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Near-infrared spectroscopy during stagnant ischemia estimates central venous oxygen saturation and mixed venous oxygen saturation discrepancy in patients with severe left heart failure and additional sepsis/septic shock

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Abstract

Introduction: Discrepancies of 5-24% between superior vena cava oxygen saturation (ScvO₂) and mixed venous oxygen saturation (SvO₂) have been reported in patients with severe heart failure. The thenar muscle tissue oxygenation (StO₂) measured with near-infrared spectroscopy (NIRS) during arterial occlusion testing decreases slower in sepsis/septic shock patients (lower StO₂ deoxygenation rate). The StO₂ deoxygenation rate is influenced by dobutamine. The aim of this study was to determine the relationship between the StO₂ deoxygenation rate and the ScvO₂-SvO₂ discrepancy in patients with severe left heart failure and additional sepsis/septic shock treated with or without dobutamine.

Methods: Fifty-two patients with severe left heart failure due to primary heart disease with additional severe sepsis/septic shock were included. SvO₂ and ScvO₂ were compared to the thenar muscle StO₂ before and during arterial occlusion.

Results: SvO₂ correlated significantly with ScvO₂ (Pearson correlation 0.659, $P = 0.001$), however, Bland Altman analysis showed a clinically important difference between both variables (ScvO₂-SvO₂ mean $72 \pm 8\%$, ScvO₂-SvO₂ difference $9.4 \pm 7.5\%$). The ScvO₂-SvO₂ difference correlated with plasma lactate (Pearson correlation 0.400, $P = 0.003$) and the StO₂ deoxygenation rate (Pearson correlation 0.651, $P = 0.001$). In the group of patients treated with dobutamine, the ScvO₂-SvO₂ difference correlated with plasma lactate (Pearson correlation 0.389, $P = 0.011$) and the StO₂ deoxygenation rate (Pearson correlation 0.777, $P = 0.0001$).

Conclusions: In patients with severe heart failure with additional severe sepsis/septic shock the ScvO₂-SvO₂ discrepancy presents a clinical problem. In these patients the skeletal muscle StO₂ deoxygenation rate is inversely proportional to the difference between ScvO₂ and SvO₂; dobutamine does not influence this relationship. When using ScvO₂ as a treatment goal, the NIRS measurement may prove to be a useful non-invasive diagnostic test to uncover patients with a normal ScvO₂ but potentially an abnormally low SvO₂.

Trial Registration: NCT00384644 ClinicalTrials.Gov.

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Introduction

Maintenance of adequate oxygen delivery (DO_2) is essential to preserve organ function, because a sustained low DO_2 leads to organ failure and death [1]. Low cardiac output states (cardiogenic, hypovolemic and obstructive types of shock), anemic and hypoxic hypoxemia are characterized by a decreased DO_2 but a preserved oxygen extraction ratio. In distributive shock, the oxygen extraction capability is altered so that the critical oxygen extraction ratio is typically decreased [2]. Measurement of mixed venous oxygen saturation (SvO_2) from the pulmonary artery is used for calculations of oxygen consumption and has been advocated as an indirect index of tissue oxygenation and a prognostic predictor in critically ill patients [3-6]. However, catheterization of the pulmonary artery is costly, has inherent risks and its usefulness remains under debate [7,8].

Not surprisingly the monitoring of central venous oxygen saturation ($ScvO_2$) was suggested as a simpler and cheaper assessment of global DO_2 to oxygen consumption ratio [1,2].

A concern with $ScvO_2$ compared with mixed venous oxygen saturation (SvO_2) is that it may not accurately reflect global hypoxia, because organs with capillary beds that drain into the inferior vena cava or coronary sinus will not be involved in this measurement. Healthy resting individuals have a $ScvO_2$ that is slightly lower than the SvO_2 [3]. In heart failure and shock, however, this situation is reversed. Most authors attribute this pattern to changes in the distribution of cardiac output that occur in periods of haemodynamic instability. In shock states, blood flow to the splanchnic and renal circulations fall, while flow to the heart and brain is maintained due to redistribution of blood away from the mesenteric and renal vascular beds and additional right heart dysfunction [4]. Discrepancies of 5 to 24% have been reported [5-7,9].

Near infrared spectroscopy (NIRS) is a technique used for continuous, non-invasive, bedside monitoring of tissue oxygen saturation (StO_2) [8,10].

We have previously shown that skeletal muscle StO_2 does not estimate SvO_2 in patients with severe left heart failure and additional severe sepsis or septic shock. However, in patients with severe left heart failure without additional severe sepsis or septic shock, StO_2 values could be used for fast noninvasive SvO_2 estimation; the trend of StO_2 may be substituted for the trend of SvO_2 [8].

We have also shown that thenar skeletal muscle StO_2 during stagnant ischemia (deoxygenation rate during arterial occlusion test) decreases slower in septic shock patients compared with patients with severe sepsis or localized infection or healthy volunteers [10].

Impaired skeletal muscle microcirculation, especially impaired deoxygenation rate during arterial occlusion test, was recently detected in patients with chronic heart failure. Dobutamine, but not levosimendan, partially reversed this impairment [11].

The aim of current study was to combine our previous findings. We tested the hypothesis that in patients with severe left heart failure and additional sepsis/septic shock the skeletal muscle deoxygenation rate during an arterial occlusion test could predict a $ScvO_2$ - SvO_2 discrepancy. The second aim was to explore the effect of dobutamine treatment on any $ScvO_2$ - SvO_2 discrepancy.

Materials and methods

Patients

The study protocol was approved by the National Ethics Committee of Slovenia; informed consent was obtained from all patients or their relatives. The study was performed between October 2004 and June 2007.

After initial hemodynamic resuscitation according to early goal-directed therapy [12] and Surviving Sepsis Campaign guidelines [13], transthoracic echocardiography for the assessment of left ventricular volume, ejection fraction (Simpson's rule) and valvular function was performed in all patients admitted to our ICU (Hewlett-Packard HD 5000, Hewlett Packard, Andover, MA, USA) by experienced ICU doctors (HM and MP) trained in echocardiography.

In patients with primary heart disease, low cardiac output, and no signs of hypovolemia, a right heart catheterization with a pulmonary artery floating catheter (Swan-Ganz CComboV CCO/ SvO_2 /CEDV, Edwards Lifesciences, Irvine, CA, USA) was performed following a decision of the treating physician. The site of insertion was confirmed by the transducer waveform, the length of catheter insertion, and chest radiography. Systemic arterial pressure was measured invasively using radial or femoral arterial catheterization. Consecutive patients with severe left heart failure due to primary heart disease (left ventricular systolic ejection fraction below 40%, pulmonary artery occlusion pressure above 18 mmHg) and additional severe sepsis/septic shock were included in our study. Severe sepsis and septic shock were defined according to the 1992 American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) consensus conference definitions [14]. Patients with heart failure confirmed by echocardiography without sepsis/septic shock were excluded. Patients with cachexia were not included.

Patients were divided into two groups depending on treatment with dobutamine or not.

All patients received standard treatment of localized infection, severe sepsis and septic or cardiogenic shock

including: source control, fluid infusion, catecholamine infusion, organ failure replacement and/or support therapy, intensive control of blood glucose and corticosteroid substitution therapy according to current Surviving Sepsis Campaign Guidelines [13]. Mechanically ventilated patients were sedated with midazolam and/or propofol infusion. Paralytic agents were not used.

Measurements

Skeletal muscle oxygenation

Thenar muscle StO₂ was measured non-invasively by NIRS (25 mm Probe, InSpectra™, Hutchinson Technology Inc., West Highland Park Drive NE, MN, USA) [8,10,15]. Maximal thenar muscle StO₂ was located by moving the probe over the thenar prominence. StO₂ was continuously monitored and stored onto a computer using InSpectra™ software. The average of StO₂ changing over a 15 second span was used. The arterial occlusion test was performed as previously reported [10]: StO₂ was monitored before and during (StO₂ deoxygenation rate) upper limb ischemia until StO₂ decreased to 40%. Upper limb ischemia was induced by rapid automatic pneumatic cuff inflation (to 260 mmHg) placed above the elbow.

Severity of disease

Sepsis-related Organ Failure Assessment (SOFA) score was calculated at the time of each measurement to assess the level of organ dysfunction [16]. Dobutamine and norepinephrine requirement represented the dose of drug during the StO₂ measurement. Use of an intra-aortic balloon pump during the ICU stay is reported.

Plasma lactate concentration was measured using an enzymatic colorimetric method (Lactate, Roche Diagnostics, Hoffman-La Roche, Basel, Switzerland) at the time of each StO₂ measurement.

Laboratory analysis

Blood was withdrawn from the superior vena cava approximately 2 cm above the right atrium and from the pulmonary artery at the time of each StO₂ measurement to determine ScvO₂ (%) and SvO₂ (%), respectively. In view of known problems arising during sampling from the pulmonary artery, including the possibility of contaminating arterial blood with pulmonary capillary blood, all samples from this site were withdrawn over 30 seconds, using a low-negative pressure technique, without inflating the balloon. A standard volume of 1 mL of blood was obtained from each side after withdrawal of dead-space blood and flushing fluid. All measurements were made using a cooximeter (RapidLab 1265, Bayer HealthCare, Leverkusen, Germany).

Data analysis

A sample size of 41 patients was estimated for a correlation coefficient of 0.6 with a desired power of 0.95 and

alpha of 0.01 (SigmaPlot 2004 for Windows, version 9.01 SyStat Software, Inc., Chicago, IL, USA).

Data was expressed as mean \pm standard deviation (SD). The Mann Whitney non-parametric test was used to compare groups. A *P* value of less than 0.05 was considered statistically significant. The Pearson correlation test was applied to determine correlation (SPSS 10.0 for Windows™, SPSS Inc., Chicago, IL, USA). In order to compare ScvO₂ and SvO₂ we calculated bias, systemic disagreement between measurements (mean difference between two measurements), precision and the random error in measuring (SD of bias) [17]. The 95% limits of agreement were arbitrarily set following Bland and Altman as the bias \pm two SD.

Results

During the study period (20 months), 2,121 patients were admitted to the 15-bed university center internal medicine ICU. In that period 151 right heart catheterizations were performed. The final sample of 52 patients was reached after exclusion of 65 patients with heart failure without sepsis/septic shock, 24 patients who did not have heart failure, 2 patients for whom consent was not given and 8 patients for whom NIRS measurements were not performed. The detailed description of our selected population is given in Table 1. Patients were all mechanically ventilated.

Intra-aortic balloon pumps were inserted in patients who were treated with percutaneous coronary intervention and stent implantation after primary cardiac arrest due to ST-elevation myocardial infarction (STEMI; *n* = 42) and cardiogenic shock. Patients with STEMI after cardiac arrest were treated with medically induced hypothermia for 24 hours. During the ICU stay and before study inclusion they all developed pneumonia. All other patients were admitted to the ICU primarily because of sepsis or septic shock.

Forty-three patients were treated with dobutamine. There was no difference between patients treated with or without dobutamine in additional hemodynamic support (Table 2). Patients treated with dobutamine had a lower cardiac index (Table 3) and a higher procalcitonin value (Table 4).

Thenar StO₂ before (basal StO₂) and during the vascular occlusion test is presented in Table 5. There was no difference between patients treated with and without dobutamine in NIRS data.

SvO₂ correlated significantly with ScvO₂ (Pearson correlation 0.659, *P* = 0.001; Figure 1); however, Bland Altman analysis showed a clinically important difference between both variables (ScvO₂-SvO₂ mean 72 \pm 8%, ScvO₂-SvO₂ difference 9.4 \pm 7.5%; Figure 2).

The ScvO₂-SvO₂ difference correlated with plasma lactate (Pearson correlation 0.400, *P* = 0.003; Figure 3)

Table 1 Description of patients

| Parameter | All (n = 52) | Treatment with dobutamine (n = 43) | Treatment without dobutamine (n = 9) | P value |
|---------------------------------|-----------------|--|--|---------|
| Age (years) | 68 ± 13 | 68 ± 14 | 69 ± 8 | 0.8 |
| Female (n) | 7 | 5 | 2 | 0.6 |
| Heart disease | | | | |
| Ischemic heart disease (n) | 42 | 36 | 6 | 0.4 |
| Aortic stenosis (n) | 6 | 4 | 2 | 0.6 |
| Dilated cardiomyopathy (n) | 1 | 1 | 0 | 0.9 |
| Myocarditis (n) | 3 | 2 | 1 | 0.6 |
| Echocardiography | | | | |
| LVEF (%) | 28 ± 5 | 25 ± 8 | 29 ± 9 | 0.1 |
| LVEDD (cm) | 5.8 ± 0.9 | 5.8 ± 0.7 | 6.0 ± 0.9 | 0.2 |
| Severe mitral regurgitation (n) | 26 | 22 | 4 | 0.8 |
| Cause of infection | | | | |
| Pneumonia (n) | 45 | 38 | 7 | 0.6 |
| Urosepsis (n) | 5 | 4 | 1 | 0.9 |
| Other (n) | 2 | 1 | 1 | 0.7 |
| SOFA score | 12.2 ± 2.5 | 12. ± 2.2 | 12.6 ± 2.6 | 0.8 |
| ICU stay (days) | 9 ± 4 | 9 ± 6 | 9 ± 5 | 0.9 |
| ICU survival (%) | 48 | 47 | 55 | 0.8 |

LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; SOFA, Sequential Organ Failure Assessment.

Table 2 Treatment of patients

| Treatment | All (n = 52) | Treatment with dobutamine (n = 43) | Treatment without dobutamine (n = 9) | P value |
|---------------------------|------------------|--|--|---------|
| Norepinephrine (mg/h, n) | 0.09 ± 0.10 (43) | 0.08 ± 0.11 (37) | 0.04 ± 0.06 (9) | 0.1 |
| Dobutamine (µg/kg/min) | - | 0.47 ± 0.25 | - | - |
| Levosimendan (n) | 23 | 17 | 6 | 0.2 |
| IAPB (n) | 20 | 15 | 5 | 0.3 |
| Mechanical ventilation(n) | 52 | 43 | 9 | 1.0 |
| FiO ₂ | 0.72 ± 0.22 | 0.73 ± 0.23 | 0.71 ± 0.23 | 0.8 |

FiO₂, fractional inspired oxygen; IAPB, intra-aortic balloon pump.

and StO₂ deoxygenation rate (Pearson correlation 0.651, $P = 0.001$; Figure 4).

In the group of patients treated with dobutamine the ScvO₂-SvO₂ difference correlated with plasma lactate (Pearson correlation 0.389, $P = 0.011$) and StO₂ deoxygenation rate (Pearson correlation 0.777, $P = 0.0001$).

In a small group of patients (n = 9) treated without dobutamine the ScvO₂-SvO₂ difference correlated with the StO₂ deoxygenation rate (Pearson correlation 0.673, $P = 0.033$); however, there was no correlation between the ScvO₂-SvO₂ difference and plasma lactate (Pearson correlation 0.503, $P = 0.139$).

Discussion

Our study confirmed the hypothesis that the skeletal muscle StO₂ deoxygenation rate correlates (or is

inversely proportional) to the ScvO₂-SvO₂ difference in patients with severe heart failure with additional sepsis/septic shock. This relation between the StO₂ deoxygenation rate and the ScvO₂-SvO₂ difference was also present in patients treated with or without dobutamine. We also showed that these patients have a clinically considerable ScvO₂-SvO₂ discrepancy. Monitoring of ScvO₂ is a simpler and cheaper assessment of global DO₂ to oxygen consumption ratio, but its use as a treatment goal in patients with severe heart failure with additional sepsis/septic shock is questionable.

The high StO₂/low SvO₂ seen in patients with severe sepsis and septic shock suggests blood flow redistribution. Thenar muscle StO₂ correlates with central venous oxygen saturation that is measured in a mixture of blood from the head and both arms [18]. In healthy

Table 3 Hemodynamic data in patients with heart failure and additional sepsis treated with and without dobutamine

| Hemodynamic data | All (n = 52) | Treatment with dobutamine (n = 43) | Treatment without dobutamine (n = 9) | P value |
|-----------------------------|-----------------|--|--|-------------|
| HR (bpm) | 113 ± 20 | 113 ± 20 | 114 ± 21 | 0.8 |
| SAP (mmHg) | 118 ± 21 | 117 ± 20 | 124 ± 27 | 0.9 |
| DAP (mmHg) | 74 ± 22 | 76 ± 22 | 66 ± 21 | 0.4 |
| PAP _s (mmHg) | 57 ± 14 | 56 ± 13 | 57 ± 16 | 0.9 |
| PAP _d (mmHg) | 28 ± 8 | 27 ± 8 | 29 ± 7 | 0.4 |
| CVP (mmHg) | 16 ± 5 | 16 ± 5 | 15 ± 5 | 0.8 |
| DO ₂ (ml/kg/min) | 406 ± 128 | 391 ± 134 | 470 ± 121 | 0.1 |
| VO ₂ (ml/kg/min) | 118 ± 42 | 116 ± 43 | 126 ± 38 | 0.5 |
| PAOP (mmHg) | 23 ± 7 | 24 ± 7 | 22 ± 8 | 0.7 |
| CI (L/min/m ²) | 2.5 ± 0.7 | 2.4 ± 0.7 | 2.9 ± 0.6 | 0.03 |
| SvO ₂ (%) | 67 ± 10% | 66 ± 10 | 71 ± 7 | 0.2 |
| ScvO ₂ (%) | 77 ± 8% | 77 ± 7 | 78 ± 10 | 0.6 |

Bold: statistically significant difference, $P < 0.05$.

CI, cardiac index; CVP, central venous pressure; DAP, diastolic arterial pressure; DO₂, delivery of oxygen; HR, heart rate; PAOP, pulmonary artery occlusion pressure; PAP_d, diastolic pulmonary arterial pressure; PAP_s, systolic pulmonary arterial pressure; SAP, systolic arterial pressure; SvO₂, mixed venous hemoglobin saturation; ScvO₂, central venous oxygen saturation; VO₂, oxygen consumption.

Table 4 Laboratory data

| Laboratory data | All (n = 52) | Treatment with dobutamine (n = 43) | Treatment without dobutamine (n = 9) | P value |
|----------------------------------|-----------------|--|--|-------------|
| Core temperature (°C) | 38.0 ± 0.9 | 37.9 ± 0.87 | 38.2 ± 0.92 | 0.5 |
| Lactate (mmol/l) | 3.5 ± 3.0 | 3.6 ± 3.3 | 3.0 ± 1.7 | 0.4 |
| CRP (mg/l) | 127 ± 78 | 124 ± 65 | 154 ± 120 | 0.6 |
| PCT (mg/l) | 6.2 ± 6.1 | 7.2 ± 6.3 | 2.5 ± 4.2 | 0.01 |
| Leucocytes (*10 ⁹ /l) | 14.0 ± 5.4 | 13.8 ± 5.3 | 15.4 ± 6.3 | 0.5 |
| Hemoglobin (g/L) | 11.6 ± 1.5 | 11.6 ± 1.6 | 11.6 ± 1.0 | 0.9 |
| Creatinine | 198 ± 160 | 162 ± 142 | 231 ± 182 | 0.1 |
| Sodium (mmol/L) | 144 ± 12 | 144 ± 11 | 147 ± 14 | 0.8 |
| Arterial blood gas analysis | | | | |
| pH | 7.35 ± 0.09 | 7.35 ± 0.08 | 7.33 ± 0.09 | 0.6 |
| pCO ₂ (kPa) | 4.7 ± 1.0 | 4.6 ± 1.0 | 5.3 ± 0.8 | 0.06 |
| pO ₂ (kPa) | 15.3 ± 5.4 | 14.6 ± 4.8 | 18.5 ± 7.4 | 0.1 |
| HCO ₃ (mmol/L) | 20.6 ± 5.6 | 20.4 ± 6.1 | 21.5 ± 3.9 | 0.5 |
| BE(mEq/l) | -5.1 ± 6.4 | -5.4 ± 6.9 | -4.2 ± 4.8 | 0.5 |
| SatHbO ₂ (%) | 97 ± 3% | 97 ± 2 | 98 ± 3 | 0.4 |

Bold: statistically significant difference, $P < 0.05$.

BE, base excess; CRP, C-reactive protein; HCO₃, bicarbonate; PCT, procalcitonin; pCO₂, partial pressure of carbon dioxide; pO₂, partial pressure of oxygen; SatHbO₂, hemoglobin oxygen saturation.

resting individuals the ScvO₂ is slightly lower than the SvO₂ [3]. Blood in the inferior vena cava has a high oxygen content because the kidneys do not utilise much oxygen but receive a high proportion of the cardiac output [19]. Blood in the inferior vena cava blood has a higher oxygen content than blood from the upper body and the SvO₂ is thus greater than the ScvO₂.

This relation changes in periods of cardiovascular instability. Scheinman and colleagues performed the earliest comparison of ScvO₂ and SvO₂ in both hemodynamically stable and shocked patients [5]. In stable

patients, ScvO₂ was similar to SvO₂. In patients with a failing heart, ScvO₂ was slightly higher than SvO₂ and in patients with shock the difference between SvO₂ and ScvO₂ was even more expressed (47.5% ± 15.11% vs. 58.0% ± 13.05%, respectively, $P < 0.001$). Lee and colleagues described similar findings [20]. Other more detailed studies in mixed groups of critically ill patients designed to test if the ScvO₂ measurements could substitute the SvO₂ showed problematically large confidence limits [6] and poor correlation between the two values [7].

Table 5 NIRS data of skeletal muscle tissue oxygenation (StO₂) during vascular occlusion test in patients with heart failure and additional sepsis

| NIRS data | All (n = 52) | Treatment with dobutamine (n = 43) | Treatment without dobutamine (n = 9) | P value |
|---|--------------|------------------------------------|--------------------------------------|---------|
| Basal StO ₂ (%) | 89 ± 8 | 88 ± 8 | 92 ± 6 | 0.1 |
| StO ₂ deoxygenation rate (%/min) | -12.6 ± 4.9 | -12.7 ± 5.2 | -12.6 ± 4.6 | 0.9 |

NIRS, near-infrared spectroscopy; StO₂, skeletal muscle tissue oxygenation.

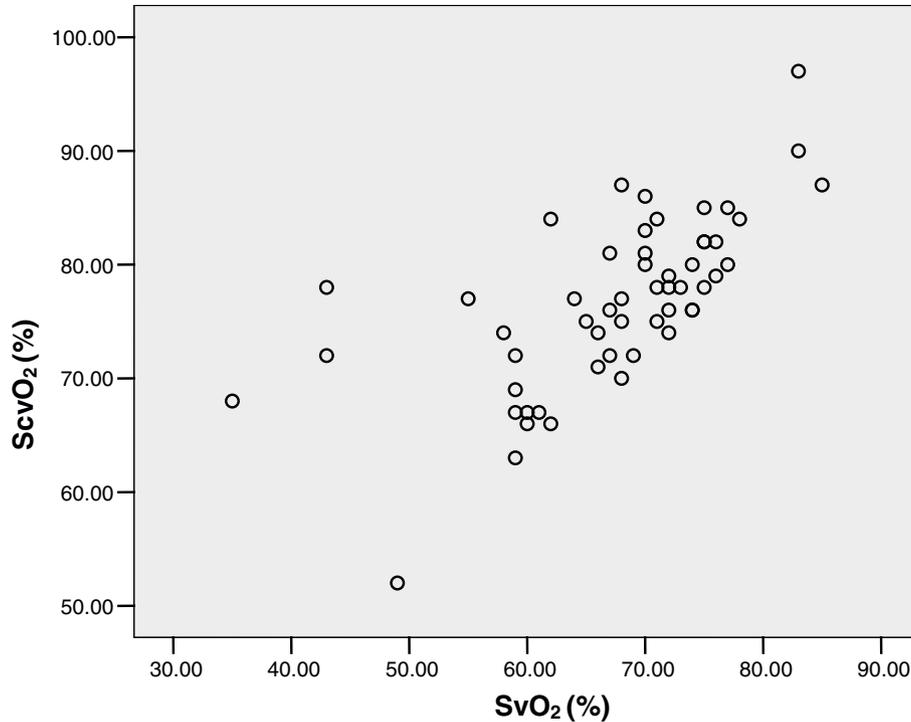


Figure 1 Correlation between mixed venous (SvO₂) and central venous saturation (ScvO₂) in patients with heart failure and additional sepsis/septic shock. Pearson correlation 0.659, *P* = 0.001.

Most authors attribute this pattern to changes in the distribution of cardiac output that occur in periods of hemodynamic instability. In shock states, blood flow to the splanchnic and renal circulations falls, while flow to the heart and brain is maintained [21]. This results in a fall in the oxygen content of blood in the inferior vena cava. As a consequence, in shock states the normal relation is reversed and ScvO₂ is greater than SvO₂ [5]. Therefore, when using ScvO₂ or StO₂ as a treatment goal, the relative oxygen consumption of the superior vena cava system may remain stable, while the oxidative metabolism of vital organs, such as the splanchnic region, may reach a level where a flow-limited oxygen consumption is achieved, together with a marked decrease in oxygen saturation. In this situation skeletal muscle StO₂ provides a false favorable impression of an adequate body perfusion, because of

the inability to detect organ ischemia in the lower part of the body.

In our study, three patients with septic shock had skeletal muscle StO₂ of 75% or less (under the lower boundary of 95% confidence interval for the mean of StO₂ in controls); they were all in septic shock (lactate value above 2.5 mmol/L) with a low cardiac index below 2.0 L/min/m². These patients were probably in an early under-resuscitated phase of septic shock. The low quantity of septic patients with low StO₂ did not allow statistical comparison of StO₂ and SvO₂/SvO₂ in these types of patients. Additional research is necessary to study muscle skeletal StO₂ in under resuscitated septic patients.

Our data are supported by previous work by Boekstegers and colleagues who measured the oxygen partial

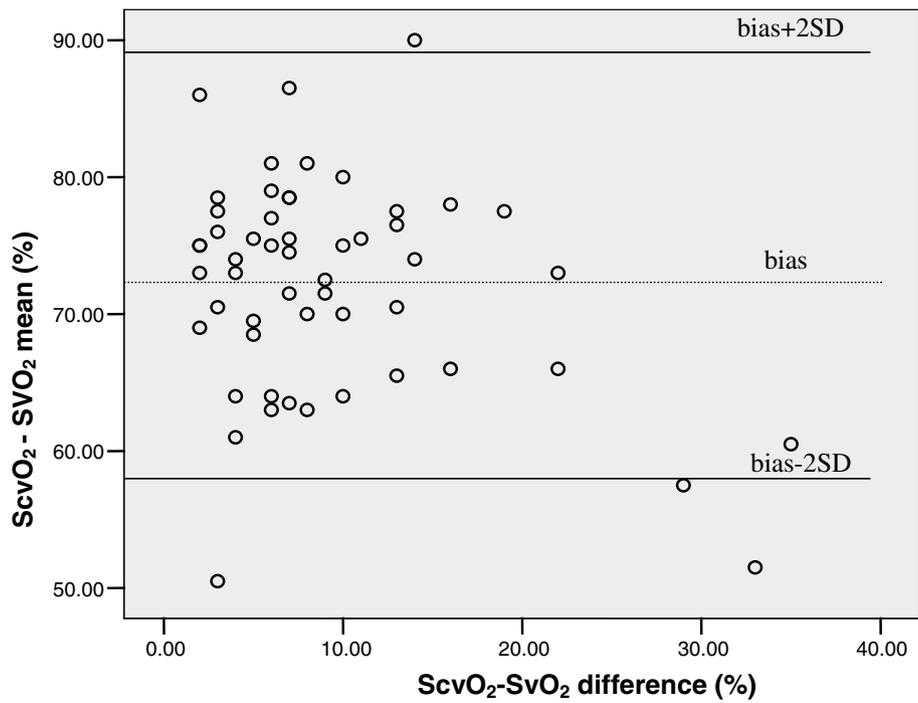


Figure 2 Bland Altman analysis of clinically important difference between mixed venous (SvO₂) and central venous saturation (ScvO₂) in patients with heart failure and additional sepsis/septic shock. ScvO₂-SvO₂ mean 72 ± 8%, Scv-Svo2 difference 9.4 ± 7.5%.

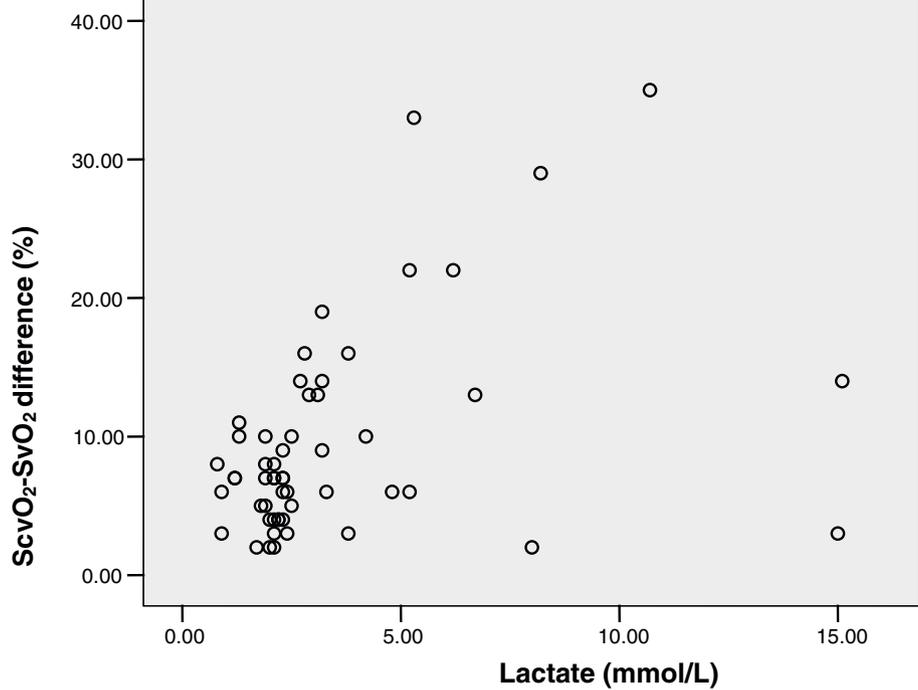


Figure 3 Correlation of mixed venous (SvO₂) and central venous saturation (ScvO₂) difference with plasma lactate (mmol/L). Pearson correlation 0.400, $P = 0.003$.

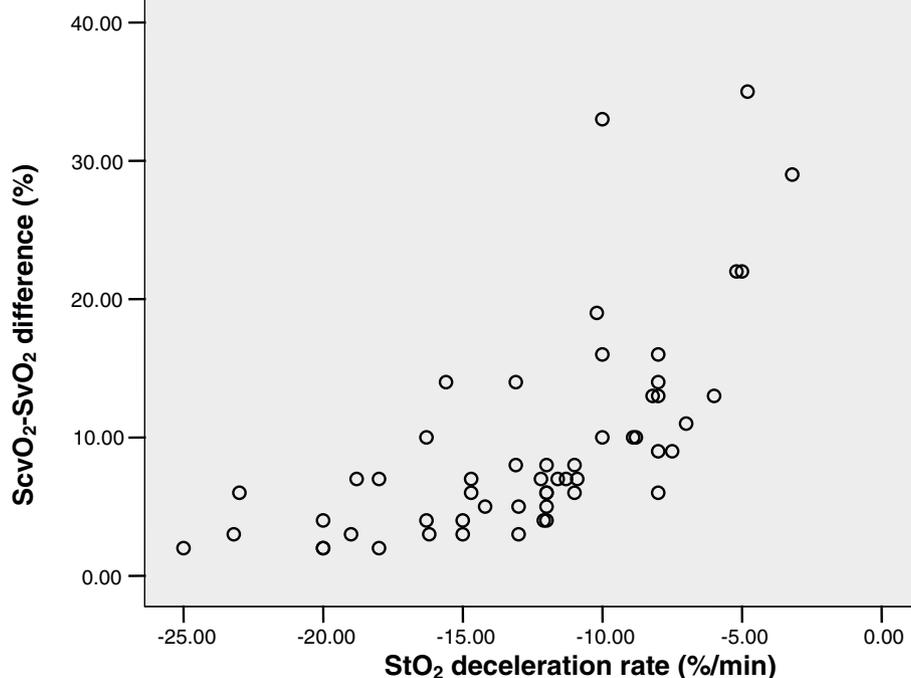


Figure 4 Correlation of central venous saturation (ScvO₂) central venous saturation (SvO₂) difference with skeletal muscle tissue oxygenation (StO₂) deceleration rate. Pearson correlation 0.651, *P* = 0.001.

pressure distribution in bicep muscle [22]. They found low peripheral oxygen availability in cardiogenic shock compared with sepsis. In cardiogenic shock the skeletal muscle oxygen partial pressure correlated with systemic oxygen delivery ($r = 0.59$, $P < 0.001$) and systemic vascular resistance ($r = 0.74$, $P < 0.001$). No correlation was found between systemic oxygen transport variables and the skeletal muscle partial oxygen pressure in septic patients. These measurements were performed in the most common cardiovascular state of sepsis in contrast to hypodynamic shock, which is only present in the very final stage of sepsis or in patients without adequate volume replacement [23]. In a following study the same authors have shown that even in the final state of hypodynamic septic shock leading to death, the mean muscle partial oxygen pressure did not decrease to below 4.0 kPa before circulatory standstill [24].

A recent study confirmed the use of NIRS and the arterial occlusion test in the assessment of peripheral muscle microcirculation impairment in patients with congestive heart failure [11]. This impairment of microcirculation was partially reversed by infusion of the inotropic agent dobutamine but not by levosimendan. In chronic heart failure patients, dobutamine increases cardiac output and improves tissue perfusion, which leads to improvement of endothelial function and tissue oxygenation. It was demonstrated that short-term (72 hours) and short-term intermittent (for five hours,

biweekly) administration of dobutamine has a sustained beneficial effect on vascular endothelial function for two weeks or longer and after four months, respectively [25,26]. Despite this effect of dobutamine on endothelial function in patients with chronic heart failure, we have not detected any difference in StO₂ deoxygenation in our mixed population of patients with left heart failure and additional sepsis/septic shock treated with or without dobutamine. Sepsis/septic shock-related microvascular changes and the lack of inclusion of end-stage heart failure patients in our study are probably causes for discrepancy between the results of our study and the study performed by Nanas and colleagues [11].

It is known that progressive chronic heart failure leads to cardiac cachexia and decreased resting energy expenditure, both of which are worst outcome predictors [27]. Previously, we have shown that in these patients metabolism is changed to the predominant utilization of lipids [28]. However, these changes happen in stages of advanced chronic heart failure, while on the other hand in patients without cachexia the resting energy expenditure is increased proportionally to a higher New York Heart Association class [29]. No patients with cardiac cachexia were included in our study. The effects of dobutamine on skeletal muscle metabolism in patients with chronic heart failure were studied by magnetic resonance spectroscopy, which indicated that dobutamine has the ability to increase cardiac output and limb

blood flow, although it does not improve oxygen delivery to the working muscle of the patients [30]. Increased resting blood flow can result in increased oxyhemoglobin content in muscle leading to increased basal StO_2 but the StO_2 deoxygenation rate should stay unchanged if the metabolic rate remains constant.

Conclusions

In patients with severe heart failure with additional sepsis/septic shock, there is a clinically important discrepancy between $ScvO_2$ and SvO_2 . However, with the use of arterial occlusion testing and measurement of the skeletal muscle deoxygenation rate, we can predict the $ScvO_2$ - SvO_2 difference and determine adequate monitoring. Dobutamine use did not change this relation. Applying these findings in practice, in a patient with severe left heart failure, first perform arterial occlusion testing to determine the StO_2 deoxygenation rate. If it is high (not prolonged as seen in sepsis/septic shock), estimate the SvO_2 by using basal StO_2 . In the case of a prolonged skeletal muscle StO_2 deoxygenation rate, look for additional sepsis, and the deoxygenation rate can estimate discrepancy between the $ScvO_2$ and SvO_2 .

Key messages

- In patients with severe left heart failure and additional severe sepsis or septic shock the $ScvO_2$ - SvO_2 discrepancy is clinically important.
- The skeletal muscle StO_2 deoxygenation rate estimates the $ScvO_2$ - SvO_2 discrepancy in patients with severe left heart failure with additional severe sepsis or septic shock.

Abbreviations

DO_2 : systemic oxygen delivery; NIRS: near infrared spectroscopy; SOFA: Sepsis-related Organ Failure Assessment Score; $ScvO_2$: central venous oxygen saturation; SD: standard deviation; STEMI: ST-elevation myocardial infarction; StO_2 : tissue oxygen consumption; SvO_2 : mixed venous oxygen saturation.

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Authors' contributions

HM contributed to original observation, conception, design, acquisition of data, analysis and interpretation, and drafting the manuscript. MP contributed to conception, design, acquisition of data, analysis and interpretation, and drafting the manuscript.

Competing interests

The authors declare that they have no competing interests.

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