

## Research Article

### Central Venous Oxygen Saturation as a Mortality Marker in Septic Shock: An Observational Study

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#### Abstract

**Background:** Septic shock is a leading cause of morbidity and mortality. Central Venous Oxygen Saturation (ScVO<sub>2</sub>) is a prognostic marker of patients in septic shock. It is influenced by the oxygen-carrying capacity of blood, organ perfusion and metabolic oxygen consumption. Tissue hypoxia may sometimes occur despite adequate global oxygen delivery. In such scenarios, ScVO<sub>2</sub> can be useful to predict increased risk of mortality. In the previous studies on ScVO<sub>2</sub>, its importance as a tissue oxygen marker and its importance in critical care have been studied. It has not been viewed as a mortality marker previously. The present study conducted to explore the association of ScVO<sub>2</sub> with 28 days mortality in patients with septic shock, admitted to the Critical Care Unit (CCU) and, to evaluate the usefulness of ScVO<sub>2</sub> as a mortality marker.

**Materials and Methods:** A prospective, observational study which was conducted on patients admitted to the CCU with septic shock. 76 patients were enrolled for study based on inclusion and exclusion criteria. Central venous sampling by Central Venous Catheter (CVC) was done for initial ScVO<sub>2</sub> value (T0) and was repeated after 6 hours of resuscitation for ScVO<sub>2</sub> value (T6) to assess the response to resuscitation. All enrolled patients were observed for a period of 28 days and were divided into 2 groups based on the outcome: Group NS (Non-Survivor group, which included patients who did not survive

at the end of 28 days) and Group S (Survivor group, which included patients who survived at the end of 28 days) and ScVO<sub>2</sub> values were compared between the survivor and non-survivor group.

**Results:** In our study, out of 76 patients, 44 patients (57.89%) were non-survivors and 32 patients (42.11%) were survivors. The mean Central Venous Oxygen Saturation (ScVO<sub>2</sub>) at the time of admission (T0) was 64.00 ± 2.74% among non-survivors and 73.22 ± 2.62% among survivors, and after six hours of resuscitation (T6) it was 63.30 ± 2.91% among non-survivors and 73.97 ± 2.31% among survivors. The sensitivity of ScVO<sub>2</sub> at T0 in terms of mortality for value < 70% was 88.64% and specificity was 81.25% (OR = 33.8, 95% CI = 9.34, 122.35) and sensitivity of ScVO<sub>2</sub> at T6 in terms of mortality for value < 70% was 93.18% and specificity was 93.75% (OR = 205, 95% CI = 32.23, 1303.97), which reflected that patients with ScVO<sub>2</sub> < 70% had a poor prognosis as compared to patients with ScVO<sub>2</sub> > 70%.

**Conclusion:** Central Venous Oxygen Saturation (ScVO<sub>2</sub>) values of less than 70% at the time of admission to CCU (T0) and six hours after the resuscitation (T6) was associated with higher 28 days mortality. From the observations and analysis of our study, it can be concluded that ScVO<sub>2</sub> can be used as a predictor of mortality in patients of septic shock.

**Keywords:** Central Venous Oxygen Saturation (ScVO<sub>2</sub>); Septic shock; Critical Care Unit (CCU)

#### Introduction

Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality and is defined as sepsis along with persistent hypotension requiring vasopressors to maintain MAP ≥ 65mm Hg, and Lactate ≥ 2mmol/L despite adequate fluid resuscitation [1]. Goal-directed therapy helps to predefine resuscitation endpoints to help clinicians at the bedside in the resuscitation of patients in septic shock. Two essential features of early goal-directed therapy are maintenance of Central Venous Pressure (CVP) > 8 mmHg and Central Venous Oxygen Saturation (ScVO<sub>2</sub>) ≥ 70% [2].

Central Venous Oxygen Saturation (ScVO<sub>2</sub>) is influenced by the oxygen carrying-capacity of blood, organ perfusion and metabolic oxygen consumption. It reflects the changes in oxygen delivery and consumption ratio. Central venous oxygen saturation (ScVO<sub>2</sub>) is a prognostic marker of patients in shock which has been underutilized in the critical care setting. Previous studies have used venous oxygen saturation as a therapeutic goal. Tissue hypoxia may sometimes occur despite adequate global oxygen delivery. Unrecognized global tissue hypoxia is associated with an increased risk of mortality and morbidity. Hence accurate detection is of prime importance. Vital signs are not sufficient for accurate and timely detection. In such scenarios, ScVO<sub>2</sub> can be useful to predict increased risk of mortality. It can be measured from a blood sample taken from the central venous catheter or pulmonary artery catheter.

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In the previous studies on ScVO<sub>2</sub>, its importance as a tissue oxygen marker and its importance in critical care have been studied. It has not been viewed as a mortality marker previously. In the present study, the association of central venous oxygen saturation with 28 days mortality in patients with septic shock admitted to the Critical Care Unit (CCU) has been explored, to evaluate the usefulness of ScVO<sub>2</sub> as a mortality marker.

## Materials and Methods

An observational, prospective study conducted in the Department of Anesthesiology and Critical care at Pt. J.N.M. Medical College & Dr. B.R.A.M. Hospital, Raipur (C.G) from April 2018 to July 2019 to predict mortality in patients admitted to the Critical Care Unit (CCU) using ScVO<sub>2</sub>% at T0 and T6. After applying inclusion and exclusion criteria, a total of 76 patients were selected for study and all of them were followed over a period of 28 days.

**Study Design:** Prospective, Observational study

**Study location:** Pt. J.N.M. Medical College and Dr. B.R.A.M. Hospital, Raipur (C.G.)

**Study Duration:** April 2018 to July 2019

**Sample size:** 76

**Sample size calculation:** Using epitool by one-tailed test, taking confidence of 95%.

**Study population:** Patients admitted to the Critical Care Unit (CCU) of Dr. B.R.A.M. Hospital.

**Inclusion Criteria:** Septic shock patients of either sex aged ≥ 18 years of age.

### Exclusion Criteria

1. Patients with contraindication to central venous catheterization.
2. Age < 18 years.
3. Patients with systolic dysfunction.
4. Patients revived by Cardio-Pulmonary Resuscitation (CPR).
5. Patients with imminent death.

### Methodology

As the patient got shifted to the CCU, the patient's medical records were reviewed; demographic data, clinical data, vital signs, diagnosis and associated co-morbidities were recorded. Sequential Organ Failure Assessment (SOFA score) and Systemic Inflammatory Response Syndrome (SIRS) criterion, Simplified Acute Physiology Score (SAPS II) were calculated at that time. Central venous catheter was inserted for monitoring of Central Venous Pressure (CVP) and evaluation of ScVO<sub>2</sub>, venous sampling by CVC was then done for initial ScVO<sub>2</sub> value (T0), and an arterial blood sample was done for lactate, pH and bicarbonate levels. Venous blood sampling by CVC was repeated after 6 hours of resuscitation for ScVO<sub>2</sub> value (T6) to assess the response to resuscitation. All enrolled patients were observed for 28 days and divided into 2 groups based on the outcome: Group NS (Non-Survivor group, which included patients who did not survive at the end of 28 days) and Group S (Survivor groups, which included patients who survived at the end of 28 days).

## Statistical analysis

Univariate analyses were used to evaluate the correlations between all the variables. Multivariate logistic regression analysis using the mortality risk factors determined by univariate analysis was used to find the independent predictor of mortality. A Receiver Operating Characteristic (ROC) curve was plotted to determine the most appropriate cut off value of central venous oxygen saturation (ScVO<sub>2</sub>) at T0 and T6 used independently to predict the mortality.

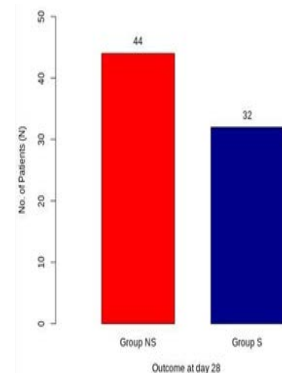
Categorical data are expressed as percent, and continuous variables are expressed as mean ± SD. Continuous variables were compared by using independent Student's t-test. Odds Ratios (OR) is given with the 95% CI. A two-tailed P-value < 0.05 was considered statistically significant.

## Results

Among 76 patients enrolled in the study 72.37% (n = 55) were male and 27.63% (n = 21) were female. Male: Female distribution in NS and S group was 37:7 and 18:14 respectively. The total number of patients who died in the follow-up duration of 28 days was 44 (57.89%) and was grouped as non-survivors whereas the remaining 32 (42.11%) patients who survived were grouped under the survivor group. The difference in gender distribution between group NS and group S was found to be statistically significant (p-value = 0.01), with odds of non-survival was found more for male gender (OR = 0.24, 95% CI = 0.08, 0.71). (Table 1), (Figures 1-3).

Variable	Groups based on Outcome (mortality at day 28)		
	Group NS	Group S	Total
Gender	n=44 (57.89%)	n=32 (42.11%)	N=76 (100%)
Male	37 (67.27%)	18 (32.73%)	55 (100%)
Female	07 (33.33)	14 (66.67%)	21 (100%)
H/O Chronic Disease			
Present	32 (64%)	18 (36%)	50 (100%)
Absent	12 (46.15%)	14 (53.85%)	26 (100%)
Ventilator Use	44 (57.89%)	32 (42.11%)	76 (100%)
Vasopressors Use	44 (57.89%)	32 (42.11%)	76 (100%)
ScVO <sub>2</sub> % < 70% at T0 to ScVO <sub>2</sub> % ≥ 70% at T6	3 (33.33%)	6 (66.67%)	9 (100%)

**Table 1:** Demographic, clinical characteristics, treatment and outcome of enrolled 76 patients.



**Figure 1:** Distribution of study subjects based on the outcome.

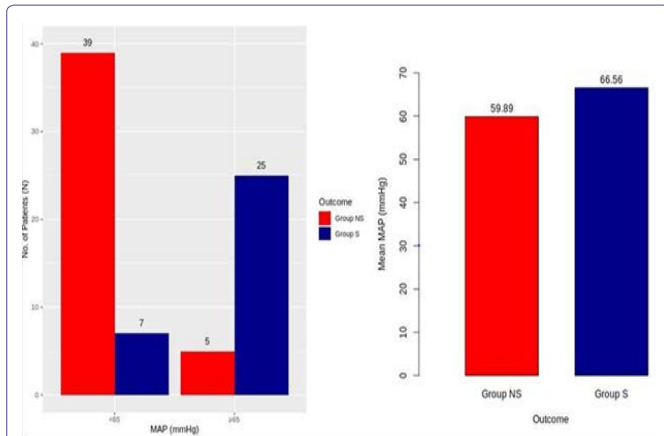


Figure 2: Distribution of Mean Arterial Pressure (MAP) and outcome.

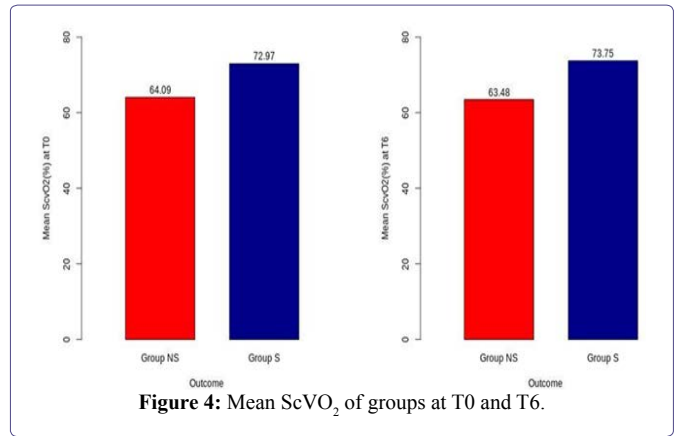


Figure 4: Mean ScVO<sub>2</sub> of groups at T0 and T6.

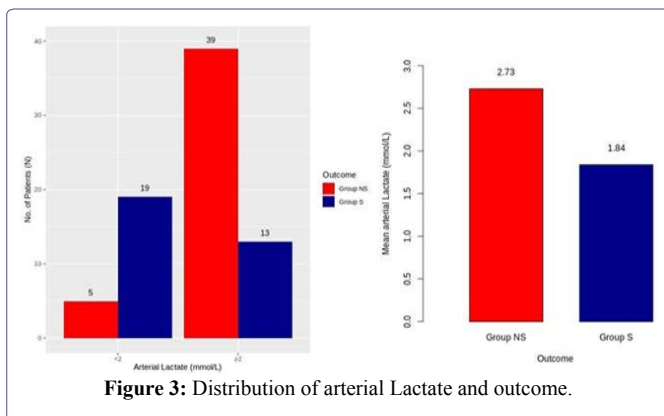


Figure 3: Distribution of arterial Lactate and outcome.

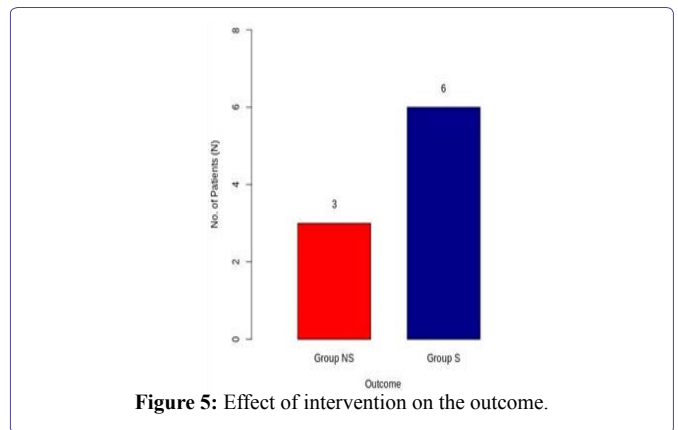


Figure 5: Effect of intervention on the outcome.

The mean Central Venous Oxygen Saturation (ScVO<sub>2</sub>) at the time of admission (T0) was 64.00 ± 2.74% among non-survivors and 73.22 ± 2.62% among survivors, and after six hours of resuscitation (T6) it was 63.30 ± 2.91% among non-survivors and 73.97 ± 2.31% among survivors. Differences between the mean of ScVO<sub>2</sub> were significant (p-value < 0.001) at both T0 and T6 (Table 2), (Figures 4-5).

Variable	Group NS (n = 44) Mean ± SD	Group S (n = 32) Mean ± SD	p-value
Age (in Years)	50.34 ± 13.01	43.53 ± 15.04	0.04
MAP (mmHg)	59.89 ± 4.16	66.56 ± 2.45	< 0.001
Arterial Lactate (mmol/L) at T0	2.73 ± 0.58	1.84 ± 0.68	< 0.001
ScVO <sub>2</sub> (%) at T0	64.09 ± 2.92	72.97 ± 2.91	< 0.001
ScVO <sub>2</sub> (%) at T6	63.48 ± 3.12	73.75 ± 2.59	< 0.001
SAPS II Score	50.34 ± 3.09	42.34 ± 2.25	< 0.001
SOFA Score	11.02 ± 1.25	7.56 ± 1.08	< 0.001

Table 2: Demographic, clinical characteristics, treatment and outcome of enrolled 76 patients.

The sensitivity of ScVO<sub>2</sub> at T0 in terms of mortality for value < 70% was 88.64% and specificity was 81.25% (OR = 33.8, 95% CI = 9.34, 122.35) and study the sensitivity of ScVO<sub>2</sub> at T6 in terms of mortality for value < 70% was 93.18% and specificity was 93.75% (OR = 205, 95% CI = 32.23, 1303.97) (Table 3).

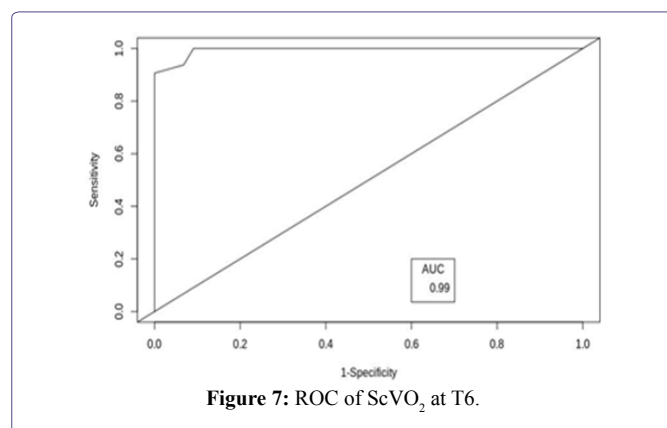
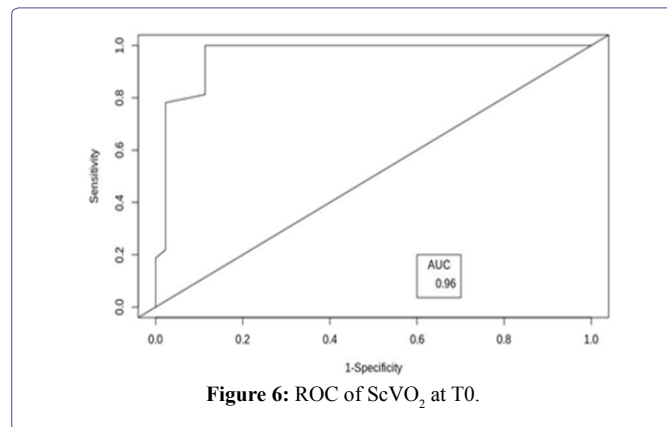
Variable	Outcome			p-value	Relative Risk for Outcome (Group NS / Group S)
	Group NS (N = 44)	Group S (N = 32)	Total (N = 76)		
Gender					
Female	7	14	21	0.01	0.24
Male	37	18	55		
Chronic Disease					
Absent	12	14	26	0.14	0.48
Present	32	18	50		
ScVO <sub>2</sub> at T0					
< 70%	39	6	45	< 0.001	33.8
≥ 70%	5	26	31		
ScVO <sub>2</sub> at T6					
< 70%	41	2	43	< 0.001	205
≥ 70%	3	30	33		
		<b>ScVO<sub>2</sub> % at T0</b>	<b>ScVO<sub>2</sub> % at T6</b>		
Sensitivity		88.64%	93.18%		
Specificity		81.25%	93.75%		
Positive Predictive Value		86.67%	95.35%		
Negative Predictive Value		83.67%	90.91%		
Positive Likelihood Ratio		4.73	14.91		
Negative Likelihood Ratio		0.14	0.07		

Table 3: Relative risk, Sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio based on ScVO<sub>2</sub> value at T0 and T6.

The ROC area under the curve for ScVO<sub>2</sub> at T0 which was assumed to be a predictor of mortality was 0.96 (p-value < 0.001). The best cut off value for ScVO<sub>2</sub> at T0 using the ROC curve was 69% with 100% sensitivity and 88.64% specificity, similarly, the ROC area under the curve for ScVO<sub>2</sub> at T6 as a predictor of mortality was 0.99 (p-value < 0.001). The best cut off value for ScVO<sub>2</sub> at T6 using ROC was 69% with 100% sensitivity and 90.91% specificity. According to the guidelines by Surviving Sepsis Campaign, the target cut off value of ScVO<sub>2</sub> was set as 70% (Table 4), (Figures 6-7).

Variable	Area Under Curve	p-value
Mean ScVO <sub>2</sub> value at T0	0.96	< 0.001
Mean ScVO <sub>2</sub> value at T6	0.99	< 0.001

**Table 4:** ROC curve for ScVO<sub>2</sub>.



The difference of the mean of lactate value was  $2.73 \pm 0.58$  mmol/L among non-survivors and  $1.84 \pm 0.68$  mmol/L among survivors which was statistically significant (p-value = 0.001) and showed higher mortality in patients with mean lactate > 2 mmol/L at the time of admission. Mean of SAPS II score was  $50.34 \pm 3.09$  among non-survivors and  $42.34 \pm 2.25$  among survivors. Mean of SOFA score was  $11.02 \pm 1.25$  among non-survivors and  $7.28 \pm 0.58$  in the survivor group. In our study, all 76 patients required ventilator support and were on vasopressors support. The presence of chronic

disease was seen in 32 patients in the NS group and 18 patients in S group, with a relative risk of 0.48 (OR = 0.48, 95% CI = 0.18, 1.26), which reflected higher mortality among patients having a history of chronic disease.

## Discussion

Central Venous Oxygen Saturation (ScVO<sub>2</sub>) has been studied as a prognostic marker and as resuscitation end-point in patients with septic shock. Rivers E, et al., (2001) showed that an early therapeutic strategy that includes aiming for the rapid normalization of ScVO<sub>2</sub> ( $\geq 70\%$ ) in patients suffering from septic shock at the time of admission to the emergency department could improve survival [3]. Since then, international guidelines have recommended targeting ScVO<sub>2</sub> > 70% during the first 6 hours of care in patients presenting with severe sepsis or septic shock.

Since 2004, international guidelines for the treatment of severe sepsis and septic shock have been issued under the auspices of the Surviving Sepsis Campaign. Following these guidelines, all patients should be treated according to Early Goal-Directed Therapy (EGDT).

Early goal-directed therapy consists of the application of a bundle of interventions that are performed following a defined algorithm during the first 6 hours of treatment of patients in septic shock. Early goal-directed therapy includes the administration of fluid boluses until a Central Venous pressure (CVP) of 8 to 12 mm Hg has been reached, followed by the use of vasopressors if necessary aiming at a Mean Arterial Pressure (MAP) of at least 65 mmHg. If ScVO<sub>2</sub> remains less than 70% and hematocrit is less than 30% then Red Blood Cell (RBC) transfusion is done to obtain a hematocrit more than 30% and if ScVO<sub>2</sub> remains less than 70%, inotropes are administered to attain ScVO<sub>2</sub> value to more than 70%.

Many scoring systems that show the severity of serious illness, such as the Acute Physiological and Chronic Health Evaluation II (APACHE-II), Sequential Organ Failure Assessment (SOFA), Simplified Acute Physiology Score (SAPS-II) for the prediction of mortality and morbidity. To the best of our knowledge, to date, no scoring systems consider the ScVO<sub>2</sub> as a mortality marker in septic shock patients. The blood lactate level increases in response to tissue hypoxia and might be more sensitive for detection of imbalance between oxygen supply and demand. Limited reports analyzed the relationship between ScVO<sub>2</sub> and mortality risk in septic shock patients. Our study aimed to determine whether Central Venous Oxygen Saturation (ScVO<sub>2</sub>) acts as a mortality marker in septic shock patients.

In a study conducted by Narula GK, et al., (2018) the 28 days mortality was 60% among patients who failed to achieve target ScVO<sub>2</sub> > 70% [4]. Gajbe S, et al., (2018) found that the mean ScVO<sub>2</sub> among non-survivors was  $53.34 \pm 4.08\%$  [5]. Worapatya P, et al., (2016) concluded that the mortality rate of patients who failed to achieve the target goals of Early Goal Directed Therapy (EGDT) which included ScVO<sub>2</sub> > 70% was found to be 93.8% [6]. Rady MY, et al., (1996) in their study concluded that after resuscitating patients with EGDT the mortality was 14% (5 patients out of 36), in patients with ScVO<sub>2</sub> < 65% and low ScVO<sub>2</sub> is associated with higher mortality, which was similar to our study [7].

In our study, all 76 patients required ventilator support. In a study by Gajbe S, et al., (2018) all 99 patients included in the study were

on ventilator support which was similar to our study which could be explained by the fact that majority of the patients who were admitted to our CCU were either transferred from other ICU for further management or postoperative cases who required ventilator support and invasive monitoring in the postoperative period [5].

Presence of chronic disease was seen in 32 patients in the group NS and 18 patients in group S, with a relative risk of 0.48 (OR = 0.48, 95% CI; 0.18, 1.26), which reflected higher mortality among patients having a history of chronic disease.

The mean SOFA score was  $11.02 \pm 1.25$  among non-survivors and  $7.28 \pm 0.58$  in the survivor group in our study, Narula GK, et al., (2018) observed the mean SOFA score of patients in ScVO<sub>2</sub> group was 11.68 as compared to 11.71 in patients of lactate clearance [4]. Similar findings were seen in a study by Lee YK, et al., (2016) where the mean SOFA score was 10 (9 - 12) among non-survivors and 7 (5 - 9) among survivors which signify higher mortality associated with patients having higher SOFA score [8].

## Conclusion

From the observations and analysis of this study, it can be concluded that Central Venous Oxygen Saturation (ScVO<sub>2</sub>) can be used as a predictor of mortality in patients of Septic shock. ScVO<sub>2</sub> values of less than 70% at the time of admission to CCU (T0) and six hours after the resuscitation (T6) was associated with higher 28 days mortality.

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