Correlation between central venous and mixed venous oxygen saturation in the elective abdominal aortic aneurysm surgery

Korelacija između saturacije kiseonikom centralne i mešane venske krvi u elektivnoj hirurgiji aneurizme abdominalne aorte

Ljiljana Šoškić*, Mladen Kočica*, Dragan Cvetković*, Biljana Miličić†,
Nebojša Ladjević‡, Ivan Palibrk§, Milica Karadžić*, Miloš Grujić*,
Milica Vještica-Mrdak‖, Arsen Ristić¶

Clinical Center of Serbia, Clinic for Cardiac Surgery, *Department of Anesthesia and
Intensive Care, Clinic for Urology, ‡Department of Anesthesia and Intensive Care,
Clinic for Abdominal Surgery, §Department of Anesthesia and Intensive Care, Clinic for
Vascular Surgery, ‖Department of Anesthesia and Intensive Care, ¶Clinic for
Cardiology, Belgrade, Serbia; University of Belgrade, Faculty of Dentistry, †Department
of Medical Statistics and Informatics, Belgrade, Serbia

Abstract

Background/Aim. The concept of utilizing central venous oxygen saturation ($ScvO_2$) to calculate cardiac index (CI) remains controversial and neither precise nor generally applicable conclusion has been reached yet. We evaluated the relationship between $ScvO_2$ and mixed venous oxygen saturation (SvO_2) in elective surgery of the abdominal aorta. The adequacy of their interchangeability was tested by comparing cardiac indices (CI) calculated by two methods in patients that underwent major vascular surgery. The aim of this study was to test the correlation between $ScvO_2$ and SvO_2 in different time frames, in patients undergoing elective abdominal aortic aneurysm (AAA) surgery as well as to determine if the use of $ScvO_2$ for calculating CI by the modified Fick equation, could be feasible and accurate surrogate for the values obtained by pulmonary artery catheter (PAC). **Methods.** This prospective observational study included 125 consecutive patients that underwent elective AAA surgery. The $ScvO_2$ and SvO_2 data, as well as CI values, were obtained and compared from samples taken in three different time frames: immediately after induction of general anesthesia (T_0), immediately after admission in the intensive care unit (ICU; T_1), and 8 h after admission in the ICU (T_2). The Fick equation, used for CI estimation from $ScvO_2$ (CI-F), for the purpose of this study, was simplified according to Walley. **Results.** There was good linear correlation between $ScvO_2$ and SvO_2 in all time frames and linear regression study revealed strongest coefficient of determination ($R^2 = 0.661$) in T_2 time-frame. There was no correlation between CI-F (i.e. CI calculated from $ScvO_2$ by modified Fick equation) and CI (measured by PAC from SvO_2) in any time-frame. **Conclusion.** The results of our study confirm that $ScvO_2$ is a reliable substitute for SvO_2 among patients undergoing elective surgery of the AAA. However, $ScvO_2$ cannot be used as a surrogate to true SvO_2 in the calculation of CI.

Key words:
aorta, abdominal; aortic aneurysm; monitoring, physiologic; oxygen; oximetry.

Apstrakt

Uvod/Cilj. Koncept korišćenja saturacije kiseonikom centralne venske krvi ($ScvO_2$), umesto saturacije mešane venske krvi (SvO_2), za izračunavanje srčanog indeksa (CI), ostaje kontroverzan s obzirom na to da još uvek nema pouzdanih podataka koji bi ukazivali da jedna saturacija može biti adekvatna zamena drugoj. Odnos između ova dva parametra testirali smo upoređivanjem vrednosti CI izračunatih na dva načina, kod elektivno operisanih bolesnika zbog aneurizme abdominalne aorte (AAA). Cilj rada bio je testiranje korela- cije između $ScvO_2$ i SvO_2 u različitim vremenima merenja kod bolesnika podvrgnutih elektivnim operacijama AAA, kao i utvrđivanje mogućnosti korišćenja $ScvO_2$ za izračuna- vanje CI, modifikovanom Fick-ovom jednačinom, kao ade- kvatne zamene vrednostima CI dobijenih merenjem putem plućnog arterijskog katetera (PAC). **Metode.** Prospektiv- nom opservacionom studijom bilo je obuhvaćeno 125 kon- sekutivnih bolesnika podvrgnutih elektivnim operacijama AAA. Podaci o $ScvO_2$ i SvO_2, kao i vrednosti CI dobijeni su uzimanjem uzoraka krvi i merenjem u tri različita vremena: posle uvoda u opštu anesteziju (T0), odmah posle prijema u

Correspondence to: Mladen Kočica, Clinical Center of Serbia, Clinic for Cardiac Surgery, Kosta Todorović St. 8, 11 000 Belgrade, Serbia. E-mail: kocica@sbb.rs

jedinicu intenzivnog lečenja (JIL) (T1), i osam sati posle dolaska u JIL (T2). Za izračunavanje CI upotrebljena je pojednostavljena Fick-ova jednačina po Walley-u, u kojoj smo koristili ScvO₂ (CI-F). **Rezultati**. Nađena je dobra linearna korelacija između vrednosti ScvO₂ i SvO₂ u svim vremenima merenja, a linearna regresiona studija pokazala je najjači koeficijent determinacije (R2 = 0.661) u T2 vremenskom okviru. Nije bilo korelacije između CI-F (CI izračunat iz ScvO2 modifikovanom Fick-ovom jednačinom) i CI (me-

ren PAC-om) u bilo kom vremenskom okviru. **Zaključak.** Rezultati studije potvrđuju da ScvO₂ može biti pouzdana zamena za SvO₂ kod bolesnika podvrgnutih elektivnim operacijama AAA. Međutim, ScvO₂ se ne može koristiti kao surogat za pravu SvO₂ u izračunavanju CI.

Ključne reči:
aorta, abdominalna; aorta, aneurizma; fiziološke funkcije, praćenje; kiseonik; oksimetrija.

Introduction

Measurement of mixed venous oxygen saturation (SvO₂) is useful indirect index of the entire body tissue oxygenation [1]. However, risk/benefit of the pulmonary artery catheter (PAC) placement remains controversial, and thus, its use has became somewhat unpopular [2, 3]. Routine use of the PAC in critically ill patients does not influence mortality and is associated with higher costs and complication rates [4, 5]. Insertion of a central venous catheter (CVC) in the superior vena cava (SVC), via the right internal jugular or subclavian vein, on the other side, remains standard of care in critically ill patients [6]. Monitoring of central venous oxygen saturation (ScvO₂) may be, therefore, the safer alternative to SvO₂.

Despite recent renewed interest in clinical applicability of serial ScvO₂ measurements, there are no published data in the available literature describing the pattern of ScvO₂ changes during major vascular surgery or possible relationships with outcome [7, 8].

The aim of this study was to test the correlation between ScvO₂ and SvO₂ in different time frames, in patients undergoing elective abdominal aortic aneurysm (AAA) surgery. Additionally, we wanted to determine if calculating cardiac index (CI) using ScvO₂, by the modified Fick equation, could be feasible and accurate surrogate for the values obtained by PAC.

Methods

This prospective observational study included 125 consecutive patients, scheduled for the elective AAA surgery, between July 2015 and April 2016, at the Clinic for Vascular and Endovascular Surgery, the Clinical Center of Serbia in Belgrade.

Patients with aortoiliac occlusive disease (Leriche's syndrome), cardiac or dialysis access shunt (fistula or graft) and emergent cases (ruptured AAA) were excluded from the study.

The study protocol was approved by the Ethics Committee of the Clinical Center of Serbia. Written informed consent was obtained from all patients before enrollment.

All operations were performed with combined (peridural and general endotracheal) anesthesia. Patients were premedicated with 5 mg im. midazolam (Dormicum®, Roche) 45 min prior to anesthesia. Peridural catheter (Perifix, B. Braun Melsungen AG) was inserted under local anesthesia at Th_{10}–L_1, or L_1–L_2, or L_2–L_3 levels, with a patient in left recumbent position. Induction proceeded with 0.2 mg/kg

midazolam and 0.6 mg/kg rocuronium bromide (Esmeron®, Merck Sharp & Dohme). Patients were connected to an anesthesia apparatus (Primus, Dräger) and anesthesia was maintained with gas mixture O_2/N_2O (FiO₂ = 0.5) and sevoflurane (Sevorane®, AbbVie) in concentration of 0.8–1.5 vol%, along with rocuronium bromide in a total dose of 100 mg. For analgesia, 6–8 mL of 0.5% levobupivacain was given every 1.5 h–2 h via the peridural catheter. Operations were completed without any use of iv. analgsics.

Median laparotomy and transperitoneal approach to the abdominal aorta (AA) and classical inguinal approach to the femoral arteries were utilized. Abdominal aortic cross clamping was done below or above the origin of renal arteries, and occasionally above the origin of *truncus coeliacus*. Reconstruction of AA included interposition of either tubular Ao graft interposition (GI) or "Y" Dacron graft (Ao-biilliac – Aii, Ao-bifemoral – AFF).

Postoperative analgesia was maintained with a bolus dose of 6–8 mL of 0.25%, levobupivacain, every 8 h, via the peridural catheter. Lungs were mechanically ventilated (Evita, Dräger).

Invasive monitoring included radial artery cannulation (Becton Dickinson off-on), for the measurement of systemic blood pressure and serial blood sampling for gas analyses (Radiometar ABL 90 flex).

Insertion of the CVC (Arrow) was performed via the right internal jugular or subclavian vein and position of its tip in SVC, for ScvO₂ measurements, subsequently verified by chest radiograph. In addition, PAC (Swan-Ganz catheter, Arrow, 7F) was also inserted for SvO₂, CO (cardiac output), and CI measurements. Thermodilution CO and CI were obtained in triplicate and averaged. Samples from CVC and PAC were taken simultaneously in following time-frames: immediately after induction of general anesthesia (T_0), immediately after admission in the ICU (T_1), and 8 h after admission in the ICU (T_2).

The Fick equation, used for CI estimation from ScvO₂ (CI-F), for the purpose of this study, was simplified according to Walley [10]

$$CI \approx 100/Hgb \times 1/(SaO_2 - SvO_2)$$

where: CI as previously explained (L/min/m²); Hgb = hemoglobin (g/L); SaO₂ = arterial oxygen saturation (%) and ScvO₂ (%).

Statistical analyses were performed using SPSS software v.23.0 (SPSS Inc., Chicago, IL, USA). Descriptive data for all groups and variables were expressed as mean ± stan-

dard deviation (SD) for continuous measures, or percent of a group for discrete measures.

A normal distribution was tested using the Koglomorov-Smirnov test. If the data were normally distributed, RM-ANOVA was used. Nonparametric data were analyzed using Fridman test. *Post hoc* analysis was performed using Bonferroni test (parametric data) and Wilcoxon test (non-parametric data).

Correlation of the CVC and PAC parameters was tested with Pearson's (parametric data) and Spearman's correlation coefficients (nonparametric data).

All reported *p* values were two-sided; differences were considered significant when *p* value was < 0.05.

Results

Preoperative and intraoperative patient characteristics are summarized in Table 1. It is noteworthy emphasizing that majority of patients were in the seventh decade of life, with significant male predominance. Almost 95% were hypertensive and more than a half had some form of coronary artery disease. Intraabdominal reconstruction (ie. GI and Aii) with infrarenal clamp was possible in more than 90% cases.

Values of observed parameters ($ScvO_2$, SvO_2, CI, CI–F), obtained in three different time frames, are summarized in Table 2. Significant changes were registered for all of them, but inter-group significance was present only for $ScvO_2$ and SvO_2.
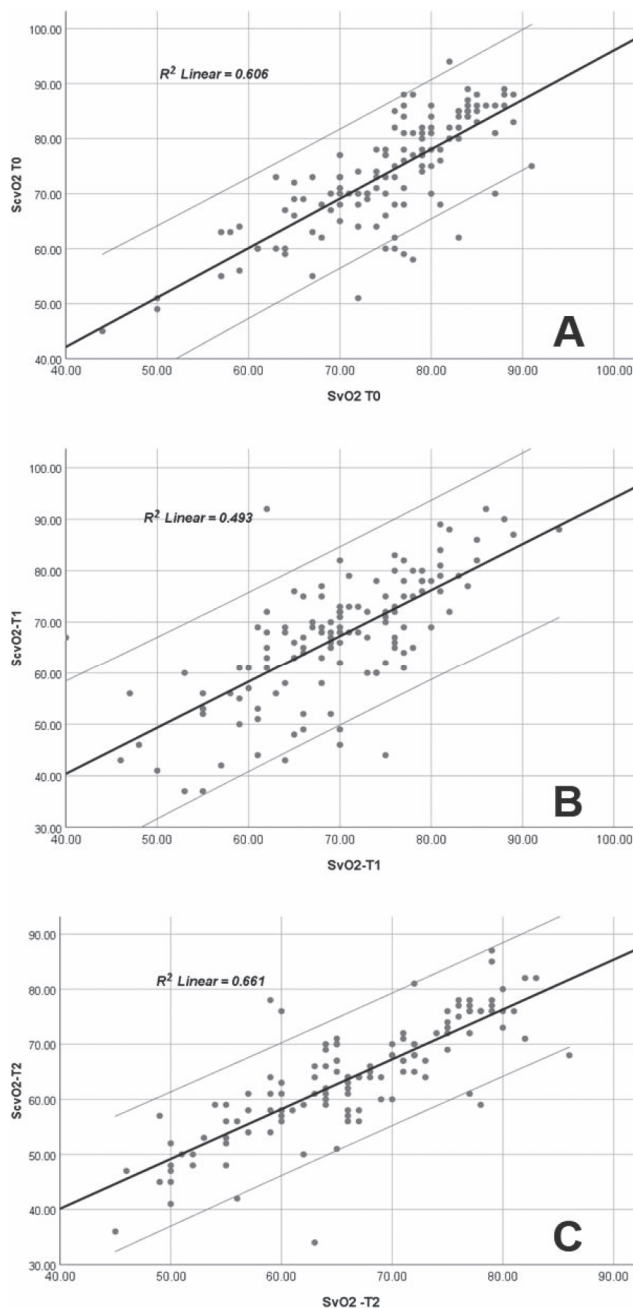

Fig. 1 – Correlation between central venous oxygen saturation ($ScvO_2$) and mixed venous oxygen saturation (SvO_2) in different time frames: A) immediately after induction of general anesthesia (T0); B) immediately after admission in the Intensive Care Unit (ICU); C) 8 h after admission in the ICU (T2).

Table 1

Demographic and clinical characteristic of patients (n = 125)

Characteristics	Values
Gender, n (%)	
male	108 (86.4)
female	17 (13.6)
Age (years), mean ± SD (Med; min-max)	66.39 ± 6.49 (66.0; 49–86)
BMI (kg/m^2),(mean ± SD (Med; min-max)	26.36 ± 3.85 (26.10; 14.70–36.50)
BSA (m^2), mean ± SD (Med; min-max)	2.00 ± 0.21 (2.03; 1.28–2.51)
Comorbidities, n (%)	
hypertension	118 (94.4)
DM	16 (12.8)
COPD	29 (23.2)
carotid surgery	14 (11.4)
CVI	17 (13.6)
CRF	14 (11.2)
CABG	11 (8.8)
valvular surgery	2 (1.6)
AP	46 (36.8)
PCI	14 (11.3)
Ao reconstruction, n (%)	
Ao-II	51 (40.8)
Ao-FF	10 (8.0)
Ao GI	64 (51.2)
Infrarenal cross clamp, n (%)	114 (91.2)
Proximal clamp time (min), mean ± SD (Med; min-max)	21.94 ± 8.09 (21.0; 9–53)
Total clamp time (min), mean ± SD (Med; min-max)	49.73 ± 20.21 (45.0; 17–118)

BMI – body mass index; BSA – body surface area; DM – diabetes mellitus; COPD – chronic obstructive pulmonary disease; CVI – cerebro-vascular insult; CRF – chronic renal failure; CABG – coronary artery bypass grafting; AP – angina pectoris; PCI – percutaneous coronary intervention; Ao-II – aortobiiliac bypass; Ao-FF – aortobifemoral bypass; Ao-GI – abdominal aortic graft interposition; Med – median.

Table 2

Analysis of selected parameters measured by central venous catheter (CVC) and pulmonary artery cateter (PAC) in different time frames

Parameters	Values	p-value [a,b]	Intergroup comparison[c,d]
ScvO$_2$ (%), mean ± SD (Med; min-max)	73.79 ± 10.12 (74.5; 45–94)	[a]0.000*	[c.1]0.000*
T0	66.82 ± 12.24 (68; 37–92)		[c.2]0.000*
– T2	63.94 ± 10.35 (64; 34–87)		[c.3]0.044*
SvO$_2$ (%), mean ± SD (Med; min-max)		[a]0.000*	
T0	75.31 ± 8.76 (77; 44–91)		[c.1]0.000*
T1	69.52 ± 9.59 (70;40–94)		[c.2]0.000*
T2	66.33 ± 9.30 (66; 45–86)		[c.3]0.000*
CI, mean ± SD (Med; min-max)		[b]0.000*	
T0	3.31 ±1.09 (3.01; 1.50–7.0)		[d.1]0.097
T1	3.34 ± 0.97 (3.20; 1.70–6.8)		[d.2]0.001*
T2	3.62 ± 0.79 (3.60; 1.30–5.90)		[d.3]0.000*
CI-F, mean ± SD (Med; min-max)		[b]0.024*	
T0	3.03 ± 1.05 (2.81; 1.27–5.93)		[d.1]0.118
T1	2.83 ± 1.02 (2.62; 1.21–6.12)		[d.2]0.001*
T2	2.64 ± 0.88 (2.49; 1.3–5.45)		[d.3]0.041*

ScvO$_2$ – central venous oxygen saturation; SvO$_2$ – mixed venous oxygen saturation; CI – cardiac index; CI-F – ScvO$_2$ for calculating CI, by modified Fick equation; T0 – immediately after induction of general anesthesia; T1 – immediately after admission in the Intensive Care Unit (ICU); T2 – 8 h after admission in the ICU; Med – median.
*statistical significance; [a]RM ANOVA; [b]Fridman-s test; [c]Bonferroni test; [d]Wilcoxon-s test ([1]p = To and T1 comparison; [2]p = To and T2 comparison; [3]p = T1 and T2 comparison).

Correlation between $ScvO_2$ and SvO_2 in different time frames is shown in Table 3. Since we established statistically significant correlation between observed parameters, a linear regression study was performed (Figure 1) and the strongest coefficient of determination ($R^2 = 0.661$) was found in T2 time-frame (Table 3, Figure 1C). These results confirmed that $ScvO_2$ could be reliable surrogate for SvO_2, particularly 8 h after admission in the ICU.

Table 3

Correlation of central venous catheter (CVC) and pulmonary artery catheter (PAC) parameters: $ScvO_2$ and SvO_2

Time-frame	Linear correlation	R^2	*p*-values
T1	0.779	0.606	0.000*
T2	0.702	0.493	0.000*
T3	0.814	0.661	0.000*

$ScvO_2$ – central venous oxygen saturation; SvO_2 – mixed venous oxygen saturation; T0 – immediately after induction of general anesthesia; T1 – immediately after admission in the Intensive Care Unit (ICU); T2 – 8 h after admission in the ICU.
*statistically significant.

Unlike expected, there was no correlation between CI-F (i.e. CI calculated from $ScvO_2$ by the modified Fick equation) and CI (measured by PAC from SvO_2) in any time-frame (Table 4).

Table 4

Correlation of central venous catheter (CVC) and pulmonary artery catheter (PAC) parameters: CI and CI-F

Time-frame	Spearman's correlation coefficient (ρ)	*p*-values
T0	0.085	0.346
T1	0.148	0.100
T2	0.069	0.444

CI – cardiac index; CI-F – CI, calculated by modified Fick equation.

Discussion

Interchangeability of $ScvO_2$ and SvO_2 values has been a matter of debate, primarily because of different sampling points and venous blood pools they represent (ie. entire body for SvO_2 and upper part of the body for $ScvO_2$)[9].

Complex relationship of these two parameters is different in healthy and diseased persons. Thus, $ScvO_2$ is slightly lower than SvO_2 in healthy individuals (76% vs. 78%, respectively), but in persons with cardiovascular instability, this relationship changes[10].

The most valuable information is trend of either $ScvO_2$ or SvO_2 changes upon applied treatment. Renewed interest in $ScvO_2$ monitoring came from the fact that lots of complications related to PAC insertion have been documented in the literature[11]. Intravascular pressure could not provide an adequate insight in the intravascular volume, which is, in turn, the only cardiac preload equivalent[12]. Sandham et al.[2] found no correlation between PAC guided therapy and outcome in non-cardiac surgical patients.

Scheinman et al.[11] compared $ScvO_2$ and SvO_2 levels in different hemodynamic states. They found no significant difference in stabile patients and patients with heart failure (54.7% vs. 56.9%, $p > 0.1$; and 61.8% vs. 58.2%, $p > 0.1$, respectively). In patients with circulatory shock, this difference was significant (58.0% vs. 47.5%, $p < 0.001$), due to poor left ventricular function and renal impairment[12, 13].

The degree of correlation between $ScvO_2$ and SvO_2 was tested by numerous studies, regardless of patient's hemodynamic status. By doing so, it was unable to find the reasons for poor correlation observed.

This main shortcoming comes from the fact that CO distribution changes in critically ill patients, thus affecting $ScvO_2$ and SvO_2 relationships[14–17]. Unlike previous, studies performed under experimentally controlled conditions found good correlation between $ScvO_2$ and SvO_2, regardless of their absolute values[18, 19]. Also, some studies emphasized the importance of similarity of trends between two parameters, while others deny the reliability of $ScvO_2$[20–22].

If we keep on mind that $ScvO_2$ depends on: hemoglobin levels, SaO_2, CO, oxygen consumption (VO_2), body temperature, analgesic level and metabolic state, keeping all, except selected one constant, than $ScvO_2$ value reflects the changes of the remaining. The relationship between $ScvO_2$ and SvO_2 is not simple. In healthy persons, absolute values of these parameters are similar, which is not necessarily true in critically ill patients. Absolute values of $ScvO_2$ may be pathological even when it is high or low[23].

Attempts to calculate CI from $ScvO_2$ is not a new concept[24]. In experimental studies, with dogs in different cardio-respiratory conditions, Reinhart et al.[20] found a good correlation (r = 0.97) between CI calculated using two different methods. Goldman et al.[24] 1968, performed similar study in human subjects. Since then, a lot of studies on human subjects in different medical conditions were designed to correlate $ScvO_2$ and SvO_2[25, 26].

During hypovolemic circulatory disturbances, CI and $ScvO_2$ showed better correlation with the extent of blood loss, than central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), arterial pressure and heart rate. Interestingly, in spite of different absolute values, the trends of $ScvO_2$ and SvO_2 changes paralleled observed hemodynamic changes. Orthostatic hypotension is commonly used, as a model of the cardiovascular disturbances associated with hypovolemia in humans[25, 27]. Median $ScvO_2$ fell from 75% to 60%, paralleling CO decrease from 4.3 to 2.7 L/min, at the onset of presyncope symptoms. However, unlike in experiments, in series of major trauma victims, there was no strong correlation of $ScvO_2$ and SvO_2 with the extent of blood loss[27, 28].

In septic patients, different trials could not find firm correlation between absolute values of $ScvO_2$ and SvO_2[29, 30], probably due to modified blood flow distribution and oxygen extraction (O_2 ER) by brain and splanchnic tissues[30, 31]. In spite of this, variations in these two parameters usually occured in a parallel manner[29, 32].

Maybe the most extensively studied were the patterns of SvO_2 and $ScvO_2$ changes in cardiac failure and myocardial infarction. Goldman et al. [24] correlated derangements of $ScvO_2$ with severity of myocardial dysfunction and subsequent response to treatment, finding that levels below 45% usually indicate the onset of cardiogenic shock. While decrease of $ScvO_2$ levels depicts the severity of disease [11], trends are associated with CO and response to treatment [33–35].

There are few papers describing SvO_2 monitoring during the aortic surgery [36, 37]. Application and removal of aortic and femoral clamps produces complex SvO_2 changes. Clamp removal and lower body reperfusion produce significant SvO_2 decrease, not necessarily reflecting a need to change cardiovascular management. However, there are very few or no data, regarding $ScvO_2$ monitoring during the abdominal aortic surgery.

Kopterides et al. [37] investigated the significance of CVC tip position. When positioned 15 cm away from the inlet of the right atrium, $ScvO_2$ overestimated SvO_2 by 8%. However, when the tip of the CVC was advanced deeper in the right atrium, $ScvO_2$ becomes an excellent surrogate, overestimating SvO_2 by only 1%.

Our study enrolled patients without pulmonary artery and superior vena cava (SVC) catheterization under fluoroscopic guidance. So, both measurements, neither $ScvO_2$ nor SvO_2, were obtained under direct visualization of the catheter tips. Our subsequent analyses of the central line tip positions, in the ICU, showed that most of them were located in SVC or proximal right atrium (RA) or SVC-RA junction. This implies that blood samples were actually obtained from different places. We used the X-ray confirmation of the CVC tip position in the ICU, to exclude the patients in whom CVC was accidentally placed in the innominate vein. Thus, we intended to test the correlation between $ScvO_2$ and SvO_2 within more limited variations of $ScvO_2$ values. It should be emphasized that it was our intention to adapt on "real-life" situation, without changing established perioperative protocols for the purposes of this study. On the other hand, PAC parameters (SvO_2 and thermodilution CI) were obtained in triplicate and then averaged. Although our results confirmed statistically significant linear correlation between $ScvO_2$ and SvO_2, almost paradoxically, the same was not true with CI-F

and CI. The most logical explanation is that, in fact, we used "different mathematics". Walley's simplification of the Fick formula, using $ScvO_2$ values to calculate CI-F, could not meet correlation criteria with thermodilution CI values obtained by PAC, using SvO_2. The ability of $ScvO_2$ measurement to estimate SvO_2 is useful but still imperfect, depending on CVC catheter placement, patient anatomy and physiologic state. Importantly, $ScvO_2$ is an increasingly less reliable substitute for SvO_2 as the cardiac performance is worsened. This should always be kept in mind when interpreting $ScvO_2$ measurements. When true SvO_2 is essential, PAC placement remains the gold standard, since it provides more data than just a calculation of CI and many patients may still benefit from it. In that sense, significant linear correlation between $ScvO_2$ and SvO_2 in our study could be seen as a result of standardized and reliable team work, resulting in absence of significant perioperative hemodynamic disturbances and mayor blood loss, allowing early detubation (within two hours postoperatively) and stabile spontaneous breathing in all patients.

Limitations of the study

This study has some limitations which have to be pointed out.

Accuracy of $ScvO_2$ measurement depends on CVC catheter placement, patient anatomy and physiologic state. Positioning of PAC and measurements was not always done by the same physician.

Conclusion

The results of our study confirm that $ScvO_2$ is a reliable substitute for SvO_2 among patients undergoing elective surgery of the abdominal aorta. It seems, when applied appropriately, that measurements of either $ScvO_2$ or SvO_2 may provide a valuable guide to circulatory management in the early postoperative period. However, this is not always true. In our study $ScvO_2$ cannot be used as a surrogate to true SvO_2 in the calculation of CI. Further studies are needed to confirm our findings. In practice, $ScvO_2$ seems especially useful in combination with vital signs and other relevant parameters.

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