Can the Sequential Organ Failure Assessment (SOFA) Score Predict Mortality of the Patients Receiving Extracorporeal Life Support?

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Objective: *To assess the applicability of the Sequential Organ Failure Assessment (SOFA) score to the patients who underwent extracorporeal life support (ECLS).*

Material and Method: *This study retrospectively reviewed the medical records of all 97 critically ill patients who underwent ECLS between January 2006 and December 2014. Demographics, comorbidities, primary diagnoses, ECLS days, length of hospital stay, presence of prior cardiac arrest and intra-aortic balloon pump, mode and indication of ECLS, clinical and laboratory data, and outcome of each patient were collected. The SOFA scores of each patient were calculated.*

Results: *The overall survival rate was 19.6%. The most common indication was postcardiotomy cardiogenic shock (26%). The SOFA score when utilized to assess the patients on the first day of ECLS treatment could not predict either removal of the ECLS or survival of the patient (mean SOFA scores of the ECLS-survivor group vs. the non-survivor group were 12.75±2.44 and 13.66±2.83; p = 0.144 and mean SOFA scores of the hospital-survivor group vs. the non-survivor group were 12.94±2.41 and 13.49±2.81; p = 0.455). However, among the ECLS survivors, the SOFA score assessed after ECLS removal could predict hospital survival as the SOFA scores of the survivor group vs. non-survivor group were 9.89±3.78 and 14.40±2.95; p = 0.003). When analyzed by the receiver-operating characteristic (ROC) curve, the area under the curve (AUC) of the SOFA score obtained on one day after ECLS removal was 0.832 (95% confidence interval [CI]: 0.676 to 0.987, p = 0.004). However, the appropriate cutoff point of the SOFA score to predict a patient's survival cannot be accurately determined because of downward bulge in the middle of the ROC curve, which represents the range of the SOFA scores of 10.50 to 15.50.*

Conclusion: *The SOFA score can be a useful tool to predict the survival of a patient after ECLS removal. The lower the SOFA score, the higher the chance of a patient's survival. However, it cannot predict the success of removal of the ECLS or survival while the patient is on ECLS, partly because of physiologic changes in various systems after ECLS insertion.*

Keywords: *Sequential Organ Failure Assessment score, SOFA score, Extracorporeal life support, ECLS*

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Extracorporeal life support or ECLS has been utilized for patients with postoperative low cardiac output following open heart surgery of complex congenital heart diseases and for critically ill patients since the early 1970s[1,2]. There are two major configurations of ECLS-the venoarterial ECLS to support the circulation and the venovenous ECLS to support the pulmonary system. In Thailand, the extracorporeal life support has become an appealing treatment during the last decade as the technology has been rapidly evolving with decreasing costs. However, the results of ECLS treatment are still unsatisfactory. Even if a patient could survive the ECLS, the hospital survival is still low. The experience of physicians taking care of patients undergoing ECLS, who are critical and complicated, may still be lacking. Predicting the results of the treatment and the outcome of the patients is frequently difficult. Therefore, a practical, objective, and reliable tool is needed to help evaluate the severity, morbidity, and mortality of the patients.

The Sequential Organ Failure Assessment or SOFA score, comprises six variables, each representing an organ system-respiration, coagulation,

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liver, cardiovascular, central nervous system, and renal. Each organ system is assigned a point value from 0, which represents normal, to 4, which represents the highest degree of dysfunction or failure[3]. Although originally designed to describe a sequence of organ dysfunction and morbidity, later studies have shown that high SOFA scores were associated with higher mortality and increased SOFA score during ICU admission also correlated with higher mortality[4,5]. As this scoring system is not complicated and can be feasible, this scoring system was selected to assess the patients in this study.

The purpose of this study is to assess the applicability of the SOFA score to the patients who underwent ECLS in order to predict the outcome of the patients.

Material and Method

After Siriraj Institutional Review Board approval was obtained, the study was conducted without consent needed. By retrospectively reviewing the medical records of all 97 critically ill patients who underwent extracorporeal life support between January 1, 2006 and December 31, 2014 at Siriraj Hospital, the research data were extracted. Demographics, comorbidities, primary diagnoses, ECLS days, length of hospital stay, presence of prior cardiac arrest and intra-aortic balloon pump, mode and indication of ECLS, clinical and laboratory data, and outcome of each patient were collected. The SOFA scores of each patient were calculated.

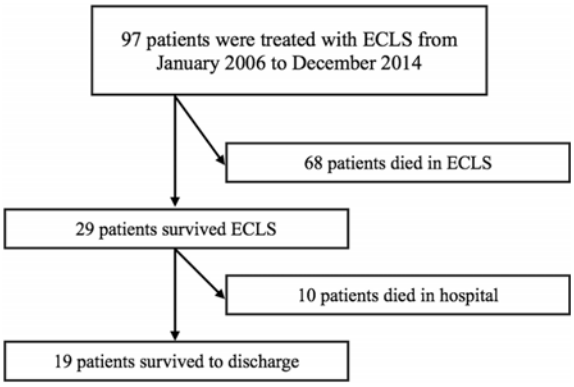
Statistical analysis

Descriptive statistics were expressed as means ± standard variation (SD). The categorical variables were tested, using the χ^2 test. The means of continuous variables were compared, using the Student's t-test. Discrimination thresholds of the SOFA score were analyzed with a receiver operating characteristic (ROC) curve. A *p*-value of less than 0.05 was considered to be statistically significant. All statistic analyses were performed with SPSS Statistics 14.0 for Windows (SPSS, Inc., Chicago, IL, USA).

Results

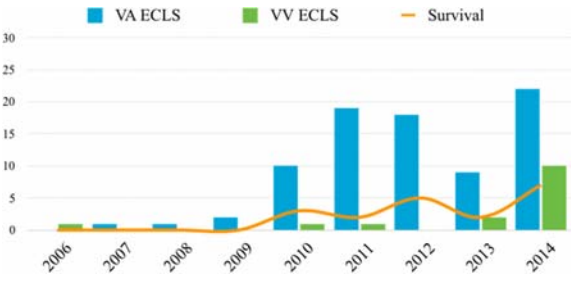
From January 1, 2006 to December 31, 2014, there were 97 patients treated with extracorporeal life support. Sixty-eight patients (70.1%) died in ECLS. The rest 29 patients (30%) could be weaned off from ECLS; however, among these, 10 patients (10.3%) didn't survive ICU. Only 19 patients (19.6%) survived to hospital discharge.

The majority of the patients were men (62.9%) with the mean age of 43.26 years. The three most common comorbidities were hypertension (34%), dyslipidemia (28.9%), and diabetes mellitus (20.6%). Coronary artery disease, chronic kidney disease, and history of treated malignancy were ranked fourth to sixth respectively. Forty-three percent of the patients had cardiac arrest before receiving ECLS. Thirty-two percent of patients were treated with intra-aortic balloon pump prior to ECLS (Table 1). The three most common primary diagnoses for intensive care unit admission and extracorporeal life support were congenital heart disease (20.6%), valvular heart disease, and acute respiratory distress syndrome (17.5% each) (Table 2). There was no statistically significant difference in terms of gender, age, comorbidity, prior cardiac arrest or IABP, and the primary diagnosis between the patients who survived to discharge and who died in the hospital (Table 1 and 2).



ECLS = extracorporeal life support

Fig. 1 Study profile.



VA ECLS = venoarterial extracorporeal life support; VV ECLS = venovenous extracorporeal life support.

Fig. 2 Extracorporeal life support at Siriraj Hospital from 2006 to 2014.

Table 1. Demographic data and patients' characteristics

	Overall (n = 97)	Survived to discharge (n = 19)	Died in hospital (n = 78)	*p*-value
Male gender	61 (62.9%)	14 (73.7%)	47 (60.3%)	0.30
Age (years)	43.26± 25.69	34.63±28.43	45.36±24.71	0.10
Hypertension	33 (34%)	6 (31.6%)	27 (34.6%)	1.00
Dyslipidemia	28 (28.9%)	3 (15.8%)	25 (32.1%)	0.26
Diabetes	20 (20.6%)	3 (15.8%)	17 (21.8%)	0.75
Coronary artery disease	19 (19.6%)	1 (5.3%)	18 (23.1%)	0.11
Ischemic stroke	4 (4.1%)	2 (10.5%)	2 (2.6%)	0.17
Chronic kidney disease	12 (12.4%)	1 (5.3%)	11 (14.1%)	0.45
Treated malignancy	11 (11.3%)	1 (5.3%)	10 (12.8%)	0.46
ECLS days	5.69±6.63	8.63±10.85	4.97±4.96	0.03
Length of stay (days)	22.49±31.18	66.58±42.82	11.76±13.68	0.00
Cardiac arrest	42 (43.3%)	7 (36.8%)	35 (44.9%)	0.61
IABP prior to ECLS	31 (32%)	4 (21.1%)	27 (34.6%)	0.29

ECLS = extracorporeal life support; IABP = intra-aortic balloon pump

Table 2. Primary diagnoses for admission to intensive care unit and extracorporeal life support

	Overall (n = 97)	Survived to discharge (n = 19)	Died in hospital (n = 78)	*p*-value
Congenital heart disease	20 (20.6%)	7 (36.8%)	13 (16.7%)	0.63
Valvular heart disease	17 (17.5%)	4 (21.1%)	13 (16.7%)	0.74
ARDS	17 (17.5%)	3 (15.8%)	14 (17.9%)	1.00
Acute coronary syndrome	16 (16.5%)	2 (10.5%)	14 (17.9%)	0.52
Coronary artery disease	12 (12.4%)	1 (5.3%)	11 (14.1%)	0.45
Pulmonary embolism	8 (8.2%)	1 (5.3%)	7 (9.0%)	0.70
Aortic dissection	8 (8.2%)	2 (10.5%)	6 (7.7%)	0.70
Cardiomyopathy	7 (7.2%)	1 (5.3%)	6 (7.7%)	0.71
Myocarditis	4 (4.1%)	2 (10.5%)	2 (2.6%)	0.17
Aortic aneurysm	3 (3.1%)	0 (0%)	3 (3.8%)	0.61
Other	5 (5.2%)	1 (5.3%)	4 (5.1%)	1.00

ARDS = acute respiratory distress syndrome

During the nine years, 82 patients (84.54%) were treated with venoarterial extracorporeal life support while 15 patients (15.46%) were treated with venovenous configuration. The survival rate in the first four years was zero. However, the overall survival rate was 19.6%, with 20.7% from venoarterial ECLS and 13.3% from venovenous ECLS. There has been an upward trend in the number of patients as well as the survival rate.

There were five major indications for extracorporeal life support-respiratory failure from severe acute respiratory distress syndrome, low cardiac output, postcardiotomy cardiogenic shock, cardiac and respiratory failure, and extracorporeal cardiopulmonary resuscitation. Postcardiotomy cardiogenic shock was the most common indication, 26% (Fig. 3) and had the highest survival rate of 36.8%. Meanwhile, none of the patients who were treated with extracorporeal cardiopulmonary resuscitation survived (Table 3).

The mean SOFA scores of the ECLS-survivor group and the ECLS non-survivor group obtained on the first day of ECLS treatment were not significantly different (12.75±2.44 and 13.66±2.83; $p = 0.144$). When comparing the mean SOFA scores between the hospital-

survivor group and the non-survivor group, there were not significantly different either (12.94±2.41 and 13.49±2.81; p = 0.455). Among the 29 patients who survived ECLS, the mean SOFA scores of the patients who survived to discharge and the patients who did not survive ICU were not statistically significant either the scores obtained on the day of ECLS placement (12.94±2.41 and 12.4±2.59; p = 0.582) or on one day before ECLS removal (11.17±3.03 and 12.3±1.89; p = 0.296). However, the SOFA score obtained on one day after ECLS removal was significantly lower in the survivor group (9.89±3.78 versus 14.40±2.95, p = 0.003) (Table 4).

The coordinates of the Receiver operating characteristic (ROC) curve are shown in the Table 5.

This chart showed the trends of the SOFA scores of the patients who could be weaned off the ECLS. The SOFA score in the non-survivor group has tended upwards over time while the score in the survivor group has tended downwards (Fig. 4).

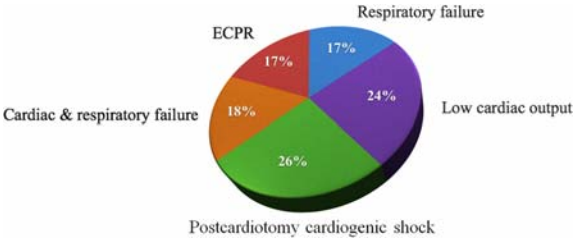
Among the twenty-nine ECLS survivors, the SOFA scores obtained on one day after removal of the extracorporeal life support were analyzed by the receiver-operating characteristic curve. The area under the curve (AUC) was 0.832 (95% confidence interval [CI]: 0.676 to 0.987, p = 0.004) (Fig. 5).

Discussion

The SOFA score when utilized to assess the patients on the day of treatment with extracorporeal life support could not predict either the patients' survival from ECLS or the hospital as the mean SOFA scores between the ECLS-survivors (n = 29) and non-survivors (n = 68) were not significantly different as well as the mean scores between the hospital-survivors (n = 19) and non-survivors (n = 78). Among the ECLS-survivors, the score when obtained during the ECLS treatment-either on the day of ECLS placement or one day before ECLS removal-still could not predict the hospital-survival. However, the SOFA score could predict the survival of a patient only after ECLS removal as the scores obtained one day after ECLS removal was significantly lower the in the survivor group. From the receiver operating characteristic analysis, the SOFA score obtained on one day after ECLS removal is a good test to predict the patient's survival (AUC = 0.832; 95% CI of 0.676 to 0.987, p = 0.004). The lower the SOFA score, the higher the chance of a patient's survival. All survivors had the SOFA score of less than 10.50, while all non-survivors had the score of more than or equal to 15.50. However, the appropriate cutoff point of the SOFA score to predict a patient's survival cannot be accurately determined because of downward bulge in the middle of the ROC curve, which represents the range of the SOFA scores of 10.50 to 15.50.

Limitations of the study

This is a retrospective, single-center study,



ECPR = extracorporeal cardiopulmonary resuscitation

Fig. 3 Indications for extracorporeal life support.

Table 3. Survival according to indication of extracorporeal life support

Indication	Survival
Postcardiotomy cardiogenic shock	36.8%
Low cardiac output	31.6%
Cardiac and respiratory failure	21.1%
Respiratory failure from ARDS	10.5%
ECPR	0%

ARDS = acute respiratory distress syndrome; ECPR = extracorporeal cardiopulmonary resuscitation

Table 4. SOFA scores over time, comparing between hospital survivors and non-survivors in patients who survived extracorporeal life support

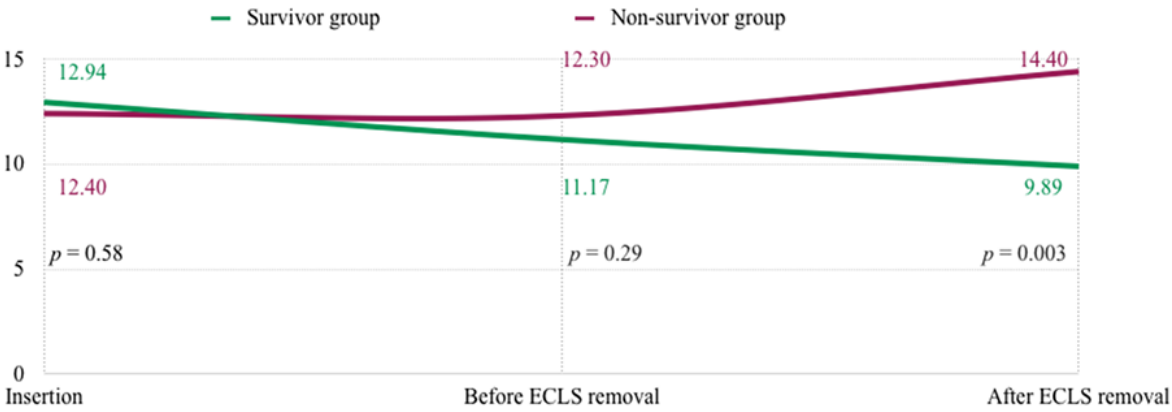
	Hospital survivors (n = 19)	Non-survivors (n = 10)	p-value
SOFA score on the first day of ECLS	12.94±2.41	12.4±2.59	0.582
SOFA score one day before ECLS removal	11.17±3.03	12.3±1.89	0.296
SOFA score one day after ECLS removal	9.89±3.78	14.4±2.95	0.003

SOFA = Sequential Organ Failure Assessment; ECLS = extracorporeal life support

Table 5. Coordinates of the ROC curve of the SOFA scores obtained on one day after removal of ECLS

Survived to discharge if SOFA score less than or equal to	Sensitivity	1-Specificity
2.00	0.000	0.000
3.50	0.053	0.000
5.00	0.158	0.000
6.50	0.211	0.000
7.50	0.263	0.000
9.00	0.368	0.000
10.50	0.579	0.100
11.50	0.579	0.200
12.50	0.632	0.300
13.50	0.789	0.400
14.50	0.947	0.400
15.50	1.000	0.600
17.50	1.000	0.900
20.00	1.000	1.000

ROC = receiver operating characteristic; SOFA = Sequential Organ Failure Assessment; ECLS= extracorporeal life support



SOFA = Sequential Organ Failure Assessment; ECLS = extracorporeal life support

Fig. 4 SOFA scores over time, comparing between hospital survivors and non-survivors in patients who survived extracorporeal life support.

which may be biased by the patient and treatment selection as the attending physician was the only one who decides whether to initiate extracorporeal life support or not and when to terminate the treatment. Moreover, the sample size of this study (ones who survived ECLS) is rather small even though the duration of the study was quite long (nine years). This might be from the patients' grave prognosis as the mean SOFA score on the first day of ECLS treatment of all patients was 13.38, which correlatedwith the mortality risk as high as 50-60% (from a prospective study in ICU patients)[4], while the mean SOFA scores in other studies ranged from 11.3 to 13[6,7]. This might partly be a result of delayed decision to initiate the extracorporeal life support because of the physicians' lack of experience during the initial period of ECLS treatment at Siriraj Hospital. It was evident that none of the patients survived during the first four years of extracorporeal life support at Siriraj Hospital while during the last five years there was an upward trend in both the number of patients and the survival rate.

Conclusion

The SOFA score could not predict the success

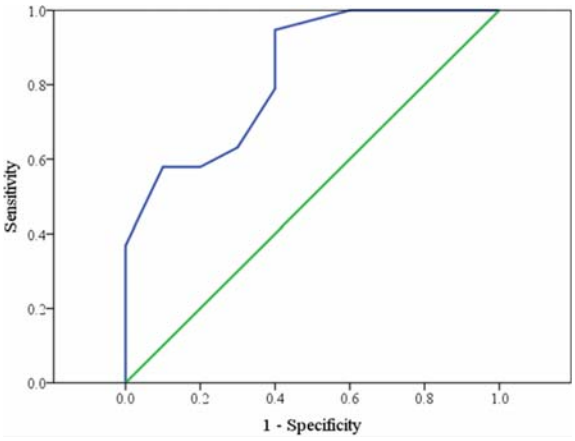


Fig. 5 Receiver operating characteristic (ROC) curve of SOFA scores obtained on one day after removal of ECLS.

of removal of the extracorporeal life support or survival to hospital discharge of a patient while he or she was receiving ECLS treatment. However the SOFA score could be a useful tool to predict the hospital survival of a patient when it was obtained after removal of extracorporeal life support. The lower the SOFA score, the higher the chance of a patient's survival, especially when the SOFA score was less than 10.50. On the other hand, the higher the SOFA score, the higher the chance of a patient's death, particularly the score of more than or equal to 15.50.

What is already known on this topic?

The extracorporeal life support has been widely utilized in Thailand during the last decade, but the results of treatment are still unsatisfactory. Predicting the results of the treatment and the outcome of the patients is frequently difficult. Therefore, a practical, objective, and reliable tool is needed to help evaluate the severity, morbidity, and mortality of the patients undergoing ECLS, who are critical and complicated.

The Sequential Organ Failure Assessment or SOFA score comprises of six variables, each representing an organ system, assigned a point value from 0 (normal) to 4 (failure). Studies have shown that high SOFA scores were associated with higher mortality and increased SOFA score during ICU admission also correlated with higher mortality.

What this study adds?

The SOFA score when utilized to assess the patients on the first day of ECLS treatment could not predict either removal of the ECLS or survival of the patient. However, among the ECLS survivors, the SOFA score assessed after ECLS removal could predict hospital survival as the lower the SOFA score, the higher the chance of a patient's survival.

Potential conflicts of interest

None.

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Sequential Organ Failure Assessment (SOFA) Score สามารถทำนายการเสียชีวิตของผู้ป่วยที่ได้รับการรักษาด้วยเครื่องพยุงการทำงานของปอดและหัวใจได้หรือไม่

ปรัญญา สากิยลักษณ์, ภาวนา ฌานวังศะ

วัตถุประสงค์: *เพื่อศึกษาการนำ Sequential Organ Failure Assessment (SOFA) score มาใช้ประเมินผู้ป่วยที่ได้รับการรักษาด้วยเครื่องพยุงการทำงานของปอดและหัวใจ (extracorporeal life support; ECLS)*

วัสดุและวิธีการ: *การศึกษานี้ได้ศึกษาข้อมูลย้อนหลังจากแฟ้มประวัติผู้ป่วยวิกฤตทั้งหมด 97 รายที่ได้รับการรักษาด้วยเครื่องพยุงการทำงานของปอดและหัวใจตั้งแต่เดือนมกราคม พ.ศ. 2549 ถึง เดือนธันวาคม พ.ศ. 2557 ข้อมูลที่เก็บประกอบด้วย ข้อมูลประชากร โรคร่วม คำวินิจฉัยโรคหลัก ระยะเวลาที่ได้รับการรักษาด้วยเครื่องพยุงการทำงานของปอดและหัวใจ ระยะเวลาที่ได้รับการรักษาในโรงพยาบาล การมีภาวะหัวใจหยุดเต้นและการใส่ intra-aortic balloon pump ก่อนการรักษาด้วยเครื่องพยุงการทำงานของปอดและหัวใจ รูปแบบและข้อบ่งชี้ในการใส่เครื่องพยุง การทำงานของปอดและหัวใจ ข้อมูลทางคลินิกและผลการตรวจทางห้องปฏิบัติการและผลการรักษา จากนั้นจะคำนวณ SOFA score ของผู้ป่วยแต่ละราย*

ผลการศึกษา: *อัตราการรอดชีวิตโดยรวมคิดเป็น 19.6% ข้อบ่งชี้ในการรักษาที่พบบ่อยที่สุดคือ ภาวะช็อคเหตุหัวใจ ภายหลังการผ่าตัด (postcardiotomy cardiogenic shock) ซึ่งคิดเป็น 26% เมื่อนำ SOFA score มาใช้ประเมินผู้ป่วยในวันแรกที่ให้รักษาด้วยเครื่องพยุงการทำงานของปอดและหัวใจ จะไม่สามารถทำนายว่าผู้ป่วยสามารถยุติการรักษาด้วยเครื่องพยุงการทำงานของปอดและหัวใจ หรือรอดชีวิตได้หรือไม่ (SOFA score เฉลี่ยในกลุ่มผู้ป่วยที่สามารถยุติการรักษาด้วยเครื่องพยุงการทำงานของปอดและหัวใจได้ คือ 12.75±2.44 ส่วน SOFA score เฉลี่ยในกลุ่มผู้ป่วยที่เสียชีวิตในระหว่างการรักษาคือ 13.66±2.83 โดยที่ p = 0.144 สำหรับ SOFA score เฉลี่ยในกลุ่มผู้ป่วยที่รอดชีวิตออกจากโรงพยาบาลได้คือ 12.94±2.41 ในขณะที่ SOFA score เฉลี่ยในกลุ่มผู้ป่วยที่เสียชีวิตในโรงพยาบาลคือ 13.49±2.81 โดยที่ p = 0.455) อย่างไรก็ตามในกลุ่มผู้ป่วยที่สามารถยุติการรักษาด้วยเครื่องพยุงการทำงานของปอดและหัวใจได้ SOFA score ที่ประเมินหลังจากการยุติการรักษา สามารถทำนายการรอดชีวิตออกจากโรงพยาบาลได้ โดย SOFA score ในกลุ่มที่รอดชีวิตคือ 9.89±3.78 ในขณะที่ SOFA score ในกลุ่มที่เสียชีวิตคือ 14.40±2.95 โดยที่ p = 0.003 เมื่อวิเคราะห์ด้วย Receiver-operating characteristic (ROC) curve พบว่า พื้นที่ใต้กราฟ (area under the curve; AUC) ของ SOFA score ที่ประเมินหลังยุติการรักษาด้วยเครื่องพยุงการทำงานของปอดและหัวใจ 1 วัน คือ 0.832 (ช่วงความเชื่อมั่น 95% คือ 0.676 ถึง 0.987, p = 0.004) อย่างไรก็ตามจุดตัดของ SOFA score ที่เหมาะสมสำหรับทำนายการรอดชีวิตของผู้ป่วยนั้นไม่สามารถบอกได้ชัดเจนเนื่องจากช่วงกลางของกราฟ ROC มีลักษณะยุบลง ซึ่งเป็นช่วงของ SOFA score 10.50 ถึง 15.50*

สรุป: *SOFA score เป็นเครื่องมือที่มีประโยชน์ในการทำนายการรอดชีวิตของผู้ป่วยภายหลังจากการรักษาด้วยเครื่องพยุงการทำงานของปอดและหัวใจ โดย SOFA score ยิ่งต่ำ ผู้ป่วยยิ่งมีโอกาสรอดชีวิตสูง อย่างไรก็ตาม SOFA score ไม่สามารถทำนายความสำเร็จในการยุติการรักษาด้วยเครื่องพยุงการทำงานของปอดและหัวใจได้ อีกทั้งไม่สามารถทำนายการรอดชีวิตของผู้ป่วยในขณะที่ผู้ป่วยยังได้รับการรักษาอยู่ด้วยส่วนหนึ่งอาจเป็นจากการเปลี่ยนแปลงทางสรีรวิทยาของระบบต่างๆ ของร่างกายภายหลังจากการรักษาด้วยเครื่องพยุงการทำงานของปอดและหัวใจ*