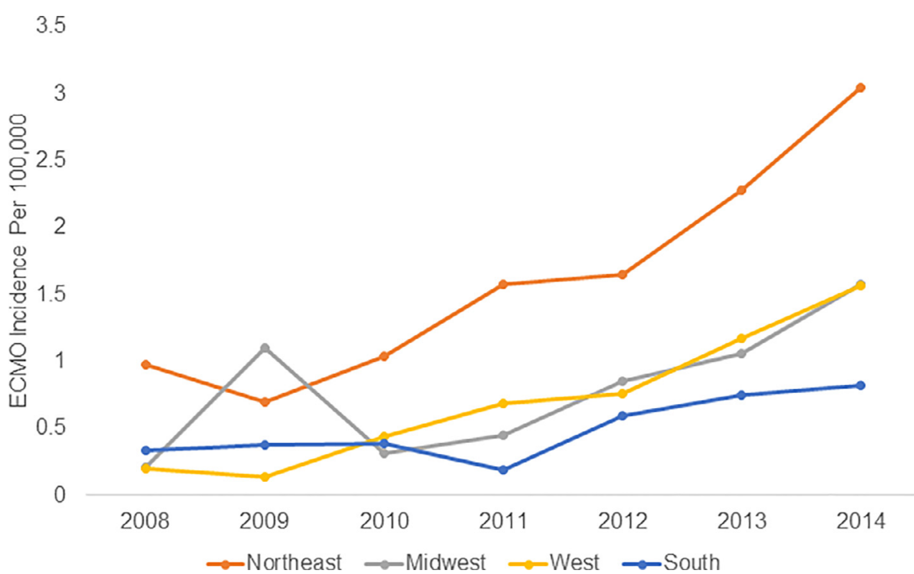

Fig. 3. Trend of ECMO incidence per 100,000, by US region.

63.0%–41.3%, $P < 0.0001$; South 80.4%–44.8%, $P < 0.0001$; the US western region 67.8%–47.8%, $P < 0.0001$) after adjusting for age and changes in the Elixhauser Comorbidity Index.

Hospital costs and LOS per ECMO admission were stable throughout the study period (Fig. 6). Heart and lung transplant cohorts incurred the highest index admission costs ($339,917.30 ± $242,724.20 and $258,111 ± $170,424.40, respectively) and longest LOS (49.5 days ± 55.6 days and 41 ± 40.0 days). Patients with cardiogenic shock had the shortest LOS (11.3 days ± 16.4 days) and, subsequently, the lowest hospital costs ($98,059 ± $101,646).

Discussion

With previous studies demonstrating a dramatic increase in ECMO utilization and mixed outcome trends, the present study was performed to provide a current perspective on the utilization of ECMO. In this study of a nationally representative sample from 2008 to 2014, we make four important observations. First, ECMO utilization increased 369% among the entire study population, with the fraction of ECMO for respiratory failure exhibiting substantial growth. Second, overall ECMO in-hospital mortality significantly declined during the 7-year study period, driven by significant decreases in postcardiotomy mortality. Patients receiving ECMO for all other indications demonstrated increased mortality over time. Third, we describe an expansion in the fraction of ECMO at small- and medium-size institutions, whereas LOS and hospital costs remained steady among survivors. Fourth, the use of ECMO per capita is not uniform across geographic regions and likely represents lack of access to suitable care in underserved areas.

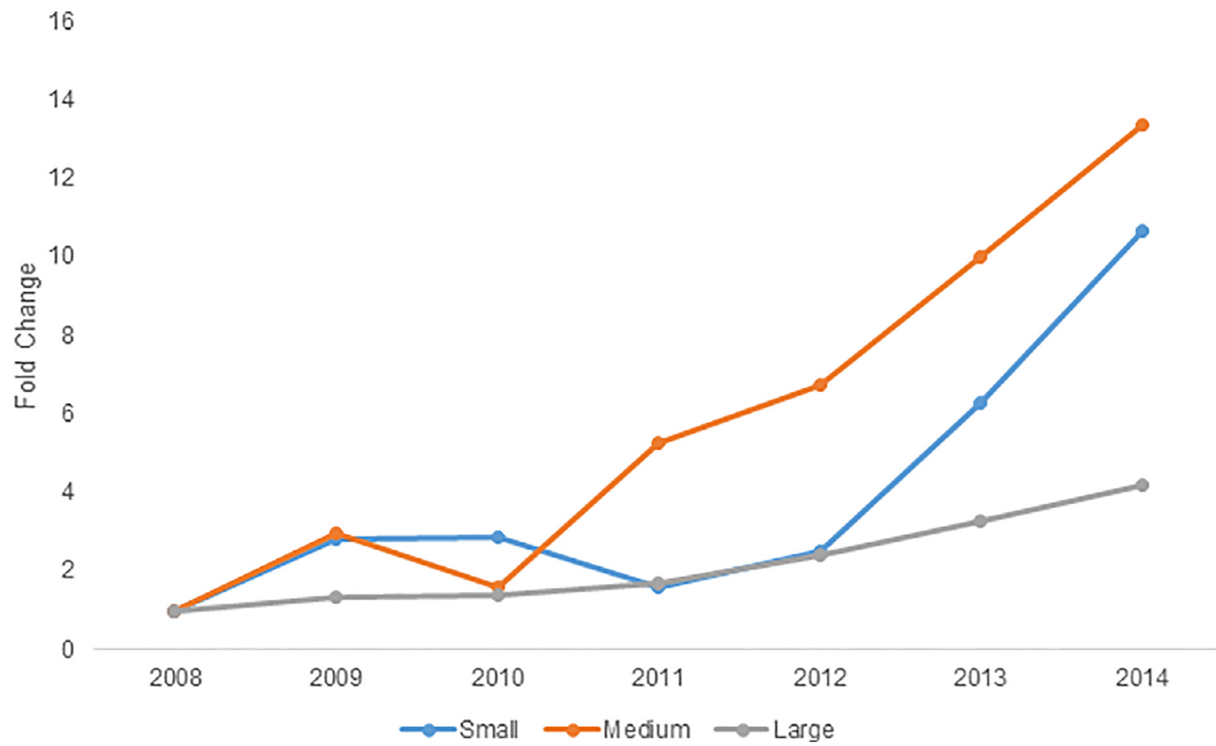

Fig. 4. Growth of ECMO hospitalizations relative to 2008, by hospital bed size.

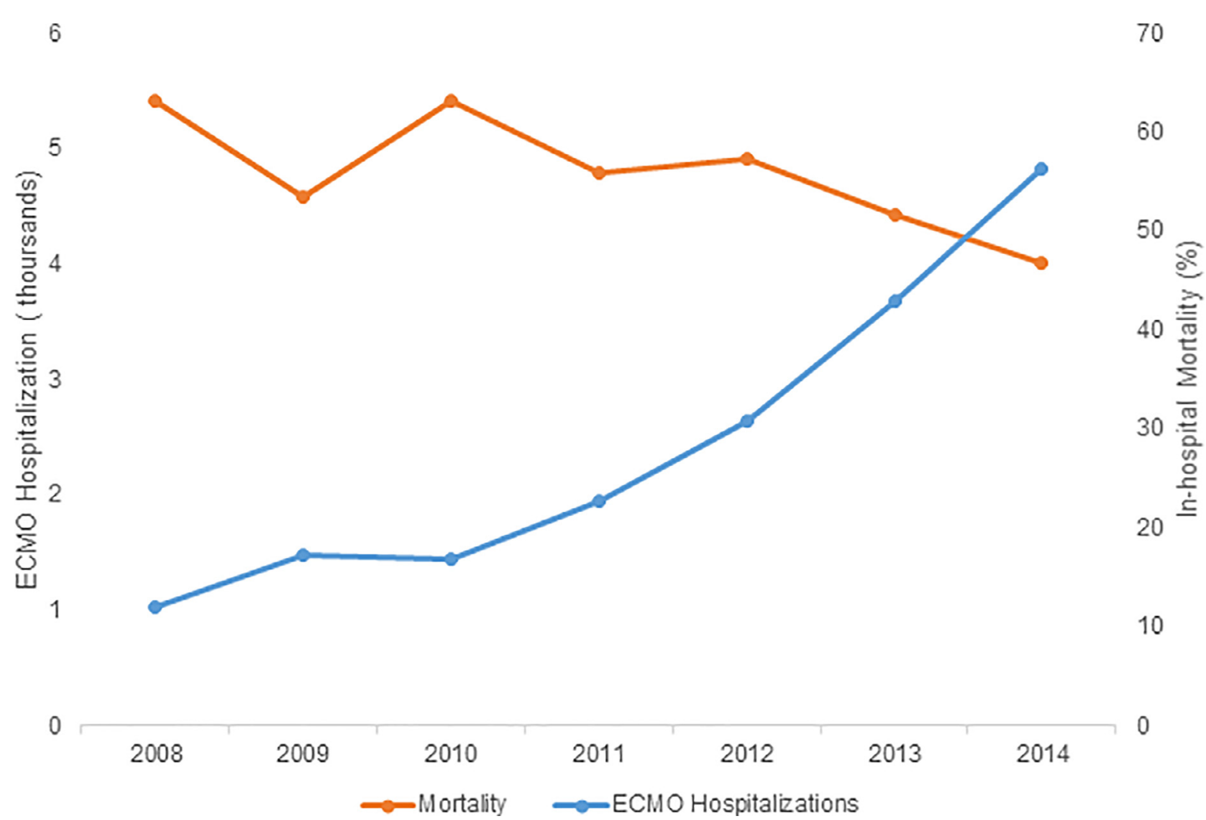

Fig. 5. Annual ECMO hospitalizations and inhospital mortality rate.

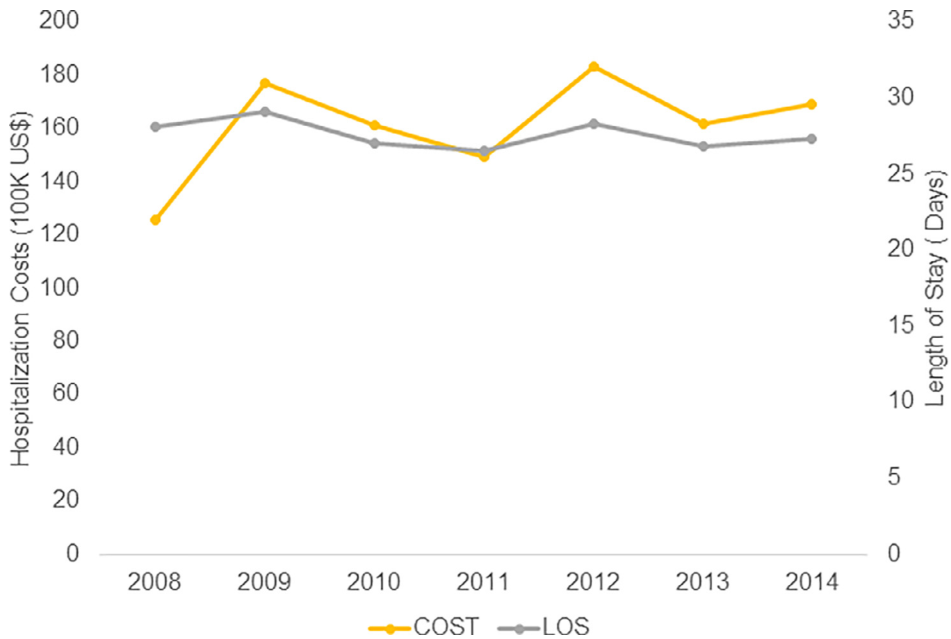

Fig. 6. Total charges per admission and median length of stay for overall ECMO hospitalizations. Charges and length of stay are reported as median US $ and days, respectively.

Multiple explanations have been proposed for the overall increase in ECMO utilization throughout the past decade, including success of ECMO in management of the 2009 H1N1 respiratory virus epidemic, recent publication of series in postcardiotomy and cardiogenic shock circulatory support, and advances in technology that have allowed increased portability of ECMO circuits.[1,13,17,22–24] Although initially described in 1972, interest in use of extracorporeal support for respiratory failure waned after a subsequent randomized controlled trial in 1979 failed to demonstrate survival benefit.[25,26] Use of ECMO to treat acute respiratory distress syndrome (ARDS) has substantially increased in the past decade, primarily supported by the randomized CESAR trial indicating a survival advantage for patients who were transferred to ECMO centers.[27] Specific explanations for the profound increase in ECMO utilization for respiratory failure can be attributed to increasing enthusiasm for ECMO application in ARDS and technical advances in cannula and circuit technology described elsewhere.[28]

The observed reduction in overall in-hospital mortality after administration of ECMO for postcardiotomy syndrome likely reflects the increased availability of competing interventional technologies and improved perioperative care. Public reporting of hospital and surgeon outcomes also have likely driven improved patient selection. Furthermore, these findings may simply be attributed to more widespread adoption of ECMO in postcardiotomy failure. Increased mortality for all other ECMO indications, including heart and lung transplantation, cardiogenic shock, and respiratory failure are likely related to increased availability of this technology. Because ECMO is increasingly utilized across the nation at various community hospitals, refinement of criteria for initiation is warranted to optimize patient outcomes and resource utilization.

The significant increase in mortality in the lung transplant group is in contrast to recent evidence for the success of ECMO as a salvage therapy for end-stage lung disease and as a bridge to lung transplantation.[5,29,30] Age-adjusted analyses of mortality across cohorts receiving ECMO for respiratory failure, cardiogenic shock, and postcardiotomy suggests that ECMO is utilized in increasingly morbid clinical scenarios that cannot be accounted for using administrative and nonphysiologic parameters. As ECMO remains the standard in the management of primary graft dysfunction after heart and lung transplantation, improved selection criteria to realize the maximal survival benefit is warranted.[2,3]

Of note, the present study highlights national disparities in the utilization of ECMO. Throughout this study period, large bed-size institutions appear to have paved the way for smaller facilities to initiate ECMO, likely attributable to the intensity of care and required resources. With the increasing volume of literature supporting successful, short-term use of ECMO in ARDS, lung transplant, and, more recently, cardiogenic shock, more reliable criteria for predicting response are emerging.[31,32] These published successes may be leading more medium and small bed-size centers to offer ECMO as a real option for selected patients. Geographically, ECMO utilization continues to increase overall but remains the highest per capita in the Northeast. These differences in ECMO utilization are likely not solely related to national discrepancies of population age or morbidity. In contrast, the geographic burden of congestive heart disease has been shown to be particularly heavy in the South, and, in fact, has moved away from the Northeast.[33] A greater concentration of ECMO-capable centers in metropolitan areas in the Northeast may be partially responsible for this finding. The mortality trend of ARDS also weighs more heavily on the South than all other regions of the United States.[34] The notable geographic differences in ECMO utilization, which do not parallel the disease patterns that most commonly lead to need for ECMO, suggest significant disparities in access to care outside the Northeast. The greatest discrepancy appeared to be within the Midwest, which was the only region with increased mortality after ECMO despite correction for population age and comorbidity. With the promising mortality benefit of ECMO for multiple indications, additional provider training and initiation of ECMO programs in all regions of the United States will be important in the current era of mechanical circulatory support.

Hospital costs per admission along with LOS among ECMO survivors remained steady throughout the study period. With increased utilization of ECMO nationally, guidelines for implementation and management require rigorous validation. Increasing complexity of cardiac surgery patients, not completely reflected by administrative measures, significantly adds to the societal burden for this technology. Contemporary literature quantifying the cost of implementation of ECMO in small and large populations notes dramatically increased charges. For example, median charges for patients undergoing lung transplantation with ECMO increased by up to 50% as compared with charges for patients who did not require ECMO.[35] In patients placed on ECMO for cardiogenic shock, Chiu et al[36] reported an incremental increase of $100,000. The present study was unable to delineate the hospitalization costs directly attributed to ECMO, possibly explaining the stable trend of costs and LOS over time. With increasing societal demands for financially sustainable ECMO, programs with more stringent outcome-based implementation and transfer criteria are increasingly crucial.

The present study has several important limitations. The NIS modified its methodology beginning in 2012 such that 20% of discharges were sampled, and we used best practices for national estimates to mitigate this factor. Trends weighting has been substantiated in earlier published works for patient-level analyses and was used to evaluate national trends over throughout this 7-year study period.[15,16] Our inclusion of all data spanning 2008–2014 allowed for a broader representation of patient outcomes among the contemporary ECMO scene. Of all ECMO cases, urban-teaching and large bed size were the most common institutional characteristics for both the 2008–2011 and 2012–2014 data. Consistent with previously published guidelines for use of this database, we did not perform hospital-level quality designations. Furthermore, we confirmed the ICD-9 coding for ECMO and the five clinical indications remained consistent across the years. With regard to billing data, the potential influence of inflation was minimized by adjustment through the Bureau of Labor Statistics Consumer Price Index. In addition, given that ECMO is a relatively rare and new therapy, an exclusion of an institution performing a large volume of ECMO in the sample may overrepresent or underrepresent the real number of ECMO patients. However, our data trends regarding utilization agree with previous publications using this data set and the ELSO database.[1,17,35,37,38]

Another limitation of the present study is that current administrative ICD-9 coding does not specify the various ECMO cannulation strategies, such as veno-venous and veno-arterial. Although we cannot identify the mode of ECMO implemented, the use of the NIS procedure-day variable allowed us to exclude patients receiving preprocedural ECMO, increasing the homogeneity of our findings. Absence of physiologic data is another significant limitation of this database. However, because the NIS is the largest nationally representative database, we performed this analysis to assess the global landscape of ECMO utilization. Finally, the NIS does not differentiate between patients who may have had more than one indication for ECMO, such as patients with respiratory failure secondary to idiopathic pulmonary fibrosis with pulmonary hypertension and subsequent cardiogenic shock. These distinctions may significantly affect the predicted mortality, and, in this relatively small sample, a single indication for ECMO may not adequately capture the true nature of the studied patient population. In light of these constraints, precedent for reliable use of the NIS has been widely established[16,33,35,36] and earlier works have supported its particular use for the study of trends on the national level.[17,35,37–40]

In conclusion, our study of the NIS throughout a 7-year period shows a growth in ECMO utilization across the United States, with improved postcardiotomy mortality. The reported observations are likely influenced by recent technologic advancements and a greater enthusiasm for ECMO implementation in selected high-risk patients with cardiac and respiratory failure. Nonetheless, our mortality analysis is limited by a lack of granular data to appropriately risk-adjust the included study cohort. Prominent geographic disparities in access to ECMO outside of the Northeast suggest the importance of broader initiation strategy for ECMO programs throughout the United States to maximize the full benefit of this technology. Initiation of ECMO and treatment of patients supported by this complex modality require financial, personnel, and equipment resource exploitation and thus have a significant economic impact. To extract the greatest benefit with the least harm, future efforts to develop clear, objective ECMO deployment criteria based on indication and predicted success will be crucial.

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"That was a good start. Love your showing six graphs at once. It will totally confuse them."