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Low and "supranormal" central venous oxygen saturation and markers of tissue hypoxia in cardiac surgery patients: a prospective observational study

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Abstract *Purpose:* To characterize incidence of low, normal and "supranormal" central venous oxygen saturation ($ScvO_2$) and the relation to markers of tissue hypoxia, course and outcome in cardiac surgery patients. *Methods:* Prospective, observational study in a university multidisciplinary 50-bed intensive care unit including 205 consecutive patients undergoing elective cardiac surgery. Data were split into training and test data sets and subjected to 50 replications of fivefold cross-validation to estimate lower and upper bounds of $ScvO_2$ indicative of impaired tissue oxygenation. *Results:* Both low ($\leq$60.8%) and supranormal ($\geq$77.4%) $ScvO_2$ were associated with an unfavorable course, while the logistic EuroSCORE for risk adjustment was comparable between groups. Incidences of abnormal $ScvO_2$ were 13.2% low and 30.7% supranormal. Patients with low $ScvO_2$ and an uneventful course initially presented with normal lactate levels, whereas patients with supranormal $ScvO_2$ displayed consistently higher serum lactate levels. High $ScvO_2$ values were associated with the use of β-mimetics and signs of systemic inflammation. Mortality rates were comparable for patient populations presenting either low (14.8%) or supranormal $ScvO_2$ (7.9%) and higher than normals (0%, $p < 0.001$). Lactate was comparably increased in patients that ultimately died, irrespective whether they had low or supranormal $ScvO_2$ values. In contrast, neither low nor supranormal $ScvO_2$ was associated with altered gastric pCO_2. *Conclusions:* High $ScvO_2$ is an under-recognized warning sign for impaired tissue oxygenation in the peri-operative period. Including values $\geq$77.4% as 'normal' impaired performance of $ScvO_2$ monitoring to predict a complicated perioperative course.

Keywords $ScvO_2$ · Lactate · Gastric tonometry · Systemic inflammation · Organ failure

Abbreviations

$aiDCO_2$	Arterio-intestinal pCO_2-gradient
AUC	Area under the curve
CABG	Coronary artery bypass graft
DO_2	Oxygen delivery
pCO_2	Partial pressure of carbon dioxide
SAPS II	Simplified Acute Physiology Score II
$ScvO_2$	Central venous oxygen saturation
SaO_2	Arterial oxygen saturation
SIRS	Systemic inflammatory response syndrome
SOFA	Sepsis-related Organ Failure Assessment
VO_2	Oxygen uptake

Introduction

It is now well accepted that macrohemodynamic assessment may fail to detect persistent tissue hypoxia, as reflected by increased lactate levels and low central venous oxygen saturation ($ScvO_2$), in a wide range of clinical conditions [1–3]. Signs of persistent tissue hypoxia indicate the need for additional resuscitation, at least in septic patients. The Early Goal-Directed Therapy trial by Rivers and colleagues [3] demonstrated that low $ScvO_2$ was not only associated with high in-hospital mortality, but also that more aggressive therapy to restore $ScvO_2$ could substantially reduce mortality.

$ScvO_2$-monitoring has been validated against mixed venous saturation and expanded to different patient cohorts as well as clinical conditions [4–7], but with mixed results. In particular, the significance of supply dependency as well as usefulness of $ScvO_2$ monitoring in interdisciplinary ICU-admissions or perioperative patients has been questioned [8]. In a recent study by Bracht et al. [9], the receiver-operating characteristics for $ScvO_2$ to predict 28-day mortality in 'mixed ICU-admissions' were very poor, with an area-under-the-curve (AUC) of only 0.53; this was clearly inferior to the SAPS II score with an AUC of 0.89. However, defining cutoff points for $ScvO_2$ in patient cohorts presenting either hypo- or hyperdynamic circulatory failure is problematic. More to the point, efforts to define the significance of "supranormal" $ScvO_2$ are scarce, and including these as 'normal' might result in overall poor performance of $ScvO_2$ as a predictor of impaired tissue oxygenation.

Moreover, two components affect the oxygen delivery/uptake relationship (DO_2/VO_2) as it is reflected in $ScvO_2$. Cardiac output and peripheral cellular oxygen utilization are frequently altered in parallel in individual patients, confounding interpretation of $ScvO_2$ values. Thus, assessment of tissue perfusion typically presents a challenge in patient groups with impaired cardiac function that is complicated by peripheral circulatory and/or mitochondrial failure [10]. Cardiac surgery in patients with impaired left ventricular function reflects such a scenario, as a whole-body inflammatory response capable of initiating peripheral circulatory failure similar to sepsis ensues in up to one-third of patients with need for vasopressors and a characteristic primed phenotype of circulating immune competent cells [11].

We therefore defined lower and upper boundaries and studied incidence of both low as well as "supranormal" $ScvO_2$ prospectively and assessed their relationship to markers of tissue oxygenation in patients undergoing elective cardiac surgery.

Materials and methods

The study was approved by the Institutional Review Board for Human Research of the Friedrich Schiller University, Jena, Germany, which permitted anonymous data analysis, waving informed consent due to the strict observational character and the routine use of central venous lines and gastric tubes in all patients enrolled. A total of 205 patients, age 18 years or older, undergoing cardiac surgery for either coronary artery bypass grafting or valve repair were enrolled between February and November 2004.

Central venous access was obtained percutaneously via the internal jugular approach using a triple lumen spectrophotometry catheter (PreSepCV, Edwards Lifesciences, Unterschleissheim, Germany) after induction of anesthesia and connected to the optical module of a Vigilance monitor (Edwards Lifesciences). In vivo calibration was performed according to the manufacturer's instruction at least on a 6-hourly basis. All patients routinely received transesophageal echocardiography, which was used in addition to postoperative chest radiography to confirm the position of the fiberoptic catheter in the central vein. Also, a gastric tonometry tube (Tonometrics TM, 14F, Datex Ohmeda) for continuous estimation of gastric CO_2 partial pressure ($prCO_2$; Tonocap TC 200, Datex-Engström, Helsinki, Finland) to calculate arterio-intestinal pCO_2-gradient ($aiDCO_2$) was placed after intubation.

Upon admission to the ICU, all patients were treated according to standard practice; no specific hemodynamic study protocol was implemented. Values for $ScvO_2$, which are otherwise frequently but not routinely monitored on our ICU, were made available to the physician in charge.

Blood gas analyses and lactate levels were assessed at least every 2–3 h via a bed-side analyzer (Radiometer ABL, Copenhagen, Denmark), which was calibrated on a daily basis and subjected to quality control by the central laboratory for clinical chemistry according to 'good clinical practice' criteria.

Patients were monitored as described above until they were hemodynamically stable, extubated and fulfilled criteria for discharge to a step-down unit, but no longer than 24 h.

A "complicated course" was defined prospectively by the end points mortality, need for veno-venous hemofiltration or ventilation for more than 24 h.

Statistical analysis

Determination of lower and upper boundaries for $ScvO_2$

Data at time point $h = 0$ h were split into training and test sets as recommended [12]. The definition of optimal lower and upper bounds for $ScvO_2$ was solely based on the training set. We used 50 replications of fivefold cross-validation to obtain estimators for the optimal lower and upper bounds for $ScvO_2$. In each cross-validation step, the optimal bounds were computed by a grid search.

Thus, three groups were defined as low, normal and supranormal $ScvO_2$, based on their immediate $ScvO_2$ values upon admission to the ICU. For a more detailed description, see the ESM.

Test statistics and data reporting

Data are presented as median and interquartile range, absolute numbers or percentages. Demographic data, hemoglobin levels, perioperative transfusion requirements, Acute Physiology and Chronic Health Evaluation II (APACHE II), Sepsis-related Organ Failure Assessment (SOFA) and Simplified Acute Physiology Score II (SAPS II) scores, EuroSCORE, laboratory data, dosage of catecholamines and markers of tissue hypoxia at a particular time were compared between the three groups using the Kruskal-Wallis test followed post hoc, if significant, by Mann-Whitney *U* test with Bonferroni correction. Differences between categorical variables were analyzed applying Fisher's exact test. For serial measurements of markers of tissue hypoxia, the area under the curve normalized for observation periods was calculated and similarly tested by Kruskal-Wallis and post-hoc Mann-Whitney *U* tests with Bonferroni correction. Changes over time, e.g., for vasoactive drugs, were assessed by Friedman repeated measure on ranks followed if significant by Tukey's test. A p value less than 0.05 was considered statistically significant. To avoid drop-out bias, the 'last-observation-carried-forward principle' was applied.

Data analysis was performed using the SPSS software package, version 15.0, and the software R (R Foundation for statistical computing, Vienna, Austria, http://www.R-project.org).

Results

Incidence of low and supranormal values for $ScvO_2$ upon admission to the ICU

Abnormal values for $ScvO_2$ were observed in over 40% of the patients upon admission to the ICU after elective cardiac surgery. A low $ScvO_2$ (determined as $\leq$60.8%) was observed less frequently (13.2% of cases) than a supranormal (determined as $\geq$77.4%) $ScvO_2$ (30.7% of cases). The supranormal $ScvO_2$ group already had higher values during the intraoperative course at some time points. However, intraoperative $ScvO_2$ values were rather high in all groups.

Demographic data

There were no statistically significant differences among the three patient groups in the assessed demographic variables of sex, preoperative left ventricular function, NYHA classification, chronic cardiovascular medication, type and duration of surgery, bypass and ischemia time, and lowest hematocrit and oxygen delivery during cardiopulmonary bypass (Table 1). While heart rates were comparable between groups at all time points, mean arterial pressure was lower in the supranormal $ScvO_2$ group in comparison with the normal $ScvO_2$ group after induction of anesthesia and 3 and 12 h after ICU admission. However, median and interquartile ranges were within normal range (see electronic supplementary material). Patients with either low or supranormal $ScvO_2$ were however on average 2–4 years older, and those with high $ScvO_2$ had a moderately lower body mass index (Table 1). Intra- and postoperative infusion management was comparable among the three patient groups (see electronic supplementary material). Of interest, hemoglobin values were significantly lower upon admission in those patients with a low $ScvO_2$, but this was corrected postoperatively as reflected in higher transfusion requirements. In the low $ScvO_2$ group, patients received more platelet concentrates intraoperatively.

The complex European System for Cardiac Operative Risk Evaluation (EuroSCORE), a logistic tool assessing 17 individual risk factors, including comorbidities as well as perioperative determinants predictive of 28-day mortality, was comparable among the groups (Table 1).

Time course of $ScvO_2$ and relation to markers of impaired tissue oxygenation

$ScvO_2$ values normalized in both the low and supranormal groups within the first 6–12 h after admission to the ICU (Fig. 1). With respect to detection of tissue hypoxia, two different patterns, most likely relating to either hypo- or hyperdynamic cardiovascular impairment, could be observed. Low $ScvO_2$ values were associated with normal lactate values for the majority of patients. Low $ScvO_2$ associated with lactate production was associated with mortality (Figs. 2, 3).

In contrast, supranormal $ScvO_2$ was paralleled by immediate and persistently increased lactate production in all patients, with even higher lactate values in those patients subsequently dying (Figs. 2, 3). Higher lactate values in these patients were detected as early as at the time of protamin bolus intraoperatively, reflecting the end of cardiopulmonary bypass and end of off-pump bypass surgery, respectively.

Thus, the combined analysis of $ScvO_2$ and lactate values as surrogates for oxidative metabolism identified patients with significant tissue hypoxia, whereas $aiDCO_2$ was not associated with unfavorable clinical outcome (Fig. 4).

The importance of high $ScvO_2$ levels as a marker of tissue hypoxia is further supported by the association of

Table 1 Demographic data of patients presenting low, normal or supranormal $ScvO_2$ upon admission to the ICU

	Low ScvO2 group ($n = 27$)	Normal ScvO2 group ($n = 115$)	Supranormal ScvO2 group ($n = 63$)	p value
Age [years]	71.0 [64.0–76.0]	67.0 [62.0–74.0]	68.0 [59.0–71.0]	0.086
Sex [no. of patients] female/male	11/16	39/76	23/40	0.784
Body mass index [kg m^{-2}]	26.6 [24.5–31.3]	27.3 [24.8–29.8]	25.2 [23.4–27.3]*	0.007
NYHA class	2.5 [2.0–3.0]	3.0 [2.5–3.0]	2.75 [2.5–3.0]	0.257
Preoperative ejection fraction [%]	60.0 [53.8–72.3]	60.0 [45.0–70.0]	55.0 [48.0–65.0]	0.124
Chronic medication				
Beta-adrenergic blocking agent	18 (66.7%)	84 (73.0%)	49 (77.8%)	0.519
Angiotensin-converting enzyme inhibitor/angiotensin II antagonists	17 (63.0%)	81 (70.4%)	44 (69.8%)	0.734
Calcium channel blocker	8 (29.6%)	14 (12.2%)	9 (14.3%)	0.091
Digitalis	5 (18.5%)	13 (11.3%)	7 (11.1%)	0.540
Nitrates	12 (44.4%)	38 (33.0%)	17 (27.0%)	0.278
Diuretics	16 (59.3%)	62 (53.9%)	34 (54.0%)	0.903
Antiplatelet drugs	18 (66.7%)	75 (65.2%)	41 (65.1%)	0.999
Statins	14 (51.9%)	68 (59.1%)	39 (61.9%)	0.672
Type of operation [no. of patients]				0.424
Coronary artery bypass graft (CABG)	16	77	39	
Valve replacement/repair	10	22	13	
Coronary artery bypass graft (CABG) and valve replacement/repair	1	12	7	
Other operations	0	0	4	
On pump/off pump surgery [no. of patients]	26/1	102/13	56/7	0.579
Duration of surgery [min]	200.0 [172.0–234.0]	200.0 [166.0–240.0]	191.0 [160.0–227.0]	0.398
Bypass time [min]	107.5 [70.8–146.8]	99.5 [76.0–118.5]	90.0 [70.5–111.5]	0.105
Ischemia time [min]	62.5 [40.8–79.3]	50.5 [40.3–73.8]	53.0 [40.0–61.8]	0.282
Oxygen delivery during bypass [ml × min^{-1} × m^{-2}]	317.3 [292.9–351.6]	338.3 [302.2–364.3]	324.7 [290.6–359.6]	0.281
Lowest hematocrit during bypass [%]	24.1 [22.6–27.1]	25.3 [21.6–27.6]	23.0 [20.4–27.4]	0.171
EuroSCORE	5.0 [4.0–7.0]	5.0 [3.0–7.0]	5.0 [3.0–7.0]	0.931
APACHE II Score	16.0 [13.0–20.0]	16.0 [12.0–19.0]	17.0 [14.0–20.0]	0.132
SAPS II Score	31.0 [26.0–35.0]	28.0 [23.0–34.0]	28.0 [24.0–36.0]	0.365
SOFA Score	6.0 [4.0–7.0]	6.0 [5.0–8.0]	6.0 [5.0–8.0]	0.454
Hemoglobin level [mmol × l^{-1}]				
0 h after admission	5.8 [5.2–6.1]*	6.2 [5.6–6.6]	6.1 [5.5–6.7]	0.030
24 h after admission	6.1 [5.6–6.5]	6.2 [5.7–6.8]	6.1 [5.4–6.5]	0.403
Transfusion requirements [no. of units of packed red cells on ICU during first 24 h]	1 [0–2]*	0 [0–0]	0 [0–2]	<0.001
Central venous oxygen saturation [%]				
After induction of anesthesia	79.0 [71.0–82.0]	78.0 [72.8–82.0]	81.0 [75.5 -85.0]*	0.032
After heparin bolus	81.0 [75.0–85.0]	80.0 [74.0–84.0]	83.0 [75.8–87.0]	0.199
After protamin bolus	72.0 [60.0–81.0]	80.0 [74.0–86.0]	84.0 [76.0–88.0]†	<0.001
Lactate [mmol/l]				
After induction of anesthesia	0.8 [0.6–1.0]	0.7 [0.6–0.9]	0.7 [0.6–0.9]	0.392
After heparin bolus	0.7 [0.7–0.9]	0.8 [0.6–1.0]	0.8 [0.7–1.1]	0.251
After protamin bolus	1.9 [1.5–3.3]	1.6 [1.2–2.4]	2.4 [1.5–3.1]*	0.004

Data are medians and interquartile range and absolute values
* $p < 0.05$ compared to normal $ScvO_2$ group
† $p < 0.05$ compared to low $ScvO_2$ group

supranormal values with mortality, which was 14.8% for low, 7.9% for high and 0% for normal $ScvO_2$ ($p < 0.001$). Surrogates of morbidity, i.e., ventilation >24 h (low $ScvO_2$: 14.8%, normal $ScvO_2$: 6.1%, supranormal $ScvO_2$: 14.3%) and hemodialysis (low $ScvO_2$: 7.4%, normal $ScvO_2$: 3.5%, supranormal $ScvO_2$: 9.5%) displayed a similar trend not reaching significance. Assuming that both low and "supranormal" $ScvO_2$s are indicative of impaired tissue oxygenation, and consequently defining lower and upper boundaries of normal, resulted in a good

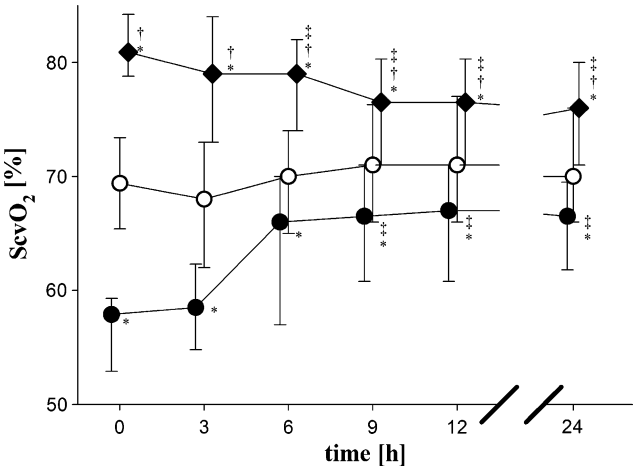

Fig. 1 Time course of $ScvO_2$ in patients classified as low (≤60.8%; *filled circle*), normal (60.9–77.3%; *open circle*) and supranormal (≥77.4%; *filled diamond*) regarding their central venous saturation. Data are medians and interquartile range. $^{*}p < 0.05$ compared to normal $ScvO_2$; $^{\dagger}p < 0.05$ compared to low $ScvO_2$; $^{\ddagger}p < 0.05$ compared to respective baseline

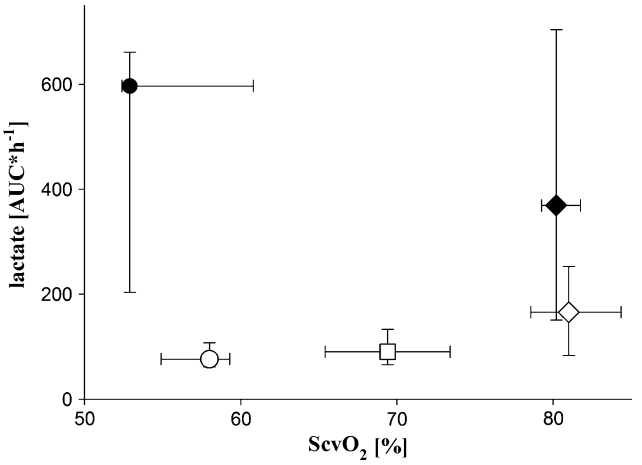

Fig. 3 Correlation of $ScvO_2$ and lactate production (as reflected in area under the curve of plasma lactate) and their association with mortality. *Circles* reflect patients with low $ScvO_2$, *squares* indicate normal $ScvO_2$ and *diamonds* high $ScvO_2$ upon admission. *Empty symbols* indicate surviving, *filled symbols* dying patients

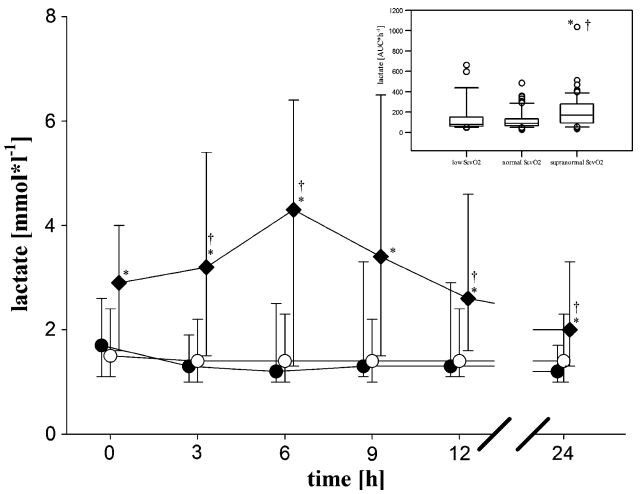

Fig. 2 Time course of lactate in patients classified as low (≤60.8%; *filled circle*), normal (60.9–77.3%; *open circle*) and supranormal (≥77.4%; *filled diamond*) regarding their central venous saturation. Data are medians and interquartile range. *Inset*: Area under curve as a measure of lactate production for each individual patient. *Box* and *whisker* plots indicate median, interquartile range, 5th and 95th percentile and outliers. $^{*}p < 0.05$ compared to normal $ScvO_2$; $^{\dagger}p < 0.05$ compared to low $ScvO_2$; $^{\ddagger}p < 0.05$ compared to respective baseline

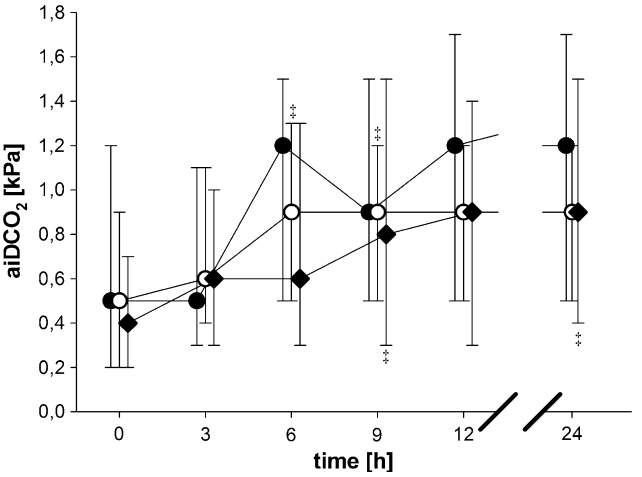

Fig. 4 Time course of arterio-intestinal pCO_2-gradient in patients classified as low (≤60.8%; *filled circle*), normal (60.9–77.3%; *open circle*) and supranormal (≥77.4%; *filled diamond*) regarding their central venous saturation. Data are medians and interquartile range. $^{*}p < 0.05$ compared to normal $ScvO_2$; $^{\dagger}p < 0.05$ compared to low $ScvO_2$; $^{\ddagger}p < 0.05$ compared to respective baseline

performance of $ScvO_2$ to predict unfavorable outcome as reflected in a sensitivity of 0.75 and a specificity of 0.69.

Possible factors for impaired oxygen extraction include use of catecholamines as well as initiation of systemic inflammatory response by the surgical insult. Both, use of β-mimetics (see ESM) and increased white blood count and procalcitonin levels as markers of systemic inflammation were associated with a supranormal $ScvO_2$ (Table 2). In addition, there was a trend towards higher blood glucose levels in the supranomal $ScvO_2$ group [blood glucose (AUC) (mmol/h): low 468.2 (406.8/543.3), normal 496.7 (418.7/565.9), supranormal 528.7

Table 2 Markers of systemic inflammation

	Low ScvO2 ($n = 27$)	Normal ScvO2 ($n = 115$)	Supranormal ScvO2 ($n = 63$)	p value
Procalcitonin [ng ml^{-1}]				
1st day postoperative	0.6 [0.5–2.9]	1.1 [0.5–3.6]	3.1 [0.9–10.3]*,†	0.002
C-reactive protein [mg l^{-1}]				
ICU admission	3.0 [3.0–5.9]	3.0 [3.0–5.9]	3.0 [3.0–8.9]	0.518
1st day postoperative	56.0 [43.8–108.3]	76.1 [55.8–93.4]	70.8 [51.7–92.9]	0.672
White blood cell count [10^3 mm^{-3}]				
ICU admission	10.0 [7.5–14.2]	11.5 [7.6–16.3]	14.0 [10.4–21.3]*,†	0.001
1st day postoperative	9.7 [7.5–10.7]	9.5 [7.5–12.1]	9.2 [7.8–12.9]	0.683

Data are medians and interquartile range

* $p < 0.05$ compared to normal ScvO2 group

† $p < 0.05$ compared to low ScvO2 group. Procalcitonin levels were measured only on day 1

(458.6/639.4), $p = 0.048$ (not significant after post-hoc adjustment for multiple testing)).

Discussion

In this study, we assessed the incidence of abnormal values for $ScvO_2$ and their relation to global as well as regional markers of impaired tissue oxygenation (i.e., serum lactate and gastric tonometry) in patients undergoing elective cardiac surgery. Our data confirm that a low $ScvO_2$ ($\leq$60.8%) occurred in approximately 13% of patients, but was associated with an unfavorable course only if paralleled by increased lactate production. However, a supranormal $ScvO_2$ ($\geq$77.4%) was observed even more frequently, i.e., in approximately one-third of patients, and appeared to be a hitherto under-recognized warning sign of impaired tissue oxygenation in the same patient population. $ScvO_2$, in particular the combined use of $ScvO_2$ and lactate levels together, was better than gastric tonometry to identify patients at risk.

Mixed and central venous O_2 saturations are influenced by arterial oxygen saturation (SaO_2) and by the balance between VO_2 and cardiac output and hemoglobin concentration. If, as is usually the case in the ICU setting, SaO_2 is normal, then $ScvO_2$ reflects the global oxygen supply-demand ratio of the tissues. Additional surrogates of impaired oxygen supply to peripheral tissues, such as serum lactate [13–15], or markers of regional perfusion, such as gastric tonometry, have been proposed as supplementary parameters to unravel persistent tissue hypoxia, though with mixed results [16–18].

The concept of consistent changes of the various surrogates for tissue hypoxia is not supported by the present data. In patients with low $ScvO_2$, lactate levels failed to provide additional information, as lactate only rose upon recovery of circulatory function in parallel with an increase in $ScvO_2$ and presumably cardiac index. On the other hand, many patients with initial low $ScvO_2$ had an uneventful course, which might reflect a compensated state of chronic congestive heart failure in the absence of other signs of tissue hypoxia. Moreover, gastric tonometry ($aiDCO_2$), unlike $ScvO_2$, failed to detect persistent tissue hypoxia. This suggests either impaired tissue oxygenation in regions other than the gut, or points to limitations of gut tonometry [17, 19, 20] and serum lactate [21]. Our results lend support to the recommendation that regional or micro-circulation assessment, e.g., with gastric tonometry, should not be used routinely [22].

A similar observation pointing towards a high sensitivity of $ScvO_2$ to identify patients at risk has been reported by Pearse et al. [23] recently for a mixed sample of patients undergoing major surgery, although the authors limited their definition of abnormal to <65% to detect cardiocirculatory compromise.

Thus, the new information that our data show is that the sensitivity of $ScvO_2$ to detect tissue hypoxia also held true for supranormal values. More to the point, lactate production was even higher in these patients. Mixed or central venous oxygen saturation has traditionally been regarded as an end point of low impact on clinical decision making in "hyperdynamic" shock where high venous saturation is common. Two mechanisms are likely responsible for the supranormal $ScvO_2$ in our population: (1) a systemic inflammatory response (SIRS) to cardiopulmonary bypass or off-pump surgery with concomitant mitochondrial dysfunction [24, 25] or (2) therapeutic measures to increase DO_2, most notably β-mimetics. SIRS as the underlying cause is supported by higher white cell counts and markers of inflammation, most notably procalcitonin on day 1, in the present subset of patients. However, higher white cell counts can also reflect β-stimulation [26]; consistent with this notion, a higher share of patients in the subgroup with supranormal $ScvO_2$ received β-mimetics. Another facet might be a higher

lactate production due to a metabolic adjustment in consequence of the use of β-mimetics [27]. This would be consistent with the tendency to higher blood glucose values in the supranormal $ScvO_2$ group. However, in pediatric cardiac surgery a raised lactate:pyruvate ratio was detected in 50% of patients with hyperlactatemia, but on the other hand the median lactate value in patients with a high lactate:pyruvate ratio was only 2.1 mmol/l (IQR 1.2/3.2), and only lactate, but not lactate:pyruvate ratio was associated with prolongation of ICU support [28]. High lactate values might also be due to cytokine mediation, correlating with pronounced SIRS, and other non-anaerobic mechanisms [21].

Any observational trial such as this study can provide only limited mechanistic information regarding therapeutic interventions. Why patients received β-mimetics in the present study remains speculative. Supranormal $ScvO_2$ would be consistent with the notion that epinephrine was started, e.g., to improve contractility rather than to normalize tissue perfusion, as use of transesophageal echocardiography is standard in our department and may lead in the light of $ScvO_2$ monitoring to an "overuse" of inotropic substances. "Adequacy" of cardiac function and output was thus achieved more or less irrespective of $ScvO_2$ as a surrogate for the DO_2/VO_2 relationship. However, this poses important concerns, since the use of epinephrine or dobutamine might worsen outcome if used liberally, i.e., to increase DO_2 above the actual need of peripheral tissues. This is consistent with data obtained in congestive (chronic) heart failure where—despite improved cardiac function—excess mortality accompanies the use of β-mimetics [11, 29, 30], and with a recent study in cardiac surgery patients, where use of dobutamine based solely on clinical judgment was associated with increased cardiac morbidity [31].

In conclusion, our data indicate that $ScvO_2$ monitoring, in particular if used along with lactate as a systemic marker of tissue hypoxia, is superior to gastric tonometry, a supposedly sensitive marker of regional flow, to detect both low output syndrome and hyperdynamic shock early in the postoperative cardiac surgery phase.

Supranormal values of $ScvO_2$, which are traditionally considered to be of limited clinical value, turned out to be under-recognized warning signs of impaired tissue oxygenation in cardiac surgery patients. Thus, our data lend support to the concept of a rather narrow corridor of safety for $ScvO_2$, e.g., as used here between 60 and 75%. The association of high $ScvO_2$ with both use of β-mimetics and unfavorable outcome raises the question as to whether the use of β-mimetics might have been too liberal in our cohourt of patients, e.g., triggered by echocardiographic estimates.

In any case, we propose that combined analysis of $ScvO_2$ and lactate levels may be used to identify patients at risk, and a high $ScvO_2$ might reflect an underrecognized warning sign in this context. Additional studies are warranted to test these results in an independent data set.

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