Venoarterial-Extracorporeal Membrane Oxygenation for Refractory Cardiogenic Shock Post-Cardiac Arrest

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Online data supplement

Methods

Patient management

Clinical features of poor outcome included absence of pupillary light reflex or corneal reflex after 72 h, absence of motor reaction to pain or extension posturing after 72 h. Electroencephalography features of poor outcome included diffuse suppression or low voltage at 24 h, burst suppression at 24 h, absence of reactivity after return to normothermia. The decision to withdraw care was made based on clinical examination and EEG findings. Patients with reactivity to stimuli on EEG were deemed to have potentially favorable outcomes and their care was pursued. In ambiguous cases, care was continued, and prognostic examination and EEG were repeated several days later. Somatosensory evoked potentials were not used because this technique is not available at the bedside in our unit.

Data collection

The following information was recorded: age; sex; severity of underlying condition(s), according to the McCabe and Jackson, and Charlson criteria [E1]; body mass index; Utstein style variables related to cardiac arrest (CA): CA cause; where CAoccurred; first rhythm monitored, duration of resuscitation (no-flow and low-flow), witnessed CA and bystander-attemptedcardiopulmonary resuscitation (CPR). The following variables were recorded during the first 24 h followingECMO implantation: Simplified Acute Physiology Score (SAPS) II [E2], Sequential Organ Failure Assessment (SOFA) score [E3]and out-of-hospital CA (OHCA) score [E4]; time between CA and VA-ECMO implantation; pre-ECMO left ventricular ejection fraction (LVEF) and aortic velocity-time integral (VTI); temperature; heart rate; respiratory rate; day-1 (day of ECLO implantation) urine output; and blood laboratory findings (leukocyte and platelet counts, hematocrit, pH, bicarbonates, arterial lactate peak, serum sodium, potassium, creatinine, urea, bilirubin, international normalized

ratio (INR), alanine aminotransferase (ALT) peak). The Survival After Veno-arterial

Extracorporeal membraneoxygenation (SAVE) score was also retrospectively calculated for

all patients [E5], and the ENCOURAGE (prEdictioN of Cardiogenic shock OUtcome foR

AMI patients salvaGed by VA-ECMO) score was calculated retrospectively for the 67

patients with OHCA of ischemic origin [E6].

Results

Outcome

The ability to differentiate between survivors and non-survivors, based on SAVE score, was

assessed with receiver operating-characteristics (ROC)–curve analysis (Fig. E3). The area

under the ROC curve was 0.66 (95% CI 0.55–0.75). To predict hospital death, a SAVE score

cut-off value of −11 had 77% (95% CI, 63–88) sensitivity and 63% (95% CI 38–84)

specificity.

Subgroup analyses of patients with OHCA due to acute coronary syndrome

For 67 (71%) of our patients,CA was due to acute coronary syndrome and occurred out-of-

hospital, in the emergency department or in the catheterization lab. Their characteristics are

described in Table E5. When the analysis was restricted to these patients, similar results were

obtained: 21 (31%) survived, and shockable rhythm (OR 0.9; 95% CI 0.01–0.8), INR >2.4

(OR 5.7; 95% CI 1.3–25.9) and admission SOFA score >14 (OR 6.2; 95% CI 1.5–25)

wereindependently associated with hospital mortality. SAVE and ENCOURAGE scores were

not independently associated with outcomes.The ability to differentiate between survivors and

non-survivors, based on the ENCOURAGE score, was assessed with ROC-curve analysis

(Figure E4). To predict hospital death, an ENCOURAGE score cut-off value of 25 had 77%

(95% CI 63–88) sensitivity and 63% (95% CI 38–84)specificity.

Table E1. ICU Admission clinical and biological characteristics of VA-ECMO–

treatedpatients

Characteristic	Entire Cohort	Survivors	Non-Survivors	*P*
	(*n*=94)	(*n*=26)	(*n*=68)	
Day-1 clinical (worst value)				
Temperature (°C)	31.9 [30.6–33.6]	32.1 [31.2–35.4]	31.8 [30.5–33.2]	0.06
Heart rate (bpm)	71 [54–116]	104 [57–121]	68 [53–110]	0.1
Urine output (mL)	525 [87–1625]	1400 [918–2250]	250 [0–1500]	<0.0001
Day-1 biological parameter (worst value)				
Leukocyte count (G/L)	18±8	20.2±8.6	17±8.1	0.09
Hematocrit (%)	29 [24–34]	31.5 [25.7–37]	26 [23–32]	0.03
Platelet count (G/L)	173±90	213±91	159±85	0.007
pH	7.11±0.16	7.17±0.16	7.08±0.16	0.02
Serum creatinine (μmol/L)	141 [113–198]	122 [93.7–159]	150 [117–198]	0.08
Serum bilirubin (μmol/L)	12 [8–16]	11 [7–13.2]	13 [8–17.7]	0.1
Arterial lactate peak (mmol/L)	11.5 [9–17]	9.6 [7.8–11.4]	12.6 [9.5–20]	<0.0001
INR	2.4 [1.6–4.8]	1.9 [1.8–2.4]	2.9 [1.9–5.5]	0.003
ALT peak[a] (IU/L)	279 [135–1230]	175 [80–490]	384 [166–1630]	0.03

Abbreviations: *INR* international normalized ratio, *ALT* alanine aminotransferase.

[a]ALT was not available for 1 non-survivor.

Table E2. Outcome measures for all 94 VA-ECMO–treated patients according to the use of intraaortic balloon pump

Outcome measure	IABP (*n*=47)	No IABP (*n*=47)	*P*
VA-ECMO duration (days)	5 [3-8]	3 [1-5]	0.1
ICU length of stay (days)	6 [2-14]	3 [1-10]	0.7
MV duration (days)	5 [3-14]	3 [2-9]	0.2
ECMO complications			
Limb ischemia	6 (12.8)	8 (17)	0.5
Fasciotomy	0 (0)	4 (9)	0.04
Amputation	0 (0)	1 (2)	0.3
Bleeding	12 (26)	12 (26)	1
Infection	10 (21)	7 (15)	0.4
VA-ECMO weaning			
Yes	16 (34)	17 (36)	0.8
No	31 (66)	30 (64)	0.7
Died on ECMO	28 (60)	30 (64)	0.8
LVAD	4 (9)	1 (2)	0.1
Heart transplantation	2 (4)	0 (0)	0.5
28-day survival	17 (36)	13 (28)	0.3
6-month survival	16 (34)	10 (21)	0.16
12-month survival	16 (34)	9 (19)	0.1

Abbreviations:*VA-ECMO* venoarterial-extracorporeal membrane oxygenation,*ICU* intensive care unit,*MV* mechanical ventilation,*IABP* intra-aortic balloon pump,*LVAD*left ventricular assist device

Continuous variables are expressed as median [IQR] and categorical variables as *n* (%).

Table E3. Main characteristics of all VA-ECMO–treated patients at ICU admission and comparisons between 1-year survivors and non-survivors

Characteristic	Entire Cohort (*n*=94)	Survivors (*n*=25)	Non-Survivors (*n*=69)	*P*
Age (y)	50.8±11.5	49.8±10.2	51.1±12	0.6
Male sex	71 (76)	19 (76)	52 (75.4)	0.9
Body mass index (kg/m^2)	26.2 [23.4–29.3]	26.2 [23.6–28.5]	26.1 [23.4–29.4]	0.9
McCabe & Jackson score for comorbidity	1 [0–2]	0 [0–1.5]	1 [0–2]	0.4
SAPS II	82 [77–88]	77 [70.5–83]	84 [78.5–88.5]	0.004
SOFA score	15 [13–17]	13 [12–14.5]	16 [14–18]	<0.0001
Organ failure[a]				
Cardiovascular system	94 (100)	25 (100)	69 (100)	–
Lung	94 (100)	25 (100)	69 (100)	–
Brain	91 (97)	23 (92)	68 (98.6)	0.1
Kidney	48 (51)	5 (20)	43 (62.3)	<0.0001
Hematological	6 (6)	1 (4)	5 (7.2)	0.6
Liver	2 (2)	0 (0)	2 (2.9)	0.4
OHCA score	41.3 [30.8–50.9]	32.9 [24.3–43.3]	43.7 [33.2–51.8]	0.002
Etiology of cardiac arrest				
Myocardial infarction	66 (70)	18 (72)	48 (69.6)	0.8
AD of chronic cardiomyopathy	8 (9)	3 (12)	5 (7.2)	0.5
Pulmonary embolism	4 (4)	2 (8)	2 (2.9)	0.3
Drug intoxication	3 (3)	0 (0)	3 (4.3)	0.3
Anaphylactic shock	3 (3)	2 (8)	1 (1.4)	0.1

Miscellaneous[b]	10 (11)	0 (0)	10 (14.5)	0.04
Witnessed CA	88 (94)	24 (96)	64 (92.8)	0.6
Attempted defibrillation	56 (60)	20 (80)	36 (52.2)	0.01
Bystander-attempted CPR	76 (81)	20 (80)	56 (81.2)	0.9
No Flow (min)	0 [0–5]	0 [0–3]	0 [0–5]	0.8
Low Flow (min)	30 [15–42.7]	30 [10–40]	30 [16–45]	0.4
Out-of-hospital CA	78 (83)	21 (84)	57 (83)	0.8
Shockable rhythm	56 (60)	20 (80)	36 (52.2)	0.01
CA-to-VA-ECMO interval (h)	7.4 [3.3–14]	10.3 [4.1–17.7]	6.5 [3–13.4]	0.1
Therapeutic hypothermia	75 (80)	19 (76)	56 (81.2)	0.6
Echocardiographic findings before ECMO implantation				
LVEF[c] (%)	15 [10–20]	15 [10–20]	15 [10–20]	0.4
Aortic VTI[d] (cm)	7 [5–9]	8 [5.8–10.5]	6 [5–8]	0.04
Day-1 clinical (worst value)				
Temperature (°C)	31.9 [30.6–33.6]	32.1 [31.1–34.9]	31.8 [30.5–33.3]	0.1
Heart rate (bpm)	71 [54–116]	105 [57–121]	68 [53–110]	0.2
Urine output (mL)	525 [87–1625]	1300 [862–2000]	250 [0–1510]	0.001
Day-1 biological (worst value)				
pH	7.11±0.16	7.17±0.16	7.09±0.16	0.05
Serum creatinine (μmol/L)	141 [113–198]	123 [99–164]	149 [117–198]	0.1
Serum bilirubin (μmol/L)	12 [8–16]	11 [7–12.5]	13 [18–17.5]	0.08
Arterial lactate peak (mmol/L)	11.5 [9–17]	9.7 [8.1–11.4]	12.6 [9.4–20]	0.001
INR	2.4 [1.6–4.8]	2 [1.5–2.4]	2.8 [1.8–5.5]	0.005
ALT peak[e] (IU/L)	279 [135–1230]	174 [79.5–425.5]	390 [167–1608]	0.02

Abbreviations; VA-ECMO, venoarterial extracorporeal membrane oxygenation; ICU, intensive care unit;

SAPS simplified acute physiology score, *SOFA* sequential organ failure assessment, *AD* acute decompensation,*CA* cardiac arrest,*CPR* cardiopulmonary resuscitation, *LVEF* left ventricular ejection fraction, *VTI*velocity-time integral, *day 1* day of ECMO implantation,*INR*international normalized ratio,*ALT* alanine aminotransferase

Continuous variables are expressed as mean ± SD or median [IQR] and compared using Student's *t*-test or Wilcoxon's rank test. Categorical variables are expressed as *n* (%) and were compared with χ^2 tests.

[a]Deemed present when the corresponding SOFA score was >2.

[b]Miscellaneous causes of CA: hypoxic CA and/or potassium disorders: 2 each; and 1 each: near drowning, myocarditis, subarachnoid hemorrhage, amniotic fluid embolism, postpartum hemorrhage, idiopathic cardiac arrhythmia.

[c]Available for 87 patients (24 survivors and 63 non-survivors);for the others, the information was not entered in the chart.

[d]Available for 67 patients (22 survivors and 45 non-survivors); for the others, the information wasnot entered in the chart.

[e]ALT was not available for 1 non-survivor.

Table E4. Univariable and multivariable analyses of factors associated with 1-year mortality

Factor	Univariable analysis OR [95% CI]	P	Multivariable analysis OR [95% CI]	P
Arterial lactate >11.5 mmol/L	5.8 [2–17.4]	0.002		
INR >2.4	7.7 [2.4–24.8]	0.001	4.8 [1.4–16.5]	0.01
Renal failure at ICU admission[a]	6.6 [2.2–19.7]	0.001		
Pre-VA-ECMO SOFA score >14	6.7 [2.3–19.3]	<0.0001	4.2 [1.4–12.9]	0.01
SAPS II >82	3.1 [1.1–8.5]	0.02		
Shockable rhythm	0.27 [0.09–0.8]	0.02		

Abbreviations: *OR* odds ratio, *CI* confidence interval, *INR* international normalized ratio, *ICU* intensive care unit, *VA-ECMO* venoarterial-extracorporeal membrane oxygenation, *SOFA* Sequential Organ Failure Assessment, *SAPS* Simplified Acute Physiology Score

[a]Defined as a renal SOFA score of 3 or 4.

Table E5. Main characteristics of patients with OHCA of ischemic origin under VA-ECMO

at ICU admission and comparisons between hospital survivors and non-survivors

Characteristic	Entire cohort (n=67)	Survivors (n=19)	Non-survivors (n=48)	P
Age (y)	53.1±9.7	50.1±9	54.1±9.8	0.1
Male sex	58 (86)	16 (84.2)	42 (87.5)	0.9
Body mass index (kg/m^2)	26.1 [23.9–28.4]	26.2 [23.8–27.7]	26.1 [23.6–29.1]	0.7
McCabe & Jackson				
comorbidity score	0.5 [0–2]	0 [0–2]	1 [0–2]	0.9
SAPS II	81 [77–86]	77 [68–82]	83 [79–88]	0.005
SOFA score	15 [13–16]	13 [12–14]	15 [14–17]	<0.0001
Organ failure[a]				
Cardiovascular system	67 (100)	19 (100)	48 (100)	–
Lung	67 (100)	19 (100)	48 (100)	–
Brain	65 (97)	18 (95)	47 (98)	0.4
Kidney	33 (49)	4 (21)	29 (60)	0.004
Hematological	2 (3)	0	2 (4)	0.3
Liver	0	0	0	–
OHCA score	40.2 [30.5–50.3]	31.9 [25.2–37.2]	42.9 [33–51.8]	0.001
No Flow (min)	0 [0–5]	1 [0–5]	0 [0–5]	0.6
Low Flow (min)	30 [20–45]	25 [13–45]	30 [20–45]	0.2
Witnessed CA	63 (94)	18 (95)	45 (94)	0.8
Attempted defibrillation	47 (70)	18 (95)	29 (60)	0.006
Bystander-attempted CPR	51 (76)	14 (74)	37 (77)	0.7
Shockable rhythm	47 (70)	18 (95)	29 (60)	0.006

Out-of-hospitalCA	67 (100)	19 (100)	48 (100)	–
CA-to-VA-ECMO interval (h)	9.1 [3.7–15.1]	11.1 [4.1–20.7]	8.2 [3.3–14.2]	0.1
Therapeutic hypothermia	54 (81)	13 (68)	41 (85)	0.1
Echocardiographic findings at ECMO implantation				
LVEF[b] (%)	15 [10–20]	15 [10–21.25]	15 [10–20]	0.3
Aortic VTI[c] (cm)	7 [5–8]	8 [5.6–11.5]	6 [5–8]	0.09
Day-1 clinical data (worst value)				
Temperature (°C)	32 [30.6–33.9]	33.7 [31–35.9]	31.8 [30.5–33.2]	0.06
Heart rate (bpm)	70 [54–117]	103 [58–121]	65 [53–110]	0.27
Day-1 urine output (mL)	750 [100–1550]	1500 [1000–2000]	350 [12.5–1475]	0.001
SAVE score risk class [E5]				0.01
I	–	–	–	
II	–	–	–	
III	4 (6)	1 (5)	3 (6)	
IV	18 (27)	10 (53)	8 (17)	
V	45 (67)	8 (42)	37 (77)	
ENCOURAGE score class[E6]				0.02
ENCOURAGE 0–12	–	–	–	
ENCOURAGE 13–18	4 (6)	3 (16)	1 (2)	
ENCOURAGE 19–22	9 (13)	2 (11)	7 (15)	
ENCOURAGE 23–27	17 (25)	8 (42)	9 (19)	
ENCOURAGE ≥28	37 (55)	6 (31)	31 (65)	
Day-1 biological data (worst value)				
pH	7.1±0.16	7.2±0.13	7.06±0.15	0.001
Serum creatinine (µmol/L)	144 [113–195]	118 [90–174]	153 [117–196]	0.1

Serum bilirubin (µmol/L)	12 [8–16]	9 [5–13]	13 [8.25–16.75]	0.021
Arterial lactate peak (mmol/L)	10.9 [8.5–14.1]	9.2 [7.9–11]	11.75 [9.1–16.6]	0.002
INR	2.2 [1.6–3.7]	1.6 [1.4–2.3]	2.7 [1.9–4.7]	0.005
ALT peak[d] (IU/L)	256 [157–969]	177 [78–460]	383 [171–1258]	0.04

Abbreviations: *VA-ECMO* venoarterial-extracorporeal membrane oxygenation, *ICU* intensive care unit, S*APS* Simplified Acute Physiology Score, *SOFA* Sequential Organ Failure Assessment, *OHCA* out-of-hospital cardiac arrest, *CA* cardiac arrest, C*PR* cardiopulmonary resuscitation, *LVEF* left ventricle ejection fraction, *VTI* velocity-time integral, *day 1* day of ECMO implantation, *SAVE* Survival After Venoarterial Extracorporeal membrane oxygenation, *ENCOURAGE* prEdictioN of Cardiogenic shock OUtcome foR AMI patients salvaGed by VA-ECMO, *INR* international normalized ratio, *ALT* alanine aminotransferase

Continuous variables are expressed as mean±SD or median [IQR] and compared using Student's *t*-test or Wilcoxon's rank test. Categorical variables are expressed as *n* (%) and were compared with χ^2 tests.
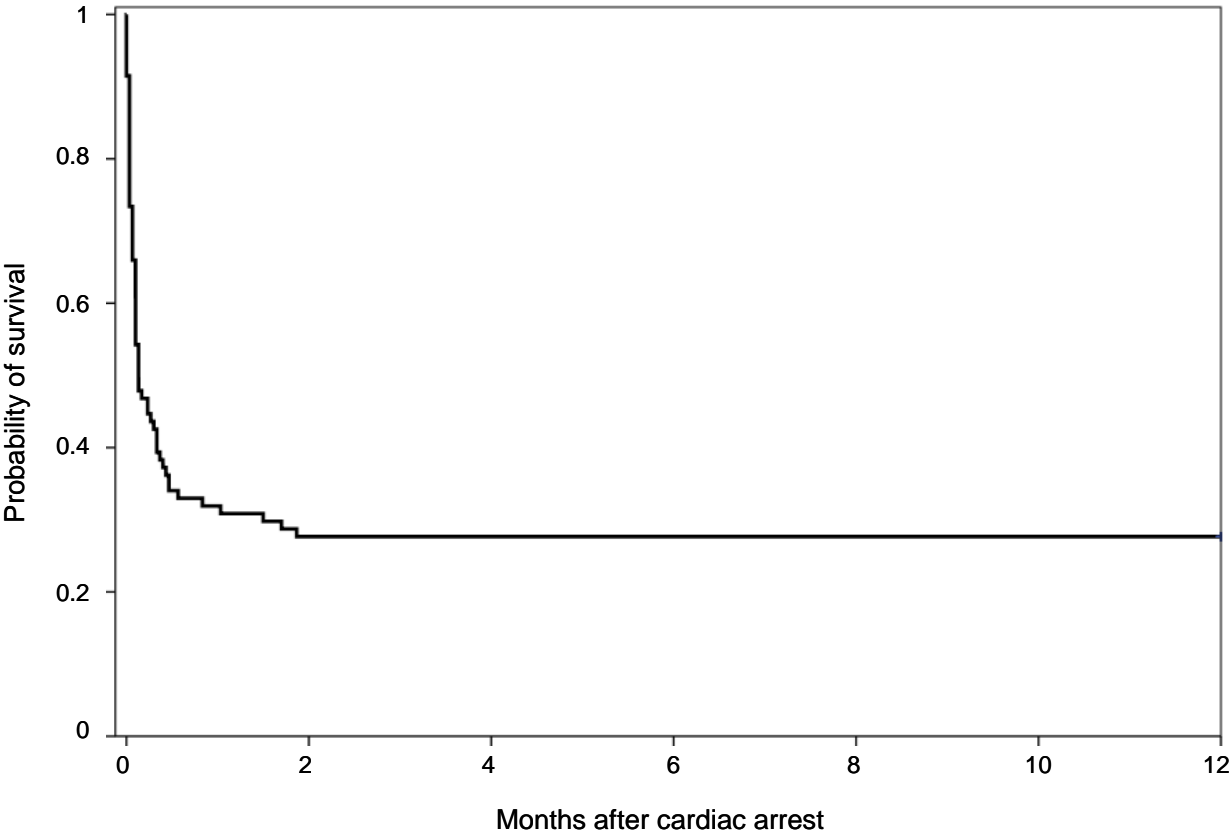
[a]Deemed present when the corresponding SOFA score was >2.

[b]Available for 63 patients (20 survivors and 43 non-survivors).

[c]Available for 47 patients (18 survivors and 29 non-survivors).

[d]Not available for 1 survivor.

Fig. E1 Kaplan–Meier probability of survival curve for all patients included in the study

Fig. E2. Kaplan–Meier probability of survival curves according to pre-venoarterial–extracorporeal membrane oxygenation Sequential Organ Failure Assessment (SOFA) score >14 or ≤14
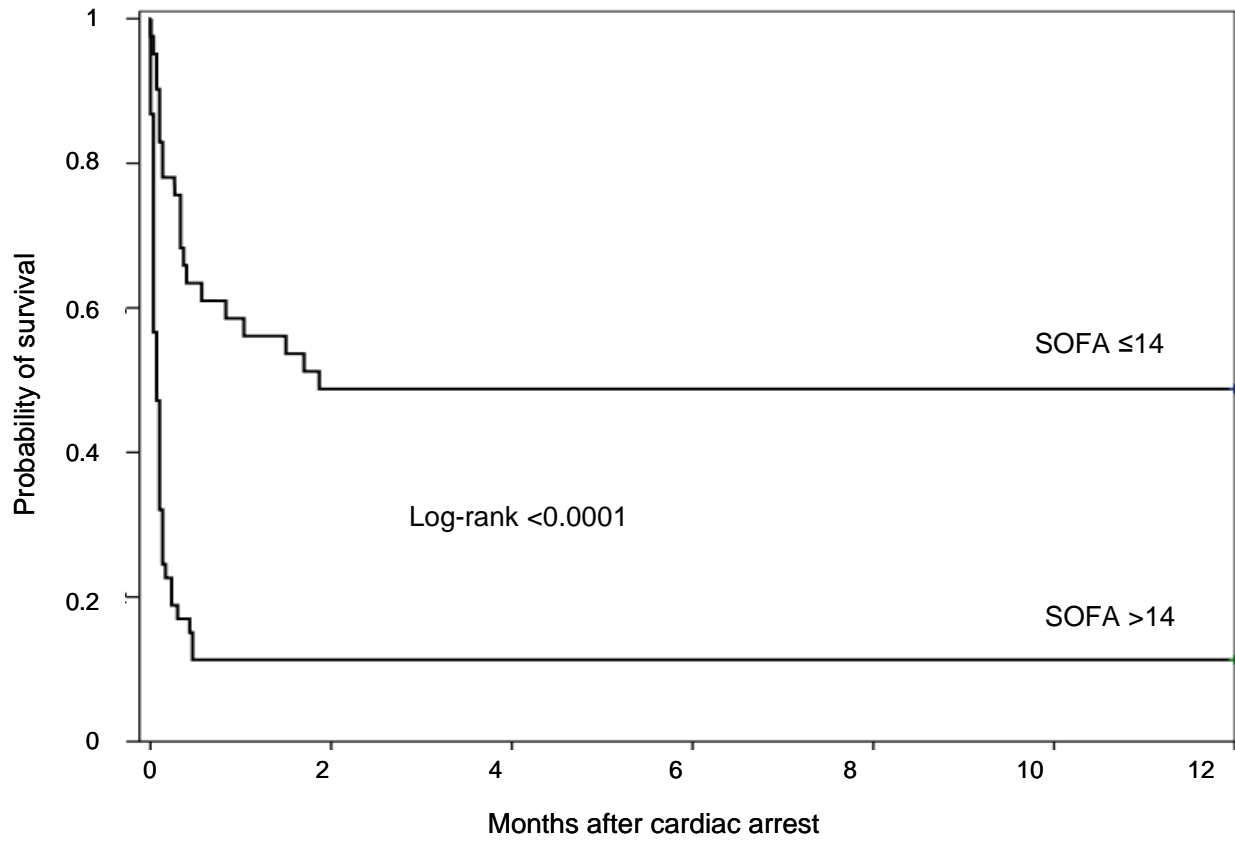
Fig. E3ROC-curve analysis of SAVE scores to predict hospital mortality for the 94 patients included in the study. Area under the ROC curve was 0.66 (95% CI 0.55–0.75).
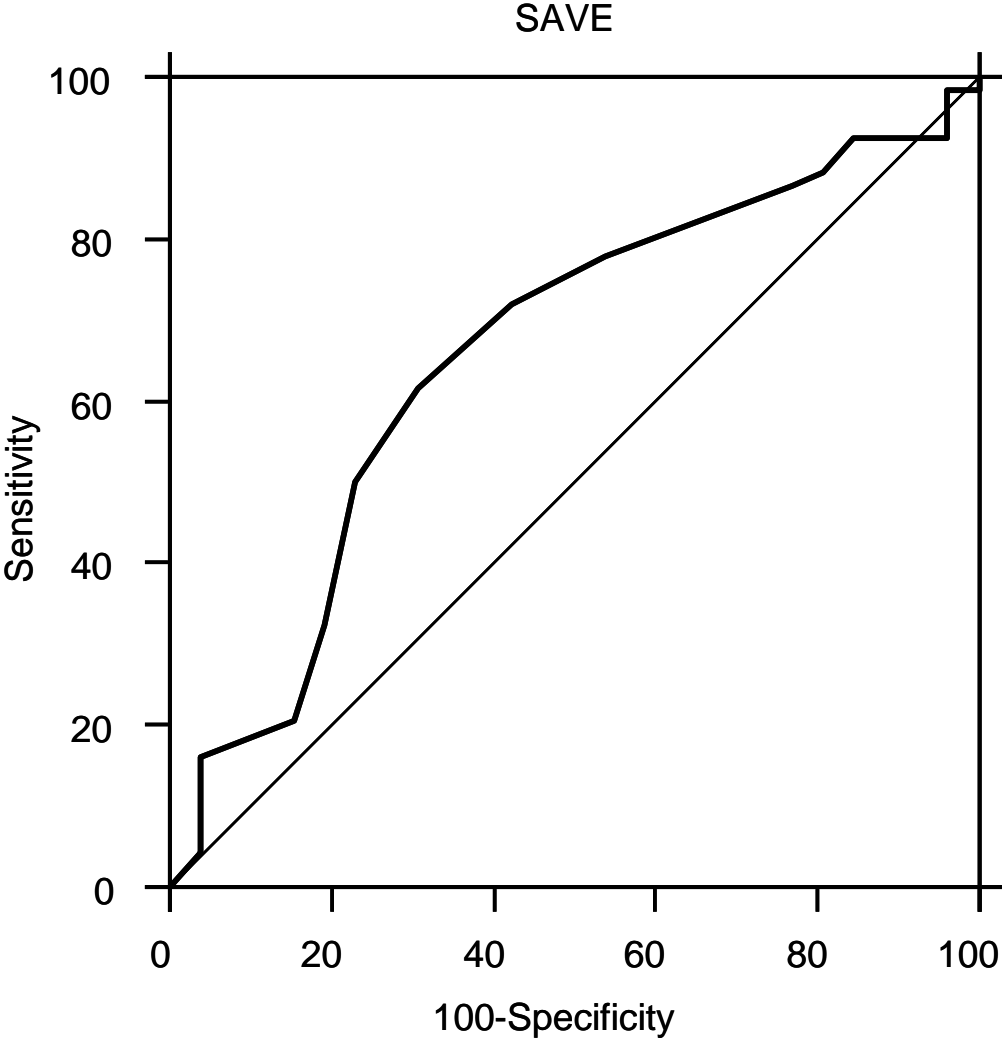
Fig. E4 ROC-curve analysis of ENCOURAGE scores to predict hospital mortality for the 67 patients with OHCA of ischemic origin. Area under the ROC curve was 0.70 (95%CI 0.58–0.81).
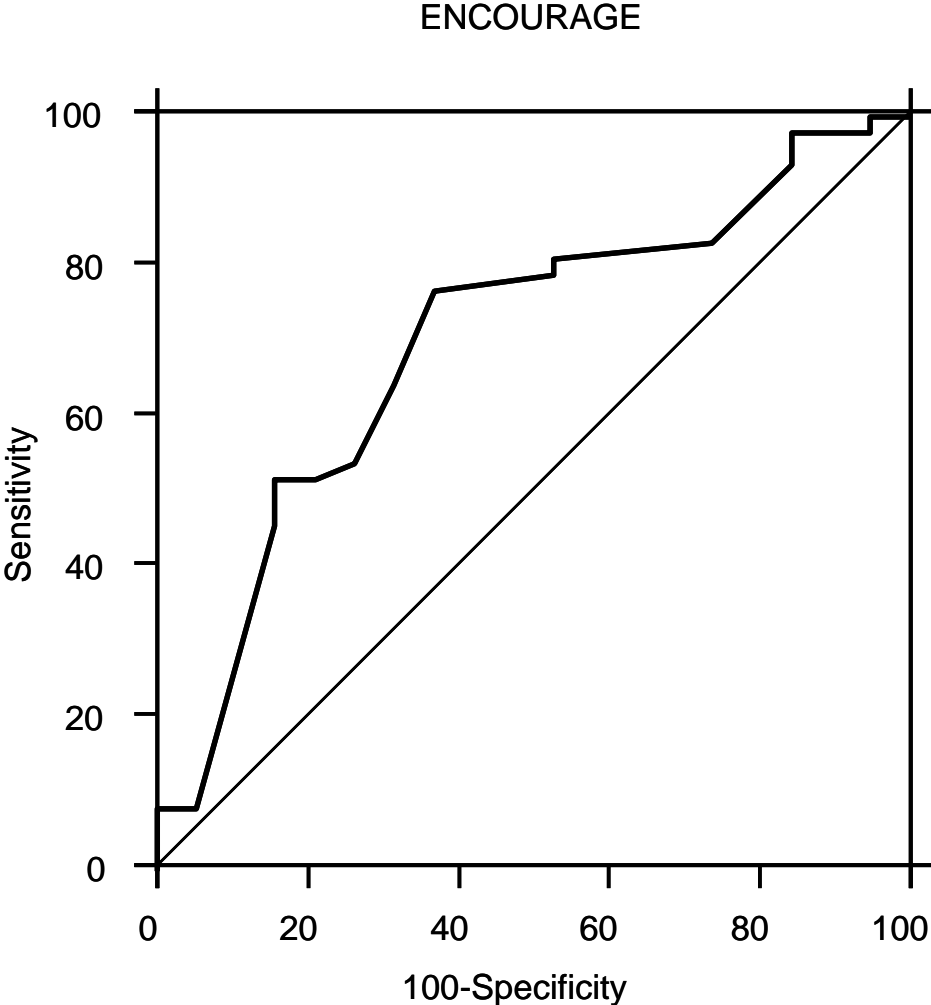
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