



# Central venous oxygen saturation/lactate ratio: a novel predictor of outcome following emergency open laparotomy

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## Abstract

**Introduction** Emergency laparotomy is associated with high rates of morbidity and mortality. The need for highly sensitive readily prognostic biomarkers is necessary to improve the outcome. We investigated the usefulness of post-operative arterial lactate and ScvO<sub>2</sub>/lactate ratio as predictors of outcome after post-operative emergency open laparotomy. To the best of our knowledge, the novel ScvO<sub>2</sub>/lactate ratio was not investigated before in emergency open laparotomy patients.

**Methods** It is a prospective observational cohort study. We investigated the usefulness of post-operative arterial lactate and ScvO<sub>2</sub>/lactate ratio as predictors of early mortality in 40 patients following emergency open laparotomy admitted to the ICU.

**Results** Admission and 24 h lactate levels were predictor of mortality with cut-off point > 3.95 mmol/L, sensitivity 100%, and specificity 93.3%, and cut-off > 3.5 mmol/L, sensitivity 100%, and specificity 96.7%, respectively. In this study, ScvO<sub>2</sub>/lactate ratio on admission was predictor of at day 7 with cut-off point < 13.95, sensitivity 100%, and specificity 96.7%  $p < 0.0001$ . Lactate at 12 and 24 h was also predictor of survival  $p < 0.0001$ . Serial arterial lactate was highly correlated to ICU length of stay; admission APACHE II and day 1; and 2 MODS and SOFA scores ( $p < 0.001$ ).

**Conclusion** Serial blood lactate as well as the novel ScvO<sub>2</sub>/lactate ratio can be useful for early predictors of mortality at 7 days. Serial lactate levels correlate to admission ICU scores APACHE II; MODS and SOFA in post-operative emergency open laparotomy patients.

**Keywords** Emergency open laparotomy · Central venous oxygen saturation (ScvO<sub>2</sub>) · Arterial lactate levels · ScvO<sub>2</sub>/lactate ratio · MODS · SOFA · APACHE II

## Introduction

Emergency laparotomy is associated with high rates of mortality and post-operative complications, as well as prolonged hospital stay [1]. Global tissue hypoxia (GTH) is often not recognized by use of routinely monitored vital signs or physical findings, such as urine output (UO).

Central venous oxygen saturation (ScvO<sub>2</sub>) and lactate have been used frequently to better guide clinicians to begin and optimize early hemodynamic treatment and determine the resolution of GTH [2]. Rivers et al. identified a subset of patients with severe sepsis and septic shock by an elevation in lactate and by optimizing early therapy—targeted at

the normalization of ScvO<sub>2</sub>—morbidity and mortality were improved [3].

Global tissue hypoxia after major surgery has been associated with a prolonged ICU course. More recently, abnormal lactate and ScvO<sub>2</sub> values obtained immediately after surgery have been found to detect latent shock, and elevated lactate and low ScvO<sub>2</sub> have been associated independently with an increased risk of complications after high-risk general surgical patients.

ScvO<sub>2</sub> have been shown to reflect circulatory insufficiencies successfully. Elevations in lactate have been associated with increased risk of morbidity and mortality in high-risk surgical patients. ScvO<sub>2</sub> has been associated independently with post-operative complications in patients who have undergone emergency laparotomy. Patients after emergency laparotomy who had prolonged ICU LOS have been found to have a significantly lower ScvO<sub>2</sub> [4].

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## Materials and methods

This is a prospective cohort observational study conducted on 40 patients, 22 males (55%) and 18 females (45%), Nasser institute hospital during 30 month duration. Patients were admitted to intensive-care unit following emergency laparotomy as specified by treating health care teams. All patients were subjected to post-operative care management according to ICU protocols. An arterial line is inserted and informed patient consent was obtained for all patients. The study was approved by critical care department and Cairo University ethical committee.

## Study criteria

### Inclusion criteria

Adult patients admitted to intensive-care unit after open emergency laparotomy for any cause and considered at high risk of post-operative complications.

**Table 1** Causes of emergency laparotomy

Cause of laparotomy	Number	Percentage (%)
Intestinal obstruction	11	27.5
Perforated DU	10	25.0
Strangulated hernia	6	15.0
Rupture appendix	5	12.5
Mesenteric vascular occlusion	3	7.5
Blunt/perforated trauma/traffic accident	4	10.0
Intra-abdominal abscess	1	2.5
Total	40	100.0

**Table 2** Need for cardio-respiratory support, ICU and hospital length of stay, and incidence of complications in survivors and non-survivors

Variable	All patients ( <i>n</i> =40)	Survivors (30)	Non-survivors (10)	<i>p</i> value
Need for vasopressors	20 (50.0%)	10 (33.3%)	10 (100.0%)	0.0004
Duration of vasopressor administration (h)	88.3 (21.3)	84.6 (23.9)	91.9 (18.9)	0.458
Need for MV	26 (65.0%)	16 (53.3%)	10 (100.0%)	0.007
Duration of MV (h)	75.4 (31.9)	59.2 (25.3)	101.4 (23.2)	0.0003
Length of ICU stay (days)	3.7 (1.2)	3.5 (1.2)	4.4 (1.2)	0.045
Length of hospital stay (days)	7.6 (2.3)	8.5 (1.7)	4.9 (1.8)	< 0.0001
Need for RRT	20 (50.0%)	11 (36.7%)	9 (90.0%)	0.008
Circulatory shock	20 (50.0%)	10 (33.3%)	10 (100.0%)	0.0004
Cardiac arrest	9 (22.5%)	1 (3.3%)	8 (80.0%)	< 0.0001
AKI	20 (50.0%)	10 (33.3%)	10 (100.0%)	0.0004
Arrhythmia	11 (27.5%)	5 (16.7%)	6 (60.0%)	0.014
CVS	6 (15.0%)	4 (13.3%)	2 (20.0%)	0.629

Data are number (percentage) or mean (standard deviation)

## Exclusion criteria

- Age less than 18 years.
- Intraoperative cardiac arrest.
- Presence of cardiogenic shock immediately before surgery.
- Patients with terminal malignancy.
- Metabolic inborn errors affecting lactate metabolism.
- Patients on metformin or any drug affecting lactate metabolism.

## Study procedure

Following ICU admission, all patients were subjected to detailed and full history taking and thorough clinical examination from the patient and/or his relatives.

In addition, routine laboratory labs plus arterial lactate and central venous oxygen saturation collected from central venous line every 6 h for 24 h. Comparative data between scores and morbidity and mortality, central venous oxygen saturation and lactate, and effect on morbidity and mortality were also collected.

## Outcome

Primary outcome is the mortality and secondary outcomes include length of hospital stay and development of major adverse events as shock, cardiac arrest, serious arrhythmias, acute kidney injury, and cerebrovascular stroke.

## Statistical methods

Data were analyzed using IBM® SPSS® Statistics version 23 (IBM® Corp., Armonk, NY, USA) and MedCalc® version 18.11.3 (MedCalc® Software bvba, Ostend, Belgium).

**Table 3** Serum lactate level and ScvO<sub>2</sub>/lactate ration in survivors and non-survivors

Variable	All patients (n=40)	Survivors (30)	Non-survivors (10)	p value
Serum lactate (mmol/l)				
On ICU admission	3.6 (1.0)	3.2 (0.8)	4.8 (0.6)	< 0.0001
At 12 h	3.3 (0.9)	2.9 (0.7)	4.3 (0.4)	< 0.0001
At 24 h	2.5 (1.1)	2.0 (0.5)	3.9 (1.2)	< 0.0001
ScvO <sub>2</sub> (%)				
On ICU admission	63.6 (7.5)	66.7 (5.2)	54.4 (5.8)	< 0.0001
At 12 h	73.2 (5.1)	75.1 (3.6)	67.4 (4.9)	< 0.0001
At 24 h	78.2 (4.7)	79.9 (2.3)	73.3 (6.7)	< 0.0001
ScvO <sub>2</sub> /lactate ratio				
On ICU admission	19.5 (7.2)	22.1 (6.3)	11.6 (2.0)	< 0.0001
At 12 h	24.6 (8.7)	27.6 (8.0)	15.7 (2.0)	< 0.0001
At 24 h	37.2 (15.2)	42.8 (12.9)	20.3 (6.4)	< 0.0001

Data are mean (standard deviation)

Continuous numerical data were presented as mean and standard deviation and intergroup differences were compared using the unpaired *t* test. Categorical data were presented as number and percentage and intergroup differences were compared using Fisher's exact test. Receiver-operating characteristic (ROC) curve analysis was used to examine the prognostic value of serum lactate or ScvO<sub>2</sub>/lactate ratio for prediction of mortality. Survival analysis was done using the Kaplan–Meier method. The log-rank test was used to compare individual Kaplan–Meier curves. *p* values < 0.05 were considered statistically significant.

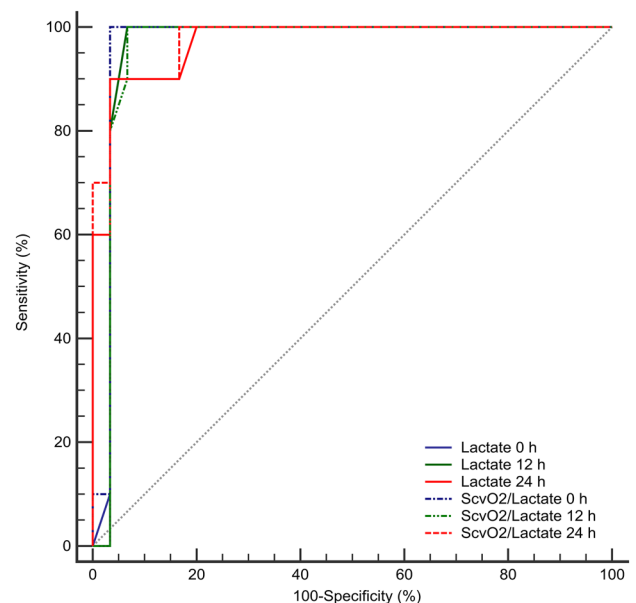
## Results

This is a prospective observational cohort study conducted on 40 post-operative patients admitted to the surgical intensive-care unit (ICU), Nasser institute hospital during the period from March 2013 to October 2015. The mean age of patients was  $59.7 \pm 12.9$  years (range 30–81 years). There were 22 males (55%) and 18 females (45%).

In our study, causes of emergency laparotomy were intestinal obstruction 11 patients (27.5%), perforated duodenal ulcer (DU) 10 patients (25%), complicated hernia 6 patients (15%), rupture appendix 5 patients (12.5%), trauma 4 patients (10%), and intra-abdominal abscess 1 patient (2.5%) (Table 1).

Out-of-study population different co-morbidities were found: 20 patients were smokers (50%), 31 patients were hypertensive (77.5%), 28 patients were diabetic (70%), 28 patients presented with history of cardiac problems including heart failure, ischemic heart disease, and valvular heart disease (70%), 11 patients had chronic renal disease (27.5%), and 6 patients had decompensated liver failure (15%).

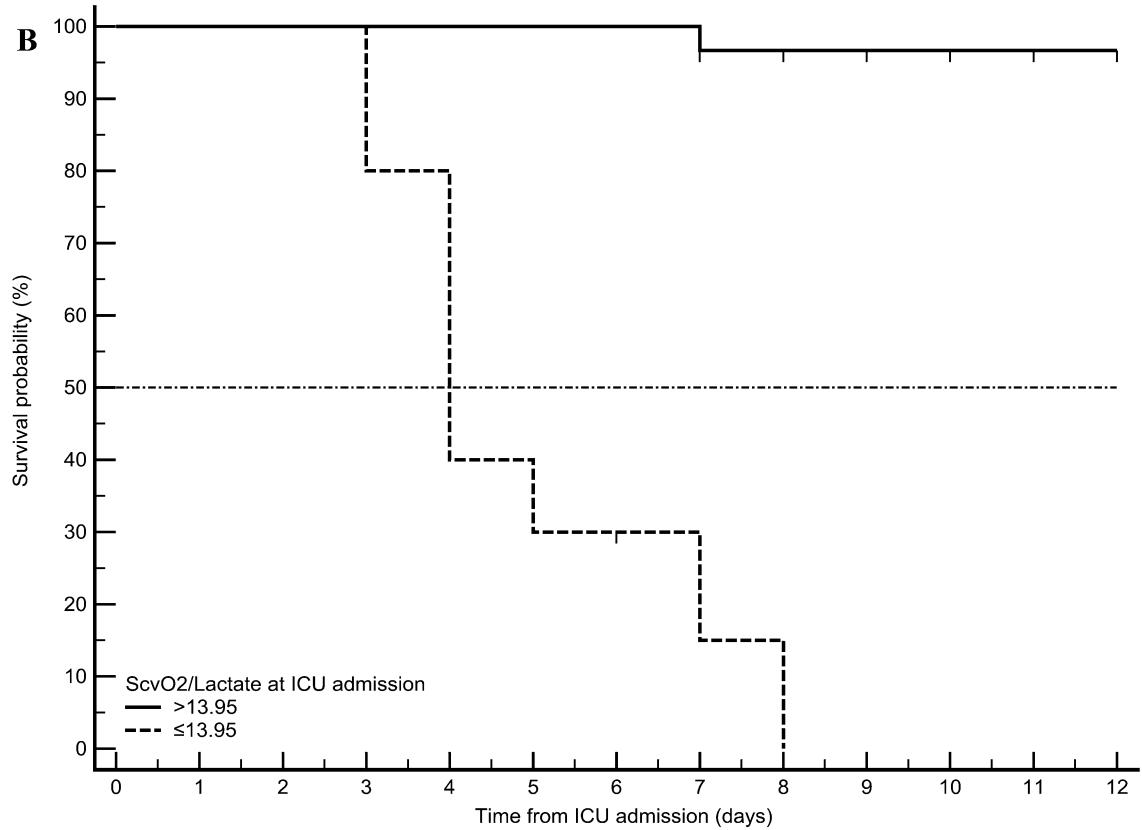
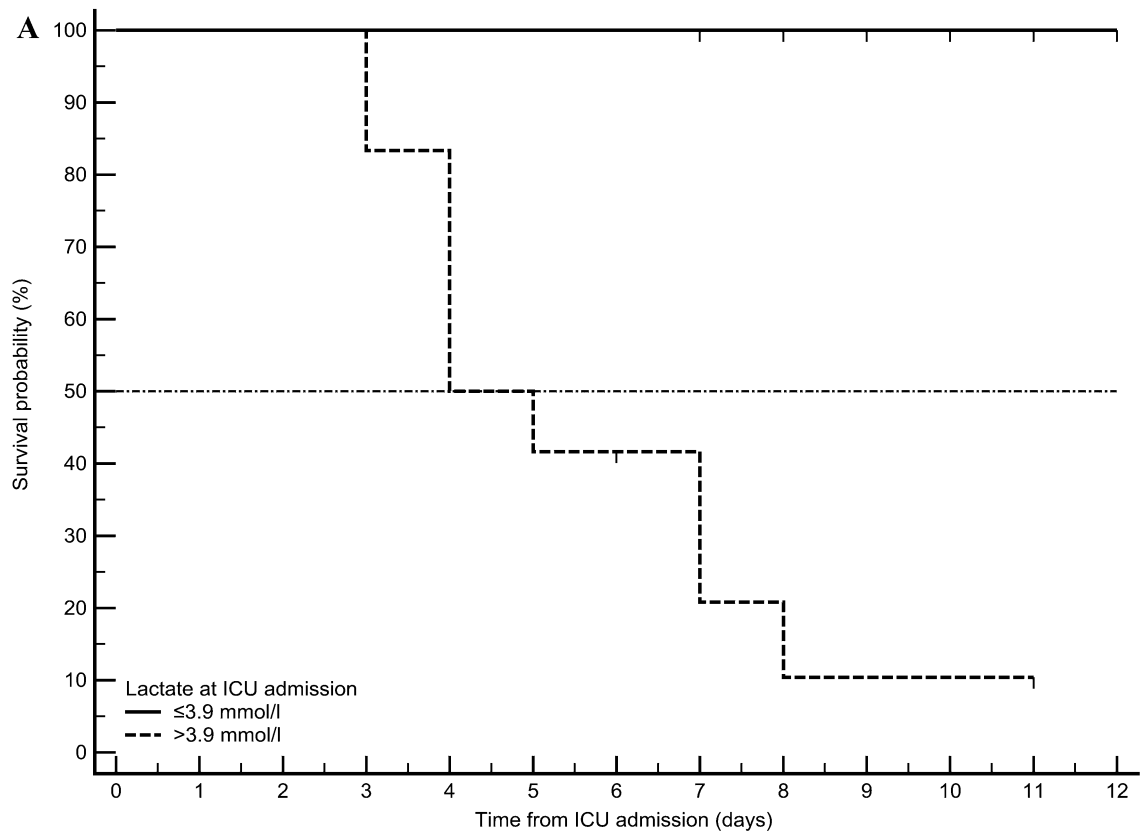
In this study, 26 patients were mechanically ventilated upon ICU admission following emergency laparotomy



**Fig. 1** Receiver-operating characteristic (ROC) curves for prediction of mortality using serum lactate level or ScvO<sub>2</sub> at ICU admission (0 h), after 12 h from ICU admission (12 h) or after 24 h from ICU admission (24 h)

(65%). Twenty patients developed renal impairment (50%) after ICU admission. Twenty-eight patients (70%) were in need for use of vasopressors with mean duration 79.5 h. In our study, mean length of stay (LOS) in ICU was  $3.7 \pm 1.2$  days with range from 2 to 8 days. Length of hospital stay was 3–12 days with mean  $7.6 \pm 2.3$  days (Table 2).

Initial and serial lactate levels at 12 h were highly predictor of mortality with cut-off point > 3.9 mmol/L and > 3.5 mmol/L with sensitivity 100% and specificity 93.3% *p* < 0.0001, respectively. In addition, lactate at 24 h at cut-off level > 2.9 mmol/L



**Fig. 2** Kaplan–Meier survival curves in patients with serum lactate  $\leq 3.9$  mmol/l or  $> 3.9$  mmol/l (upper plot, **a**) and in patients with ScvO<sub>2</sub>/lactate ratio  $> 13.95$  or  $\leq 13.95$  (lower plot, **b**) at ICU admission. Median survival in patients with serum lactate  $> 3.9$  mmol/l is 4 days (95% CI 4–7 days) and could not be estimated in patients with serum lactate  $\leq 3.9$  mmol/l. The difference between the survival curves of both subgroups is statistically significant (Log-rank test Chi squared, 39.128; *df* 1; *p* value  $< 0.0001$ ; hazard ratio could not be estimated). Likewise, median survival in patients with ScvO<sub>2</sub>/lactate ratio  $\leq 13.95$  is 4 days (95% CI 4–7 days) and could not be estimated in patients with ScvO<sub>2</sub>/lactate ratio  $> 13.95$ . The difference between the survival curves of both subgroups is statistically significant (Log-rank test Chi squared, 43.816; *df*, 1; *p* value  $< 0.0001$ ; hazard ratio, 382.6; 95% CI 65.8–2226.1)

is highly predictor of mortality with sensitivity 90% and specificity 96.7%  $p < 0.0001$  (Table 4 and Fig. 1).

### Correlations of serial blood lactate levels with length of stay in ICU

There was highly significant positive correlation between lactate OA, 12 and 24 h, and length of stay in ICU (correlation coefficient 0.522, 0.551, and 0.554), respectively;  $p < 0.001$ .

Kaplan–Meier curves showed the significant importance of initial and serial lactate levels and initial and serial ScvO<sub>2</sub>/lactate ratio as predictor of mortality in open emergency laparotomy patients admitted to the ICU (Figs. 2, 3, 4).

In our study, central venous oxygen saturation/lactate ratio on admission was predictor of survival at day 7 with cut-off point  $\leq 13.95$ , sensitivity 100%, and specificity 96.7%  $p < 0.0001$  (Table 4; Fig. 1).

### Correlation of arterial lactate to APACHE II, MODS D1, and SOFA D1 critical illness scores

Admission arterial lactate; lactate at 12 and 24 h was highly correlated with APACHE II score day 1 ( $p < 0.001$ ) and correlation coefficient was (0.67; 0.649; 0.569).

Admission arterial lactate; lactate at 12 and 24 h was highly correlated with MODS score day 1 ( $p < 0.001$ ) and correlation coefficient was (0.737; 0.747; 0.767).

Admission arterial lactate; lactate at 12 and 24 h was highly correlated with SOFA score day 1 ( $p < 0.001$ ) and correlation coefficient was (0.632; 0.617; 0.579) (Fig. 5).

### Relations of lactate with survival at day 7

There was highly significant positive relation between lactate OA, at 12 h and 24 h, and mortality as  $p$  value was  $< 0.0001$  (Table 3; Fig. 1).

### ROC curve of ScvO<sub>2</sub>/lactate ratio with mortality

In our study, central venous oxygen saturation/lactate ratio on admission was predictor of survival with AUC 0.970, cut-off point  $\leq 13.95$ , sensitivity 100%, and specificity 96.7%  $p < 0.0001$  (Fig. 1).

In our study, central venous oxygen saturation/lactate ratio At 12 h was predictor of survival with AUC 0.962, cut-off point  $\leq 19.74$ , sensitivity 100%, and specificity 93.3%  $p < 0.0001$  (Table 4; Fig. 1).

In our study, central venous oxygen saturation/lactate ratio At 24 h was predictor of survival with AUC 0.977, cut-off point  $\leq 25$ , sensitivity 90%, and specificity 96.7%  $p < 0.0001$  (Table 4; Fig. 1).

### Discussion

Emergency open laparotomy poses unique challenges to both the surgeon and anesthetics. Emergency open laparotomy is usually done in patients who are not prepared preoperatively such patients may be dehydrated, hypotensive; with varying degrees of biochemical derangement and very sick with ongoing sepsis.

Emergency surgery may be done by junior staff of surgeons and anesthesiologists, so post-operative complications may be increased.

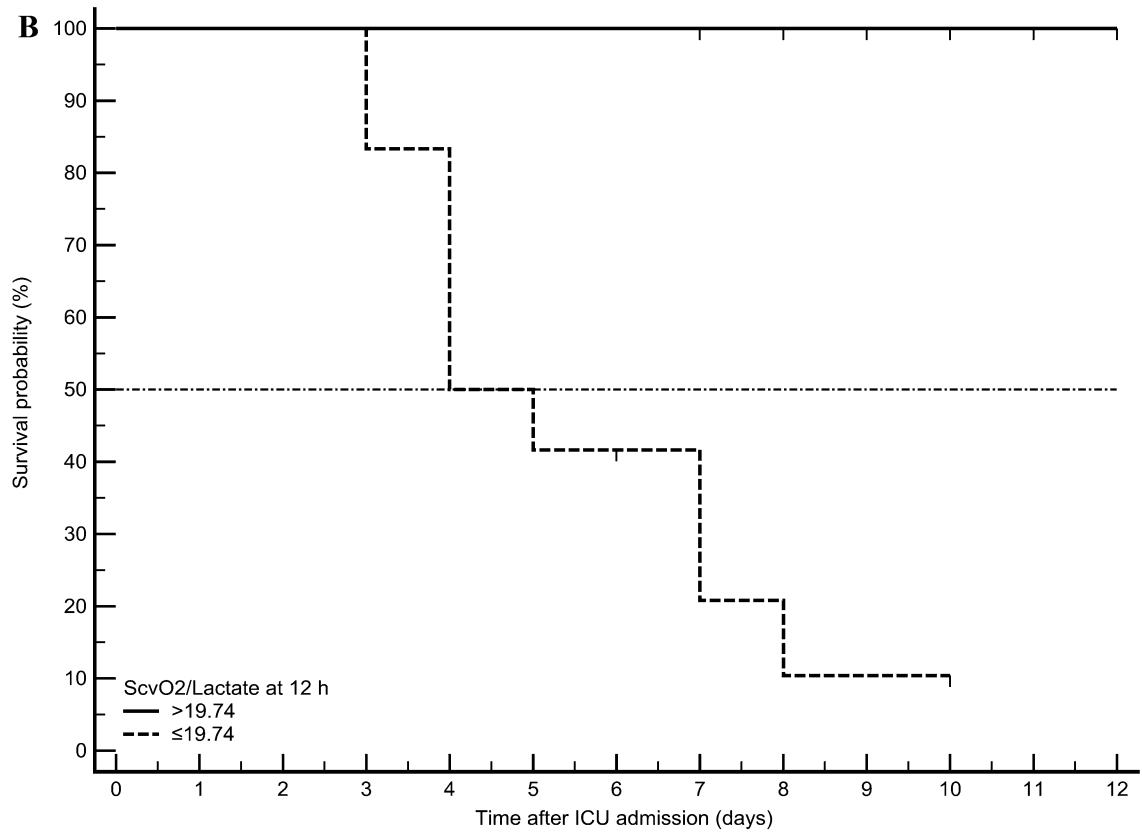
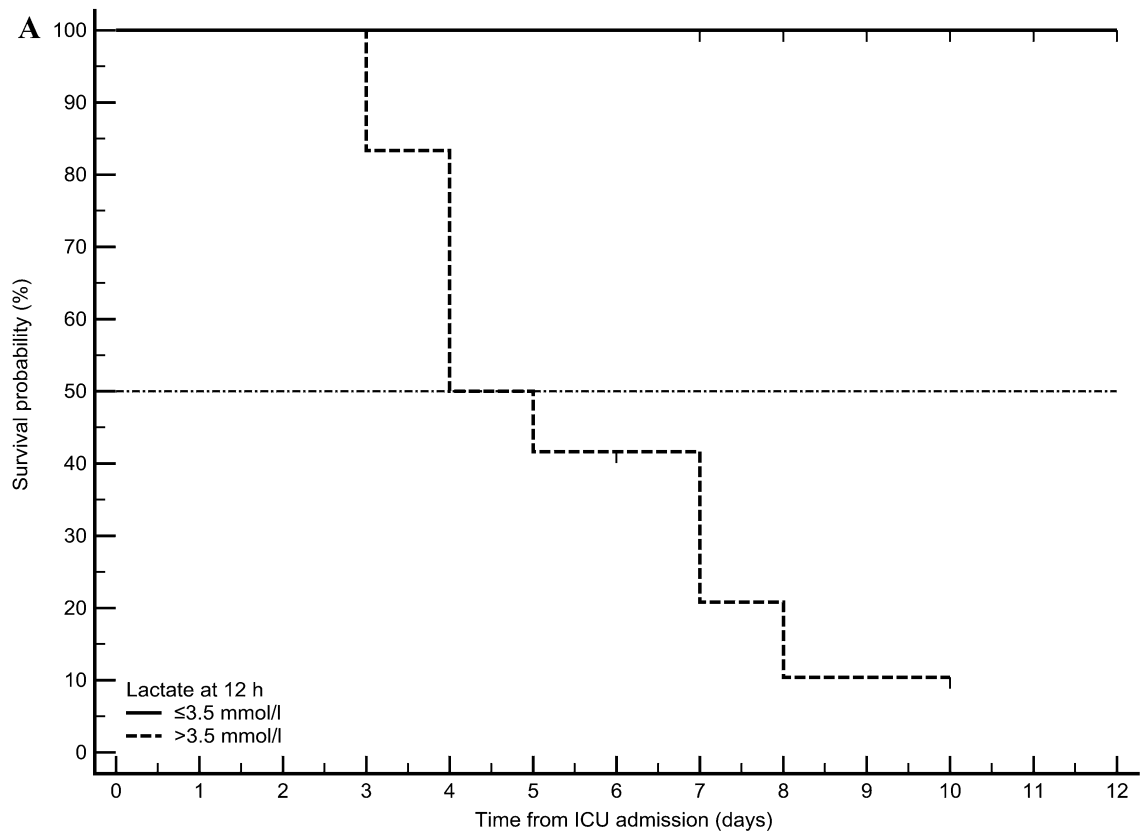
Emergency laparotomy can lead to serious complications and attentive monitoring is a must. The ongoing imbalance between oxygen demand and oxygen supply is an initiator for the cascade of events leading to multiple organ dysfunction syndrome. Prompt detection and management of hypoperfusion state is, therefore, the key for better survival [5].

Standard indicators of perfusion, such as blood pressure or urine output, have been proved repeatedly to be inaccurate. Therefore, the need for accurate assessment tool of hypoperfusion is essential to suppress the incidence of organ dysfunction in these patients [6].

Central venous oxygen saturation (ScvO<sub>2</sub>) and blood lactate have been found to be valuable indicators for evaluating the degree of hypoperfusion in patients with different disease processes [3, 4, 7].

In our study, 26 patients were mechanically ventilated after admission to ICU following emergency laparotomy (65%). This agrees with Litton et al. [8] who reported that 51% of patients need mechanical ventilation after major surgery.

In our study, there was highly significant positive relation between serial lactate in the 1st 24 h after ICU admission and mortality as  $p$  value was  $< 0.001$ ; this is similar to the results obtained by Hu [9].



**Fig. 3** Kaplan-Meier survival curves in patients with serum lactate  $\leq 3.5$  mmol/l or  $> 3.5$  mmol/l (upper plot, **a**) and in patients with ScvO<sub>2</sub>/lactate ratio  $> 19.74$  or  $\leq 19.74$  (lower plot, **b**) at 12 h from ICU admission. Median survival in patients with serum lactate  $> 3.5$  mmol/l is 4 days (95% CI 4–7 days) and could not be estimated in patients with serum lactate  $\leq 3.5$  mmol/l. The difference between the survival curves of both subgroups is statistically significant (log-rank test chi-squared, 39.128; *df* 1; *p* value  $< 0.0001$ ; hazard ratio could not be estimated). Likewise, median survival in patients with ScvO<sub>2</sub>/lactate ratio  $\leq 19.74$  is 4 days (95% CI 4–7 days) and could not be estimated in patients with ScvO<sub>2</sub>/lactate ratio  $> 19.74$ . The difference between the survival curves of both subgroups is statistically significant (log-rank test chi-squared, 39.128; *df* 1; *p* value  $< 0.0001$ ; hazard ratio could not be estimated)

Beebee concluded that patients who developed severe Global Tissue Hypoxia which was defined as ScvO<sub>2</sub>  $< 70\%$  and lactate  $\geq 4$  mmol/L have longer lengths of ICU stay; time on mechanical ventilation and more complications following post-CABG or valve surgery. He also concluded that the use of ScvO<sub>2</sub> and lactate allows rapid identification of occult hypoperfusion post cardiac surgery and can positively affect the outcome. The use of our results agrees also with André Meregalli [10], who reported that increased lactate level was associated with increased incidence of major adverse events and mortality in 44 hemodynamically stable high-risk surgical patients and Husain et al. [11] who showed that elevated the initial and 24-h lactate levels correlated significantly with 30-day mortality in 137 surgical ICU patients.

In our study, the cut-off point for the mortality prediction at day 7 of admission lactate was  $> 3.9$  mmol/L with sensitivity 100% and specificity 93.3%. Ole Kruse et al. [12] also found that a cut-off point for admission lactate 2.5 mmol/L is predictor of 30-day mortality with sensitivity 86% and specificity 77%.

Our results confirm one of the largest studies depicting lactate clearance in major trauma patients; Heinonen et al. [13] who reported that the survival rate of patients with lactate values  $< 2.5$  mmol/L was 88% and of the patients with high lactate levels that cleared within 24 and 48 h, the survival rates were 81% and 71%, respectively. They concluded that arterial lactate clearance trends are reliable simple predictor of outcome following major trauma [13].

In our study, we found that ScvO<sub>2</sub>/lactate ratio on admission to ICU was predictor for mortality at cut-off point  $\leq 13.95$  with sensitivity 100%, and specificity 96.7%; this agrees with Zante et al. [14], who reported that the ratio of ScvO<sub>2</sub>/lactate at ICU admission is a better predictive power of 28-day mortality in patients after cardiac surgery than the individual values with the optimal cut-off-value was 29.61. This value led to a sensitivity of 81.25% and a specificity of 73.66%.

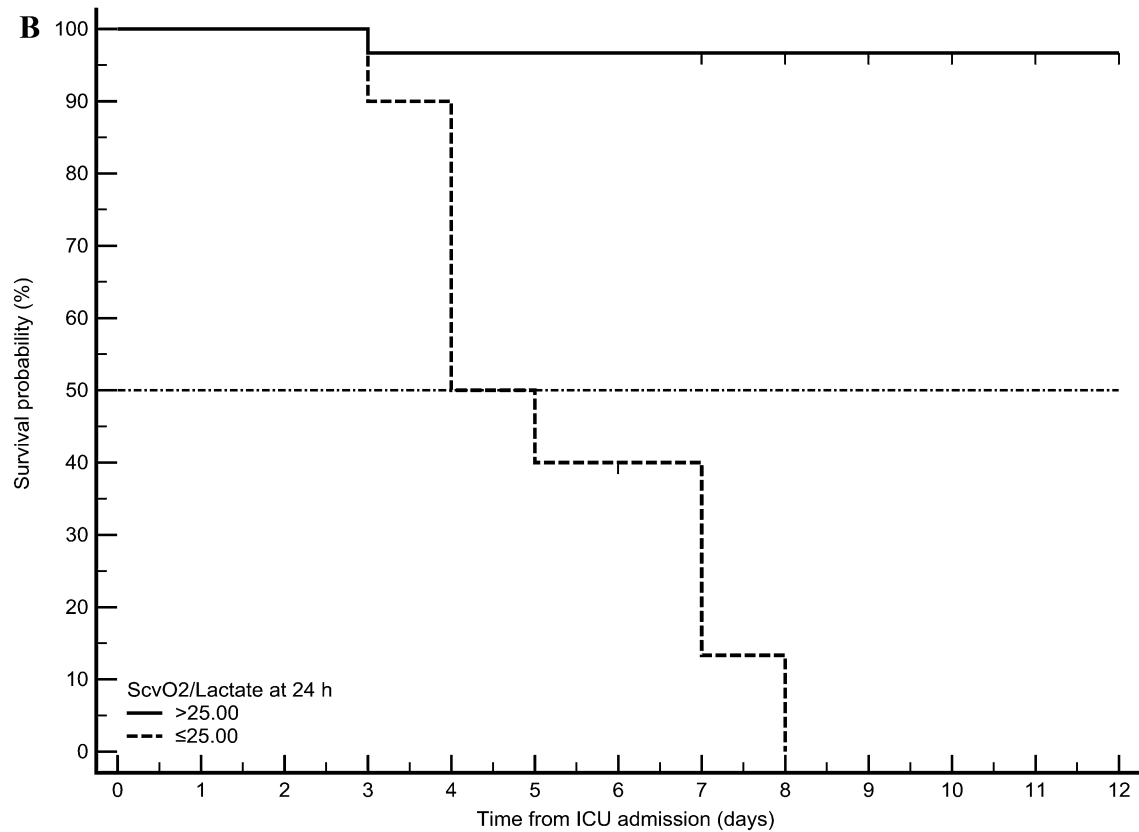
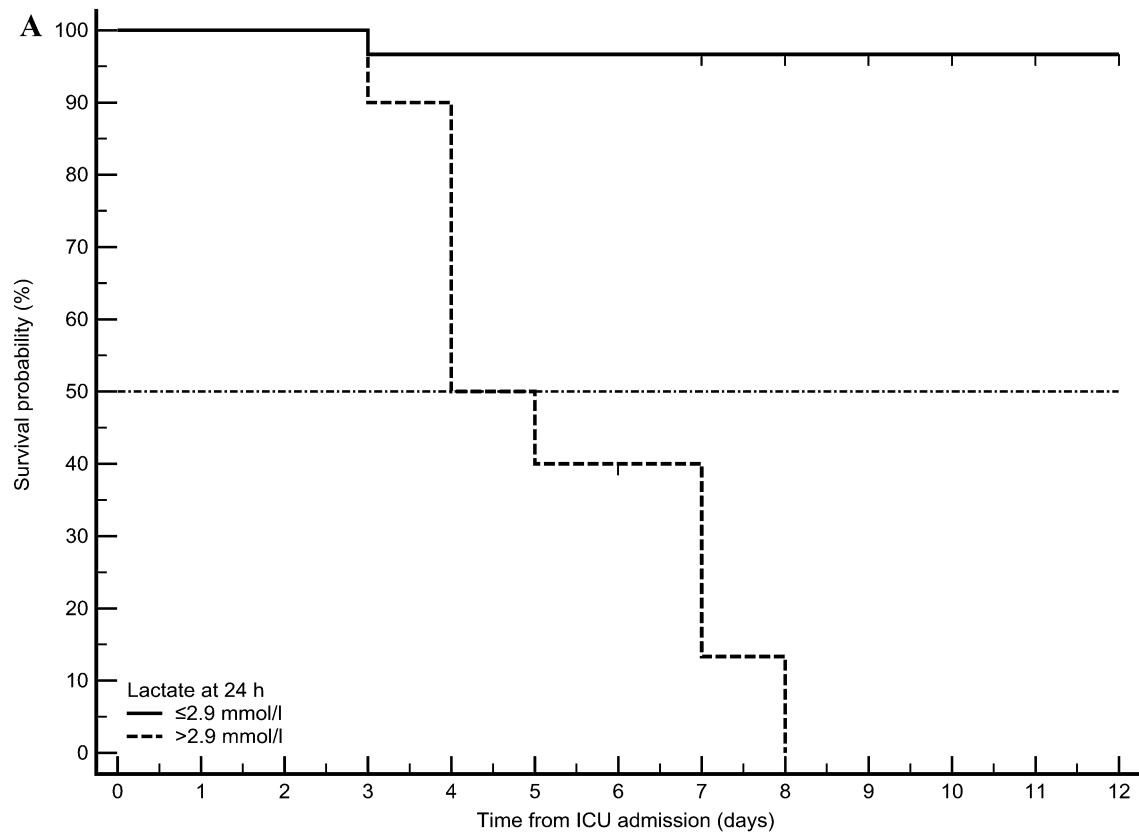
In our study, mortality at day 7 was 25%; this agrees with D. I. Saunders [15] who reported that 30-day mortality was 24.4% after emergency laparotomy. Also Clarke [16] showed that 30-day mortality was 19.6% after emergency laparotomy and Vester-Andersen et al. [17] reported that 90-day mortality in 2803 patients after emergency abdominal surgery was 18.4%. Peden et al. also reported that mortality after emergency open laparotomy in United Kingdom was 16% in 1587 patients [18]. In patients older than 65 years; 1 year mortality reached 34% [19] Also emergency laparotomy during hospital stay and remote from admission is associated with high morbidity and  $> 40\%$  mortality [20] This can be explained by the associated admission co-morbidities and the resistant hospital organisms infections in addition to complications of the prolonged hospital stay.

Emergency open laparotomy in the already admitted critically ill patients showed mortality 55.6%; the authors concluded that the high mortality is anticipatable based on concurrent abnormal physiology [21].

## Conclusion

A highly significant correlation  $< 0.001$  was detected between admission and serial arterial lactate levels and ICU length of stay; admission APACHE II; SOFA and MODS.

Serial blood lactate and ScvO<sub>2</sub>/lactate ratio are reliable predictors of post-operative open laparotomy outcome in critically ill patients with the latter providing 100% sensitivity and 90% specificity at admission cut-off  $\leq 13.95$ ,





**Fig. 4** Kaplan–Meier survival curves in patients with serum lactate  $\leq 2.9$  mmol/l or  $> 2.9$  mmol/l (upper plot, **a**) and in patients with ScvO<sub>2</sub>/lactate ratio  $> 25.0$  or  $\leq 25.0$  (lower plot, **b**) at 24 h from ICU admission. Median survival in patients with serum lactate  $> 2.9$  mmol/l is 4 days (95% CI 4–7 days) and could not be estimated in patients with serum lactate  $\leq 2.9$  mmol/l. The difference between the survival curves of both subgroups is statistically significant (log-rank test chi-squared, 37.668; *df* 1; *p* value  $< 0.0001$ ; hazard ratio, 191.2; 95% CI 35.7–1023.3). Likewise, median survival in patients with ScvO<sub>2</sub>/lactate ratio  $\leq 25.0$  is 4 days (95% CI 4–7 days) and could not be estimated in patients with ScvO<sub>2</sub>/lactate ratio  $> 25.0$ . The difference between the survival curves of both subgroups is statistically significant (log-rank test chi-squared, 37.668; *df*, 1; *p* value  $< 0.0001$ ; hazard ratio, 191.2; 95% CI 35.7–1023.3)

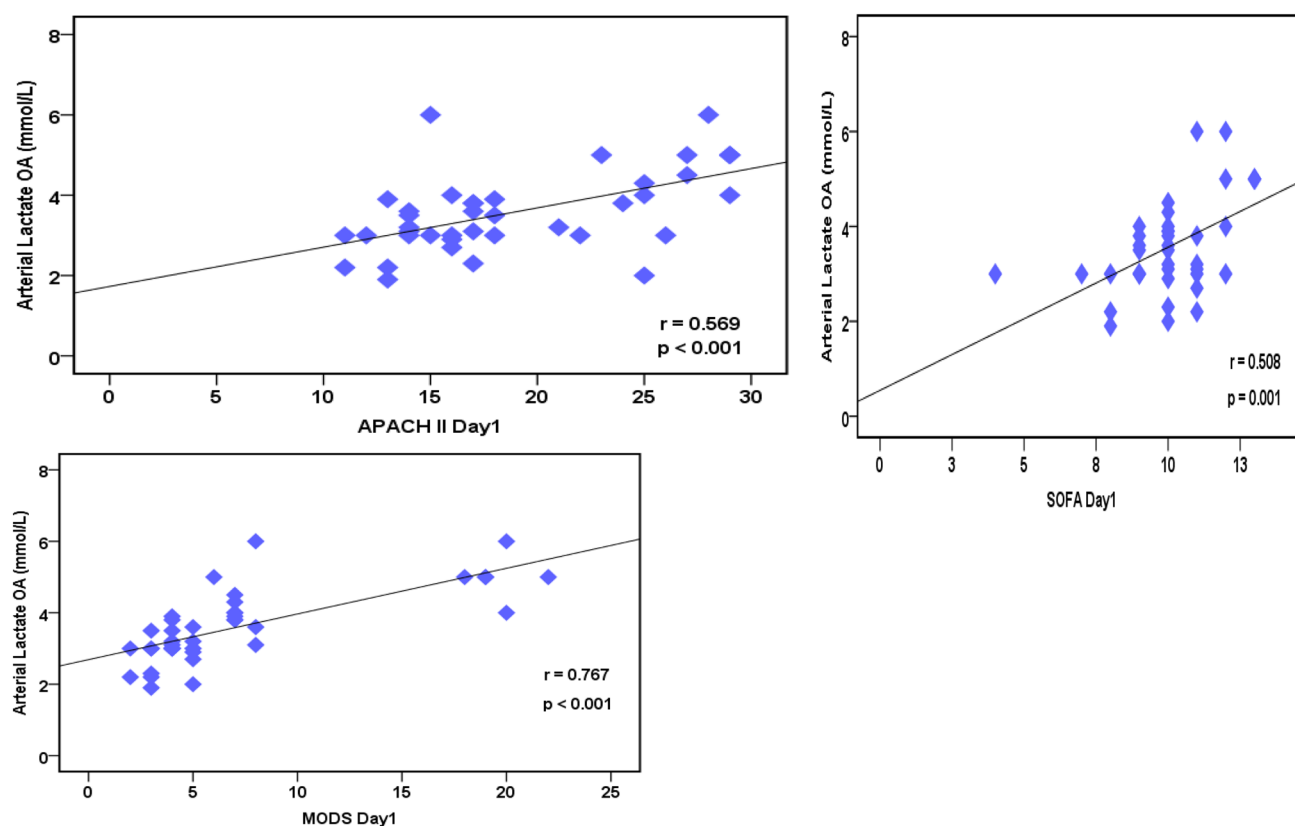
and at 12 h, sensitivity 100%, and specificity 93.3%. cut-off  $\leq 19.74$  and At 24 h, cutoff  $\leq 25.00$  can provide sensitivity 90% and specificity 96.7% for mortality prediction.

Serial ScvO<sub>2</sub>/lactate ratio can improve risk stratification and guide early rapid management to provide better outcome in post-operative emergency open laparotomy patients admitted to the ICU.

**Table 4** Receiver-operating characteristic (ROC) curve analysis for the value of serum lactate or ScvO<sub>2</sub>/lactate ratio for prediction of mortality in patients undergoing emergency laparotomy

ROC metric	Predictor					
	Serum lactate			ScvO <sub>2</sub> /lactate ratio		
	At ICU admission	At 12 h	At 24 h	At ICU admission	At 12 h	At 24 h
AUC	0.965	0.963	0.972	0.970	0.962	0.977
SE	0.032	0.034	0.023	0.030	0.034	0.020
95% CI	0.853–0.998	0.850–0.997	0.863–0.999	0.861–0.999	0.848–0.997	0.871–1.000
z statistic	14.59	13.85	20.56	15.57	13.69	23.73
p value	$< 0.0001$	$< 0.0001$	$< 0.0001$	$< 0.0001$	$< 0.0001$	$< 0.0001$
Youden index J	0.93	0.93	0.87	0.97	0.93	0.87
Cutoff criterion	$> 3.9$	$> 3.5$	$> 2.9$	$\leq 13.95$	$\leq 19.74$	$\leq 25.00$
Sensitivity (%)	100	100	90	100	100	90
95% CI	69.2–100.0	69.2–100.0	55.5–99.7	69.2–100.0	69.2–100.0	55.5–99.7
Specificity (%)	93.3	93.3	96.7	96.7	93.3	96.7
95% CI	77.9–99.2	77.9–99.2	82.8–99.9	82.8–99.9	77.9–99.2	82.8–99.9
+ LR	15	15	27	30	15	27
95% CI	3.9–57.2	3.9–57.2	3.9–187.5	4.4–206.1	3.9–57.2	3.9–187.5
– LR	0.00	0.00	0.10	0.00	0.00	0.10
95% CI	–	–	0.02–0.7	–	–	0.02–0.7
+ PV (%)	83.3	83.3	90	90.9	83.3	90
95% CI	56.7–95.0	56.7–95.0	56.4–98.4	59.3–98.6	56.7–95.0	56.4–98.4
– PV (%)	100	100	96.7	100	100	96.7
95% CI	–	–	81.9–99.5	–	–	81.9–99.5

ROC receiver-operating characteristic (ROC) curve, AUC, area under the ROC curve, SE, standard error, 95% CI 95% confidence interval, + LR positive likelihood ratio, – LR negative likelihood ratio, + PV positive predictive value, – PV negative predictive value



**Fig. 5** Correlation of arterial lactate to APACHE II, MODS D1 and SOFA D1 critical illness scores

**Electronic supplementary material** The online version of this article (<https://doi.org/10.1007/s00068-019-01188-0>) contains supplementary material, which is available to authorized users.

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### Compliance with ethical standards

**Conflict of interest** All authors confirm they have no conflict of interest.

**Ethical approval** The research was approved by the local ethical committee of the Critical Care Department and then the Ethical committee of Faculty of Medicine Cairo University.

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