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The prognostic role of the CHA_2DS_2-VASc score in patients with acute myocardial infarction receiving extracorporeal membrane oxygenation following out-of-hospital cardiac arrest

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ABSTRACT

Aims: The CHA_2DS_2-VASc scoring system has been widely used for stroke risk stratification in patients with atrial fibrillation, yet evidence regarding its prognostic value in other critical settings remains limited. This study aimed to assess the utility of the CHA_2DS_2-VASc score in predicting mortality in patients with acute myocardial infarction (AMI) who received veno-arterial extracorporeal membrane oxygenation (VA-ECMO) support following out-of-hospital cardiac arrest.

Methods: This retrospective study included 41 patients with AMI requiring VA-ECMO after OHCA. Baseline demographics, clinical characteristics, and prognostic scores, including CHA_2DS_2-VASc, SAVE (Survival After Veno-Arterial ECMO), Glasgow Coma Scale (GCS), and acute physiology and chronic health evaluation (APACHE) II were recorded. Patients were categorized into three risk groups based on the CHA_2DS_2-VASc score: low (0 points), moderate (1 point), and high (≥2 points). According to the SAVE score, patients were classified into five risk groups: class I (≥5 points), class II (1–4 points), class III (−4 to 0 points), class IV (−9 to −5 points), and class V (≤−10 points). The primary outcome was in-hospital mortality.

Results: The overall in-hospital mortality rate was 58.5%. Patients with high risk group had a significantly higher mortality risk (HR: 3.12, 95% CI: 1.28-7.63, p=0.008). The SAVE score had the highest diagnostic performance, with a sensitivity of 81.2% and specificity of 76.5% (AUC=0.80). CHA_2DS_2-VASc (AUC=0.74) and APACHE II (AUC=0.72) also demonstrated good predictive performance. While CHA_2DS_2-VASc maintained a balanced sensitivity (70.8%) and specificity (64.7%), APACHE II had higher sensitivity (75.7%) but lower specificity (58.8%). GCS demonstrated the lowest diagnostic performance (AUC=0.68).

Conclusion: While the SAVE score, a risk model specifically designed for VA-ECMO, provides a strong prognostic evaluation, the CHA_2DS_2-VASc score could be a simple and easily applicable tool for early risk stratification in this high-risk population.

Keywords: CHA2DS2-VASc score, extracorporeal membrane oxygenation, cardiogenic shock, mortality

INTRODUCTION

Out-of-hospital sudden cardiac arrests (OHCA) continue to be a significant clinical issue, with acute coronary syndromes being the most prevalent etiological factor, especially in patients above 35 years of age.[1] Rapid and effective intervention is crucial in cardiac arrest. Although standard cardiopulmonary resuscitation (CPR) approaches can effectively reestablish circulation in numerous cases, they may be insufficient in ensuring optimal tissue perfusion and oxygenation for patients with refractory cardiac arrest.[2] In these complex scenarios, extracorporeal membrane oxygenation (ECMO) has been proposed as a promising rescue option. Specifically, veno-arterial ECMO (VA-ECMO) serves as a temporary cardiopulmonary support system by performing the heart's pumping function and the lungs' oxygenation, thereby preserving organ perfusion and increasing survival likelihood.[3,4]

The application of ECMO requires substantial resources and is an invasive procedure, with varying success rates among patients.[5-7] Hence, forecasting the prognosis of patients receiving ECMO therapy is crucial for avoiding unnecessary aggressive treatments and optimizing resource utilization. At this stage, various scoring systems have been developed as potential tools for predicting survival. One such scoring system is the SAVE (survival after veno-arterial ECMO) score, designed to predict survival in patients receiving VA-ECMO for refractory cardiogenic shock. This model assesses key clinical variables, including age, weight, underlying cardiac diagnosis, pre-ECMO organ dysfunction (such as

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renal or hepatic impairment), duration of intubation before ECMO initiation, and various vital signs or hemodynamic parameters.[8] Other scoring systems include the ENCOURAGE mortality risk score, Sequential Organ Failure Assessment (SOFA), Simplified Acute Physiology Score (SAPS) II, and Acute Physiology and Chronic Health Evaluation (APACHE) II.[9-11] However, their diagnostic performance differs between studies and continues to be an important area of investigation.[8-11]

The CHA_2DS_2-VASc score is designed to evaluate stroke risk in patients with atrial fibrillation and incorporates key cardiovascular risk factors, including congestive heart failure (CHF), hypertension, age (≥75 and 65–74), diabetes, previous stroke/transient ischaemic attack (TIA), vascular disease, and female sex.[12] Thus, it functions as a practical tool that indicates a patient's chronic comorbidity load. Additionally, its prognostic value has been validated in several studies conducted on populations beyond atrial fibrillation.[13-15] However, its effectiveness in predicting survival outcomes in patients undergoing ECMO therapy after cardiac arrest remains unexplored.

Considering that the SAVE and CHA_2DS_2-VASc scoring systems incorporate essential cardiovascular risk factors, we assumed that the CHA_2DS_2-VASc score might function as a useful prognostic tool for estimating survival outcomes in patients undergoing ECMO therapy after cardiac arrest. Therefore, this study aimed to compare the prognostic value of the VA-ECMO score and CHA_2DS_2-VASc score in predicting survival outcomes in patients with acute myocardial infarction (AMI) undergoing ECMO therapy following OHCA.

METHODS

This retrospective study was conducted on OHCA patients who underwent ECMO therapy at the coronary and cardiovascular surgery intensive care unit (ICU) of Lokman Hekim University Health Practice and Research Center between January 2020 and December 2024. The study was approved by the Lokman Hekim University Non-interventional Clinical Researches Ethics Committee (Date: 30.12.2024, Decision No: 2024/13) and was carried out in accordance with the relevant ethical guidelines and the Helsinki Declaration (2013 Brazil revision). The need for informed consent was waived under the approval of the local ethics committee due to the retrospective design.

During the study period, a total of 2054 who admitted to the emergency department due to OHCA were retrospectively evaluated. Exclusion criteria included patients under 18 years old, those with chronic obstructive pulmonary disease, those with myocarditis, those with previous ECMO treatment, those with refractory VT/VF, those with heart or lung transplantation, those with malignancy or terminal organ failure, those diagnosed with severe neurological impairment or brain death, cases of profound pre-resuscitation hypothermia (<28°C), pregnant women, and patients with incomplete medical records. Following the exclusion criteria, a total of 42 patients were included in the final analysis.

Data Collection and Definitions

The hospital's electronic information system and patient files were used to gather demographic and clinical data. Pre-existing severe neurological disease or injury, malignancy, or other comorbidities with an extremely short expected survival, along with severe peripheral vascular disease, were regarded as contraindications for ECMO.[16,17] CHF was defined as recently decompensated heart failure, independent of left ventricular ejection fraction (LVEF) or the detection of moderate-to-severe left ventricular systolic dysfunction on cardiac imaging, even in asymptomatic cases.[18] Hypertension was defined as prior use of antihypertensive medications or a systolic/diastolic blood pressure of ≥140/90 mm Hg. Diabetes mellitus was defined as prior insulin or antidiabetic drug use or a fasting glucose level of ≥126 mg/dl. Transient ischemic attack (TIA) and systemic embolism were considered equivalent risk factors for stroke.[19] A history of myocardial infarction, peripheral arterial disease, or complex aortic plaques was considered indicative of vascular disease. Chronic renal failure (CRF) was defined as the presence of kidney damage or a glomerular filtration rate (GFR) below 60 mL/min/1.73 m^2 for at least 3 months. Acute renal failure (ARF) was defined as a creatinine level exceeding 1.5 mg/dl, regardless of the need for renal replacement therapy. Acute liver failure (ALF) was defined as total bilirubin ≥33 µmol/L or ALT/AST levels >70 U/L at the initiation of ECMO. The definition of acute central nervous system dysfunction (CNS) dysfunction included neurotrauma, stroke, encephalopathy (confusion or impaired consciousness), cerebral embolism, seizures, and epileptic syndromes.[20]

In the CHA_2DS_2-VASc scoring system, 1 point was assigned for CHF, hypertension, diabetes mellitus, age 65–74 years, female sex, and vascular disease, while 2 points were given for age ≥75 years and a prior stroke/TAI.[12] Patients were categorized into two groups according to their admission CHA_2DS_2-VASc score: the low risk group (CHA_2DS_2-VASc score 0), moderate risk group (CHA_2DS_2-VASc score), and the high risk group (CHA_2DS_2-VASc ≥ 2).[21]

The SAVE score was assessed using previously established factors, including age, weight, pre-existing cardiac disease, organ dysfunction before ECMO (such as renal or hepatic impairment), intubation duration before ECMO initiation, and various hemodynamic or vital parameters.[8] Based on the SAVE score, patients are classified into five risk groups: class I risk (≥5 points), class II (1–4 points), class III (−4 to 0 points), class IV (−9 to −5 points), and class V (≤−10 points). Higher SAVE scores indicate better survival chances, while lower scores correlate with increased mortality risk.[8]

ECMO Procedure

At our institution, ECMO initiation and weaning protocols align with widely accepted clinical strategies. Peripheral VA-ECMO cannulation was performed in the ICU using the percutaneous Seldinger technique via the femoral vessels. To prevent thromboembolic complications during ECMO support, unfractionated heparin infusion was administered, targeting an activated clotting time (ACT) of 180–200 seconds and an activated partial thromboplastin time (aPTT) of 60–80 seconds. The ECMO pump flow rate was adjusted

to maintain adequate perfusion and hemodynamic stability, with additional support provided as needed through fluid resuscitation, blood products, inotropes, or vasopressors. Neurological function was regularly assessed using the Glasgow Coma Scale (GCS), including evaluations of consciousness, motor responses, and sensory function. For sedated patients, daily sedation interruptions were performed to facilitate neurological assessment. ECMO weaning was considered once the patient achieved hemodynamic stability, either with minimal pharmacological support or independently. The patient's circulatory status was evaluated at an ECMO flow rate of 1 L/min, and ECMO support was discontinued if sufficient perfusion was maintained without mechanical assistance.

Statistical Analysis

All data were analyzed with STATA/MP v.16 software (StataCorp LLC, Texas, USA). Numerical data determined to be normally distributed based on the results of Kolmogorov-Smirnov tests are given as mean±standard deviation values, while non-normally distributed variables are given as median (25^{th}-75^{th} quartiles) values. Student T test or Mann-Whitney U test were used for comparisons between two groups. Categorical variables were presented as numbers and percentages, and comparisons between groups were performed using Chi-square and Fisher-exact tests. Mortality was evaluated using Cox regression analysis, and the results were expressed as hazard ratios (HR) with 95% confidence intervals (CI). ROC curve analysis was used to assess diagnostic performance, with threshold values determined via the Youden index method. AUC curves were compared using a nonparametric approach, employing the generalized U-statistics method to estimate the covariance matrix, as previously described by DeLong et al.[22] Significance was accepted at $p<0.05$ (*) for all statistical analyses.

RESULTS

A total of 41 patients were included in the study, with a mean age of 54.5±11.7 years, and the majority being female (58.5%). Among the patients, 51.2% were smokers, while 31.7% had hypertension, 53.7% had diabetes mellitus, 70.7% had coronary artery disease (CAD), 24.4% had chronic heart failure (CHF), 9.8% had a history of stroke, and 29.3% had chronic kidney disease (CKD). The median CHA_2DS_2-VASc score was 2, and 56.1% of the patients were classified as high-risk according to this scoring system. All patients underwent percutaneous coronary intervention (PCI), with the most common AMI location being the anterior wall. Intra-aortic balloon pump (IABP) support was used in 51.2% of the patients. The median duration of ECMO support was 6.5 days (IQR: 2–9 days), while the median total hospital stay was 16 days (IQR: 16–25 days). The in-hospital mortality rate was 58.5%.

The demographic characteristics of the patients are presented in Table 1 in detail. Demographic variables significantly associated with mortality included older age (HR: 1.04, 95% CI: 1.0–1.08, p=0.039), hypertension (HR: 3.10, 95% CI: 1.25–7.69, p=0.018), diabetes mellitus (HR: 2.38, 95% CI: 1.02–5.76, p=0.048), and CAD (HR: 3.16, 95% CI: 1.05-9.49, p=0.040). The other demographic variables were not associated with mortality (Table 1).

The pre-ECMO clinical findings of the patients are presented in detail in Table 2. Patients with ARF had a higher risk of mortality. However, no significant association was found between mortality and other clinical findings (Table 2).

The prognostic scoring systems and clinical severity scores of the patients are presented in Table 3. The CHA_2DS_2-VASc score was significantly higher in the non-survivor group compared to the survivor group (3.0 vs. 1.5, p<0.001) (Figure 1). Patients classified as high risk based on the CHA_2DS_2-VASc score had a significantly higher mortality risk (HR: 3.12, 95% CI: 1.28-7.63, p=0.008). Similarly, the SAVE score was significantly lower in non-survivors than in survivors (-12.0 vs. -5.0, p=0.002) (Figure 1). Risk stratification based on SAVE score classes demonstrated a significant association with mortality. Compared to class III (reference group), patients in class IV had a higher mortality risk (HR: 3.11, 95% CI: 1.10–10.22, p=0.039), while those in class V had an even greater mortality risk (HR: 7.30, 95% CI: 2.16-24.66, p=0.001). Regarding clinical severity scores, lower GCS scores (HR: 0.75, 95% CI: 0.58–0.96, p=0.031) and higher APACHE II scores (HR: 1.07, 95% CI: 1.01–1.13, p=0.026) were significantly associated with increased mortality (Table 3).

To prevent multicollinearity, age, hypertension, and diabetes mellitus, which are core components of the CHA_2DS_2-VASc score, were not included as separate variables in the multivariable model. Furthermore, the variance inflation factor (VIF) between CAD and the CHA_2DS_2-VASc score was high (VIF=11.6), indicating a strong collinearity between these variables. For this reason, CAD was omitted from the multivariable regression analysis. Additionally, components of the SAVE and APACHE II scores were excluded from the regression model due to high collinearity. The multivariable regression model showed that the high-risk group based on the CHA_2DS_2-VASc score and class IV and V classifications based on the SAVE score were independent predictors of mortality (Table 4). The survival rate was 48% in the moderate-risk group and 23% in the high-risk group. On the other hand, the survival rate was 52% in class III, 31% in class IV, and 16% in class V (Figure 2, Table 4).

Among the assessed prognostic risk scoring systems, the SAVE score exhibited the highest predictive accuracy, with an AUC of 0.80 (95% CI: 0.64–0.91), indicating a strong discriminatory ability. Furthermore, it demonstrated the highest sensitivity (81.2%) and specificity (76.5%), suggesting its superior capacity to identify high-risk patients while minimizing false-positive classifications. The CHA_2DS_2-VASc score (AUC=0.74, 95% CI: 0.57–0.86) and APACHE II score (AUC=0.72, 95% CI: 0.56–0.86) also exhibited good predictive performance. While CHA_2DS_2-VASc maintained a relatively balanced sensitivity (70.8%) and specificity (64.7%), APACHE II demonstrated a higher sensitivity (75.7%) but lower specificity (58.8%), indicating a greater likelihood of detecting high-risk patients at the cost of increased false-positive rates. The GCS had the lowest predictive performance among the evaluated scores, with an AUC of 0.68 (95% CI: 0.53–0.83) (Table 5).

Table 1. Demographic characteristics of the study population

Variables	All population n=41	Survival		Univariable regression		
		Survived n=17	Died n=24	HR	95% CI	p
Age, years	54.5±11.7	54.1±10.2	54.8±12.8	1.04	1-1.08	0.039*
Female, n (%)	24 (58.5)	10 (58.8)	14 (58.3)	0.66	0.28-1.54	0.335
Weight, kg	76.0±18.0	77.1±19.6	75.2±17.2	0.99	0.97-1.01	0.323
BMI, kg/m²	25.4±5.2	26.3±5.3	24.8±5.2	0.97	0.89-1.05	0.399
Smoking, n (%)	21 (51.2)	9 (52.9)	12 (50.0)	0.55	0.23-1.28	0.162
Comorbidity, n (%)						
Hypertension	13 (31.7)	4 (23.5)	9 (37.5)	3.10	1.25-7.69	0.015*
Diabetes mellitus	13 (31.7)	5 (29.4)	8 (33.3)	2.38	1.02-5.76	0.048*
CAD	29 (70.7)	11 (64.7)	18 (75.0)	3.16	1.05-9.49	0.040*
CHF	10 (24.4)	4 (23.5)	6 (25.0)	1.27	0.49-3.24	0.622
Stroke	4 (9.8)	1 (5.9)	3 (12.5)	2.51	0.74-8.53	0.142
CRF	12 (29.3)	6 (35.3)	6 (25.0)	0.97	0.38-2.49	0.956
CPR duration, minutes	46.1±11.6	46.8±7.3	45.6±14.1	0.99	0.96-1.03	0.648
AMI location, n (%)						
Anterior	26 (63.4)	11 (64.7)	15 (62.5)	ref		
Inferior	11 (26.8)	3 (17.6)	8 (33.3)	1.52	0.65-3.57	0.333
Other	4 (9.8)	3 (17.6)	1 (4.2)	0.21	0.03-1.54	0.123
IABP, n (%)	21 (51.2)	9 (52.9)	12 (50.0)	0.79	0.35-1.78	0.567

The data are expressed as the mean±SD, median (IQR), or frequency (%). * indicates statistical significance at p<0.05. AMI: Acute myocardial infarction, BMI: Body-mass index, CAD: Coronary artery disease, CHF: Chronic heart failure, CI: Confidence interval, CPR: Cardiopulmonary resuscitation; CRF: Chronic renal failure, HR: Hazard ratio, IABP: Intra-aortic balloon pump, ref: Reference category

Table 2. Pre-extracorporeal membrane oxygenation clinical findings of the study population

Variables	All population n=41	Survival		Univariable regression		
		Survived n=17	Died n=24	HR	95% CI	p
Intubation, h	10.0 (7.0-16.0)	9.0 (6.0-14.0)	11.0 (7.0-16.0)	1.02	0.92-1.09	0.126
DBP > 40 mm Hg	8 (19.5)	5 (29.4)	3 (12.5)	0.48	0.14-1.63	0.242
PP ≤ 20 mm Hg	26 (63.4)	9 (52.9)	17 (70.8)	2.16	0.88-5.31	0.095
Ejection fraction, %,	29.8±6.1	29.1±7.1	30.2±5.4	1.04	0.97-1.1	0.250
sPAP, mmHg	34.3±5.8	35.6±6.1	33.3±5.5	0.95	0.87-1.04	0.251
Laboratory findings						
Hemoglobin, g/dl	12.3±1.8	12.2±2.1	12.3±1.5	1.06	0.85-1.32	0.621
WBC, 10^3/uL	8.6±2.9	8.0±3.2	9.0±2.6	1.05	0.93-1.19	0.433
LDL, mg/dl	120.6±28.9	116.9±31.4	123.3±27.4	1.01	0.99-1.02	0.240
Triglyceride, mg/dl	156.6±81.5	147.9±73.1	162.7±87.9	1.00	0.98-1.01	0.493
TT, mmol/L	24.1±10.3	25.3±9.5	23.3±11.0	0.98	0.94-1.02	0.267
ALT, UI/L	134.2±99.9	113.5±108.1	148.9±93.3	1.00	0.98-1.01	0.185
AST, UI/L	226.0±150.6	226.5±139.8	225.7±160.8	1.00	0.98-1.01	0.890
Creatinine, mg/dl	1.8±0.4	1.8±0.5	1.8±0.4	0.96	0.39-2.33	0.924
UREA	39.0 (26.0-64.0)	39.0 (25.0-58.0)	43.0 (27.5-75.0)	1.01	0.97-1.02	0.219
CRP, mg/L	10.1 (4.7-35.0)	9.3 (4.7-35.0)	14.1 (8.1-35.0)	1.00	0.98-1.01	0.609
Albumin, g/dl	3.7 (3.4-3.9)	3.9 (3.4-3.9)	3.6 (3.4-3.9)	0.98	0.91-1.06	0.597
HCO, mmol/L	17.5±3.2	17.6±2.8	17.4±3.4	1.01	0.88-1.17	0.857
Acute organ failures						
Renal failure	24 (58.5)	7 (41.2)	17 (70.8)	2.28	1.02-5.34	0.044*
Liver failure	28 (68.3)	9 (52.9)	19 (79.2)	2.20	0.81-5.95	0.122
CNS dysfunction	8 (19.5)	2 (11.8)	6 (25.0)	1.16	0.46-2.93	0.754
ECMO duration, days	6.5 (2-9)	7 (2-10)	5 (2-8)	0.92	0.68-1.23	0.106
Hospital duration, days	16 (10-25)	25 (17-30)	13 (8-15)	-	-	-

The data are expressed as the mean±SD, median (IQR), or frequency (%). * indicates statistical significance at p<0.05. ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CI: Confidence interval, CNS: Central nervous system, CRP: C-reactive protein, DBP: Diastolic blood pressure, ECMO: Extracorporeal membrane oxygenation, HCO: Bicarbonate, HR: Hazard ratio, LDL: Low-density lipoprotein, PP: Pulse pressure, sPAP: Systolic pulmonary artery pressure, TT: Total bilirubin, WBC: White blood cell count

Table 3. Association of prognostic scores and clinical severity indices with mortality

Variables	Survival		Univariable regression		
	Survived n=17	Died n=24	HR	95% CI	p
CHA_2DS_2-VASc	1.5 (1.0-3.0)	3.0 (1.5-4.0)	1.58	1.26-1.99	<0.001*
Moderate risk, n (%)	11 (64.7)	7 (29.2)	ref		
High risk, n (%)	6 (35.3)	17 (70.8)	3.12	1.28-7.63	0.008*
SAVE score	-5.0 [(-9.0)-(-3.0)]	-12.0 [(-17.0)-(-8.0)]	0.89	0.83-0.96	0.002*
Risk class, n (%)					
III	9 (52.9)	4 (16.7)	ref		
IV	5 (29.4)	9 (37.5)	3.11	1.10-10.22	0.039*
V	3 (19.6)	11 (45.8)	7.30	2.16-24.66	0.001*
GCS	7.2±2.2	5.4±1.6	0.75	0.58-0.96	0.031*
APACHE II score	25.1±7.4	31.0±6.4	1.07	1.01-1.13	0.026*

The data are expressed as the mean±SD, median (IQR), or frequency (%). * indicates statistical significance at p<0.05. APACHE II: Acute physiology and chronic health evaluation II, CI: Confidence interval, GCS: Glasgow Coma Scale, HR: Hazard ratio, SAVE: Survival after veno-arterial ECMO

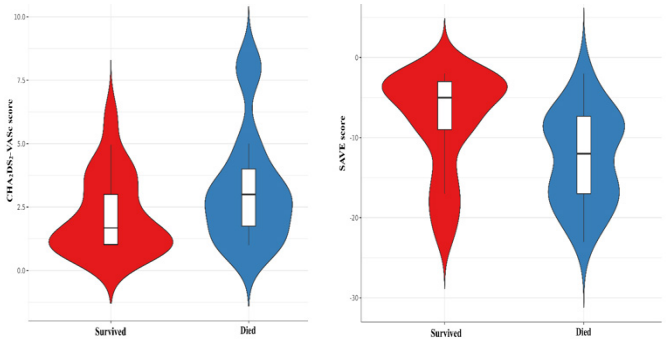

Figure 1. Comparison of CHA_2DS_2-VASc and SAVE scores between survived and died patients
SAVE: Survival after veno-arterial ECMO

Table 4. Independent predictor of mortality

Variables	Multivariable regression			Survival rate (%)
	HR	95% CI	p	
CHA_2DS_2-VASc				
Moderate risk, n (%)	ref			48.0
High risk, n (%)	2.72	1.29-6.49	0.045*	23.0
SAVE score				
Risk class, n (%)				
III	ref			52.0
IV	3.09	1.08-10.05	0.048*	31.0
V	5.57	1.57-19.82	0.008*	16.0
APACHE II score	1.03	0.97-1.09	0.231	-

The data are expressed as the mean±SD, median (IQR), or frequency (%). * indicates statistical significance at p<0.05. APACHE II: Acute physiology and chronic health evaluation II, GCS: Glasgow Coma Scale, HR: Hazard ratio, CI: Confidence interval, SAVE: Survival after veno-arterial ECMO

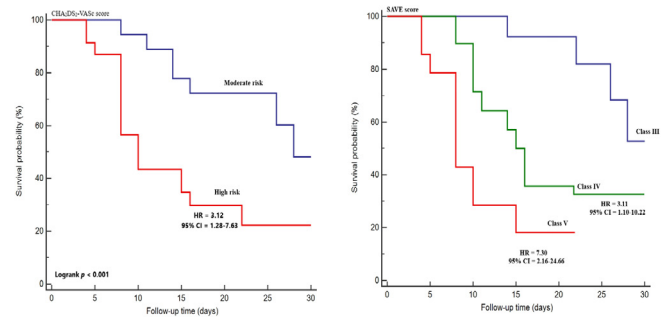

Figure 2. The survival rate according to CHA_2DS_2-VASc and SAVE score classifications

Table 5. Diagnostic performance of prognostic risk scores in predicting mortality

	AUC±SE	95%CI	Sens.	Spec.	Threshold
APACHE II	0.72 ± 0.08	0.56-0.86	75.7	58.8	>24
GCS	0.68 ± 0.08	0.53-0.83	73.7	57.5	≤6
CHA_2DS_2-VASc	0.74 ± 0.08	0.57-0.86	70.8	64.7	≥2
SAVE score	0.80 ± 0.07	0.64-0.91	81.2	76.5	<-6

APACHE II: Acute physiology and chronic health evaluation II, CI: Confidence interval, GCS: Glasgow Coma Scale; SAVE: Survival after veno-arterial ECMO, Sens: Sensitivity, Spec: Specificity

DISCUSSION

To the best of our knowledge, this is the first study to investigate the prognostic value of the CHA_2DS_2-VASc score in AMI patients undergoing ECMO following OHCA. Our findings indicate that CHA_2DS_2-VASc and other prognostic scores were significantly higher in non-survivors compared to survivors. Although the SAVE score demonstrated the highest diagnostic performance in predicting in-hospital mortality, the CHA_2DS_2-VASc score exhibited an acceptable predictive value. These findings suggest that the CHA_2DS_2-VASc score may serve as a feasible screening tool for pre-ECMO mortality risk assessment.

Studies conducted on OHCA patients have reported post-ECMO 30-day mortality rates varying between 43% and 76%.[23-26] In line with these studies, the survival rate observed in our study was 58.5%. Although general scoring systems such as APACHE II, SAPS II, and SOFA are widely used for mortality prediction in the heterogeneous population of ICUs, their limitations in patients undergoing ECMO have been reported.[8,11,27] A previous study reported that APACHE II scores demonstrated lower mortality rates compared to the SAVE score. In the same study, Bland-Altman analysis revealed a mean predicted mortality difference of 17.6% (95% CI: 7.6%–27.6%, p<0.0001) between the SAVE and APACHE II scores. Additionally, APACHE II was shown to underestimate mortality compared to SAVE up to an 80% mortality threshold, beyond which it provided higher mortality estimates.[28] This finding indicates that APACHE II might undervalue the potential benefits of ECMO in low-risk patients while overestimating disease severity in high-risk

patients. Our findings not only support but also extend the outcomes of these studies. In the present study, although ICU risk scores (APACHE II, GCS) and the ECMO-specific risk score (SAVE) were elevated in deceased patients, the SAVE score exhibited superior sensitivity and specificity.

The better diagnostic performance of the SAVE score over ICU-specific scoring systems may be due to several factors. Firstly, GCS and APACHE II were originally designed for the general ICU population without ECMO, meaning they may not fully capture the unique physiological status and risks of patients requiring VA-ECMO. In contrast, the SAVE score was developed specifically from VA-ECMO patient data, making it inherently more tailored to this population. Secondly, all of our patients experienced OHCA and underwent immediate PCI prior to ECMO initiation. Given that revascularization can partially restore cardiac function and improve hemodynamic stability, the physiological parameters incorporated into the APACHE II score at ICU admission may not fully reflect the initial severity of shock at the time of arrest. It has been emphasized that the APACHE II score may not accurately reflect the true severity of a patient's condition at the time of arrest, potentially leading to an underestimation of risk, especially in subgroups with lower mortality risk and rapidly correctable conditions.[28] Finally, patient profile differences may also contribute to variations in scoring system performance. In the cohort where the SAVE score was established, CHF (33%), AMI (29%), valvular heart disease (17%), and refractory VT/VF (13%) were the most common conditions,[8] whereas in our VA-ECMO series, all cases were AMI.

In fact, numerous studies on cardiac arrest patients have shown that patient profile can be an important prognostic indicator.[29-32] In a recent comprehensive analysis of more than 5.000 ECMO patients, advanced age was found to be a significant factor reducing survival probability. The survival rate for the 65–74 age group was 32% lower than that of the 18–49 age group, and for patients over 75, it was 46% lower.[33] Similarly, female sex or presence of comorbidities, such as diabetes mellitus, hypertension, CHF, has been found to be an independent predictor of mortality after ECMO.[31,34-36] These findings indicate that the risk factors encompassed in the CHA_2DS_2-VASc score, such as age and the burden of comorbidities, may play a crucial role in determining survival probability after ECMO. To our knowledge, this is the first study to report that an elevated CHA_2DS_2-VASc score is associated with higher post-ECMO mortality in OHCA patients. Based on the ROC curve analysis, a cutoff value of ≥2 was established for mortality risk, which corresponded with the general risk classification defined by the European Society of Cardiology (ESC) guidelines.[21] The CHA_2DS_2-VASc score exhibited sensitivity comparable to ICU risk scores. Although its specificity was limited, it remained higher than that of ICU risk scores. This aligns with the regression analysis results, where it was identified as an independent predictor. Furthermore, several studies conducted on cardiac arrest patients, have demonstrated the prognostic role of the CHA_2DS_2-VASc score.[14,37-41] The score's prognostic role is likely due to the cumulative pathophysiological effects of its components. Advanced age, hypertension, and diabetes, major components of the CHA_2DS_2-VASc score, are associated with progressive microvascular damage and decreased organ reserve, which can hinder recovery from global ischemic injury after cardiac arrest. Diabetes and hypertension impair cerebral and myocardial circulation, worsening ischemia-reperfusion injury and reducing the likelihood of full neurological recovery. Additionally, CHF and vascular disease indicate a limited cardiopulmonary reserve and widespread atherosclerosis, meaning that when cardiac arrest occurs in these patients, it is typically more severe, and even if circulation is restored, organ recovery remains challenging. In summary, a high CHA_2DS_2-VASc score identifies a physiologically fragile subgroup with an increased risk of poor outcomes after ECPR.

Although the SAVE score clearly outperformed CHA_2DS_2-VASc in our analysis, patients requiring emergent ECMO often present with limited real-time data, making a fast and feasible scoring tool valuable in early decision-making, triage, or counseling. The SAVE score requires specific ECMO-related variables that may not be immediately accessible at the time of emergent cannulation, whereas the CHA_2DS_2-VASc score relies on chronic patient factors (age, sex, and comorbid conditions) and can be readily calculated by most clinicians familiar with cardiology risk assessment. Given that vascular comorbidities, advanced age, and chronic disease burden are major contributors to mortality in VA-ECMO patients,[31,34-36] the CHA_2DS_2-VASc score could be a useful tool for predicting survival in this setting. While the CHA_2DS_2-VASc cutoff value of ≥2 identified in the ROC analysis aligns with the threshold reported in the ESC atrial fibrillation (AF) guidelines,[21] its sensitivity and specificity differ across various patient populations.[42,43] In the OHCA setting, the CHA_2DS_2-VASc score may provide risk stratification with varying sensitivities and specificities at different threshold values. This emphasizes the need for further studies in larger, multicenter VA-ECMO cohorts to identify alternative cutoff points that ensure the most accurate balance between sensitivity and specificity. Nonetheless, our results suggest that once the CHA_2DS_2-VASc score reaches ≥2, the patient's cumulative comorbidity burden becomes a significant predictor of adverse outcomes in this emergent setting.

Limitations

This study has several limitations. First, it is a single-center, retrospective study with a relatively small sample size, which may limit the generalizability of the findings to broader OHCA cohorts, restrict causal inferences, and increase the risk of type II errors. Second, long-term outcomes of the patients were not assessed, preventing an evaluation of the extended prognostic impact of CHA_2DS_2-VASc score. Third, our study excluded certain extremely high-risk patient, such as those with advanced multi-organ failure, myocarditis, or prior heart/lung transplantation, conditions that overlap with critical components of the SAVE score. This exclusion might have contributed to the underrepresentation of patients with higher SAVE scores, which could have influenced the predictive performance. Lastly, other ECMO-specific scoring

systems were not included in the comparative analysis, which could have provided a more comprehensive assessment of risk stratification in this patient population. To address these limitations, larger, multicenter, prospective studies with long-term follow-up and external validation are needed to further investigate the prognostic utility of CHA_2DS_2-VASc and SAVE scores in ECMO patients.

CONCLUSION

This study demonstrates that the CHA_2DS_2-VASc score, while originally developed for thromboembolic risk assessment in atrial fibrillation, may serve as a valuable adjunctive tool for mortality prediction in patients undergoing VA-ECMO after cardiac arrest. Together with established ECMO-specific indices such as the SAVE score, CHA_2DS_2-VASc can contribute to a more accurate risk stratification and guide clinical decision-making. However, it remains crucial to integrate this information with a comprehensive clinical assessment and acute arrest-related factors.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was approved by the Lokman Hekim University Non-interventional Clinical Researches Ethics Committee (Date: 30.12.2024, Decision No: 2024/13)

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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