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Central venous-to-arterial carbon dioxide difference: an additional target for goal-directed therapy in septic shock?

Received: 26 October 2007
Accepted: 6 June 2008

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Electronic supplementary material The online version of this article (doi:10.1007/s00134-008-1199-0) contains supplementary material, which is available to authorized users.

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Abstract Objective: To test the hypothesis that, in resuscitated septic shock patients, central venous-to-arterial carbon dioxide difference [P(cv-a)CO₂] may serve as a global index of tissue perfusion when the central venous oxygen saturation (ScvO₂) goal value has already been reached. **Design:** Prospective observational study. **Setting:** A 22-bed intensive care unit (ICU). **Patients:** After early resuscitation in the emergency unit, 50 consecutive septic shock patients with ScvO₂ > 70% were included immediately after their admission into the ICU (T0). Patients were separated in Low P(cv-a)CO₂ group (Low gap; n = 26) and High P(cv-a)CO₂ group (High gap; n = 24) according to a threshold of 6 mmHg at T0. **Measurements:** Measurements were performed every 6 h over 12 h (T0, T6, T12). **Results:** At T0, there was a significant difference between Low gap patients and High gap patients for cardiac index (CI) (4.3 ± 1.6 vs.

2.7 ± 0.8 l/min/m², P < 0.0001) but not for ScvO₂ values (78 ± 5 vs. 75 ± 5%, P = 0.07). From T0 to T12, the clearance of lactate was significantly larger for the Low gap group than for the High gap group (P < 0.05) as well as the decrease of SOFA score at T24 (P < 0.01). At T0, T6 and T12, CI and P(cv-a)CO₂ values were inversely correlated (P < 0.0001). **Conclusion:** In ICU-resuscitated patients, targeting only ScvO₂ may not be sufficient to guide therapy. When the 70% ScvO₂ goal-value is reached, the presence of a P(cv-a)CO₂ larger than 6 mmHg might be a useful tool to identify patients who still remain inadequately resuscitated.

Keywords Venous CO₂ · ScvO₂ · Lactate · Septic shock · Goal-directed therapy · Cardiac index

Introduction

The early haemodynamic management of septic shock patients has recently been codified [1]. Rivers et al. show that an early optimisation (within the very first 6 h of treatment) targeting central venous oxygen saturation (ScvO₂) and general haemodynamic parameters improved outcome in septic shock [2]. At the onset of septic shock,

ScvO₂ appears to be a strong indicator of the balance between O₂ demand and supply. In ICU-resuscitated patients however, ScvO₂ or mixed venous oxygen saturation (SvO₂) [3, 4], is often larger than 70% in spite of evidence of abnormal tissue oxygenation. This oxygen extraction defects might be related to severe microcirculatory disorders [5] and/or mitochondrial damage and/or impairment of cellular respiration [6] resulting in most of

the cases in elevated ScvO₂ or SvO₂ values [7, 8]. After early resuscitation, ScvO₂ may therefore not be sufficient to guide titration of fluid loading and vasopressor therapy.

Several studies have already shown that venous-to-arterial carbon dioxide difference, calculated with mixed venous blood sample [P(v-a)CO₂], and cardiac index (CI) are inversely correlated in case of non-septic [9–11] and septic circulatory failure [12–14]. Vallet et al. [15] emphasized on the importance of blood flow in the increased venous-to-arterial carbon dioxide tension difference in a canine model of isolated limb. Nevriere et al. [16] confirmed that increased P(v-a)CO₂ was mainly related to the decrease in cardiac output as P(v-a)CO₂ was increased in ischemic hypoxia but not in hypoxic hypoxia for the same degree of O₂ supply-dependency. In a recent review Lamia et al. [17] stated that P(v-a)CO₂ could be considered as a marker of adequacy of venous blood flow to remove the total CO₂ produced by the peripheral tissues. Interestingly, Cushieri et al. [18] found an inverse correlation between central venous-to-arterial carbon dioxide tension difference P(cv-a)CO₂ and CI values suggesting that a simple central venous blood sample instead of a pulmonary arterial blood sample was to be considered for this purpose.

The major aim of this study was therefore to test in ICU-resuscitated septic patients the hypothesis recently published by Vallet et al. [19] that the P(cv-a)CO₂ value could be used as a reflection of inappropriate tissue perfusion when a ScvO₂ larger than 70% has already been reached. A second aim was to confirm whether P(cv-a)CO₂ was inversely correlated to CI.

Materials and methods

Setting and eligibility

The study was a prospective observational case series of adult patients. The study was conducted in a 22-bed ICU of a University Hospital. All new admitted patients in this ICU, coming from the emergency unit, with the following criteria were screened for the study: (1) septic shock defined by the criteria of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference [1]; (2) patients intubated and mechanically ventilated; (3) hyperlactatemia > 2 mmol/l; (4) ScvO₂ > 70%; (5) age > 18 years and absence of pregnancy.

Patient management in emergency and intensive care units

From diagnosis in the emergency unit to the first 24 h hospitalisation in the ICU, study patients were resuscitated to reach the following goals as recommended by the

international guidelines for septic shock [1]: (1) mean arterial pressure (MAP) ≥ 65 mmHg and diastolic arterial pressure (DAP) ≥ 40 mmHg; (2) ScvO₂ ≥ 70%; (3) urine output ≥ 0.5 ml/kg/h; (4) normalisation of serum lactate.

Our standard septic shock resuscitation treatment was administrated in sequence until the following goals were reached:

1. Diagnosis of septic shock with lactate measurement followed by 30–40 ml/kg crystalloid fluid loading over 1 h (500 ml/10 min).
2. Norepinephrine titrated to obtain a MAP ≥ 65 mmHg and a DAP ≥ 40 mmHg.
3. ScvO₂ measurement: fluid loading of 500 ml crystalloid and/or colloid every 10 min until ScvO₂ reached a value ≥ 70%.
4. Blood transfusion if ScvO₂ remained < 70% and Ht < 30%.
5. Dobutamine at a dose of 5mcg/kg/min if Ht > 30% and ScvO₂ < 70%.
6. After 6 h when lactate level remained higher than 2 mmol/l: cardiac output was measured by a Pulse Indexed Continuous Cardiac Output (PiCCo) monitor (Pulsion, Medical Systems AG, Munich, Germany) in order to optimise oxygen delivery (DO₂) and reach an ScvO₂ ≥ 70%: successive colloid “fluid challenge” of 500 ml over 15 min until CI variation during the challenge became less than 15%, transfusion if Ht < 30% and ScvO₂ < 70%, dobutamine if ScvO₂ remained lower than 70%.
7. If ScvO₂ remained lower than 70% after this DO₂ optimisation, attempts to lower oxygen consumption were instituted (fever control and/or mechanical ventilation after tracheal intubation and/or increase in sedation and/or pain medication).

Others procedures within the first 24 h

1. After bacterial samples, eradication of any septic focus with early large probabilistic antibiotics and surgery when needed.
2. Prescription of low dose hydrocortisone if patients were treated by norepinephrine for more than 6 h as recommended [20].
3. Prescription of drotrecogin alpha activated (Xigris®) as recommended [21].

Study protocol

The protocol was approved by the ethics committee of our institution for human subjects. Consent was waived as no therapeutic intervention was required and all

measurements were routinely required in septic shock patients. The time of inclusion (T0) and study enrolment was considered as the time at which the PiCCo monitoring was started after ICU admission. The transit time in the emergency room between diagnosis of septic shock and enrolment in ICU was registered.

MAP, HR, CI, SaO₂, ScvO₂, O₂ extraction ratio ($ERO_2 = (SaO_2 - ScvO_2)/SaO_2$), P(cv-a)CO₂ and serum lactate were measured at 0, 6 and 12 h after inclusion (T0, T6, T12).

After inclusion, patients with persistent hyperlactatemia, despite early haemodynamic optimisation and sedation with intubation and mechanical ventilation, were separated into two groups according to the initial (T0) value of P(cv-a)CO₂. Patients with a P(cv-a)CO₂ < 6 mmHg were considered as belonging to the Low gap group; those with a P(cv-a)CO₂ ≥ 6 mmHg were considered as belonging to the High gap group. The cut off value of 6 mmHg was chosen according to previous studies [13, 22]. There was no therapeutic recommendation guided by the P(cv-a)CO₂ value. Treatment was strictly targeted to lower the high lactate while keeping the ScvO₂ ≥ 70%.

Patients of both groups were compared for age, diagnosis, SAPS 2, APACHE 2, SOFA score, biomarkers, treatment received at time of inclusion (T0), SOFA score at T24 and mortality at day 28. Patients of the Low gap group and the High gap group were compared for all haemodynamic parameters, biomarkers and lactate concentration at each time: T0, T6 and T12. At each different time, correlations between CI and P(cv-a)CO₂, lactate concentration and P(cv-a)CO₂, and CI and ScvO₂ were evaluated.

Haemodynamic and metabolic measurements

MAP and SaO₂ were continuously measured using an arterial catheter and pulse oximetry. Lactate blood concentration was determined after arterial sampling. Central venous oxygen saturation was obtained from a sample taken from the central venous line in the superior vena cava (position verified by X-ray, the tip of catheter being superimposed on the 4th right intercostal space, just above the azygos cross). Cardiac index (l/min/m²) was obtained with the PiCCo monitor by averaging of three transpulmonary thermodilution measurements made with cold saline solution (15 ml). P(cv-a)CO₂ was calculated as the difference between PcvCO₂ and PaCO₂ respectively obtained from central venous blood and arterial blood samples.

Statistical analysis

For comparison between Low gap group and High gap group we used 2-way ANOVA for time-course of MAP,

ScvO₂, P(cv-a)CO₂, CI, lactate over T0, T6 and T12, and for SOFA score between T0 and T24. If there was a significant interaction between groups and time Student's *T*-tests were performed. Data were expressed as mean ± standard deviation (SD). A *P*-value ≤ 0.05 was considered statistically significant. Correlations between CI, P(cv-a)CO₂, ScvO₂ and lactate concentration were assessed using the Spearman test. Statistical analysis was performed by the Statview 5.0 software.

Results

Patients (Table 1)

From April 2006 to May 2007, 56 new septic shock patients who were admitted in the ICU and who had been previously resuscitated in the emergency unit were considered eligible. At the time of ICU admission, all patients had a blood lactate level above 2 mmol/l and thus required cardiac output monitoring (cf [Methods](#)). Six patients (11%) were excluded because their ScvO₂ at T0 was lower than 70% (64 ± 5%). At T0, all these six patients had a P(cv-a) CO₂ larger than 6 mmHg (11.0 ± 5.7 mmHg) and a CI of 2.6 ± 1.0 l/min/m². Three of them survived.

A total of 50 patients were therefore finally included in this descriptive study. The mean time between septic shock diagnosis in the emergency unit and enrolment in the study was 8.0 ± 4.5 h. At T0, 26 patients had a P(cv-a) CO₂ less than 6 mmHg (Low gap group), and 24 had a P(cv-a) CO₂ larger than 6 mmHg (High gap group). There was no significant difference between the two groups for age, gender, APACHE II, SAPS II, SOFA score, time between diagnosis and enrolment and treatment received at T0 (Table 1). Eighty-eight percent of the patients (44/50) received norepinephrine and 18% (9/50) dobutamine with no difference between groups regarding the number of patients treated and the mean infusion rate.

From T0 to T24, the decrease in SOFA score was significantly larger for Low gap patients than for High gap patients: -8% [- 30, +20] versus +10.3% [- 20, +50]; *P* = 0.005. At T24, the Low gap patients had a significantly lower SOFA score than the High gap patients: 11.8 ± 3.7 versus 14.6 ± 3.4; *P* < 0.01 (Fig. 1). Mortality rate at D28 for all patients was 44% (22/50): 34% (9/26) for Low gap group and 54% (13/24) for High gap group; *P* = 0.16.

Initial data (Table 1)

At T0, Low gap group patients had a significantly lower P(cv-a)CO₂ than patients of the High gap group: 3.2 ± 1.3 versus 8.9 ± 2.6 mmHg, *P* < 0.0001.

Table 1 Characteristics of patients at T0

	All patients (n = 50)	Low gap group (n = 26)	High gap group (n = 24)	P value
Age (years)	54 ± 17	51 ± 13	55 ± 20	0.53
Gender: male (%)	30 (60)	16 (62)	14 (58)	0.45
Weight (kg)	73 ± 18	74 ± 21	71 ± 16	0.65
Time between diagnosis and enrolment (h)	8 ± 4.5	8.3 ± 4.5	7.6 ± 4.6	0.62
APACHE II	22 ± 9	22 ± 7	23 ± 13	0.68
SOFA	13 ± 4	13 ± 4	13 ± 5	0.95
SAPS II	61 ± 16	62 ± 17	61 ± 14	0.87
Temperature (°C)	37.5 ± 0.8	37.3 ± 0.7	37.7 ± 0.7	0.69
Diagnosis n (%)				
Pneumonia	14 (28)	9 (34)	5 (21)	0.28
Peritonitis	16 (32)	8 (31)	8 (33)	0.85
Urosepsis	4 (8)	1 (4)	3 (13)	0.26
Others	16 (32)	8 (31)	8 (33)	0.85
Culture positive n (%)	29 (58)	15 (58)	14 (58)	0.96
Antibiotics given in T0 n (%)	50 (100)	26 (100)	24 (100)	1
Antibiotics adequate n (%)	46 (92)	24 (92)	22 (92)	0.93
Catecholamine n (mcg/kg/min)				
Norepinephrine n (mcg/kg/min)	44 (0.4 ± 0.8)	23 (0.4 ± 0.7)	21 (0.5 ± 0.8)	0.52
Dobutamine n (mcg/kg/min)	9 (6.9 ± 3.1)	5 (7.2 ± 2.8)	4 (6.3 ± 3.7)	0.61
Other therapy n (%)				
Activated protein C	8 (16)	4 (15)	4 (17)	0.9
Hydrocortisone substitution	26 (52)	14 (54)	12 (50)	0.78
CVVHDF	8 (16)	5 (19)	3 (12)	0.51
Haemodynamic parameters				
MAP (mmHg)	69 ± 12	70 ± 14	68 ± 10	0.5
Cardiac index (l/min/m ²)	3.5 ± 1.5	4.3 ± 1.6	2.7 ± 0.6	<0.0001
Heart rate (beats/min)	101 ± 24	100 ± 19	103 ± 22	0.35
Biologic parameters				
Lactate (mmol/l)	6.5 ± 4	5.6 ± 3.6	7.5 ± 3.7	0.07
ScvO ₂ (%)	77 ± 5	78 ± 5	75 ± 5	0.07
ERO ₂ (%)	19 ± 8	17 ± 9	21 ± 6	0.05
P(cv-a) CO ₂ (mmHg)	5.9 ± 3.5	3.2 ± 1.3	8.9 ± 2.6	<0.0001
Hb (g/dl)	10.5 ± 2	10.6 ± 2	10.7 ± 1.8	0.84
SaO ₂ (%)	96 ± 5	95 ± 7	96 ± 3	0.43
PaO ₂ /FiO ₂ (mmHg)	186 ± 62	174 ± 58	202 ± 60	0.12
PaCO ₂ (mmHg)	36 ± 7	38 ± 9	36 ± 6	0.37
Arterial (pH)	7.29 ± 0.09	7.29 ± 0.07	7.28 ± 0.1	0.41

Emergency transit time time between diagnosis of septic shock in emergency unit and ICU admission; *APACHE* Acute Physiology and Chronic Health Evaluation; *SOFA* Sepsis-related Organ Failure Assessment; *IGS* Index Gravity Score; *CVVHDF* Continuous Veno Venous Hemo Dia Filtration; *MAP* mean arterial pressure; *ScvO₂* central venous oxygen saturation; *ERO₂* Oxygen extraction ratio ((SaO₂ - ScvO₂)/SaO₂); *P(cv-a)CO₂* central venous-arterial carbon dioxide difference; *Hb* haemoglobin value; *SaO₂* arterial oxygen saturation
Mean values ± SD

There was no significant difference between Low gap group and High gap group for all other initial parameters except for CI (4.3 ± 1.6 vs. 2.7 ± 0.8 l/min/m², *P* < 0.0001) and ERO₂ (17 ± 9 vs. 21 ± 6%, *P* = 0.05) (Table 1; Fig. 1).

Evolution between T0 and T12

At each stage of the protocol, all patients had a ScvO₂ larger than 70% with no statistical difference between groups (Fig. 1).

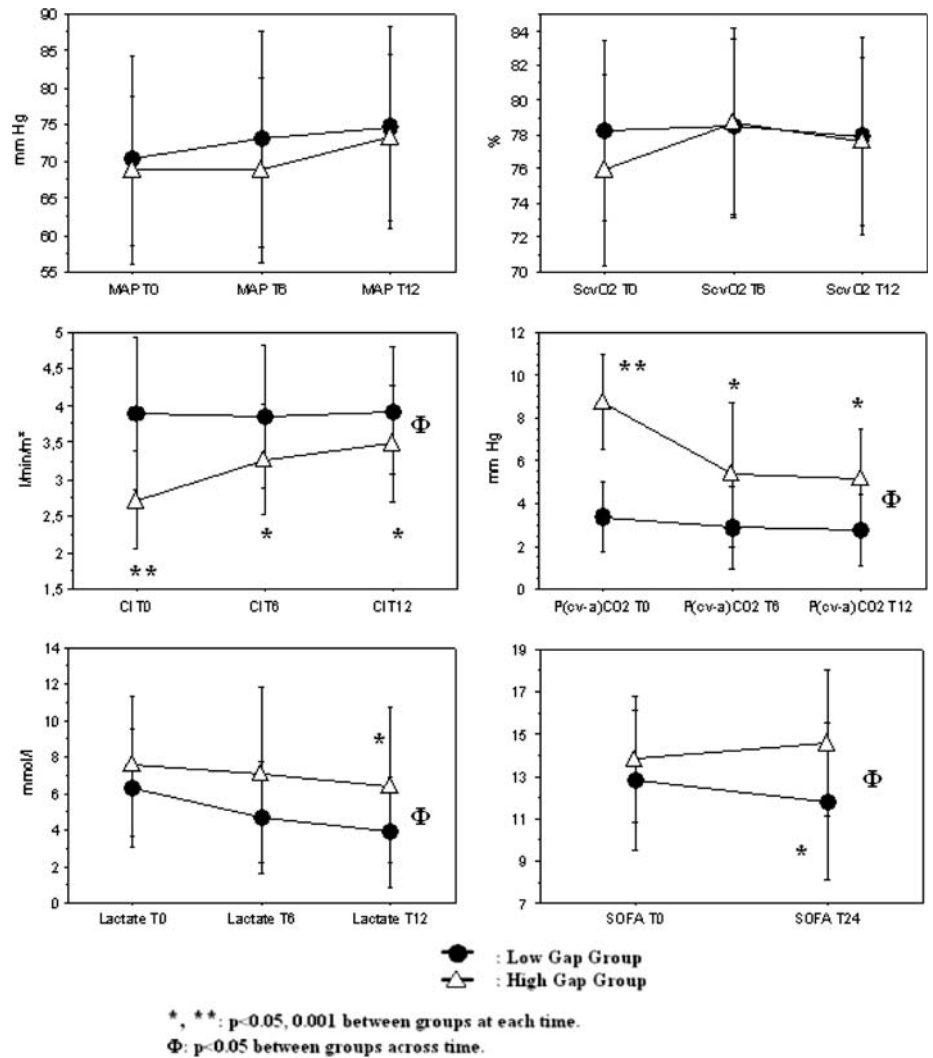
During the first 12 h after admission in the ICU, all study patients received a mean of 1.1 ± 0.9 l of colloid

fluid loading and 1.2 ± 0.7 red blood cell unit with no significant difference between the two groups. At T12, there was no significant difference regarding norepinephrine infusion rate: (0.6 ± 0.4 and 0.5 ± 0.7 mcg/kg/min for Low gap and High gap patients, respectively) nor in the number of patients receiving dobutamine.

At T6 and T12, there was a significant difference between the two groups for CI, P(cv-a)CO₂ values, and lactate concentration at T12. (Fig. 1).

From T0 to T12, the clearance of lactate concentration ((lactateT12-lactateT0)/(lactateT0) × 100) was significantly larger for the Low gap patients than for the High gap patients: -38 ± 39% versus -17 ± 33%, *P* = 0.04.

Fig. 1 Evolution of MAP (mmHg), ScvO₂ (%), CI (l/min/m²), P(cv-a)CO₂ (mmHg), and lactatemia (mmol/l) at T0, T6, T12 and SOFA score at T0 and T24 and comparison between groups. Expressed as mean ± SD



Correlation analysis

At T0, T6 and T12, CI and P(cv-a)CO₂ were inversely correlated : T0: $r = 0.57$, $P < 0.0001$; T6: $r = 0.58$, $P < 0.0001$ and T12: $r = 0.58$, $P < 0.0001$ (Figure 1 of ESM). At each time of the protocol, there was no correlation between CI and ScvO₂ values: T0: $r = 0.15$, $P = 0.29$; T6: $r = 0.26$, $P = 0.07$. T12 : $r = 0.24$, $P = 0.1$. At T0, there was no correlation between P(cv-a)CO₂ and lactate concentration: $r = 0.17$, $P = 0.22$. At T6 and T12, P(cv-a)CO₂ and lactate were weakly correlated: T6: $r = 0.37$, $P = 0.003$ and T12: $r = 0.36$, $P = 0.008$.

Discussion

Similar to what has been recently reported after admission into ICUs in a multi-centre observational study [4], a

minority of our patients kept a ScvO₂ lower than 70%. Indeed, 89% of the resuscitated septic patients had a ScvO₂ larger than 70%. Among them, those who kept an initial P(cv-a)CO₂ lower than 6 mmHg presented a lower lactate concentration and a higher lactate clearance during the next 12 h and a significant and larger decrease in SOFA score on day 1 than patients who presented with an initial P(cv-a)CO₂ higher than 6 mmHg. These results suggest that the presence of a high P(cv-a)CO₂ value could be a useful tool to identify patients who still remain inadequately resuscitated despite a ScvO₂ larger than 70% have already been reached.

The main part of our results was that resuscitated-septic patients could have a ScvO₂ larger than 70% but have significantly different P(cv-a)CO₂ and CI. This point was a key result of our study demonstrating that, after the early resuscitation with “normalisation” of DO₂/VO₂ ratio (assessed by an ScvO₂ > 70%), 48% (24/50) of our septic patients kept an enlarged P(cv-a)CO₂

(larger than 6 mmHg). In those patients, lactate tended to be higher and cardiac output and ScvO₂ tended to be lower than in patients with a P(cv-a)CO₂ < 6 mmHg (Table 1). An enlarged venous-to-arterial CO₂ gap can then be explained by: (1) an increase in venous PCO₂ secondary to low flow-induced CO₂-stagnation [16, 23]; (2) an increase in respiratory quotient with persistent additional CO₂ production (VCO₂), relative to the O₂ uptake, secondary to the buffering of excess hydrogen ions by bicarbonate [15, 24, 25]; (3) an increase in CO₂ production and stagnation although an ScvO₂ > 70%. For this last explanation, we can notice that at T0 (Table 1) a larger P(cv-a)CO₂ difference is observed (8.9 ± 2.6 vs. 3.2 ± 1.3 mmHg, *P* < 0.001) together with a lower CI (2.7 ± 0.8 vs. 4.3 ± 1.6 l/min/m², *P* < 0.0001) and ScvO₂ (75 ± 5 vs. 78 ± 5 mmHg; *P* = 0.07) and a higher ERO₂ (21 ± 6 vs. 17 ± 9%, *P* = 0.05). This is consistent with a certain degree of hypoperfusion and previous results as those presented by Bakker et al. [13]. Interestingly, the capacitance of tissues for CO₂ is very high compared to O₂ (20 to 40-fold) and Cohen et al. [26], in a model of haemorrhagic shock in swine, noted that the normalisation of VCO₂ in response to resuscitation was mainly dependent on tissue perfusion and was delayed when compared to the normalisation of VO₂ which increased more rapidly as O₂ supply limitation was overcome. Last, defects in O₂ extraction capabilities related to microcirculatory disorders [5, 27] and/or mitochondrial damage [6] can occur in septic shock resulting in an apparent normal DO₂/VO₂ ratio (with high ScvO₂ and low ERO₂) despite persistence of tissue hypoperfusion and hypoxia [28]. The conjunction of those possible physiological features might explain the possibility to observe at the same time a combination of a ScvO₂ larger than 70% and high P(cv-a)CO₂ values. In that context, O₂ supply may be apparently adapted to the tissue O₂ extraction capabilities although the bulk tissue perfusion remains insufficient to wash out the accumulating tissue CO₂ produced by the resuscitated metabolism. As the increase in tissue CO₂ during hypoperfusion is also accompanied by an increase in venous CO₂ [16], we can argue that targeting only the 70% ScvO₂ goal value may not be sufficient to guide therapy in ICU-resuscitated septic patient: using P(cv-a)CO₂ seems to be relevant to identify patients who still remain inadequately resuscitated.

Several studies demonstrated a relationship between mixed venous-to-arterial carbon dioxide difference [P(v-a)CO₂] and CI in circulatory failure [9, 11, 29, 30] and septic shock [12, 31]. For the authors, P(v-a)CO₂ can be considered as a marker of the adequacy of the venous blood efflux to remove the total CO₂ produced by the peripheral tissues. Recently, Cuschieri et al. [18] showed that this correlation still existed when the venous-to-arterial CO₂ tension difference was calculated with

PcvCO₂ measured from a central venous blood sample. For septic shock patients, our results are in agreement with those of Cuschieri et al. since we found a correlation between CI and P(cv-a)CO₂. Our results showed that this correlation did not exist between CI and ScvO₂ values probably because the relationship between ScvO₂ and CI is almost flat at high ScvO₂ values. Thus, P(cv-a)CO₂ could be considered as a better indirect assessment of systemic blood flow than ScvO₂ in resuscitated-septic shock patients.

At the time of enrolment (T0), all patients have already been resuscitated in the emergency unit according to an algorithm targeting ScvO₂. All included patients had successfully reached the ScvO₂ goal value and were kept resuscitated following the same guidelines for the next 12 h. Without any obvious difference in treatment received, patients who had a low P(cv-a)CO₂ value on admission in the ICU had a higher lactate clearance for the next 12 h. A previous study revealed the weak correlation between mixed venous-arterial carbon dioxide difference and lactate level [32]. Our results agree with those of this study as there was no correlation between the lactate level and the P(cv-a)CO₂ value at baseline, but indicate that a persistently high P(cv-a)CO₂ better predicts a lower lactate clearance than a Low P(cv-a)CO₂. Moreover Low P(cv-a)CO₂ patients presented a significant decrease in SOFA score at day 1 when patients with an initial high P(cv-a)CO₂ value did not (Fig. 1). Although the mortality rate was not significantly different between the two groups (35 vs. 54%, *P* = 0.16) the prognosis seems far better for Low gap patients with decrease in organ failure [33] and with a higher lactate clearance [28, 34, 35]. A larger size for our study population may have produced a significant statistical difference.

We believe that we do not have enough proof today to advocate that a ScvO₂ of 70% is a sufficient target to optimize tissue perfusion. Considering our results one may suggest that this target value could certainly be higher than 70% (75% or more) and/or that applying a resuscitation algorithm based on a ScvO₂ ≥ 70% combined with a P(cv-a)CO₂ < 6 mmHg would be requested [19]. We feel that the presence of a ScvO₂ ≥ 70% with a P(cv-a)CO₂ > 6 mmHg reveals a persistent inadequate haemodynamic status and that the good practice remains to test the “hypoperfusion hypothesis” by increasing CI and re-check global haemodynamics after intervention. We are aware however that complementary studies are warranted in order to confirm our results. At this time, we cannot know whether P(cv-a)CO₂ was high because patients were under-resuscitated or were not responders to the resuscitation protocol applied at our Institution. We feel nevertheless that our approach is coherent with the physiology of adapting the magnitude of blood flow to the magnitude of CO₂ produced by the tissues [17].

Conclusion

When a 70% ScvO₂ value is the recommended goal to target resuscitation at the very early phase for the septic patient management (its utility being proved [2] and transferred into guidelines [1] for continuous monitoring

in order to track down low values [36, 37]), our results suggest that a P(cv-a)CO₂ value larger than 6 mmHg might be a useful tool to identify patients who remain inadequately resuscitated. Further research is required to determine the best use of this parameter as a treatment end-point.

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