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Prognostic value of APACHE II and SAVE scores in adult patients treated with extracorporeal cardiopulmonary resuscitation

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Abstract

Purpose

The primary purpose of our study is to determine the accuracy and consistency of different evaluation systems including APACHE II scoring system and Survival After Veno-arterial ECMO (SAVE) score on predicting the prognosis of adult patients with ECPR.

Methods

We reviewed 74 adult patients underwent ECPR from June 2016 to July 2021. The primary endpoint examined was survival at hospital discharge or 28 days. The predicted accuracy of SAVE and APACHE II scoring systems was evaluated by binary logistic analysis and ROC curve, and the predicted consistency of the two grading systems was evaluated by Bland Altman plots.

Results

Overall, 43 (58.1%) patients finally died. On multivariable analysis, APACHE II score (OR = 1.372, 95%CI: 1.056–1.782, P = 0.018) was independently associated with increased 28-day mortality. The variable independently associated with decreased 28-day mortality included increased SAVE score (OR = 0.757, 95%CI: 0.643–0.890, P = 0.001). ROC analysis showed cut-off values to predict 28-day mortality for APACHE II score, namely 35.5 (sensitivity 79.1%, specificity 74.1%, AUC 0.81, 95%CI: 0.70–0.91), for SAVE score, namely − 6.5 (sensitivity 61.1%, specificity 83.7%, AUC 0.86, 95%CI:0.78–0.95), combined multivariate ROC analysis of both two parameters showed an AUC of 0.90 (95%CI: 0.83–0.97). In the Bland Altman plot for ECPR, mean $\text{mortality}_{\text{APAHCE II}}$ was not statistically different from mean $\text{mortality}_{\text{SAVE}}$ (P = 0.99, mean difference $\text{mortality}_{\text{APAHCE II}}$-$\text{mortality}_{\text{SAVE}}$=0.00%, 95%CI: -6.89–6.89%), meanwhile APACHE II and SAVE agreed well (95% limit of agreement:-59.29–59.29%) .

Conclusion

APACHE II and SAVE scores were fairly accurate in predicting prevention in adult ECPR patients and the predictive results of the two scoring systems are highly consistent.

Introduction

Cardiac arrest (CA) is the most critical emergency, the mortality rate of which could be 80–90% as reported[1–3]. Despite the progress of conventional cardiopulmonary resuscitation (CCPR) and the management of post-CPR care, mortality and neurologic prognosis in patients has remained poor[4]. Extracorporeal membrane oxygenation (ECMO) is a method for temporarily maintaining cardiopulmonary function during heart or respiratory failure[5]. In recent years, extracorporeal cardiopulmonary resuscitation (ECPR) is increasingly used in the treatment of patients with cardiac arrest, especially those who are difficult to succeed in a short period of time. ECMO can restore blood flow in patients with cardiac arrest to provide adequate perfusion, especially cerebral perfusion, which is the main cause of death in these population. Although it seems that ECPR could improve outcomes compared to CCPR, there is no perfect evaluation system to predict the prognosis of ECPR patients. This paper retrospectively analyzes the prognostic factors of adult ECPR patients and discusses the predictive value of APACHE II and SAVE scoring system in the prognosis of adult ECPR patients.

Methods

1.1 data collection

A total of 103 adult patients who were treated with ECPR in our Emergency Department from June 2016 to July 2021 were reviewed. Patients who younger than 18 years old (2 cases) or older than 80 years old (4 cases) were excluded. 23 cases were excluded for supporting by ECMO less than 24 hours. Finally, 74 patients were included in our study. General data, vital signs, laboratory indicators and other data of patients were collected.

1.2 ECMO management

Cannulations for all ECMO supports including distal perfusion catheters(DPCs) were performed percutaneously at bedside using the Seldinger technique. The surgeons empirically selected the cannula size according to the height, weight and gender of patients at time of initial ECMO cannulation. Centrifugal pumps, oxygenators, heparin-coated catheters were produced by Maquet, Germany.

Patients were closely monitored by our trained ECMO team. Echocardiography and laboratory indicators were examined every day to assess recovering and weaning in patients. Systemic anticoagulation was achieved by infusing intravenously unfractionated heparin. The anticoagulation monitoring system included activated partial thromboplastin time (aPTT), activated clotting time (ACT), platelet count (cells/μL) and fibrinogen levels (mg/dL). The ACT was repeated every 6 hour with a target value of 140–180 seconds. The aPTT was repeated every 6–8 hour to maintain aPTT of 45 to 60 seconds.

1.3 Statistical methods

Shaprio-Wilk analysis was used to test the normality of continuous data. The continuous data that obeyed or approximately obeyed normal distribution were expressed by mean ± standard deviation (mean ± SD), using Student’s t test. The continuous of skewness distribution were expressed by median with interquartile range and analyzed with Mann-Whitney U test. Categorical variables were expressed as percentages and compared with the chi-square test or Fisher’s exact test. Multivariable logistic regression was used to analyze the related factors of 28-day mortality of VA-ECMO patients. ROC curve was used to analyze the threshold of influencing factors. The Bland Altman plot was used to assess the agreement of mortality risks predicted by different scoring systems. All analyses were conducted by SPSS 25.0 software (IBM, Armonk, NY, USA). The results were deemed statistically significant when p values of 0.05 or less.

Results

Baseline analyses were demonstrated in Table 1. The 74 patients with cardiac arrest underwent ECMO for a total of 560 days. The median age of patients was 45 (34,57) years, and 32.4% (n = 24) were female. 79.7% (n = 59) of patients received blood transfusions, including red blood cells in 54 patients, platelets in 41 patients and plasma in 31 patients. The median amount of RBCs, PLTs and FFPs infusion was 0.91 (0,2.13) ml/kg/d, 0.32 (0,1.23) ml/kg/d and 0 (0,0.96) ml/kg/d respectively. The median APACHE II score of all the 74 patients was 36 (33,37) and the median SAVE score was − 8 (-12,-3). The median APACHE II score of the survivor group was 33 (30,36), significantly lower than that of the non-survival group [37 (36,39), $P < 0.001$]. Meanwhile, the median SAVE score in the survivor group was − 3 (-6,1), which was statistically significant compared with the non-survival group [-10 (-14,-8), $P < 0.001$]. There were also statistically significant differences between the survivor group and the non-survival group in lymphocyte count [1.50 (1.06,3.34) vs 2.86 (1.43,4.96), $P = 0.046$], fresh frozen plasma transfusion [0 (0,0.18) vs 0.08 (0,1.41), $P = 0.029$]. At the same time, the non-survival group had a higher rate of continuous renal replacement therapy (CRRT) (88.4% vs 61.3%, $P = 0.011$).

Table 1
Description of cohort

Variables	All patients (n = 74)	Survivor (n = 31)	Non-survivor(n = 43)	*P* value
Age(years), median (IQR)	45(34–57)	45(34–58)	45(32–54)	0.776
Male gender, n(%)	50(67.6)	18(58.1)	32(74.4)	0.208
Hypertension,(%)	19(25.7)	6(19.4)	13(30.2)	0.419
CHD,n(%)	9(12.2)	4(12.9)	5(11.6)	1.000
Diabetes,n(%)	11(14.9)	3(9.7)	8(18.6)	0.340
Smoking history,n(%)	21(28.4)	6(19.4)	15(34.9)	0.194
Drinking history,n(%)	5(6.8)	4(12.9)	1(2.3)	0.154
ECMO cause				0.109
Myocarditis,n(%)	37(50)	12(38.7)	25(58.1)	
AMI,n(%)	12(16.2)	8(25.8)	4(9.3)	
Others,n(%)	25(33.8)	11(35.5)	14(32.6)	
SAVE score, median (IQR)	-8(-12,-3)	-3(-6,1)	-10(-14,-8)	< 0.001
APACHE II score, median (IQR)	36(33–37)	33(30–36)	37(36–39)	< 0.001
WBC count($*10^9$/L), median (IQR)	15.42(11.19,21.88)	16.53(11.22,23.19)	14.40(11.08,20.60)	0.522
Neutrophil count($*10^9$/L), median (IQR)	10.81(7.04,18.66)	11.89(8.11,19.83)	9.81(6.6,18.48)	0.278
Lymphocyte count($*10^9$/L), median (IQR)	2.48(1.21,3.67)	1.50(1.06,3.34)	2.86(1.43,4.06)	0.046
Hemoglobin(g/L),mean ± SD	128 ± 22	123 ± 17	131 ± 24	0.097
HCT,mean ± SD	0.384 ± 0.066	0.367 ± 0.049	0.397 ± 0.074	0.062
Platelet count(*109/L), median (IQR)	185(131,245)	183(151,232)	189(127,246)	0.969
RDW, median (IQR)	12.8(12.3,13.2)	12.8(12.4,13.2)	12.9(12,13.2)	0.780
ALT(U/L), median (IQR)	237.6(102.7,470.8)	126.2(68.4,367.5)	295.8(163.5,484.5)	0.095
AST(U/L), median (IQR)	451.1(111.0,915.6)	269.7(102.6,683.1)	634.7(111.8,1222.8)	0.321
Cr(umol/L), median (IQR)	108.3(87.5,135.8)	102.7(82.7,121.5)	117.8(92.2,140.2)	0.148

Variables	All patients (n = 74)	Survivor (n = 31)	Non-survivor(n = 43)	*P* value
Urea(mmol/L), median (IQR)	7.30(5.53,10.02)	8.44(5.67,9.70)	7.05(5.46,10.02)	0.487
potassium(mmol/L),mean ± SD	3.9 ± 0.8	3.9 ± 0.6	4.0 ± 1.0	0.597
sodium(mmol/L),mean ± SD	141.9 ± 5.9	141.6 ± 5.1	142.1 ± 6.5	0.736
chlorine(mmol/L),mean ± SD	104.3 ± 5.9	105.5 ± 4.5	103.5 ± 6.7	0.139
calcium(mmol/L),mean ± SD	1.99 ± 0.24	2.00 ± 0.21	1.98 ± 0.26	0.785
procalcitonin(ng/ml), median (IQR)	1.42(0.18,6.09)	1.02(0.33,4.94)	1.42(0.11,10.12)	0.763
NT-proBNP(pg/ml), median (IQR)	1565(453,7072)	2156(546,7191)	1341(370,3086)	0.118
hs-TNT, median (IQR)	2619(199,8641)	2619(319,6440)	3604(163,10376)	0.493
CRRT,n(%)	57(77.0)	19(61.3)	38(88.4)	0.011
IABP,n(%)	26(35.1)	7(22.9)	19(44.2)	0.084
RBC transfusion(ml/kg/d), median (IQR)	0.91(0,2.13)	0.76(0,2.61)	1.11(0,1.68)	0.868
PLT transfusion(ml/kg/d), median (IQR)	0.32(0,1.23)	0(0,1.21)	0.36(0,1.27)	0.582
FFP transfusion,(ml/kg/d), median (IQR)	0(0,0.96)	0(0,0.18)	0.08(0,1.41)	0.029
Abbreviations: CHD, coronary heart disease; AMI,acute myocardial infarction; SAVE score, survival after veno-arterial ECMO score; APACHE II score, acute physiology and chronic health evaluation II score; WBC, white blood cell; HCT, hematocrit; RDW, red blood cell distribution width; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cr, creatinine; NT-proBNP, N-terminal pro-B-type natriuretic peptide; hs-TNT, high-sensitivity troponin T; CRRT, continuous renal replacement therapy; IABP, intra-aortic balloon pump; FFP, fresh frozen plasma.				

The multivariable logistic model of 28-day mortality is shown in Table 2. On multivariable analysis, APACHE II score (OR = 1.372, 95%CI: 1.056–1.782, P = 0.018) was independently associated with increased mortality. The variable independently associated with decreased mortality included increased SAVE score (OR = 0.757, 95%CI: 0.643–0.890, P = 0.001). Figure 1a shows that APACHE II score was positively correlated with the probability of 28-day mortality. When the APACHE score was higher than 32, the probability of 28-day mortality was significantly increased. As shown in Fig. 1b, the SAVE score was negatively correlated with the probability of 28-day mortality. The probability of 28-day mortality could be as high as 80% when SAVE score lower than − 9. ROC analysis showed cut-off values to predict 28-day mortality for APACHE II score, namely 35.5 (sensitivity 79.1%, specificity 74.1%, AUC 0.81, 95%CI: 0.70–0.91), for SAVE score, namely − 6.5

(sensitivity 61.1%, specificity 83.7%, AUC 0.86, 95%CI: 0.78–0.95), combined multivariate ROC analysis of both two parameters showed an AUC of 0.90 (95%CI: 0.83–0.97) while APACHE II and SAVE score together to have a highly significant combined effect on 28-day mortality (P < 0.001), as shown in Fig. 2.

Table 2
Multivariable model of mortality

Variables	**Missing data(%)**	**Univariable Logistic Regression**		**Multivariable Logistic Regression**	
		OR (95%CI)	**P**	**OR (95%CI)**	**P**
APACHE II score	0	1.518(1.231–1.871)	< 0.001	1.372(1.056–1.782)	0.018
SAVE score	0	0.728(0.632–0.840)	< 0.001	0.757(0.643–0.890)	0.001
FFP transfusion	0	2.037(1.035–4.009)	0.039	1.746(0.591–5.519)	0.313
CRRT	0	0.208(0.064–0.678)	0.009	0.450(0.081–2.510)	0.363
Lymphocyte count	0	1.291(0.991–1.682)	0.059	1.089(0.758–1.567)	0.644
Abbreviations: APACHE II score, acute physiology and chronic health evaluation II score; SAVE score,survival after veno-arterial ECMO score; FFP, fresh frozen plasma; CRRT, continuous renal replacement therapy.					

Figure 3 shows the Bland Altman plot between the predicted mortality from APACHE II and SAVE. For ECPR patients, mean $\text{Mortality}_{\text{APAHCE II}}$ was not statistically different from mean $\text{Mortality}_{\text{SAVE}}$ (P = 0.99, mean difference $\text{mortality}_{\text{APAHCE II}}$-$\text{mortality}_{\text{SAVE}}$=0.00%, 95%CI: -6.89–6.89%), meanwhile APACHE II and SAVE agreed well (95% limit of agreement: -59.29–59.29%).

Discussion

In recent years, ECMO technology is increasingly used in the treatment of refractory circulatory failure and cardiac arrest[6–8]. Kim SJ, et al conducted a meta-analysis ravealing that ECPR showed improved survivor comparing to CCPR[9]. American Heart Association Guidelines[10] also recommend ECPR for cardiac arrest. In a study involving 156 patients[8], ECPR can effectively improve the prognosis of the nervous system, of course, it needs to be verified by larger sample of studies. Therefore, we believe that ECMO should be more widely used in emergency department, where is the first window for most of patients with cardiac arrest, especially for patients with out-of-hospital cardiac arrest(OHCA). At present, there is a lack of international evaluation system for predicting the prognosis of patients with ECPR.

We conducted a retrospective study of 74 adult patients treated with ECPR, and a total of 31 patients survived. The survival rate(41.9%) was slightly higher than the data of international studies[5, 11]. At the same time, we found that both APACHE II and SAVE score could predict the prognosis of patients. ROC curve analysis showed that the area under the curve of the two scoring systems was similar, and the specificity of SAVE score was slightly higher while the combined multivariate ROC analysis of both two parameters showed an AUC of 0.90 (95%CI: 0.83–0.97), showing an excellent predictive value. The coincidence rate of the two scoring systems in predicting the mortality of patients with ECPR reached 91.9% (68/74).

APACHE II score has been widely used to evaluate and predict the prognosis of various types of critically ill patients[12–15] since it was proposed. There was a study revealing low evaluation value of APACHE II score in critically ill patients after cardiac surgery, and they attributed this to the lack of specificity of the APACHE II score in patients with heart disease [16]. For the reason that the subjects of our study were patients with respiratory and cardiac arrest treated with ECPR, all patients obtained a lower Glasgow score, which further reduced the differentiation of APACHE II scores. However, in our study, APACHE II score is quite accurate in predicting the prognosis of ECPR patients. As shown in the figure, there was a remarkable increase in probability of 28-day mortality if APACHE II score was more than 32.

ELSO recommended SAVE (Survival After Veno-arterial ECMO) score to evaluating the severity of patients with VA-ECMO[17]. As compared to APACHE II score, SAVE score is more specific in the evaluation of cardiovascular disease, but there is still a lack of large sample data to prove the value of SAVE in predicting the prognosis of adult patients with ECPR. In our cohort, SAVE score also showed considerable predictive accuracy. When the SAVE score is less than − 9, the mortality rate can be as high as 80%. Compared with the vital signs and internal environment contained in the APACHE II score, the SAVE score emphasizes more the importance of the primary disease, the functional status and support of organs, which is consistent with our clinical experience. Besides, studies[18, 19] have shown that ECMO patients with acute kidney injury or acute liver failure tend to have a poorer prognosis.

According to our study, we recommend that the combination of APACHE II and SAVE scores could be used to predict prognosis in adult patients with ECPR considering the different emphases of the two scoring systems. Given the high cost[20], the frequent and fatal complications of ECMO and the uncertainty of outcome, it is of great necessity for us to conduct a detailed evaluation of patients to maximize the benefits of ECMO. If patients achieve both high APACHE II score and low SAVE score, the necessity of ECMO treatment should be reconsidered.

Our ECMO center is located in the emergency department, which is the primary area of care for cardiac arrest, especially OHCA patients. When a cardiac arrest patient enters the emergency channel, the ECMO team can be mobilized as soon as possible to assess the patient's condition and initiate ECMO, which can greatly reduce the time it takes for personnel to arrive and transfer equipment and this may be one of the reasons why the survivor rate of ECPR in our center is slightly higher than the international data. As the last line of defense for critically ill patients, ECMO should be vigorously promoted, besides, we believe that it is particularly important to carry out ECMO treatment in the emergency departments.

This paper still has some limitations, as a retrospective single-center study, the sample size collected of our study is small, so we still need larger sample size and multicenter data support. In addition, APACHE II and SAVE scores are cumbersome, which may be difficult in clinical frontline application.

Conclusion

Both APACHE II and SAVE score can predict the prognosis of adult ECPR patients, and the two scoring systems have strong consistency.

Declarations

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Authors' contributions

Yi Zhu and Yue Zou participated in the design of the study and drafted the manuscript. Yong Mei, Jinru Lv performed the statistical analysis. Hao Zhou, Zhongman Zhang, Di An and Tao Ding participated in patient management, data collection and analysis. Wei Li conceived the study and manuscript revision. XuFeng Chen was responsible for the study design, data collection and provided finanical support. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (Jiangsu Province Hospital)(No.2020-SR-226).

Consent for publication

All authors Consent for publication.

Competing interests

All authors declare no conflicts of interest.

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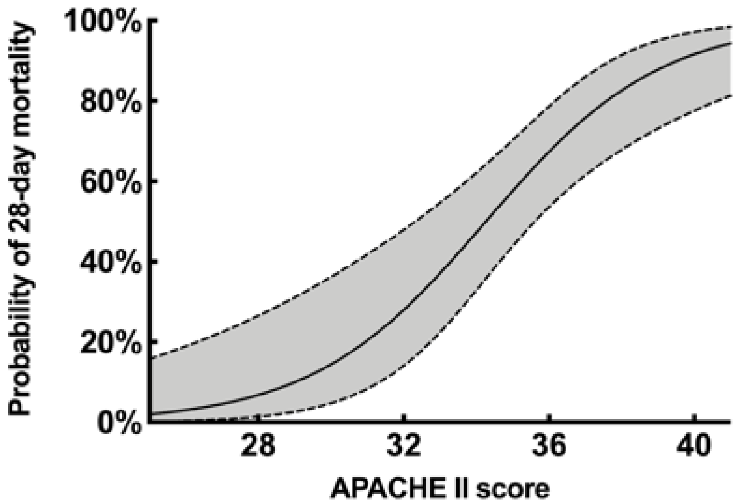
Figures



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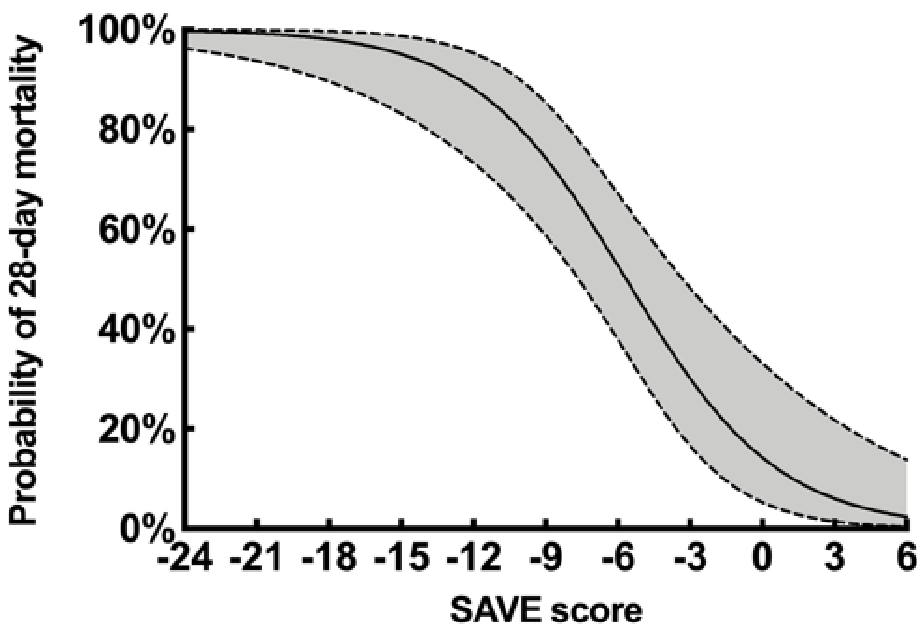

B

Figure 1

a.Predictive probability of 28-day mortality as a function of APACHE II score during ECMO treatment.

Abbreviations: APACHE II score, acute physiology and chronic health evaluation II score.

b.Predictive probability of 28-day mortality as a function of SAVE score.

Abbreviations: SAVE score, survival after veno-arterial ECMO score.

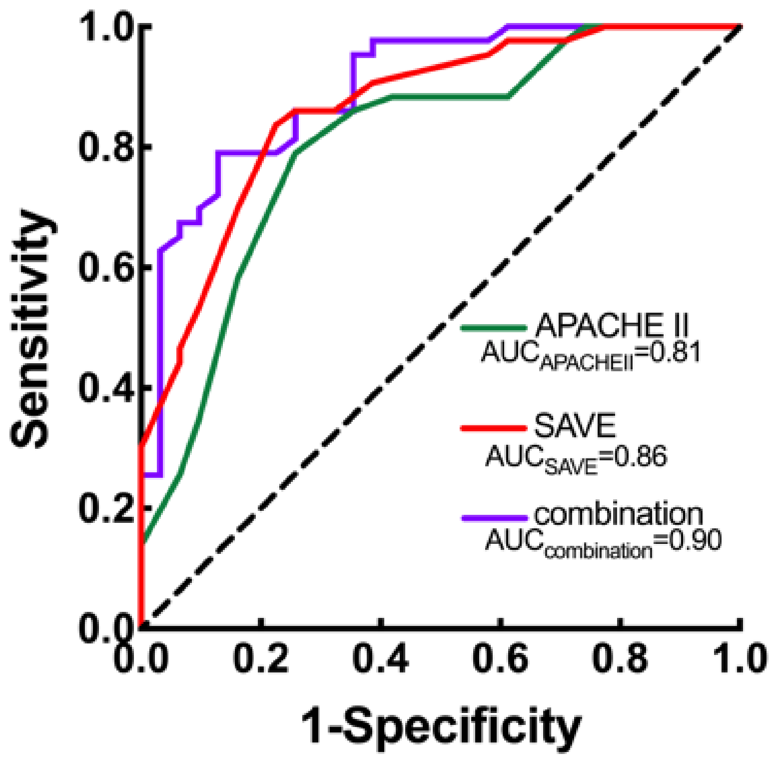

Figure 2

ROC curve for predicting prognosis of APACHE II and SAVE scores.

Abbreviations: APACHE II score, acute physiology and chronic health evaluation II score; SAVE score, survival after veno-arterial ECMO score.

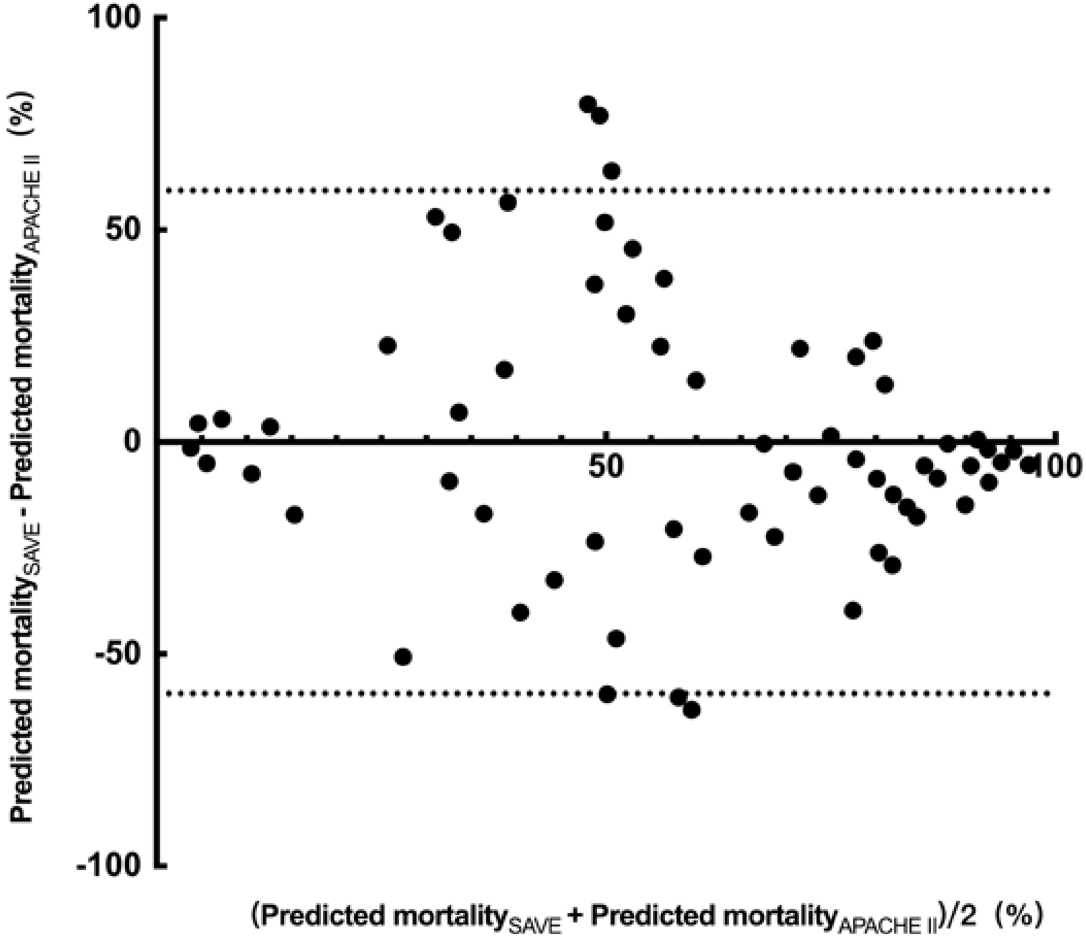

Figure 3

Bland-Altman plot of mortality predicted by SAVE and APACHE II score.

Abbreviations: APACHE II score, acute physiology and chronic health evaluation II score; SAVE score, survival after veno-arterial ECMO score.