Original Article

Extracorporeal Membrane Oxygenation in New York State
Trends, Outcomes, and Implications for Patient Selection

Jaya Batra, BA; Nana Toyoda, MD; Andrew B. Goldstone, MD; Shinobu Itagaki, MD, MS; Natalia N. Egorova, PhD; Joanna Chikwe, MD

Background—Utilization of extracorporeal membrane oxygenation (ECMO) is expanding despite limited outcome data defining appropriate use.

Methods and Results—To quantify determinants of early and 1-year survival after ECMO in adult patients, we conducted a retrospective cohort analysis of 1286 patients aged ≥18 years who underwent ECMO in New York State from 2003 to 2014. Median follow-up time was 4.9 months (range, 0–12 months). ECMO utilization increased from 13 patients in 8 hospitals in 2003 to 330 patients in 30 hospitals in 2014. Compared with patients undergoing ECMO before 2009, later patients were older (54.4 versus 52.3 years; *P*=0.013) and more likely to have major comorbidity including chronic kidney disease (25.2% versus 13.2%; *P*=0.02) and liver disease (20.0% versus 10.7%; *P*=0.001). In the overall cohort, 30-day mortality was 52.2% (95% confidence interval, 49.5–54.9). Mortality at 30 days was 65.2% for patients aged ≥75 years (n=73/112) and 74.6% in patients who required cardiopulmonary resuscitation (n=91/122). Survival at 1 year was 38.4% (95% confidence interval, 35.7–41.0). The 30-day mortality and 1-year survival improved across the study period. In multivariable analysis, earlier year of ECMO, lower hospital volume, indication for ECMO after a cardiac procedure, cardiopulmonary resuscitation before ECMO placement, and age >65 years were independent predictors of worse survival.

Conclusions—Outcomes of ECMO have improved despite increasing comorbidity. Extreme mortality after ECMO in elderly patients and patients requiring cardiopulmonary resuscitation indicates that less invasive therapeutic or palliative modalities may be more appropriate in this end-of-life setting. **(*Circ Heart Fail*. 2016;9:e003179. DOI: 10.1161/CIRCHEARTFAILURE.116.003179.)**

Key Words: extracorporeal circulation ■ heart arrest ■ heart failure ■ mortality ■ shock, cardiogenic

Extracorporeal membrane oxygenation (ECMO) is an established rescue therapy for severe respiratory failure, cardiogenic shock, and cardiac arrest refractory to conventional therapeutic modalities including ventilatory and high-dose inotropic support.[1] ECMO for severe respiratory failure provides gas exchange without circulatory support by continuously draining, oxygenating, and returning central venous blood via an external centrifugal pump.[1–5] Circulatory collapse is treated with venoarterial ECMO, in which central venous blood is continuously drained, oxygenated, and pumped to the arterial circulation, providing cardiac output of up to 6 L/min.[1–6] Both modalities require specialist perfusion and critical care support.[1] Use of ECMO in newborns and infants is well established, and the modality has been increasingly applied in complex adult populations for indications including acute respiratory failure, acute heart failure, acute coronary syndrome, and cardiogenic shock after cardiac procedures, including percutaneous coronary intervention, cardiac surgery, and heart–lung transplantation.[1,7–13] Patients undergoing this invasive procedure are therefore a particularly high-risk population, and single-center series indicate that in-hospital mortality after ECMO for circulatory collapse is close to 50%, with fewer than 20% of patients discharged home, and 6-month survival as low as 30%.[13–17]

See Clinical Perspective

Utilization of ECMO has increased 6-fold since 2008 with ≈3000 patients receiving ECMO in the United States in 2012.[9] This expansion has occurred in the absence of supporting data from clinical trials or mandatory registries, and recent consensus guidelines state that, "With the re-emergence of ECMO at many centers, the trade-offs between complete cardiopulmonary support versus complexity of intervention and monitoring and potential for complications … need to be defined,"[1]

Received May 24, 2016; accepted November 9, 2016.

From the Department of Cardiovascular Surgery (J.B., N.T., S.I., J.C.) and Department of Population Health Science and Policy (N.N.E.), Icahn School of Medicine at Mount Sinai, New York, NY; and Department of Cardiothoracic Surgery, Stanford University School of Medicine, CA (A.B.G.).

Preliminary data from this study was presented at the American College of Cardiology 65th Annual Scientific Session and Expo, April 2–4, 2016, in Chicago, IL.

The Data Supplement is available at http://circheartfailure.ahajournals.org/lookup/suppl/doi:10.1161/CIRCHEARTFAILURE.116.003179/-/DC1.

Correspondence to Joanna Chikwe, MD, Department of Cardiovascular Surgery, Mount Sinai Hospital, 1190 Fifth Ave, New York, NY 10029. E-mail Joanna.Chikwe@mountsinai.org

We, therefore, analyzed a statewide patient cohort to identify determinants of survival after ECMO in adult patients.

Methods

Study Design

We performed a retrospective cohort analysis to evaluate clinical outcomes after ECMO using the Statewide Planning and Research Cooperative System (SPARCS), an all-payer, administrative database that prospectively collects patient-level data on every inpatient hospitalization in New York State. Patients in SPARCS are allocated unique identifiers that permit longitudinal analysis of individual outcomes across multiple admissions and discharges. All patients, aged ≥18 years, who received ECMO between January 1, 2003, and December 31, 2014, were identified. ECMO use was defined using the *International Classification of Diseases, Ninth Revision*, Clinical Modification procedure code, 39.65. For patients with >1 ECMO procedure code during the study period, the earliest reported procedure was defined as the index procedure. Patients with non–New York State residency were excluded. Use of ECMO was validated by individual chart review in 5% (n=49) of patients in the cohort with a positive predictive value of 98%. The study was approved by the Program for Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai and the New York State Department of Health data protection review board. These approvals included a waiver of informed consent.

Indications for ECMO Use

To characterize the primary indication for ECMO use, patients were allocated into one of the following mutually exclusive categories: complications after heart transplant (abbreviated as post transplant), acute coronary syndrome, circulatory collapse after a cardiac procedure (post procedure), acute heart failure, or respiratory failure (Table 1). The algorithm for assigning indication categories was hierarchical. For example, a patient was only considered for the acute coronary syndrome category if they did not meet the criteria for complications after heart transplant. These categories were based on suggested indications for percutaneous mechanical circulatory support identified in recent consensus guidelines.[1]

Indication categories were defined using a combination of *International Classification of Diseases, Ninth Revision*, Clinical Modification, procedure and diagnosis codes (Table I in the Data Supplement). Procedure codes were drawn from the index admission record, and, for patients transferred to the index hospitalization from another hospital within 24 hours, the admission immediately preceding it. SPARCS reports dates corresponding to all procedures, and the date of procedure relative to ECMO placement was incorporated into the categorization algorithm. Diagnosis codes were drawn from the index admission record only. SPARCS does not report dates associated with diagnoses, but it does include a flag to distinguish diagnoses present on admission from those that developed during the hospital course. To avoid categorization based on diagnoses that developed as complications of ECMO placement, only diagnosis codes present at the time of admission were considered.

A subset of patients could not be matched into any of the 5 indication categories. These records were reviewed individually and, where the indication for ECMO placement could not be determined, excluded from analysis. The remaining patients made up the study cohort. Baseline demographics for the study cohort were defined using *International Classification of Diseases, Ninth Revision*, Clinical Modification diagnosis codes, from both the index admission and previous inpatient hospitalizations within 2 years of the index visit (Tables II and III in the Data Supplement). From the index record, only diagnoses present at the time of admission were considered.

Study End Points

The primary outcome was all-cause mortality. Secondary outcome measures included stroke, major bleeding, and acute kidney injury (Table IV in the Data Supplement). Dates of death were identified using the full Social Security Death Master File (current as of May 29, 2015) and SPARCS inpatient and emergency department admissions. Stroke was defined as any cerebrovascular event in which either a postoperative iatrogenic complication on the index admission or a primary diagnosis of a hemorrhagic or ischemic cerebrovascular event of any subsequent admission was recorded. This definition excluded transient ischemic attacks. Major bleeding events were identified by a diagnosis of postoperative bleeding, intracerebral hemorrhage, hemopericardium, cardiac tamponade, gastrointestinal hemorrhage, hematuria, hemarthrosis, hemoptysis, epistaxis, or retinal or choroidal hemorrhage during the index admission or requiring subsequent hospital admission within 30 days. Acute kidney injury was defined as a diagnosis of acute renal failure because of nontraumatic causes during the index admission or as a primary diagnosis on any subsequent admission within 30 days.

For patients with index admissions in 2014, outcomes were censored on December 31, 2014, the most recent follow-up date available in SPARCS. For all other patients, outcomes were censored at 1 year after index discharge.

Statistical Analysis

We compared baseline demographics and outcomes over 3 time periods—2003 to 2008, 2009 to 2011, and 2012 to 2014—using χ^2 tests for categorical variables and ANOVA tests for continuous variables. Starting in 2009, ECMO utilization increased sharply in New York State. For this reason, we grouped together patients who received ECMO before 2009 and divided the second half of the study period into cases performed between 2009 and 2011 and between 2012 and

Table 1. Description of Indication Categories and Diagnostic Criteria

Indication Category	Diagnostic Criteria*
Complications after heart transplant	Heart transplant before ECMO during index hospitalization
Acute coronary syndrome	Diagnosis code on admission indicative of acute myocardial infarction, or percutaneous coronary intervention anytime during index admission, or ECMO preceding coronary artery bypass graft procedure during index admission
Circulatory collapse following a cardiac procedure	ECMO on the day of or following cardiac procedure, including valve operation, coronary bypass graft procedure, and repair or dissection and aneurysm, during index admission
Acute heart failure	Diagnosis code on index admission indicative of acute cardiac failure, or ECMO with or without cardiac procedure, including valve operation, coronary bypass graft procedure, and repair or dissection and aneurysm during index admission
Respiratory failure	Diagnosis code on admission indicative of acute respiratory failure, or lung transplant during index admission

ECMO indicates extracorporeal membrane oxygenation.

*The algorithm for assigning indication categories is hierarchical. For example, a patient was only considered for the acute coronary syndrome category if he/she did not meet the criteria for complications following heart transplant. *International Classification of Diseases, Ninth Revision*, Clinical Modification diagnosis and procedure codes are available in Table I in the Data Supplement.

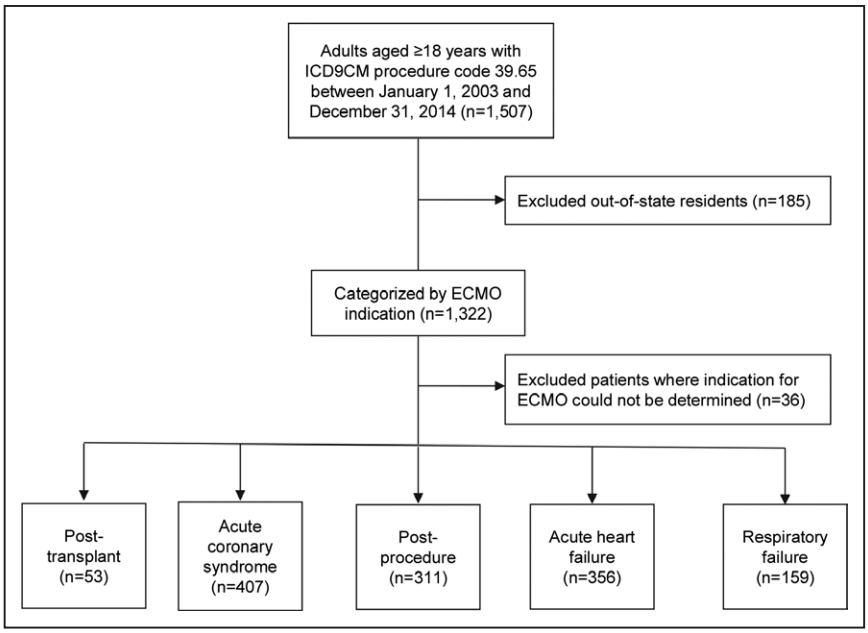

Figure 1. Flow diagram of study design. ECMO indicates extracorporeal membrane oxygenation; and ICD-9-CM, *International Classification of Diseases, Ninth Revision*, Clinical Modification.

2014. Continuous variables were reported as means with SDs, and categorical variables were reported as proportions.

Survival curves for the primary end point of survival within 12 months after ECMO were estimated by the Kaplan–Meier method. Survival estimates with 95% confidence intervals (CIs) were derived from the life table. Differences in survival between indication groups were analyzed using a log-rank test with Sidak adjustment for multiple comparisons. Secondary outcome variables were analyzed using cumulative incidence functions. Gray test was used to detect outcome differences between indication groups.

A multivariable logistic regression model was used to identify risk factors associated with 30-day mortality. Age was defined as a binary variable with flags for patient aged ≤65 and >65 years. Index procedure year was defined as a class variable with years 2003 to 2008 combined in a single level within the class and each subsequent year defined as a unique level. Annual hospital ECMO volume was also included as a covariate: quartiles were created based on hospital ECMO volume for each year of the study period. All statistical tests were 2 tailed. An α level of 0.05 was considered statistically significant, with 95% CIs provided where appropriate. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

Trends in ECMO Utilization

A total of 1507 patients aged ≥18 years were identified. Out-of-state residents (12.3%; n=185) were excluded, leaving 1322 patients. An additional 36 patients (2.4%) were excluded because the indication for ECMO use could not be determined. The remaining 1286 patients made up the study cohort (Figure 1). The number of patients undergoing ECMO in New York State increased from 13 in 2003 to 330 in 2014 (Figure 2). Compared with patients undergoing ECMO before 2009, later patients were older (54.4 versus 52.3 years; *P*=0.013) and more likely to have major comorbidity including chronic kidney disease (25.2% versus 13.2%; *P*=0.02) and liver disease (20.0% versus 10.7%; *P*=0.001). The proportion of patients who required ECMO after a cardiac procedure decreased across the study period (33.1% versus 22.0%; *P*=0.003), whereas the proportion of patients who underwent

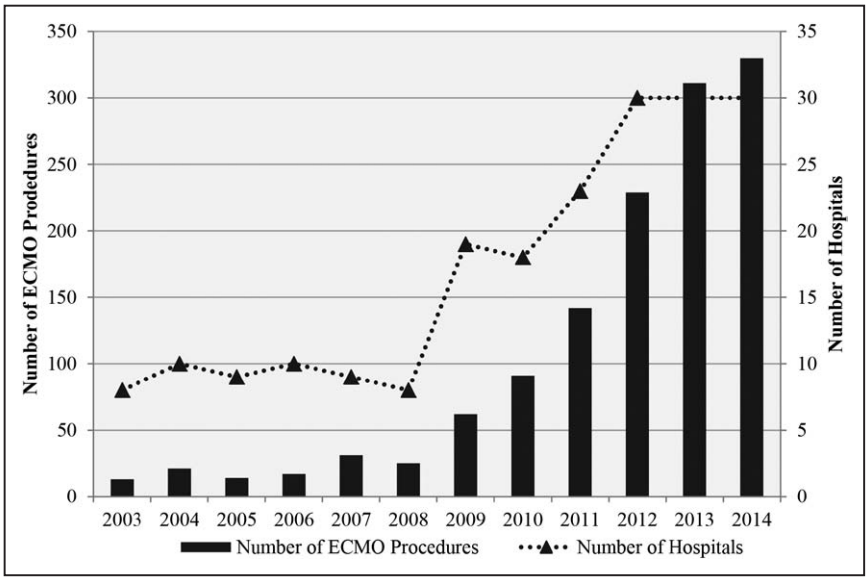

Figure 2. Trends in the use of extracorporeal membrane oxygenation (ECMO).

ECMO in the setting of acute heart failure increased (19.0% versus 29.2%; *P*=0.03). The proportion of patients who underwent ECMO for respiratory failure, acute coronary syndrome including myocardial infarction, and post-transplant remained relatively constant (Table 2).

The number of centers performing ECMO increased from 8 in 2003 to 30 in 2014 (Figure 2), with a sharp increase beginning in 2009. The mean number of ECMO procedures carried out annually by each hospital quadrupled over the study period (2.2 placements annually from 2003 to 2008 versus 9.7 placements annually from 2012 to 2014; *P*<0.001). In 2014, 50% of all hospitals (n=15) carried out between 1 and 5 procedures, and 6 hospitals performed >10 procedures (range, 12–101 procedures).

Mortality

In the overall cohort, 30-day mortality was 52.2% (95% CI, 49.5–54.9%), and 90-day mortality was 57.5% (95% CI, 54.9–60.3%). Survival at 1 year was 38.4% (95% CI, 35.7–41.0%). The 30-day, 90-day, and 1-year mortality (Figure 3) all decreased significantly over the study period (Table 3). Outcomes by ECMO indication at 30 days, 90 days, and 1 year after ECMO placement are shown in Table 4.

In multivariable analysis, several patient-level characteristics were associated with increased 30-day mortality: age >65 years (odds ratio [OR], 2.20; 95% CI, 1.37–3.52), coronary artery disease (OR, 1.45; 95% CI, 1.02–2.06), chronic kidney disease (OR, 1.50; 95% CI, 1.10–2.04), and liver disease (OR, 1.42; 95% CI, 1.02–1.98; Table 5). Cardiopulmonary resuscitation before ECMO placement was also associated with increased mortality (OR, 2.62; 95% CI, 1.76–3.91). Mortality at 30 days was 65.2% for patients aged ≥75 years (n=73/112) and 74.6% in patients who underwent cardiopulmonary resuscitation (n=91/122). Year of ECMO procedure was an independent predictor of survival, with patients undergoing ECMO between 2012 and 2014 more likely to survive to 30 days than patients undergoing ECMO between 2003 and 2008 (Table 5). Annual hospital volume was also independently associated with 30-day mortality. Compared with those in the lowest hospital volume quartile, procedures performed in the highest volume quartile were associated with lower mortality (OR, 0.58; 95% CI, 0.39–0.86; Table 5).

Morbidity

The cumulative incidence of major complications at 30 days differed by indication: risks of stroke, major bleeding, and acute kidney injury were highest in ECMO instituted after heart transplantation, whereas the lowest risks were seen in patients with ECMO instituted for acute heart failure and respiratory failure (Table 4). No significant difference was observed in the cumulative incidences of these complications across the study period. A total of 116 patients underwent bridged open heart surgery

Table 2. Trends in Baseline Characteristics of Adult Patients Undergoing Extracorporeal Membrane Oxygenation

	2003–2008 (n=121)	2009–2011 (n=295)	2012–2014 (n=870)	*P* Value
Demographics				
Age, mean (SD), y	52.3 (16.9)	51.2 (16.6)	54.4 (16.2)	0.013
Male sex, n (%)	70 (57.9)	189 (64.1)	548 (63.0)	0.51
Nonelective admission, n (%)	98 (81.0)	252 (85.4)	758 (87.1)	0.08
Transferred from a different hospital, n (%)	35 (28.9)	106 (35.9)	358 (41.1)	0.005
Baseline comorbidities, n (%)				
Atrial fibrillation	34 (28.1)	66 (22.4)	220 (25.3)	1.00
Coronary artery disease	74 (61.2)	155 (52.5)	477 (54.8)	0.50
Congestive heart failure	70 (57.9)	157 (53.2)	481 (55.3)	0.93
Cerebrovascular disease	10 (8.3)	21 (7.1)	48 (5.5)	0.16
Peripheral vascular disease	<10* (<8.3)	17 (5.8)	53 (6.1)	0.86
Coagulation or platelet disorder	22 (18.2)	39 (13.2)	192 (22.1)	0.02
Chronic kidney disease	16 (13.2)	73 (24.8)	219 (25.2)	0.02
Chronic obstructive pulmonary disease	27 (22.3)	72 (24.4)	239 (27.5)	0.15
Liver disease	13 (10.7)	39 (13.2)	174 (20.0)	0.001
Indication, n (%)				
Post-transplant	<10* (<8.3)	13 (4.4)	33 (3.8)	0.34
Acute coronary syndrome	35 (28.9)	83 (28.1)	289 (33.2)	0.13
Postprocedure	40 (33.1)	80 (27.1)	191 (22.0)	0.003
Acute heart failure	23 (19.0)	79 (26.8)	254 (29.2)	0.03
Respiratory failure	16 (13.2)	40 (13.6)	103 (11.8)	0.48

*Small cell sizes (numbers <10) are suppressed based on our Data Use Agreement with the Statewide Planning and Research Cooperative System.

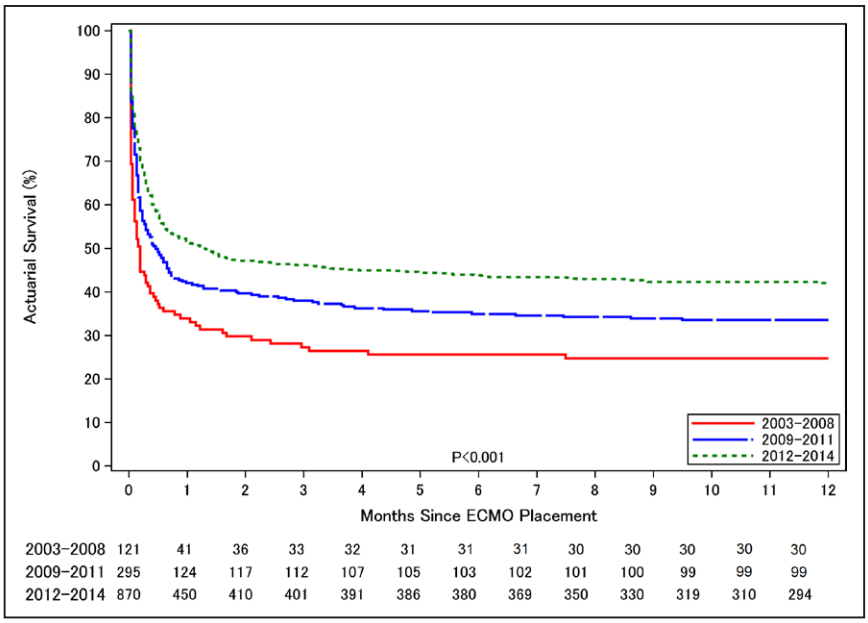

Figure 3. Kaplan–Meier unadjusted 1-year survival estimates after extracorporeal membrane oxygenation (ECMO) by year of admission.

during the index admission or after being transferred to another site of care within 24 hours of index discharge, including 11 for heart transplant, 70 for ventricular assist device placement, 17 for coronary artery bypass graft, 4 for aortic operation, and 28 for valve replacement or repair. Many patients had >1 procedure. Overall, 30-day mortality after bridged procedures was 25% with no significant difference between procedures.

Discussion

This analysis of adult patients undergoing ECMO in New York State demonstrates a rapid increase in utilization of ECMO over the past decade for all patient types. Although there has been significant improvement in 1-year survival rates over this time frame, this rescue strategy remains associated with high rates of both mortality and major morbidity, particularly in older patients. The number of hospitals with ECMO capabilities has also increased, with a wide variation observed in individual hospital ECMO volume. There seemed to be a significant correlation between hospital volume and clinical outcomes.

The sharp increase in ECMO utilization in New York State beginning in 2009 echoes nationally reported trends and occurs in parallel with increased usage of other forms of mechanical circulatory support, including intra-aortic balloon

Table 3. Outcomes After Extracorporeal Membrane Oxygenation by Year of Admission

	2003–2008 (n=121)	2009–2011 (n=295)	2012–2014 (n=870)	*P* Value
Disposition at discharge, n (%)				
Dead	80 (66.1)	172 (58.3)	444 (51.0)	<0.001
Discharged home	13 (10.7)	40 (13.6)	164 (18.9)	<0.001
Home healthcare	28 (23.1)	80 (27.2)	248 (28.5)	0.24
Other	0 (0)	<10* (<3.4)	14 (1.6)	0.22
Mortality, n (%) [95% CI]				
30-d	80 (66.1) [57.7–74.4]	171 (58.0) [52.6–63.6]	420 (48.3) [45.0–51.6]	<0.001
90-d	88 (72.7) [64.6–80.3]	183 (62.0) [56.5–67.6]	469 (53.9) [50.6–57.3]	<0.001
1-y	91 (75.2) [67.3–82.5]	196 (66.4) [61.0–71.8]	504 (58.1) [54.8–61.4]	<0.001
Other outcomes during index admission or within 30 d of ECMO, n (%) [95% CI]†				
Acute kidney injury	29 (24.0) [16.8–31.8]	61 (20.7) [16.3–25.5]	182 (20.9) [18.3–23.7]	0.60
Major bleeding	35 (28.9) [21.1–37.2]	102 (34.7) [29.3–40.1]	278 (32.0) [29.0–35.1]	0.93
Stroke	<10* (<8.3)	29 (9.8) [6.8–13.6]	76 (8.7) [7.0–10.7]	0.32

CI indicates confidence interval; and ECMO, extracorporeal membrane oxygenation.

*Small cell sizes (numbers below 10) are suppressed based on our Data Use Agreement with the Statewide Planning and Research Cooperative System.

†We report outcomes within 30 days of ECMO placement for index hospitalizations with a length of stay of <30 days and in-hospital outcomes for index hospitalizations >30 days.

Table 4. Morbidity and Mortality by Indication for Extracorporeal Membrane Oxygenation

	Post-Transplant (n=53)	Acute Coronary Syndrome (n=407)	Postcardiotomy (n=311)	Acute Heart Failure (n=356)	Respiratory Failure (n=159)	*P* Value
Mortality, n (%), [95% CI]						
30-d	23 (43.4) [31.4–57.7]	228 (56.0) [51.4–60.9]	199 (64.0) [58.7–69.3]	166 (46.6) [41.6–51.9]	55 (34.6) [27.8–42.5]	<0.001
90-d	28 (52.8) [40.2–66.6]	248 (60.9) [56.2–65.7]	216 (69.5) [64.3–74.5]	184 (51.7) [46.6–57.0]	64 (40.3) [32.6–48.3]	<0.001
1-y	30 (56.6) [43.9–70.1]	263 (64.8) [60.0–69.4]	232 (74.8) [69.9–79.5]	200 (56.2) [51.2–61.4]	66 (41.5) [34.3–49.6]	<0.001
Other outcomes during index admission or within 30-d of discharge, n (%) [95% CI]						
Acute kidney injury	17 (32.1) [20.0–44.8]	88 (21.6) [17.8–25.7]	80 (25.7) [21.0–30.7]	46 (13.0) [9.7–16.6]	41 (25.9) [19.3–32.8]	<0.001
Major bleeding	26 (49.1) [35.1–61.6]	134 (32.9)[28.4–37.5]	130 (41.8) [36.3–47.2]	90 (25.3) [20.9–29.9]	35 (22.0) [15.9–28.7]	<0.001
Stroke	<10* (<18.9)	46 (11.3) [8.5–14.6]	23 (7.4) [4.8–10.6]	27 (7.6) [5.1–10.6]	<10* (<6.3)	0.01

*Small cell size (numbers <10) are suppressed based on Data Use Agreement with Statewide Planning and Research Cooperative System.

counterpulsation and percutaneous indwelling mechanical assist devices.[10,11] Expansion in the use of mechanical circulatory support devices may result from more liberal application, suggested by the greater age and comorbidity of patients later in the study period and from greater availability of both expertise and percutaneous options. For example, although pulsatile mechanical support devices are largely restricted to centers with ventricular assist device programs, the availability of centrifugal pumps, including portable preassembled packs, has allowed for the expansion of ECMO use beyond cardiac operating rooms to emergency departments, cardiac catheterization laboratories, and critical care units.[1,6] In cardiac surgery units, ECMO is increasingly used as a bail-out strategy after cardiac surgery, including heart and lung transplantation.[8,9]

Expansion in both the availability and application of ECMO may explain the progressive improvements in 30-day and 12-month outcomes observed between 2003 and 2014, despite the fact that patients later in the cohort were older with more comorbidities. Earlier placement of ECMO before circulatory or respiratory collapse complicated by multiorgan failure or need for prolonged cardiopulmonary resuscitation has been associated with improved early clinical outcomes.[15] In addition, it seems likely that increased institutional experience with ECMO over the study period contributed to improved patient selection, management, and outcomes.

Outcomes of patients on ECMO are a specific focus in the 2016 Thoracic Organ Transplantation Committee proposal to better stratify the most medically urgent heart transplant candidates in the heart allocation system.[18] In this proposal, patients on venoarterial ECMO are designated the highest priority status, primarily because of their high mortality without transplant. Among the arguments against this stratification is the poor post-transplant prognosis: in the United Network for Organ Sharing draft proposal, the 1-year mortality of 25 registry patients who underwent ECMO followed by heart transplant in the index admission between 2010 and 2011 was 24%, which is comparable to a 1-year mortality of 18.2% for this subgroup in our study cohort.[18,19] Additional criteria, such as indication for or duration of ECMO or the duration of previous cardiopulmonary resuscitation efforts, may be warranted to identify patients for whom heart transplant would likely be futile. An argument for the stratification of patients on ECMO as high priority for heart transplant is the relatively low number of these patients. However, this is unlikely to remain the case: our analysis shows increasingly steep growth in ECMO utilization, and it has been suggested that the revised heart allocation stratification may incentivize additional use of ECMO in candidates listed for heart transplant.[19]

This study also has broader implications for patient selection. Age has previously been shown to be an independent risk factor for increased mortality after ECMO, which we confirmed in this analysis.[8,16,17] Mortality was particularly high in the small group of patients aged ≥75 years. Clearly, significant questions surround the expanded use of this highly invasive and resource intensive modality in a patient group for whom the intervention seems futile. Concentrating experience at an institutional level through specialized Shock Teams may help to optimize patient selection. A mandatory national clinical registry that builds on the voluntary registry maintained by the Extracorporeal Life Support Organization and contains longitudinal data on all patients undergoing ECMO could also provide greater clarity on patient subgroups that may be better served by other therapeutic or palliative modalities.

Strengths and Limitations

The main advantage of using a mandatory, statewide database that allows for longitudinal follow-up is the opportunity to analyze key patient outcomes in a large patient population both during and after hospital admission, in a range of hospital settings. Other available clinical databases, such as the Society of Thoracic Surgeons Adult Cardiac Database and the Extracorporeal Life Support Organization registry, are limited to clinical outcomes during the index admission or within 30 days. Linking of the Society of Thoracic Surgeons database with Medicare data allows for longer term follow-up but limits analysis to patients aged ≥65 years of age who are enrolled in Medicare Fee-For-Service. There are, however, significant limitations in administrative data sets such as the one utilized in this study, primarily centering on the accuracy and completeness of coding and the lack of key clinical information. The study is limited by the absence of several confounding variables that are not included in the data set, including clinical parameters such as the timing, duration, and type of cardiopulmonary resuscitation; severity of organ dysfunction; specific indication for ECMO; and the method, duration, and effectiveness of ECMO placement. Finally, the data set

Table 5. Predictors of 30-Day Mortality After ECMO

Predictor of Mortality	OR	95% CI
Demographics		
Age, y		
18–65	Reference	
>65	2.20	1.37–3.52
Male sex	0.89	0.69–1.14
Nonelective admission	0.88	0.60–1.30
Transferred from a different hospital	1.25	0.96–1.62
Baseline comorbidities		
Atrial fibrillation	0.86	0.64–1.15
Coronary artery disease	1.45	1.02–2.06
Congestive heart failure	0.73	0.56–0.96
Cerebrovascular disease	1.09	0.66–1.81
Peripheral vascular disease	1.02	0.61–1.71
Coagulation or platelet disorder	1.38	1.01–1.88
Chronic kidney disease	1.50	1.10–2.04
Chronic obstructive pulmonary disease	1.06	0.80–1.41
Liver disease	1.42	1.02–1.98
Year of admission		
2003–2008	Reference	
2009	0.78	0.39–1.57
2010	0.68	0.37–1.27
2011	0.86	0.49–1.51
2012	0.49	0.29–0.83
2013	0.55	0.33–0.91
2014	0.54	0.32–0.90
Annual hospital ECMO volume		
0–25th percentile (1–6 procedures)	Reference	
26–50th percentile (7–17 procedures)	1.28	0.89–1.83
51–75th percentile (21–41 procedures)	0.74	0.50–1.08
76–100th percentile (52–101 procedures)	0.58	0.39–0.86
Indication		
Acute coronary syndrome	Reference	
Post-transplant	1.14	0.52–2.50
Post-cardiac procedure	1.74	1.08–2.81
Acute heart failure	1.32	0.85–2.07
Respiratory failure	0.81	0.46–1.43
Support before ECMO placement		
Mechanical ventilator for >96 h	0.80	0.63–1.03
Intra-aortic balloon pump	1.30	0.97–1.74
Cardiopulmonary resuscitation	2.62	1.76–3.91

CI indicates confidence interval; ECMO, extracorporeal membrane oxygenation; and OR, odds ratio.

C statistic = 0.710; Hosmer–Lemeshow Goodness-of-fit test, P=0.937.

provides no information on functional outcome and no data on patients hospitalized outside of New York State, potentially causing us to underestimate the rate of secondary end points.

Conclusions

Between 2003 and 2014, use of ECMO to rescue circulatory and respiratory collapse increased 20-fold in New York State, with a concomitant modest improvement in patient survival despite significantly increased baseline comorbidity. This rescue strategy remains associated with high rates of both mortality and major morbidity, particularly after cardiopulmonary resuscitation and in elderly patients, who may be better served by a more selective approach in the end-of-life setting.

Sources of Funding

This study was funded by a grant from the Medical Student Training in Aging Research Program from the American Federation for Aging Research and the National Institute on Aging.

Disclosures

None.

References

1. Rihal CS, Naidu SS, Givertz MM, Szeto WY, Burke JA, Kapur NK, Kern M, Garratt KN, Goldstein JA, Dimas V, Tu T. 2015 SCAI/ACC/HFSA/STS clinical expert consensus statement on the use of percutaneous mechanical circulatory support devices in cardiovascular care (endorsed by the American Heart Association, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of Value by the Canadian Associaton of Interventional Cardiology – Association Canadienne de Cardiologie d'intervention). *J Cardiac Failure*. 2015; 65:499–515.
2. Zapol WM, Snider MT, Hill JD, Fallat RJ, Bartlett RH, Edmunds LH, Morris AH, Peirce EC 2nd, Thomas AN, Proctor HJ, Drinker PA, Pratt PC, Bagniewski A, Miller RG Jr. Extracorporeal membrane oxygenation in severe acute respiratory failure. A randomized prospective study. *JAMA*. 1979;242:2193–2196.
3. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, Hibbert CL, Truesdale A, Clemens F, Cooper N, Firmin RK, Elbourne D; CESAR Trial Collaboration. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet*. 2009;374:1351–1363. doi: 10.1016/S0140-6736(09)61069-2.
4. Brodie D, Bacchetta M. Extracorporeal membrane oxygenation for ARDS in adults. *N Engl J Med*. 2011;365:1905–1914. doi: 10.1056/NEJMct1103720.
5. Richard C, Argaud L, Blet A, Boulain T, Contentin L, Dechartres, A, Dejode J, Donetti L, Fartoukh M, Fletcher D, Kuteifan K, Lasocki S, Liet J, Lukaszewicz A, Mal H, Maury E, Osman D, Outin H, Richard J, Schneider F, Tamion F. Extracorporeal life support for patients with acute respiratory distress syndrome: report of a consensus conference. *Ann Intensive Care*. 2014; 4:15.
6. Burkhoff D, Sayer G, Doshi D, Uriel N. Hemodynamics of Mechanical Circulatory Support. *J Am Coll Cardiol*. 2015;66:2663–2674. doi: 10.1016/j.jacc.2015.10.017.
7. Mugford M, Elbourne D, Field D. Extracorporeal membrane oxygenation for severe respiratory failure in newborn infants. *Cochrane Database Syst Rev*. 2008;3:CD001340.
8. Stretch R, Sauer CM, Yuh DD, Bonde P. National trends in the utilization of short-term mechanical circulatory support: incidence, outcomes, and cost analysis. *J Am Coll Cardiol*. 2014;64:1407–1415. doi: 10.1016/j.jacc.2014.07.958.
9. McCarthy FH, McDermott KM, Kini V, Gutsche JT, Wald JW, Xie D, Szeto WY, Bermudez CA, Atluri P, Acker MA, Desai ND. Trends in U.S. extracorporeal membrane oxygenation use and outcomes: 2002-2012. *Semin Thorac Cardiovasc Surg*. 2015;27:81–88. doi: 10.1053/j.semtcvs.2015.07.005.

10. Maxwell BG, Powers AJ, Sheikh AY, Lee PH, Lobato RL, Wong JK. Resource use trends in extracorporeal membrane oxygenation in adults: an analysis of the Nationwide Inpatient Sample 1998-2009. *J Thorac Cardiovasc Surg*. 2014;148:416–21.e1. doi: 10.1016/j.jtcvs.2013.09.033.
11. Tramm R, Davies AR, Pellegino VA, Romero L, Hodgson C. Extracorporeal membrane oxygenation for critically ill adults. *Cochrane Database Syst Rev*. 2015;1:CD010381.
12. Chang CH, Chen HC, Caffrey JL, Hsu J, Lin JW, Lai MS, Chen YS. Survival analysis after extracorporeal membrane oxygenation in critically ill adults: A Nationwide Cohort Study. *Circulation*. 2016;133:2423–2433. doi: 10.1161/CIRCULATIONAHA.115.019143.
13. Feldman D, Pamboukian SV, Teuteberg JJ, Birks E, Lietz K, Moore SA, Morgan JA, Arabia F, Bauman ME, Buchholz HW, Deng M, Dickstein ML, El-Banayosy A, Elliot T, Goldstein DJ, Grady KL, Jones K, Hryniewicz K, John R, Kaan A, Kusne S, Loebe M, Massicotte MP, Moazami N, Mohacsi P, Mooney M, Nelson T, Pagani F, Perry W, Potapov EV, Eduardo Rame J, Russell SD, Sorensen EN, Sun B, Strueber M, Mangi AA, Petty MG, Rogers J; International Society for Heart and Lung Transplantation. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. *J Heart Lung Transplant*. 2013;32:157–187. doi: 10.1016/j.healun.2012.09.013.
14. Takayama H, Truby L, Koekort M, Uriel N, Colombo P, Mancini DM, Jorde UP, Naka Y. Clinical outcome of mechanical circulatory support for refractory cardiogenic shock in the current era. *J Heart Lung Transplant*. 2013;32:106–111. doi: 10.1016/j.healun.2012.10.005.
15. Rastan AJ, Dege A, Mohr M, Doll N, Falk V, Walther T, Mohr FW. Early and late outcomes of 517 consecutive adult patients treated with extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. *J Thorac Cardiovasc Surg*. 2010;139:302–11, 311.e1. doi: 10.1016/j.jtcvs.2009.10.043.
16. Flécher E, Anselmi A, Corbineau H, Langanay T, Verhoye JP, Félix C, Leurent G, Le Tulzo Y, Malledant Y, Leguerrier A. Current aspects of extracorporeal membrane oxygenation in a tertiary referral centre: determinants of survival at follow-up. *Eur J Cardiothorac Surg*. 2014;46:665–671; discussion 671. doi: 10.1093/ejcts/ezu029.
17. Schmidt M, Burrell A, Roberts L, Bailey M, Sheldrake J, Rycus PT, Hodgson C, Scheinkestel C, Cooper DJ, Thiagarajan RR, Brodie D, Pellegrino V, Pilcher D. Predicting survival after ECMO for refractory cardiogenic shock: the survival after veno-arterial-ECMO (SAVE)-score. *Eur Heart J*. 2015;36:2246–2256. doi: 10.1093/eurheartj/ehv194.
18. Callahan LR. UNOS Policy Department. Proposal to modify the adult heart allocation system. OPTN/UNOS Thoracic Organ Transplantation Committee public comment proposal. https://optn.transplant.hrsa.gov/governance/public-comment/adult-heart-allocation-changes-2016/. Accessed August 17, 2016.
19. Kobashigawa J, Teuteberg J, Colvin M, Edwards L, Duan T, Luu M, Patel J, Vega JD, Meyer D; Forum Participants. Proceedings of the AST heart allocation meeting at the American Transplant Congress, Philadelphia, Pennsylvania, May 4, 2015. *Clin Transplant*. 2016; 30:641–648. doi: 10.1111/ctr.12717.

CLINICAL PERSPECTIVE

Utilization of extracorporeal membrane oxygenation in adults has increased six-fold since 2008 with ≈3000 patients receiving extracorporeal membrane oxygenation in the United States in 2012, but supporting data from clinical trials or mandatory registries to define appropriate use are limited. This analysis of 1286 adult patients who underwent extracorporeal membrane oxygenation in New York State between 2003 and 2014 showed that mortality improved over this time frame even as patient age and baseline comorbidity rose. Higher volume centers seemed to have better outcomes. However, we observed high rates of morbidity and mortality, particularly in elderly patients and those requiring cardiopulmonary resuscitation, highlighting the important role of a more selective approach in the utilization of this highly invasive and resource intensive modality in these end-of-life settings.

Extracorporeal Membrane Oxygenation in New York State: Trends, Outcomes, and Implications for Patient Selection

Jaya Batra, Nana Toyoda, Andrew B. Goldstone, Shinobu Itagaki, Natalia N. Egorova and Joanna Chikwe

Circ Heart Fail. 2016;9:
doi: 10.1161/CIRCHEARTFAILURE.116.003179
Circulation: Heart Failure is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 1941-3289. Online ISSN: 1941-3297

SUPPLEMENTAL MATERIAL

Supplemental Table 1. Criteria used to define ECMO indication groups. The algorithm is hierarchical (e.g. a patient is only considered for the acute coronary syndrome category if he does not meet the criteria for complications following heart transplant).

Indication Category	International Classification of Diseases, 9th Edition, Clinical Modification codes
1. Complications post heart transplant	Heart transplant Procedure codes (ECMO placed on the day of or after heart transplantation) 3751
2. Acute coronary syndrome	ST elevated myocardial infarction Diagnosis codes (primary diagnosis or present on admission) 4100, 41000, 41001, 41002, 4101, 41010, 41011, 41012, 4102, 41020, 41021, 41022, 4103, 41030, 41031, 41032, 4104, 41040, 41041, 41042, 4105, 41050, 41051, 41052, 4106, 41060, 41061, 41062, 4108, 41080, 41081, 41082 Non-ST elevated myocardial infarction Diagnosis codes (primary diagnosis or present on admission) 4107, 41070, 41071, 41072, 4109, 41090, 41091, 41092 Percutaneous coronary intervention Procedure code (ECMO placed anytime relative to procedure) 0066, 1755, 3601, 3602, 3603, 3604, 3605, 3606, 3607, 3608, 3609 Coronary artery bypass graft Procedure code (ECMO placed prior to procedure) 3610, 3611, 3612, 3613, 3614, 3615, 3616, 3617, 3619
3. Cardiac failure following cardiac procedure	Valvuloplasty or valvotomy Procedure code (ECMO placed on day of or after procedure) 350, 3500, 3501, 3502, 3503, 3504, 351, 2510, 3511, 3512, 3513, 3514 Valve replacement Procedure code (ECMO placed on day of or after procedure) 352, 3520, 3521, 3522, 3523, 3524, 3525, 3526, 3527, 3528 Other valve operations Procedure code (ECMO placed on day of or after procedure) 3596, 3597 Operation on structures adjacent to heart valves Procedure code (ECMO placed on day of or after procedure) 353, 3531, 3532, 3533, 3534, 3535, 3539 Septal operation Procedure code (ECMO placed on day of or after procedure) 354, 3541, 3542, 355, 3550, 3551, 3552, 3553, 3554, 3555, 356, 3560, 3561, 3562, 3563, 357, 3570, 3571, 3572, 3573, 3598 Coronary artery bypass graft Procedure code (ECMO placed on day of or after procedure)

Indication Category	International Classification of Diseases, 9th Edition, Clinical Modification codes
	3610, 3611, 3612, 3613, 3614, 3615, 3616, 3617, and 3619 Cardiotomy and pericardiotomy Procedure code (ECMO placed on day of or after procedure) 371, 3710, 3711, 3712 Pericardiectomy and excision of lesions of heart Procedure code (ECMO placed on day of or after procedure) 3731, 3732, 3733, 3734, 3735, 3736, 3737 Other repair of heart and pericardium Procedure code (ECMO placed on day of or after procedure) 3749 Open repair of major dissection or aneurysm with coronary vessel involvement Procedure code (ECMO placed on day of or after procedure) 3691 Open repair of major dissection or aneurysm with aortic involvement Procedure code (ECMO placed on day of or after procedure) 3834, 3844, 3845, 3864, 3804, 3814 Open repair of major dissection or aneurysm with thoracic vessel involvement Procedure code (ECMO placed on day of or after procedure) 3835, 3865, 3805, 3815 Open repair of major dissection or aneurysm with abdominal vessel involvement Procedure code (ECMO placed on day of or after procedure) 3836, 3846, 3866, 3806, 3816 Endovascular aortic repair Procedure code (ECMO placed on day of or after procedure) 3971, 3973, 3978 Implantable heart assist device Procedure code (ECMO placed on day of or after procedure) 3765, 3766, 3760
4. Acute heart failure	Rheumatic valve disease Diagnosis code (primary diagnosis or present on admission) 394, 3940, 3941, 3942, 3949, 395, 3950, 3951, 3952, 3959, 396, 3960, 3961, 3962, 3963, 3968, 3969, 397, 3970, 3971, 3979 Non-rheumatic valve disease Diagnosis code (primary diagnosis or present on admission) 4240, 4241, 4242, 4243 Myocarditis Diagnosis code (primary diagnosis or present on admission) 422, 4220, 4229, 3912, 07423, 03282

Indication Category	International Classification of Diseases, 9th Edition, Clinical Modification codes
	Pericarditis Diagnosis code (primary diagnosis or present on admission) 420, 4200, 4209, 3910, 03641, 07421 Cardiomyopathy Diagnosis code (primary diagnosis or present on admission) 425, 4250, 4251, 4252, 4253, 4254, 4255, 4257, 4258, 4259 Conduction disorders Diagnosis code (primary diagnosis or present on admission) 426, 4260, 4261, 42610, 42611, 42612, 42613, 4262, 4263, 4264, 4265, 42650, 42651, 42652, 42653, 42654, 4266, 4267, 4268, 42681, 42682, 42689, 4269 Cardiac dysrhythmia Diagnosis code (primary diagnosis or present on admission) 427, 4270, 4271, 4272, 4273, 42731, 42732, 4274, 42741, 42742, 4275, 4276, 42760, 42761, 42769. 4278, 42781, 42789, 4279 Acute heart failure Diagnosis code (primary diagnosis or present on admission) 42820, 42821, 42823, 42830, 42831, 42833, 42840, 42841, 42843, 4281 Shock Diagnosis code (primary diagnosis or present on admission) 7855, 78550, 78551, 78552, 78559 Aneurysm and dissection of heart Diagnosis code (primary diagnosis or present on admission) 4141, 41410, 41411, 41412, 41419 Aortic dissection Diagnosis code (primary diagnosis or present on admission) 4410, 44100, 44101, 44102, 44103 Ruptured aortic aneurysm Diagnosis code (primary diagnosis or present on admission) 4411, 4413, 4415, 4416 Hemothorax Diagnosis code (primary diagnosis or present on admission) 8602, 8603 Pneumohemothorax Diagnosis code (primary diagnosis or present on admission) 8604, 8605 Cardiac injury Diagnosis code (primary diagnosis or present on admission)

Indication Category	International Classification of Diseases, 9th Edition, Clinical Modification codes
	8610, 86100, 86101, 86102, 86103 <u>Iatrogenic cardiac complications</u> Diagnosis code (primary diagnosis or present on admission) 9960, 99600, 99601, 99602, 99603, 99604, 99609, 9961, 99661, 99662, 99671, 99672, 99674, 99683, 9971 <u>ECMO placement prior to cardiac procedure</u> Procedure codes for heart transplant and all procedure codes defined in group 3 with ECMO placed prior to date of procedure.
5. Respiratory failure	<u>Acute respiratory failure</u> Diagnosis code (primary diagnosis or present on admission) 51881, 51882, 51884, 7991 <u>Pulmonary embolism</u> Diagnosis code (primary diagnosis or present on admission) 4151 <u>Pulmonary congestion</u> Diagnosis code (primary diagnosis or present on admission) 514 <u>Acute pulmonary edema</u> Diagnosis code (primary diagnosis or present on admission) 5184 <u>Pulmonary collapse</u> Diagnosis code (primary diagnosis or present on admission) 512, 5180 <u>Pneumonia</u> Diagnosis code (primary diagnosis or present on admission) 00322, 0203, 0204, 0205, 0212, 0221, 0310, 0391, 0521, 0551, 0730, 0830, 1124, 1140, 1144, 1145, 11505, 11515, 11595, 1304, 1363, 4800, 4801, 4802, 4803, 4808, 4809, 481, 4820, 4821, 4822, 4823, 48230, 48231, 48232, 48239, 4824, 48240, 48241, 48242, 48249, 4828, 48281, 48282, 48283, 48284, 48289, 4829, 483, 4830, 4831, 4838, 4841, 4843, 4845, 4846, 4847, 4848, 485, 486, 5130, 5171 <u>Influenza</u> Diagnosis code (primary diagnosis or present on admission) 487, 4870, 4871, 4878, 488 <u>Other lower respiratory infections</u> Diagnosis code (primary diagnosis or present on admission) 466, 4660, 4661, 46611, 46619, 510, 5100, 5109, 511, 5110, 5111, 5118, 51181, 51189, 5119, 513, 5130, 5131 <u>Acute bronchitis</u> Diagnosis code (primary diagnosis or present on admission)

Indication Category	International Classification of Diseases, 9th Edition, Clinical Modification codes
	490, 4910, 4911, 49121, 49122 <u>Emphysema</u> Diagnosis code (primary diagnosis or present on admission) 4920, 4928 <u>Acute bronchiectasis</u> Diagnosis code (primary diagnosis or present on admission) 4941, 49421, 49322 <u>Cystic fibrosis</u> Diagnosis code (primary diagnosis or present on admission) 2770 <u>Pneumoconioses</u> Diagnosis code (primary diagnosis or present on admission) 500, 501, 502, 503, 504, 505 <u>Other environmental exposures</u> Diagnosis code (primary diagnosis or present on admission) 495, 4950, 4951, 4952, 4953, 4954, 4955, 4956, 4957, 4958, 4959, 5060, 5061, 5062, 5063, 507, 5070, 5071, 5078, 508, 5080, 5081, 5088, 5089 <u>Pulmonary fibrosis</u> Diagnosis code (primary diagnosis or present on admission) 515, 5163 <u>Bronchus and lung malignancies</u> Diagnosis code (primary diagnosis or present on admission) 135, 162, 1620, 1622, 1623, 1624, 1625, 1628, 1629 <u>Iatrogenic lung injury</u> Diagnosis code (primary diagnosis or present on admission) 5185, 99684 <u>Other acute respiratory conditions</u> Diagnosis code (primary diagnosis or present on admission) 516, 5160, 5162, 5168, 5169, 517, 5171, 5172, 5173, 5178, 5181, 5182, 5183, 5186, 5187, 5188, 51883, 51889 <u>Lung transplant</u> Procedure code (anytime during index admission) 335, 3350, 3351, 3352

Supplemental Table 2. Definitions of baseline comorbidities

Baseline characteristic	International Classification of Diseases, 9th Edition, Clinical Modification codes
Atrial fibrillation	Diagnosis codes (from index and prior admissions) 4273, 42731, 42732
Coagulation or platelet disorders	Diagnosis codes (from index and prior admissions) 286, 2861-2865, 28652, 28653, 28659, 2866, 2867, 2869, 287, 2870-2873, 28730, 28731, 28732, 28733, 28739, 2874, 2875, 2878, 2879
Coronary artery disease	<u>Un-revascularized</u> Diagnosis codes (from index and prior admissions) 410, 4100, 41000, 41001, 41002, 4101, 41010, 41011, 41012, 4012, 40120, 41021, 41022, 4103, 41030, 41031, 41032, 4104, 41040, 41041, 41042, 4105, 41050, 41051, 41052, 4106, 41060, 41061, 41062, 4107, 41070, 41071, 41072, 4108, 41080, 41081, 41082, 4109, 41090, 41091, 41092, 411, 4110, 4111, 4118, 41181, 41189, 412, 413, 4130, 4131, 4139, 414, 4140, 41400, 41401, 41402, 41403, 41404, 41405, 41406, 41407, 4142, 4143, 4144, 4295, 4296, 4297, 42971, 42979 <u>Prior percutaneous coronary intervention</u> Diagnosis codes (from index and prior admissions) V4582 Procedure codes (from prior admissions) 0066, 1755, 3601, 3602, 3603, 3604, 3605, 3606, 3607, 3608, 3609 <u>Prior coronary artery bypass grafting</u> Diagnosis codes (from index and prior admissions) V4581 Procedure codes (from prior admissions) 3610, 3611, 3612, 3613, 3614, 3615, 3616, 3617, 3619
Peripheral vascular disease	Diagnosis codes (from index and prior admissions) 4400, 4401, 4402, 44020, 44021, 44022, 44023, 44024, 44029, 4403, 44030, 44031, 44032, 4404, 4408, 4409, 4471, 9961, 99662, 99674, V434
Cerebrovascular disease	Diagnosis codes (from index and prior admissions) 3623, 36230, 36231, 36232, 36233, 36234, 36235, 36236, 36237, 3466, 34660, 34661, 34662, 34663, 430, 431, 432, 4320, 4321, 4329, 433, 4330, 43300, 43301, 4331, 43310, 43311, 4332, 43320, 43321, 4333, 43330, 43331, 4338, 43380, 43381, 4339, 43390, 43391, 434, 4340, 43400, 43401, 4341, 43410, 43411, 4349, 43490, 43491, 435, 4350, 4351, 4352, 4353, 4358, 4359, 436, 437, 4370, 4371, 4372, 4373, 4374, 4375, 4376, 4377, , 99702, 4378, 4379, 438, 4380, 4381, 43810, 43811, 43812, 43813, 43814, 43819, 4382, 43820, 43821, 43822, 4383, 43830, 43831, 43832, 4384, 43840, 43841, 43842, 4385, 43850, 43851, 43852, 4386, 4387, 4388, 43881, 43882, 43883, 43884, 43885, 43889, 4389
Congestive heart failure	Diagnosis codes (from index and prior admissions) 39891, 428, 4280, 4281, 4282, 42820, 42821, 42822, 42823, 4283, 42830, 42831, 42832, 42833, 4284, 42840, 42841, 42842, 42843, 4289, 429, 4290, 4291, 4292, 4293, 4294, 4295, 4296, 4297, 42971, 42979, 4298, 42981, 42982, 42983, 42989, 4299
Chronic obstructive pulmonary disease	Diagnosis codes (from index and prior admissions) 491, 4910, 4911, 4912, 49120, 49121, 49122, 4918, 4919, 492, 4920, 4928, 493, 4930, 49300, 49301, 49302, 4931, 49310, 49311, 49312, 4932, 49320, 49321, 49322, 4938, 49380, 49381, 49382, 4939, 49390, 49391, 49392, 494, 4940, 4941,

Baseline characteristic	International Classification of Diseases, 9th Edition, Clinical Modification codes
	496
Chronic kidney disease	Non-dialysis-dependent Diagnosis codes (from index and prior admissions) 403, 4030, 40300, 40301, 4031, 40310, 40311, 4039, 40390, 40391, 404, 4040, 40400, 40401, 40402, 40403, 4041, 40410, 40411, 40412, 40413, 4049, 40490, 40491, 40492, 40493, 582, 5820, 5821, 5822, 5824, 5828, 58281, 58289, 5829, 583, 5830, 5831, 5832, 5834, 5836, 5837, 5838, 58381, 58389, 5839, 585, 5851, 5852, 5853, 5854, 5855, 5859, 586, 587, 588, 5880, 5881, 5888, 58881, 58888, 5889, V420, V56 Dialysis-dependent Diagnosis codes (from index and prior admissions) V560, V561, V562, V563, V5631, V5632, V568, V451, V4511, V4512, 5856
Liver disease	Diagnosis codes (from index and prior admissions 070, 0700, 0701, 0702, 07020, 07021, 07022, 07023, 0703, 07030, 07031, 07032, 07033, 0704, 07041, 07042, 07043, 07044, 07049, 0705, 07051, 07052, 07053, 07054, 07059, 0706, 0707, 07070, 07071, 0709, 456, 4560, 4561, 4562, 45620, 45621, 4563, 4564, 4565, 4566, 4568, 570, 571, 5710, 5711, 5712, 5713, 5714, 57140, 57141, 57142, 57149, 5715, 5716, 5718, 5719, 572, 5720, 5721, 5722, 5723, 5724, 5728, 573, 5730, 5731, 5732, 5733, 5734, 5735, 5738, 5738, 7824, 7891, 7895, 78951, 78959, 7904, 7905, 7948, V427

Supplemental Table 3. Support measures used during index admission

Supportive Measure	International Classification of Diseases, 9th Edition, Clinical Modification codes
Mechanical ventilator for >96 hours	Procedure code (from index hospitalization or previous admission with date of transfer within 24 hours of index admission) 9672
Pulsating balloon	Procedure code (from index hospitalization or previous admission with date of transfer within 24 hours of index admission) 3761
Cardiopulmonary resuscitation	Procedure code (from index hospitalization or previous admission with date of transfer within 24 hours of index admission) 9960, 9393

Supplemental Table 4. Definition of secondary endpoints and 30-day complications

Outcome	International Classification of Diseases, 9th Edition, Clinical Modification codes
Stroke	Iatrogenic stroke Diagnosis code (from index hospitalization or primary diagnosis of subsequent admissions) 99702 Hemorrhagic stroke Diagnosis codes (from index hospitalization or primary diagnosis of subsequent admissions) 430, 431, 432, 4320, 4321, 4329 Ischemic stroke Diagnosis codes (from index hospitalization or primary diagnosis of subsequent admissions) 43301, 43311, 43321, 43331, 43381, 43391, 43401, 43411, 43491
Acute kidney injury	Diagnosis code (from index hospitalization or primary diagnosis of subsequent admissions) 5849
Major bleeding event	Post-operative hemorrhage Diagnosis codes (from index hospitalization or primary diagnosis of subsequent admissions) 99811 Intracerebral hemorrhage Diagnosis codes (from index hospitalization or primary diagnosis of subsequent admissions) 430, 431, 432, 4320, 4321, 4329 Hemopericardium or cardiac tamponade Diagnosis codes (from index hospitalization or primary diagnosis of subsequent admissions) 4230 and 4233 Gastrointestinal hemorrhage Diagnosis codes (from index hospitalization or primary diagnosis of subsequent admissions) Acute 4560, 45620, 4590, 53021, 5310, 53100, 53101, 5312, 53120, 53121, 5320, 53200, 53201, 5322, 53220, 53221, 5330, 53300, 53301, 5332, 53320, 53321, 5340, 53400, 53401, 5342, 53420, 53421, 5693, 578, 5780, 5781, 5789 Chronic 5314, 53140, 53141, 5316, 53160, 53161, 5324, 53240, 53241, 5326, 53260, 53261, 5330, 53300, 53301, , 5334, 53340, 533401, 5336, 53360, 53361, 5344, 53440, 53441, 5346, 53460, 5346, 53501, 53511, 53521, 53531, 53541, 53551, 53561, 53571 Hematuria

	Diagnosis codes (from index hospitalization or primary diagnosis of subsequent admissions) 5997, 59970, 59971 <u>Hemarthrosis</u> Diagnosis codes (from index hospitalization or primary diagnosis of subsequent admissions) 7191, 71910, 71911, 71912, 71913, 71914, 71915, 71916, 71917, 71918, 71919 <u>Hemoptysis</u> Diagnosis codes (from index hospitalization or primary diagnosis of subsequent admissions) 7848, 7863, 78630, 78639 <u>Epistaxis</u> Diagnosis codes (from index hospitalization or primary diagnosis of subsequent admissions) 7847 <u>Retinal/choroidal hemorrhage</u> Diagnosis codes (from index hospitalization or primary diagnosis of subsequent admissions) 36281, 36243, 36361, 36362