

# Mortality and Regional Oxygen Saturation Index in Septic Shock Patients: A Pilot Study

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**Background:** Peripheral muscle tissue oxygenation determined noninvasively using near-infrared spectroscopy may help to identify tissue hypoperfusion in septic patients. The aim of this study was to investigate regional oxygen saturation index (rSO<sub>2</sub>) in the brachioradialis (forearm) muscle by comparing measurements in healthy subjects and in intensive care unit (ICU) septic shock patients, and determine whether brachioradialis muscle rSO<sub>2</sub> is associated with poor outcome in ICU septic shock patients.

**Methods:** We conducted a prospective observational study in healthy volunteers (n = 50) and ICU septic shock patients (n = 19). Brachioradialis (forearm) rSO<sub>2</sub> measurements in healthy volunteers at rest and in ICU septic shock patients were compared. Pulmonary artery catheter monitoring was used in ICU patients.

**Results:** Significant differences in rSO<sub>2</sub> were observed between healthy volunteers and ICU septic shock patients at ICU admission (68.7 ± 4.9 vs. 55.0 ± 13.0; *p* < 0.001). When comparing septic shock survivors and nonsurvivors, significant differences were observed in rSO<sub>2</sub> at baseline (64.5 ± 8.9 vs. 47.5 ± 10.7; *p* < 0.01), 12 hours (67.3 ± 9.6 vs. 45.0 ± 14.9; *p* < 0.01), and 24 hours (65.7 ± 7.0 vs. 50.1 ± 10.3; *p* < 0.01). Lactate concentration was lower in survivors than nonsurvivors at 24 hours (12.0 ± 7.5 mmol/L vs. 23.2 ± 12.5 mmol/L; *p* < 0.04). Cardiac index was greater in nonsurvivors than survivors at baseline (4.6 + 1.9 L/min/m<sup>2</sup> vs. 3.0 + 0.9 L/min/m<sup>2</sup>; *p* < 0.05) and 12 h (3.9 + 0.5 L/min/m<sup>2</sup> vs. 3.1 + 0.3 L/min/m<sup>2</sup>; *p* < 0.05).

**Conclusions:** We observed that septic shock patients with forearm skeletal muscle rSO<sub>2</sub> ≤60% throughout first 24 hours after ICU admission had significantly greater mortality rate than patients with forearm skeletal muscle rSO<sub>2</sub> >60% throughout this critical time.

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Hemodynamically unstable patients with shock or septic shock benefit from an early, goal-directed therapy and aggressive management.<sup>1,2</sup> Initial resuscitation in the intensive care unit (ICU), or ideally in the Emergency Department, should be aimed at obtaining an adequate hemodynamic index and thus guarantee optimal tissue perfusion. By ensuring prompt, early oxygen delivery to tissues, we can reverse and prevent secondary ischemic injuries that lead to multiple organ dysfunction and poor outcomes, therefore increasing morbidity and mortality.<sup>3,4</sup> Early detection and prevention of situations in which an imbalance between oxygen delivery (DO<sub>2</sub>) and oxygen consumption (VO<sub>2</sub>) occurs should be the main end point for the optimal and correct resuscitation of patients with septic shock. Noninvasive techniques such as near-infrared spectroscopy (NIRS)<sup>5–8</sup> have been proven to evaluate oxygen saturation and blood flow in peripheral tissues.<sup>8–10</sup> Tissue oxygen saturation (StO<sub>2</sub>) and oxygen saturation index (rSO<sub>2</sub>) have been proposed as a marker of tissue perfusion depending on the device used and the location of the measurement<sup>6–14</sup> Although several studies<sup>15–18</sup> have detected changes in vascular reactivity using NIRS during and after a calibrated ischemic challenge, the relationship between skeletal muscle rSO<sub>2</sub> and mortality in septic patients has not been assessed.

We hypothesized that rSO<sub>2</sub> measurements in skeletal muscle of resting healthy subjects may differ from rSO<sub>2</sub> measurements in the first 24 hours of treatment of ICU septic shock patients, that skeletal muscle rSO<sub>2</sub> could identify tissue oxygenation deficiency in ICU patients with septic shock, and that an rSO<sub>2</sub> threshold in ICU septic shock patients might distinguish survivors and nonsurvivors. The objectives of this study were (1) to compare brachioradialis rSO<sub>2</sub> in healthy subjects and ICU septic shock patients, (2) to determine the association between brachioradialis rSO<sub>2</sub> and mortality, and (3) to determine a threshold brachioradialis rSO<sub>2</sub> that might be useful to guide resuscitation.

## PATIENTS AND METHODS

Prospective, observational, controlled study was conducted in a 30-bed medical-surgical ICU in a tertiary univer-

sity hospital. Ethical approval was granted by the Institutional Ethics Board, and signed informed consent was obtained from all patients or relatives and healthy volunteers. The NIRS data were not used in patients' management and did not interfere with patient care.

## Study Populations

### Control Group

Fifty healthy volunteers (mostly hospital physicians and medicine students) were included in this study. Two hundred and fifty readings were obtained. Inpatients were not eligible for inclusion in this phase of the study.

### Septic Shock Group

Nineteen consecutive adult patients were admitted under mechanical ventilation to the ICU with septic shock defined according to the International Sepsis Conference American College of Chest Physicians/Society of Critical Care Medicine criteria.<sup>19</sup> We excluded patients with bilateral upper extremity fractures, amputations, hematomas over forearms, or morbid obesity (corporal mass index >30).

Global hemodynamic variables included the heart rate, central venous pressure (CVP), mean arterial pressure (MAP), cardiac index (CI), cardiac output, pulmonary artery occlusion pressure (PAOP), and central venous oxygen saturation. All measurements were obtained using standard equipment. Serum lactate (SL) and base deficit (BD) were obtained as markers of resuscitation. These variables were determined at baseline, 12 hours, and 24 hours from ICU admission. The patients were treated with fluid resuscitation and vasopressor therapy as required. Treatment of septic shock was standardized according to the local guidelines adapted from the Surviving Sepsis Campaign guidelines.<sup>20</sup> The vasopressor agent of choice was norepinephrine titrated to the 2  $\mu\text{g}/\text{kg}/\text{min}$  maximum dose to maintain the MAP above 65 mm Hg. Epinephrine or dopamine was not used. Fluid resuscitation was administered by fluid bolus challenge with crystalloids and/or artificial colloids to increase stroke volume and/or allow the vasopressor doses to be decreased

when required. Intravenous hydrocortisone (200 mg/d) was administered to all the subjects, but adrenocorticotropic hormone tests were not performed. Human activated protein C was not used in any study subject. In accordance with our local guidelines, each subject was monitored through an arterial catheter. In addition, 16 of 19 septic shock subjects were concomitantly monitored with a pulmonary artery catheter (Edwards, Irvine, CA).

### Oxygen Saturation Index Measurements

After informed consent was obtained, for healthy volunteer and ICU septic shock patients, an INVOS 5100 *SomaSensor* probe was placed on the medial forearm at a distance 5 cm distal to the elbow of each subject to obtain skeletal muscle  $\text{rSO}_2$  measurements. For ICU septic shock patients,  $\text{rSO}_2$  was recorded at baseline, 12 hours, and 24 hours during the first ICU day.

The skeletal muscle  $\text{rSO}_2$  measurements were performed by a commercially available NIRS spectrometry system with noninvasive, nonsterile, and nonreusable disposable skin surface probe (INVOS 5100C Oximeter and adult *SomaSensor* model SAFB-SM, Somanetics Corporation, Troy MI; www.somanetics.com; Fig. 1). The *SomaSensor* is connected to preamplifier, which is placed close to the patients and amplifies the  $\text{rSO}_2$  signal. The signal is then carried to a display unit where the values and trends are displayed on the screen. This system updates display of skeletal muscle  $\text{rSO}_2$  at 10-second intervals, and precalibration device is not required. The system will operate for up to 120 minutes on battery.

The NIRS devices use reflectance mode probes that have one 1.5-mm optical fiber to illuminate the tissue and two optical fibers to detect the backscattered light from the tissue (Fig. 1). The spatial separation between the illumination fiber and two detection fibers is 30 mm and 40 mm, respectively. The NIRS measurement depth increases with the distance between the illuminating and detecting fibers.<sup>6</sup> The 40-mm separated fiber therefore measures a greater and deeper tissue volume than the 30-mm separated fiber. By subtracting the spectral absorbance measured by the 30-mm fiber from that

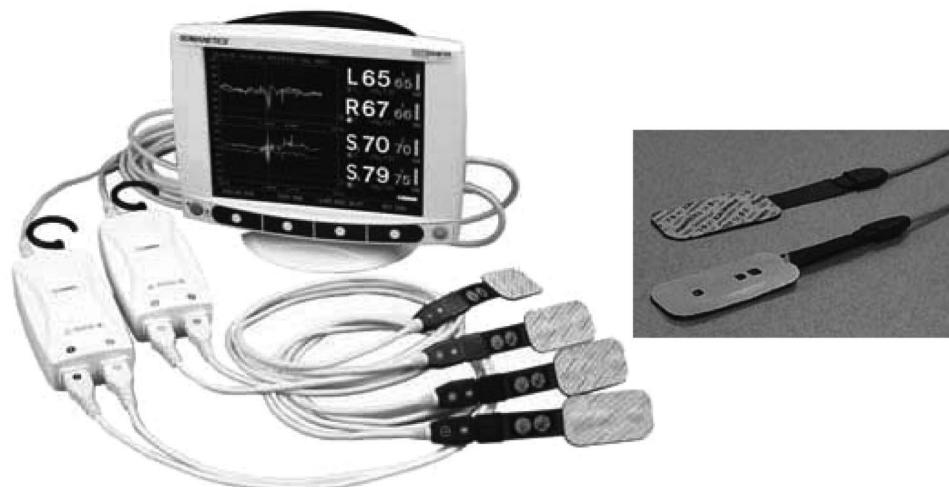


Figure 1. The INVOS 5100 Cerebral/Somatic Oximeter monitor and SomaSensor.

measured by the 40-mm fiber, the spectral absorbance between these two probing depths is then determined and used to calculate the regional oxygen saturation index (rSO<sub>2</sub>).<sup>14,21</sup>

The measurement is of functional oxygen saturation or percentage of hemoglobin bound to oxygen as a function of hemoglobin available for binding. The subtraction process reduces potential errors caused by skin pigmentation,<sup>22</sup> skin blood oxygen changes, and small variations in adipose tissue thickness when used.<sup>7</sup> The INVOS 5100 NIR system functions with two NIR probes, one with 30-mm and the other with 40-mm spacing between NIR light send and receive optical fiber tips. Spacing between optical fiber tips is proportional to the depth of the elliptical path of penetration of NIR light through tissue. The 30-mm signal is subtracted from the 40-mm signal, with the intention of subtracting the skin and subcutaneous fat layer artifact (30 mm probe) from underlying skeletal muscle (40 mm probe).<sup>23</sup>

### Data Collection

To obtain the normal reference range of skeletal muscle rSO<sub>2</sub> for comparison, 250 readings in 50 human volunteers were obtained. Septic shock patient data were collected on admission at ICU (within the first 6 hours), within 12 hours ( $\pm 2$  hours), and at 24 hours ( $+2$  hours). Global hemodynamic variables, markers of resuscitation, and skeletal muscle rSO<sub>2</sub> values were recorded simultaneously. APACHE II score<sup>24</sup> was determined in all patients within 24 hours of ICU admission to record the severity of illness. In addition, organ failure was assessed using the Sequential Organ Failure Assessment scoring system.<sup>25</sup>

### Statistical Analysis

Discrete variables are expressed as counts (percentage) and continuous variables as means  $\pm$  standard deviations or medians within the 25th to 75th interquartile (IQR) range. For the demographic and clinical characteristics of the patients, differences between groups were assessed using the  $\chi^2$  test and Fisher's exact test for categorical variables and the Student's *t* test, Mann-Whitney *U* test, or Kruskal-Wallis test for continuous variables. A logistic regression model was used to assess the association between skeletal rSO<sub>2</sub> (continuous independent variable) and mortality (dependent dichotomous variable). The association was expressed as the odds ratio (OR) for one unit increase in skeletal rSO<sub>2</sub>. In addition, the logistic regression model was used to obtain a predicted probability of mortality. These predicted probabilities were then plotted against skeletal muscle rSO<sub>2</sub> on a graph.

The predictive values for skeletal rSO<sub>2</sub> and the other variables of resuscitation were calculated using a receiver operator characteristic (ROC) curve, and the area under the ROC curve was computed. We calculate the area under ROC curve because the area does not depend only on a particular portion of the plot, such as the point closest to the diagonal or the sensibility at 90%, but on the entire plot, and provides a comprehensive picture of the ability of a test to make a distinction over all decision thresholds. The ROC graph was a plot of all the sensibility/specificity pairs resulting from continuously varying the decision threshold over the entire range of results observed.

Finally, to determine a threshold value of skeletal muscle rSO<sub>2</sub> that might be used as a new "end point" of treatment of septic shock patients, we performed a post hoc analysis according to different cutoffs for rSO<sub>2</sub> (50%, 60%, and 70%), and the sensitivity and specificity were calculated for each one. The better cutoffs of skeletal rSO<sub>2</sub> were used for outcome analysis. Data analysis was performed using SPSS for Windows 13.0 (SPSS, Chicago, IL). The significance level for all analyses was defined as  $p < 0.05$ .

## RESULTS

### Controls

Reference values were obtained from 250 measures in 50 healthy volunteers. Mean ( $\pm$  standard deviation) age (in years) was  $33.0 \pm 9.5$  with a median of 30 (IQR = 27.0–37.0). Thirty-one subjects were female (62%). The mean skeletal muscle rSO<sub>2</sub> in healthy subjects was  $67.3\% \pm 7.1$  with a median of 67.0% (IQR = 63.0–72.0). We found no differences in skeletal muscle rSO<sub>2</sub> between male and female subjects ( $67.1\% \pm 7.4$  vs.  $67.7\% \pm 6.6$ ;  $p = 0.77$ ).

### Septic Shock Patients

Nineteen septic shock patients were enrolled. The mean APACHE II score was  $24.4 \pm 7.5$  points with an overall observed mortality of 57.9%. Table 1 shows additional demographic data and baseline physiologic data with simultaneous measurements of skeletal muscle rSO<sub>2</sub>. No patients died within the first 48 hour, and the length of stay in ICU was no different ( $p = 0.62$ ) between surviving and nonsurviving patients (Table 1).

The mean baseline value of skeletal muscle rSO<sub>2</sub> in septic shock patients ( $55.0\% \pm 13.0\%$ ) was significantly lower than in healthy subjects ( $67.3\% \pm 7.1\%$ ;  $p < 0.001$ ). Nonsurvivors had lower levels of skeletal muscle rSO<sub>2</sub> than survivors in each study period (interval of measurement; Fig. 2). Global hemodynamic variables, SL, and BD are shown in Figure 3, A–G. We found no significant differences in MAP, CVP, PAOP, central venous oxygen saturation, SL, and BD between the groups (Fig. 3, A–G). Cardiac index at admission and 12 hours of presentation was higher in nonsurvivors (Fig. 3, E). SL levels were significantly lower in survivors only at 24 hours (Fig. 3, F). Hemoglobin levels were unchanged throughout the study period in septic shock patients:  $9.9 \pm 1.9$ ,  $8.7 \pm 1.7$ , and  $9.4 \pm 1.8$  for baseline, 12 hours, and 24 hours, respectively. Other variables associated with mortality (Table 1) were as follows: aging, severity of illness (APACHE II score), multiorgan dysfunction (Sequential Organ Failure Assessment score), and vasopressor support dosage. In addition, SL concentration and fluid resuscitation were not significantly different.

We calculated the predicted probability of death according to baseline skeletal muscle rSO<sub>2</sub> using the logistical regression analysis. Each point of increase in skeletal muscle rSO<sub>2</sub> was associated with a 15% decrease in the probability of death (OR = 0.85; 95% confidence interval, 0.73–0.98;  $p < 0.05$ ; Fig. 4). Predicted probability of death for other variables was not significant (data not shown).

**TABLE 1.** Baseline Characteristics of the 19 Septic Shock Patients

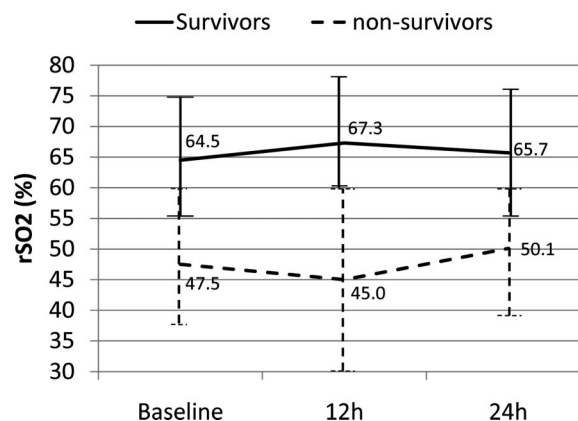
Variable	All Patients (n = 19)	Survivors (n = 8)	Nonsurvivors (n = 11)
Demographics data			
Age (yr), mean (SD)	65.0 (12.3)	61.0 (14.9)	68.5 (9.0)
Men, n (%)	13 (72.2)	6	7
Site of infection, n (%)			
Respiratory	11 (57.9)	5	6
Abdominal	6 (31.6)	2	4
Urinary	2 (10.5)	1	1
Severity of illness			
APACHE II score at day 1, mean (SD)	24.4 (7.5)	19.2 (5.1)	28.2 (6.4)*
SOFA score at day 1, mean (SD)	9.0 (2.6)	7.1 (1.3)	10.4 (2.5)*
Baseline hemodynamic data			
MAP (mm Hg), mean (SD)	73.6 (7.8)	75.9 (7.3)	71.8 (8.1)
CI (L/min/m <sup>2</sup> ), mean (SD)	4.0 (1.8)	3.0 (0.9)	4.6 (1.9)*
PAWP (mm Hg), mean (SD)	12.2 (2.8)	12.0 (5.6)	12.3 (1.5)
SvO <sub>2</sub> (%), mean (SD)	65.8 (7.9)	63.9 (8.3)	67.0 (7.9)
CVP (mm Hg), mean (SD)	13.6 (4.4)	13.1 (4.8)	14.1 (4.2)
Baseline biochemical data			
SL (mM /L), mean (SD)	35.2 (41.6)	19.8 (13.8)	47.6 (52.3)
BD, mean (SD)	7.0 (4.8)	4.9 (2.9)	8.7 (5.4)
Basal hemoglobin levels (mg %)	9.9 (1.9)	10.3 (2.2)	9.6 (1.7)
Therapy			
Norepinephrine (μg/kg/min)	0.7 (0.8)	0.3 (0.2)	1.0 (0.9)*
Volume infusion at first 12 h (mL)	1934 (865)	1456.5 (535)	2411.3 (901)
Baseline brachioradialis rSO <sub>2</sub> (%), mean (SD)	55.0 (13.0)	64.5 (8.9)	48.5 (10.7)*
ICU length of stay† (days)			
Mean (SD)	9.7 (8.9)	8.5 (6.4)	10.5 (10.0)
Median (IQR, 25%–75%)	7 (2–15)	8 (2–14.5)	4 (2–20)
Mortality rate, n (%)	11 (57.9%)	NA	NA

\*  $p < 0.05$ .

† Only in survivors.

APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment; PAWP, pulmonary capillary wedge pressure; NA: not applicable.

Based on post hoc analysis (data not shown), a cutoff value of 60% (sensitivity 73% and specificity 63%) was considered for defining the “low” threshold skeletal muscle rSO<sub>2</sub> value. Twelve patients (63.1%) had a baseline skeletal muscle rSO<sub>2</sub> ≤ 60%, nine of whom (75.0%) died, compared with only two deaths out of the seven patients (28.6%) with skeletal muscle rSO<sub>2</sub> > 60% ( $p = 0.02$ ). This represents a ninefold increase in the risk of death (OR = 9.3; 95% confidence interval, 1.3–65.6) despite similar levels of illness (Table 2).

**Figure 2.** Skeletal muscle rSO<sub>2</sub> in 19 septic shock patients (survivors and nonsurvivors) within the first 24 hours of presentation ( $p < 0.05$  for all comparisons).

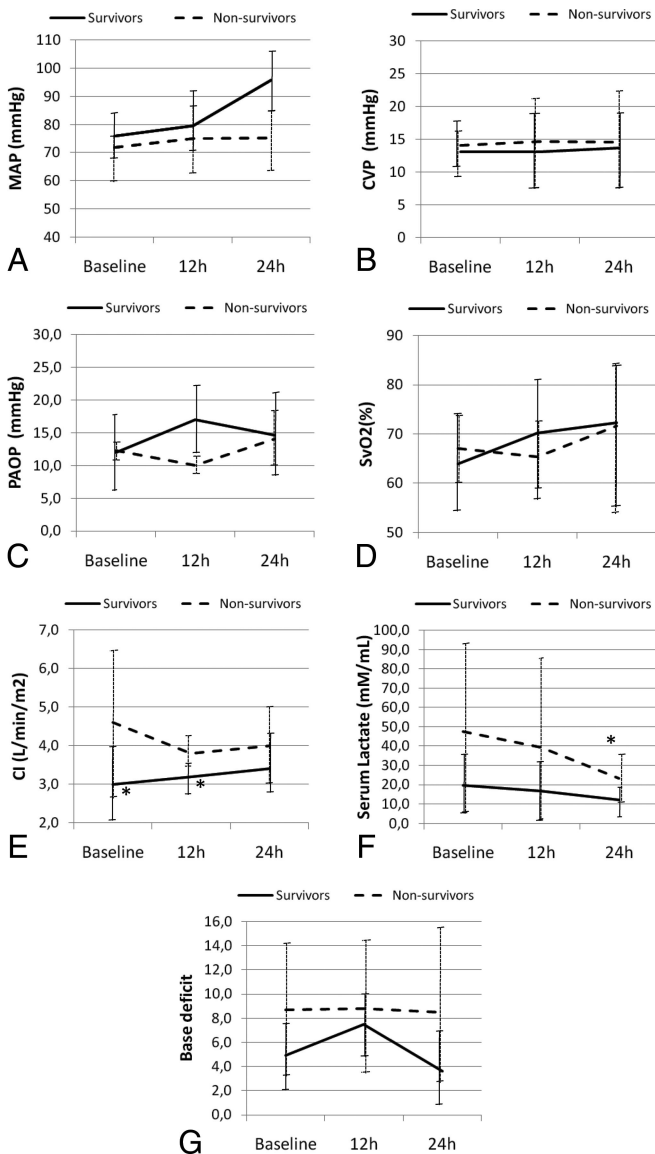
Finally, the discrimination of baseline and 24-hour measurements for skeletal muscle rSO<sub>2</sub> was assessed using ROC. The area under the ROC curve (Fig. 5) showed consistent mortality discrimination for baseline (0.96; 95% confidence interval, 0.88–1.00;  $p = 0.003$ ) and 24-hour skeletal muscle rSO<sub>2</sub> values (0.90; 95% confidence interval, 0.75–1.00;  $p = 0.01$ ), and it also showed that skeletal muscle rSO<sub>2</sub> performed better than other baseline variables (Table 3).

## DISCUSSION

The novel NIRS device (INVOS 5100), which incorporates a nonocclusive and noncontinuous technique of measurement, identifies severe tissue hypoperfusion (low skeletal muscle rSO<sub>2</sub>) in septic shock patients and correlates with mortality. The most important finding in our study is that despite a similar severity of illness, 9 of 12 patients with skeletal muscle rSO<sub>2</sub> ≤ 60% died, representing a near 10-fold increase in the risk of death compared with patients with skeletal muscle rSO<sub>2</sub> > 60%.

Previous studies in other populations and using other devices<sup>6,15–18</sup> have suggested an association between tissue oxygen saturation and hypoperfusion. Using NIRS-derived thenar tissue oxygen saturation (StO<sub>2</sub>), Skarda et al.<sup>18</sup> observed lower values in patients with severe sepsis (75% ± 15%) than in healthy volunteers (87% ± 6%;  $p = 0.013$ ). In addition, Creteur et al.<sup>15</sup> reported that septic patients had a lower baseline StO<sub>2</sub> compared with ICU nonseptic patients and with healthy volunteers. Our study generally agrees with those two studies, but differs from them in two important aspects: (1) we used a brachioradialis muscle site as other authors have done<sup>6</sup> because the INVOS SomaSensor is not designed for the thenar site; (2) we performed a nonocclusive and noncontinuous determination of skeletal muscle rSO<sub>2</sub> to avoid the variability of measurement observed using occlusion techniques. Other studies on non-septic patients<sup>26–29</sup> had similar results.

As expected, baseline levels of CI, mixed venous hemoglobin O<sub>2</sub> saturation (SvO<sub>2</sub>), MAP, pulmonary capillary wedge pressure, SL, CVP, and BD were unable to differentiate survivors from nonsurvivors.<sup>30</sup> Monitoring skeletal



**Figure 3.** Values of standard global measures of resuscitation in survivors and nonsurvivors. (A) Mean arterial pressure; (B) Central venous pressure; (C) Pulmonary artery occlusion pressure (PAOP); (D) Mixed venous hemoglobin O<sub>2</sub> saturation; (E) Cardiac index; (F) Serum lactate and (G) Base deficit (\* *p* < 0.05).

muscle rSO<sub>2</sub> with NIRS avoids the inherent limitation of following lactate or classical hemodynamic parameters. Interstitial lactate concentration may be higher than normal in well-oxygenated skeletal muscle,<sup>31,32</sup> but this would be due to a transient insufficient O<sub>2</sub> supply to that tissue. Blood lactate concentration may be higher than normal due to more global hypoperfusion or insufficient O<sub>2</sub> supply. Skeletal muscle rSO<sub>2</sub> may provide a more accurate reflection of oxygen delivery because it represents the balance between the oxygen supply to the capillaries directly beneath the sensor (monitoring site) and oxygen consumption at that site. Additionally, rSO<sub>2</sub> is a variable indicative of O<sub>2</sub> extraction from hemoglobin (Hb). In comparison with Sao<sub>2</sub>, and possibly SvO<sub>2</sub>, a more accurate picture of hypoxia might be derived from (local) tissue Hb oxygen saturation measurement or monitoring by rSO<sub>2</sub>.

CI measurements were significantly different at baseline and 12 hours, but PAOP and SvO<sub>2</sub> were not different in survivors versus nonsurvivors. rSO<sub>2</sub> reflects an indicator of tissue (hypo) perfusion and oxygenation, but not SvO<sub>2</sub>; CI and rSO<sub>2</sub> differed; In addition, SvO<sub>2</sub> tended to increase during resuscitation. Despite the increase in CI, peripheral skeletal muscle tissue supply may be decreased.<sup>33</sup> There are several mechanisms that might explain skeletal muscle hypoperfusion and, thus, the lower skeletal muscle rSO<sub>2</sub> in patients with high CI due to septic shock. Patients with severe sepsis or septic shock mainly perfuse critical organs, such as brain, heart, or liver, at the expense of peripheral tissues, such as skin or muscle.<sup>34</sup> In addition, microvascular blood flow through local skeletal muscle is altered and varies widely in hemodynamically stable septic patients.<sup>35</sup>

Our results differ from those observed by other investigators<sup>15,16,36,37</sup> because they found similar StO<sub>2</sub> values in injured patients and healthy volunteers. De Blasi et al.<sup>36</sup> found no significant differences in StO<sub>2</sub> in the brachioradialis muscle either at baseline or during cuff inflation between septic shock, postsurgery, and healthy subjects. Pareznik et al.<sup>16</sup> found comparable thenar muscle baseline StO<sub>2</sub> values in patients with septic shock and normal volunteers. Recently, Gomez et al.<sup>37</sup> reported no significant differences in thenar muscle baseline StO<sub>2</sub> between trauma patients and healthy subjects. These discrepancies may be due, in part, to differences in oxygen measured by different devices, the site chosen for measurement, and/or differences in the subset cohort. We found a difference in forearm skeletal muscle rSO<sub>2</sub> between healthy subjects and critically ill septic shock patients. In addition, based on this pilot study, differences between two commercially available NIRS tissue hemoglobin oxygen saturation devices measuring skeletal muscle rSO<sub>2</sub> and StO<sub>2</sub> cannot be defined, but a difference was observed between rSO<sub>2</sub> in healthy subjects and critically ill septic shock patients.

Finally, there are several technical considerations that should be taken into account when interpreting data obtained with different NIRS devices. In the near-infrared range, oxyhemoglobin (HbO<sub>2</sub>), deoxyhemoglobin (Hb), and oxidized cytochrome oxidase (CytOx) have characteristic absorption spectra. To derive concentration changes simultaneously for Hb, HbO<sub>2</sub>, and CytOx, values for absorption at four near-infrared wavelengths are often used. Several algorithms have been published, all of which vary in terms of the light wavelengths used, the presence of other chromophores, and the precise values for the absorption coefficients chosen.<sup>38–40</sup> Two recent studies have applied most of the published algorithms to the same dataset and revealed striking differences in the concentration changes calculated.<sup>14,41</sup> In addition, the increase in the distance traveled by each photon is expressed as “differential pathlength factor” (DPF), which is crucial for interpreting NIRS data. The DPF applied is derived from studies in healthy adults<sup>42</sup>; it may vary in other situations and

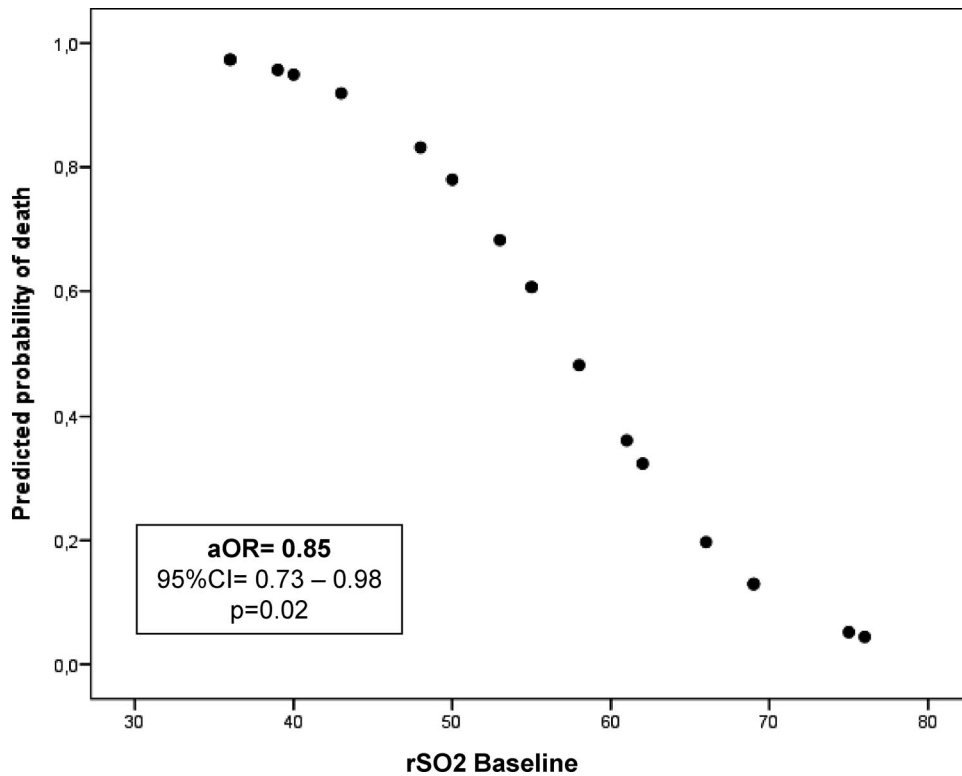


Figure 4. Predicted probability of death according to baseline skeletal muscle rSO<sub>2</sub>.

TABLE 2. Levels of Severity of Illness and Basal Resuscitation Variables in Septic Shock Patients According to Basal Skeletal Muscle rSO<sub>2</sub>

Variable	Skeletal rSO <sub>2</sub> ≤60% (n = 12)	Skeletal rSO <sub>2</sub> >60% (n = 7)	p
APACHE II score, mean (SD)	24.5 (8.0)	24.3 (7.2)	0.95
SOFA score, mean (SD)	8.9 (2.9)	9.1 (2.3)	0.88
CI (L/min/m <sup>2</sup> ), mean (SD)	4.3 (2.0)	3.5 (1.2)	0.48
MAP (mm Hg), mean (SD)	76.6 (5.3)	69.1 (9.3)	0.10
SvO <sub>2</sub> (%), mean (SD)	64.1 (8.5)	68.5 (6.8)	0.34
SL (mM/L), mean (SD)	30.8 (29.5)	42.3 (57.9)	0.96
BD, mean (SD)	6.9 (5.8)	7.2 (3.2)	0.61
Mortality rate, n (%)	8 (72.7%)	2 (28.6%)	0.02

it is also wavelength dependent. What is more, the DPF may also change within the same subject over a period of time if the state of the tissue or tissue geometry is altered,<sup>43</sup> opening up the possibility of different interpretations of the results.<sup>44</sup> In addition, these values may change not only in the same patient but also within various tissue beds in the same individual and different pathologic conditions. Thus, “normal” and critically “abnormal” tissue oxygenation values should probably be determined according to the critically ill patient population and the NIRS device used.

This study has several potential limitations that should be addressed. First, the small sample size of this pilot study precludes any broader conclusions. However,

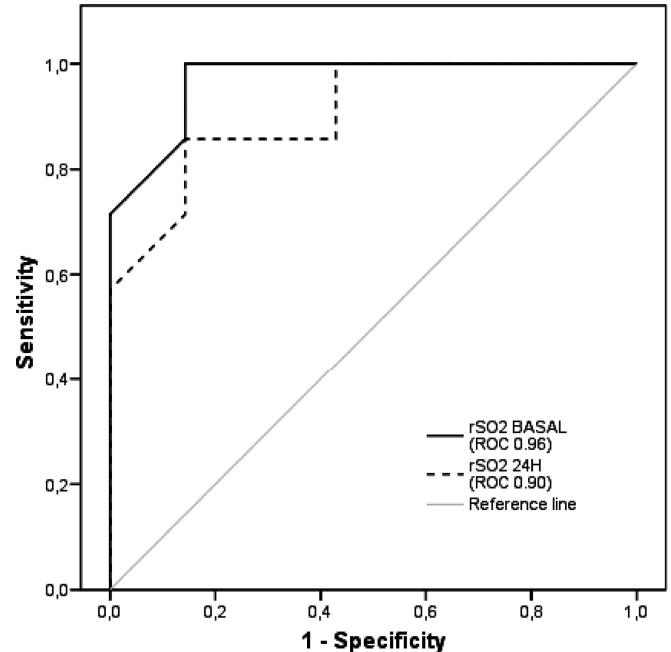


Figure 5. Receiver operating characteristic curves for skeletal muscle rSO<sub>2</sub>.

the results confirmed our hypothesis that low skeletal muscle rSO<sub>2</sub> values during early resuscitation would help to identify patients with poor outcome by recognizing

**TABLE 3.** Discriminative Power of Standard Variables of Resuscitation

Variable	Area Under the ROC Curve	95% Confidence Intervals	p
CI	0.79	0.56–1.00	0.059
SL	0.70	0.44–0.95	0.15
SvO <sub>2</sub>	0.64	0.35–0.94	0.34
CVP	0.56	0.27–0.86	0.14
MAP	0.31	0.57–5.85	0.19
BD	0.16	–4.06 to –0.31	0.16

early any alteration in tissue oxygen despite normalization of hemodynamic variables.

Second, NIRS does not directly measure microcirculatory blood flow. However, many studies<sup>45,46</sup> have observed that NIRS measures correlate well with global and specific organ perfusion parameters. In addition, the near-infrared light (680–800 nm) easily crosses biological tissues, which have a low absorption power, and is absorbed only by hemoglobin, myoglobin, and oxidized cytochrome, but the contribution of these latter two factors to the light attenuation signal is very small.<sup>47,48</sup> Therefore, the NIRS signal is limited to vessels that have a diameter <1 mm (arterioles, capillaries, and venules),<sup>49</sup> and may be a useful tool for noninvasive monitoring microcirculation in septic patients.

Third, the control group comprised healthy volunteers who did not undergo sedation and mechanical ventilation, both of which are treatments that may potentially reduce muscle oxygen consumption. However, an increase in oxygen demand has been widely reported in sepsis patients.<sup>50–52</sup>

Fourth, StO<sub>2</sub> (Inspectra, Hutchinson Technology, Inc.) and rSO<sub>2</sub> (Invos) measurements are based on similar NIRS technology. Our results agree with previous studies<sup>6,18–29</sup> that suggest that skeletal muscle StO<sub>2</sub> measurement is a sensitive and easy technique for assessing hypoperfusion.

Finally, the resuscitation period in the emergency department before admission to ICU was not recorded. A more aggressive resuscitation in ER could be associated with better skeletal rSO<sub>2</sub> at baseline. However, 60% of our patients had skeletal rSO<sub>2</sub> <60% on admission to ICU. Skarda et al.<sup>18</sup> reported a delay of about 24 hours from presentation to the first NIR data, resulting in a relatively stable situation.

In conclusion, we have established that forearm skeletal muscle rSO<sub>2</sub> differs in healthy subjects and ICU septic shock patients at ICU admission and throughout resuscitation. We found that ICU septic shock patients with forearm skeletal muscle rSO<sub>2</sub> ≤60% throughout the first 24 ICU hours had greater mortality rate than patients with forearm skeletal muscle rSO<sub>2</sub> >60% throughout this critical time. Further studies using this technology are warranted to confirm our results.

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