

Original Articles

A Simple Scoring System to Predict Survival after Venoarterial Extracorporeal Membrane Oxygenation

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Abstract: Patients undergoing consideration for venoarterial extracorporeal membrane oxygenation (VA ECMO) require an immediate risk profile assessment in the setting of incomplete or no information. A retrospective cohort study of 100 patients undergoing VA ECMO placement at three institutions was carried out. Variables strongly associated with survival to discharge were used to calculate a risk stratification score. Indications for VA ECMO support included postcardiotomy shock (24%), ischemic etiologies (33%), nonischemic cardiomyopathy (32%), and other etiologies (11%). Pre-VA ECMO arrest occurred in 69%, and 30% of patients underwent cannulation during arrest. Survival to discharge was 38%. Three variables demonstrated a strong trend toward predicting survival to discharge: lactate >10 mmol/L ($p = .054$), albumin <3 g/dL ($p = .062$), and platelet

count <180 K/uL ($p = .064$), and these variables were included in a scoring system. The extremes of age and duration of pre-VA ECMO ventilation were associated with a dismal prognosis and were also included. These five variables were used to construct a mortality prediction score. A score of 0 was associated with 10% expected mortality, whereas a score of 4+ was associated with 100% expected mortality. Mortality increased in a stepwise fashion with increasing scores. The expected mortality closely paralleled the observed mortality. A simple scoring system composed of easily collected variables may help predict mortality. However, it is not intended to replace an experienced clinician's judgment, but to enhance it. **Keywords:** ECMO, circulatory assistance, temporary, shock, statistics, risk analysis/modeling, cardiomyopathy. *J Extra Corpor Technol. 2019;51:133–9*

Venoarterial extracorporeal membrane oxygenation (VA ECMO) is increasingly used in the setting of cardiogenic shock or cardiac arrest to support oxygenation, improve hemodynamics, and allow for end-organ perfusion. It may be used as a bridge to recovery, or to further interventions such as percutaneous coronary intervention, left ventricular assist device insertion, heart transplant, or other cardiac surgery (1). As it is frequently used emergently with incomplete clinical information, it is usually used as a “bridge to decision.” However, VA ECMO requires significant financial and human resources, and thus, some degree of patient selection is critical to appropriately allocate this expensive but lifesaving therapy to those with a reasonable chance of deriving benefit (2–4).

As VA ECMO is frequently instituted at the bedside in emergent settings, mechanisms to predict outcomes rapidly but with some degree of accuracy are needed. Several survival prediction models for severe respiratory failure requiring venovenous ECMO have been devised (5–9). Several institutional studies and a few registry studies have described predictors of survival after VA ECMO for cardiogenic shock or cardiac arrest (10–12). However, very few survival prediction models exist, with varying degrees of complexity (13–18). We describe our experience with VA ECMO for cardiogenic shock and cardiac arrest patients at three affiliated institutions with the goal of creating a simple risk stratification scoring system easily implemented at the bedside to predict survival to discharge.

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MATERIALS AND METHODS

This study was a retrospective cohort study of all patients undergoing VA ECMO placement at three affiliated

academic institutions from 2010 to 2017. Data regarding pre-ECMO parameters, cannulation strategies, and outcomes including complications, and weaning were collected. The primary binary endpoint was survival to discharge. This work has been reported in line with the STROCSS criteria (19). The study was approved by the New York Methodist Hospital Institutional Review Board (Board Ref #1382246; date of approval 2/5/2019).

Patients underwent VA ECMO for cardiogenic shock or cardiac arrest in the setting of postcardiotomy shock, acute myocardial infarction/ischemic cardiomyopathy, non-ischemic cardiomyopathy, or rarely pulmonary or other etiologies. Cardiogenic shock was typically defined as 1) a systolic blood pressure of less than 90 mmHg despite the use of maximum doses of vasopressors; 2) a cardiac index less than 2.0 L/m² despite the use of inotropic agents and other forms of mechanical support, including intra-aortic balloon pump (IABP) counterpulsation or impella (Abiomed, Danvers, MA); 3) elevated filling pressures, including pulmonary capillary wedge pressure greater than 16 mmHg or central venous pressure greater than 18 mmHg, or pulmonary edema on chest x-ray; and 4) evidence of end-organ malperfusion, including oliguria, elevated lactate levels, and markers of renal or hepatic function. Pre-ECMO hemodynamic and laboratory variables collected were the last values available within 24 hours of ECMO placement. A creatinine level of 4 mg/dL was assigned to any patient on hemodialysis at the time of ECMO cannulation. Contraindications for VA ECMO included the presence of 1) advanced age, 2) neurologic injury, 3) active bleeding or absolute contraindications to anticoagulation, 4) active malignancy, 5) prolonged downtime after cardiac arrest, 6) severe sepsis, or 7) any other factor thought to represent a profound limitation of life expectancy. The final decision to institute VA ECMO was made by the treating physicians, including cardiothoracic surgeons, interventional and heart failure cardiologists, and cardiac intensivists. Patients were treated in a uniform manner with regard to cannulation techniques, anticoagulation strategies, and other aspects of post-operative management across all three centers as most of the treating team members, including surgeons and perfusionists, are the same at all centers.

The VA ECMO circuit consisted of either the Bio-Medicus (Medtronic, Minneapolis, MN) or the CentriMag (Levitronix, Waltham, MA) pump, and a Quadrox-D oxygenator (Maquet, Wayne, NJ). The circuits were similar across all patients. Femoral, axillary, and central aortic arterial cannulation and femoral, internal jugular, and central right atrial venous cannulation strategies were used depending on the clinical scenario and surgeon preference. Bedside femoral cannulation was most commonly performed in emergent scenarios precluding patient transfer as in the intensive care unit or emergency room, or in the

cardiac catheterization suite at the time of percutaneous coronary intervention. The arterial cannulae used were the Fem-Flex cannula (Edwards Lifesciences Corp, Irvine, CA) and the BioMedicus cannula (Medtronic). The venous cannula used was the RAP venous cannula (LivaNova, London, UK). Central aortic and right atrial cannulation was most commonly used in the setting of postcardiotomy shock after cardiac surgery in the operating room. Axillary cannulation was used semi-electively when a patient failed to wean from femoral VA ECMO as a preferred long-term cannulation strategy to allow for patient mobilization or in the setting of lower extremity vascular complications secondary to femoral cannulation. Ipsilateral antegrade limb perfusion sheaths as a general institutional policy were used in all cases of femoral cannulation when feasible, either by percutaneous placement with or without ultrasound guidance or via surgical cutdown. IABP and impella were used at the discretion of the treating physician for left ventricular decompression, particularly in the absence of cardiac ejection. Patients were heparinized to an activated clotting time of 250 seconds for cannulation and maintained at a partial thromboplastin time of 45–60 seconds during the course of VA ECMO support, except in the presence of bleeding complications or severe coagulopathy secondary to thrombocytopenia or hepatic dysfunction with an elevated international normalized ratio, in which case, heparin dosages were reduced or held. Activated clotting times were measured using the i-STAT handheld blood analyzer (Abbott Laboratories, Abbott Park, IL) and i-STAT kaolin-activated clotting time activator (Abbott Laboratories).

Statistical Analysis

Continuous variables were described as the mean and standard deviation and compared with the Student's *t* test. Categorical variables were described as frequency and percentages and compared with the chi-squared test or Fisher's exact test, as appropriate. A *p* value of .05 or less was considered significant. All variables were assessed for correlation with survival to discharge on univariate analysis. Those variables with a *p* < .2 were included in a multivariable logistic regression analysis. Continuous variables were dichotomized using the 50th percentile as a cutoff. Variables strongly associated with survival to discharge on multivariable regression analysis were used to calculate a risk score for survival after VA ECMO placement. Each factor was given a weight of one, and a score was determined based on the number of such variables. The observed mortality rate for each score was determined. Furthermore, the expected mortality and confidence interval for each score were determined by regressing the score to the probability of death as described by Ryan et al. (20) The number of risk factors (*x*) was regressed to the natural logarithm of the ratio of the

probability of dying to the probability of living (y). The slope and y -intercept of this curve as well as their 95% confidence intervals were determined and used to develop the equation which describes this relationship as the following: $y = -1.58(x) + 2.23$. The expected mortality and 95% confidence interval for a given number of risk factors could, thus, be calculated from this relationship. All analyses were performed with Stata 13 (StataCorp LLC, College Station, TX).

RESULTS

Between 2010 and 2017, 100 patients underwent VA ECMO placement for cardiogenic shock or cardiac arrest at our three institutions (57, 39, and 4 patients, respectively). The mean age was 56 years and 44% were female. Indications for VA ECMO support included postcardiotomy shock after cardiac surgery in 24%, ischemic cardiomyopathy (including acute myocardial infarction) in 33%, nonischemic cardiomyopathy in 32%, and other etiologies in 11%. Cardiac arrest before VA ECMO occurred in 69% with an average downtime of 33 minutes, and 30% of patients underwent cannulation during cardiac arrest (extracorporeal cardiopulmonary resuscitation [ECPR]). Peripheral cannulation was used in 91% of cases and central aortic/right atrial cannulation in 9%. Of those undergoing peripheral cannulation, 96% were via femoral cannulation and 4% were via axillary cannulation. Of those undergoing initial femoral cannulation, 7% underwent conversion to central or axillary cannulation for a variety of reasons, including lower extremity ischemia, differential cyanosis, or to allow for mobilization. IABP was used in 44% and impella in 10% for left ventricular decompression.

In univariable analysis, pre-ECMO factors significantly associated with survival to discharge included lactate level (10.5 vs. 7.6 mmol/L; $p = .021$), albumin level (2.7 vs. 3.2 g/dL; $p = .008$), platelet count (163 vs. 210 K/uL; $p = .015$), and hematocrit (31.8 vs. 36.2%; $p = .010$). Demographic, hemodynamic, and laboratory parameters are listed in Table 1. Although age was not associated with survival to discharge, very advanced age was detrimental as no patient aged older than 80 years survived to discharge (Figure 1). Similarly, although disease chronicity (as determined by duration of pre-ECMO mechanical ventilation) was not associated with survival to discharge, very prolonged periods of illness were detrimental as no patient with a duration of pre-ECMO mechanical ventilation of five or more days survived to discharge (Figure 2).

Patients remained on VA ECMO support for an average of 8.6 days. Two patients underwent emergent cardiac surgery while on VA ECMO support (one coronary artery bypass surgery and one pulmonary embolectomy). Both remained on VA ECMO support postoperatively and did

not survive to discharge. One patient was weaned from VA ECMO support and underwent subsequent mitral valve replacement and coronary artery bypass grafting, and another was weaned and underwent subsequent left ventricular assist device placement. Both patients survived to discharge. Overall, 58% of patients were successfully weaned from VA ECMO support, and of these, 71% survived to discharge. The overall survival to discharge was 38%.

In multivariable analysis, although no single variable independently predicted decreased survival to discharge with statistical significance, three variables demonstrated a strong trend: lactate >10 mmol/L (OR .25; $p = .054$), albumin <3 g/dL (OR .30; $p = .062$), and platelet count <180 K/uL (OR .32; $p = .064$ [Table 2]) and were included in the scoring system. The extremes of age and duration of pre-ECMO mechanical ventilation were associated with a dismal prognosis. For this reason and because of their clinical relevance, these parameters, although not demonstrating significance in multivariable analysis, were also included. These five variables were used to construct a survival prediction score, where each parameter was assigned a value of 1, with a range of possible scores from 0 to 5 (Table 3).

The observed and expected mortality of each score are displayed in Table 4. A score of 0 was associated with 10% expected mortality, whereas a score of 4 was associated with 100% expected mortality. Mortality increased in a stepwise fashion with increasing scores.

DISCUSSION

In the present study describing the VA ECMO experience at three affiliated institutions, the overall survival to discharge was 38%. Albumin and lactate levels and platelet count demonstrated strong trends toward decreased survival to discharge. In addition, the extremes of age and duration of pre-ECMO mechanical ventilation were also associated with dismal survival to discharge. These parameters were incorporated into a survival prediction score. Low scores predicted a high likelihood of survival to discharge, whereas higher scores portended a poor prognosis.

Despite its lifesaving potential, ECMO is fraught with complications, most commonly bleeding and thrombotic complications, the two of which create a constant dilemma between the need for anticoagulation and hemostasis (2–4). In addition, neurologic injury, vascular complications, renal failure, shock liver, and sepsis are all well-described sequelae (2–4). Allocation of this heroic resource to those most likely to benefit is crucial to appropriately allocate limited precious financial and human resources and to avoid prolonging patient suffering and the associated

Table 1. Pre-ECMO patient characteristics.

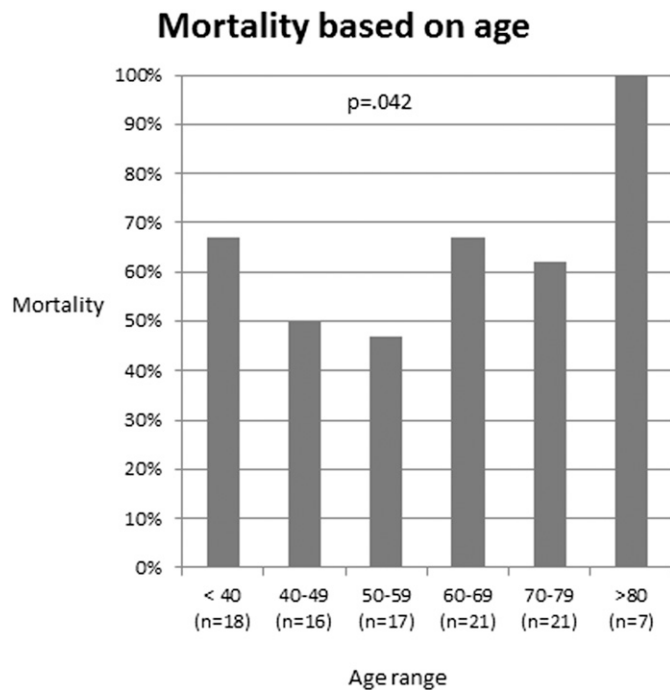
	Survival to Discharge		p Value	
	Overall (100)	No (62)		Yes (38)
Age (years)	56.4	58.1	52.9	.153
Female (%)	44 (44)	29/44	15/44	.432
Body surface area (m ²)	1.89	1.88	1.90	.660
ECPR (%)	30 (30)	22/30	8/30	.114
Cardiac arrest (%)	69 (69)	42/69	27/69	.817
Downtime (minutes)	33	38.6	24.6	.067
Etiology				.171
Postcardiotomy shock (%)	24 (24)	18/23	5/23	
Ischemic cardiomyopathy (%)	33 (33)	17/49	16/33	
Nonischemic cardiomyopathy (%)	32 (32)	18/32	14/42	
Other (%)	11 (11)	8/11	3/11	
Postcardiotomy shock (%)	24 (24)	18/23	5/23	.061
Mechanical ventilation time (days)	1.2	1.7	.5	.2
Lactate (mmol/L)	9.3	10.5	7.6	.021
pH	7.24	7.24	7.24	.865
Bicarbonate (mmol/L)	19.3	19.2	19.6	.747
Albumin (g/dL)	2.9	2.7	3.2	.008
Total bilirubin (mg/dL)	1.7	1.9	1.4	.236
Alanine aminotransferase (unit/L)	300	361	203	.354
Aspartate aminotransferase (unit/L)	476	597	284	.201
Creatinine (mg/dL)	2	2.1	1.7	.109
PO ₂ (mmHg)	124	129	132	.560
Platelet count (K/uL)	181	163	210	.015
International normalized ratio	1.88	2.02	1.67	.247
White blood cell count (K/uL)	19.4	16.1	26.4	.294
Hematocrit (%)	33.5	31.8	36.2	.010
Ejection fraction (%)	39	41	36	.331

emotional trauma inflicted on the family in the setting of medical futility (21).

Analyses of the variables associated with survival after long-term implantable ventricular assist devices underscore

the importance of a thorough evaluation focusing on age, functional status, and comorbidities, including end-organ function (22,23). The circumstances surrounding a patient in cardiogenic shock or cardiac arrest are distinctly different with regard to the frequent need for an immediate risk profile assessment in the setting of incomplete or no information (24). Age, lactate levels, etiology of cardiogenic shock, end-organ function, and prior cardiac arrest are all known to predict survival after ECMO (13–18). However, the abundance of studies and variables studied allow for limited utility in survival prediction in any given emergent clinical scenario.

Only a few survival prediction models exist for VA ECMO. Schmidt et al. created the SAVE scoring system using the Extracorporeal Life Support Organization (ELSO) registry to predict survival to discharge (13). While incorporating a large number of patients from a registry, limitations include exclusion of ECPR patients and the cumbersome nature of the score, which requires several variables to calculate. The ENCOURAGE score was created using a bi-institutional database and predicts survival to ICU discharge (15). Whereas the model demonstrated good discriminatory power, it was somewhat cumbersome for use in the emergent setting and is only applicable to patients in cardiogenic shock from acute myocardial infarction. Validation of various other risk prediction models designed for critically ill patients, including the Acute Physiology and Chronic Health

**Figure 1.** Mortality based on age.

Mortality based length of pre-ECMO mechanical ventilation

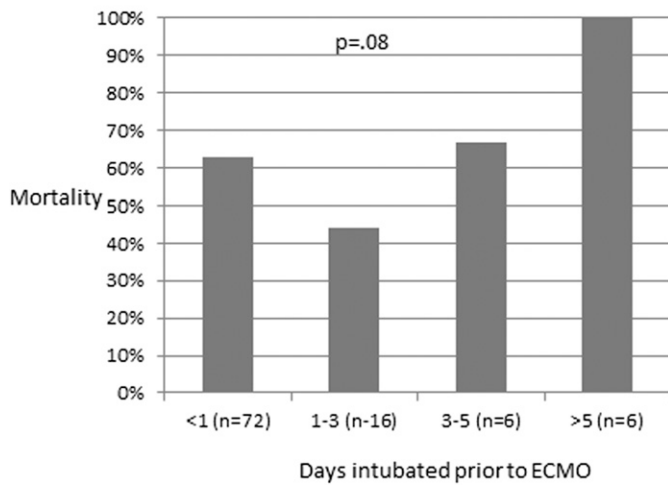


Figure 2. Mortality based on length of pre-ECMO mechanical ventilation.

Evaluation; Age, Creatinine, and Ejection Fraction; Sequential Organ Failure Assessment (SOFA); GRACE model, Dutch University Hospital; SHOCK trial and registry; and Simplified Acute Physiology score, has demonstrated variable discriminatory power in the VA ECMO population (13–15,18,25).

One study assessing outcomes after short-term ventricular assist device placement created a simple scoring system but included preoperative and postoperative day 3 variables (23). The argument was made that in emergent scenarios, laboratory and hemodynamic assessments tend to vary indiscriminately, rendering any score calculated at this time unreliable, and that the accuracy of such scores is improved when calculated at a time when these parameters have stabilized. The unsaid implication is that patients should be liberally placed on mechanical support, with risk prediction models used shortly thereafter to guide withdrawal of care. This, of course, raises numerous ethical and cost-effectiveness concerns.

In the present study, albumin and lactate levels and platelet count demonstrated strong trends toward survival

Table 2. Independent predictors of survival to discharge.

	Ratio	p Value	95% Confidence Interval
Albumin <3 g/dL	.30	.062	.09–1.06
Lactate >10 mmol/L	.25	.054	.06–1.03
Hematocrit <33%	.62	.467	.17–2.28
Platelets <180 K/uL	.32	.064	.09–1.07
Age >56 years	.37	.126	.10–1.32
Postcardiotomy shock	.96	.965	.15–6.08
Creatinine >2 mg/dL	.78	.713	.21–2.90
ECPR	.43	.261	.10–1.86
Intubated >1.3 days	.76	.744	.14–4.01

Table 3. Parameters included in the mortality prediction score.

Parameter	Points
Intubated >5 days	1
Lactate >10 mmol/L	1
Platelets <180 K/uL	1
Albumin <3 g/dL	1
Age >80 years	1

to discharge and were included in the scoring system. Albumin has not been demonstrated in prior ECMO studies to be associated with survival, although it is a component of other risk prediction models for critically ill patients such as the Child–Pugh score for cirrhosis mortality and the Charlson comorbidity index. Similarly, platelet count, although not an independent predictor of mortality after ECMO in most studies, is also a component of other risk prediction models for critically ill patients such as the SOFA score. Both are likely markers of chronic illness and may suggest a lack of reserve and the inability of such patients to tolerate the severe shock scenario, leading to institution of ECMO. Furthermore, damage to blood components from the ECMO circuit can create significant thrombocytopenia, and preexisting thrombocytopenia may, thus, exacerbate the resulting coagulopathy observed after prolonged periods of ECMO support. Lactate levels typically correlate with the length of time of preexisting shock. It has been well described as a predictor of survival after VA ECMO and is a parameter in other such scoring systems (15,17), although conflicting results are observed here as well (16,24). Interestingly, lactate levels were not assessed in the creation of the ELSO registry–based SAVE score but have subsequently been demonstrated to improve outcome prediction when combined with the SAVE score (14).

Age and illness chronicity defined as duration of pre-ECMO hospital stay or mechanical ventilation have demonstrated an association with survival after venoarterial (13) and venovenous ECMO (5–9) in prior studies and are variables included in the other risk scores. In the present study, these parameters did not emerge as independent predictors of survival on multivariable regression using the 50th percentile as a cutoff value. However, the upper extremes of age (>80 years) and duration of pre-ECMO mechanical ventilation (>5 days) were associated with abysmal survival rates as no patient

Table 4. Mortality prediction score.

Points	Observed Mortality	Expected Mortality (%)	95% CI (%)
0	32% (6/19)	10	4–20
1	56% (20/36)	35	7–78
2	74% (20/27)	72	11–98
3	87% (13/15)	87	17–99.8
4+	100% (3/3)	100	26–100

older than 80 years or intubated greater than 5 days survived to discharge. This is notable, given the inherent selection bias such that any patient older than 80 years was otherwise likely to be a very favorable ECMO candidate, given that this age represents a relative contraindication for ECMO at our institution.

The expected mortality as determined using this risk score showed an overlap of confidence intervals, such that we can only say that patients with a score of 4+ have significantly increased mortality compared with those with a score of 0. This is likely due to underpowering. In addition, each risk factor, while given an equal weight of 1, actually carries a different risk of mortality as can be observed by the differing odds ratios and mortality rates. Thus, any given score, although assigned a given expected mortality, actually carries a risk of mortality that is different based on which factors it was composed of. However, the simplicity gained from such a system with even weighting of each factor is a benefit gained by this shortcoming. The utility of a risk score relies on its ability to predict mortality and its practicality and ease of use.

Regardless of the accuracy of the predictions made by the risk scoring system, there is evidence that an expert surgical opinion is as accurate, if not better. This merely reflects the fact that an expert clinician can not only assess prognosis but also take into account the institutional facilities available and the patients' and families' wishes. Thus, our score is only meant to augment the judgment of clinicians to better equip them at making decisions (24).

Limitations of this study include those inherent to a retrospective analysis using chart review, including incomplete data, potential inaccuracies in data, and potential for selection bias. A major limitation was the small sample size. The patient cohort included an inhomogeneous group of etiologies, including ischemic and non-ischemic cardiomyopathy as well as postcardiotomy shock and a variety of cannulation strategies. However, dividing the cohort into more homogenous groups would significantly limit statistical power, given the small sample size. Data on right ventricular function and pulmonary congestion were not readily available but are known to predict outcomes after ECMO. In addition, because of differences in clinical practice across centers, extrapolation of results may be of limited value. Age greater than 80 years and duration of pre-ECMO mechanical ventilation greater than 5 days should represent absolute contraindications rather than parameters in a scoring system, considering that they perfectly predicted mortality. However, we are hesitant to suggest that any patient be denied consideration for ECMO based on such a small population sample, and therefore, these parameters were incorporated into the scoring system rather than considered as absolute contraindications.

CONCLUSIONS

In conclusion, mortality after VA ECMO as a salvage therapy for cardiogenic shock remains high. A simple scoring system composed of easily collected preoperative variables may help predict mortality in these patients. Such a scoring system can be used to provide prognostic information that would ultimately guide patient management and counseling of patients' families. However, it is not intended to replace, but rather to be used in conjunction with, an experienced clinician's judgment to influence the decision in a particular case to place a patient on VA ECMO.

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