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The ratios of central venous to arterial carbon dioxide content and tension to arteriovenous oxygen content are not associated with overall anaerobic metabolism in postoperative cardiac surgery patients

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Abstract

Background

The aim of the present study was to evaluate the ability of the ratios of central venous to arterial carbon dioxide content and tension to arteriovenous oxygen content to predict an increase in oxygen consumption (VO_2) upon fluid challenge (FC).

Methods and results

110 patients admitted to cardiothoracic ICU and in whom the physician had decided to perform an FC (with 500 ml of Ringer's lactate solution) were included. The arterial pressure, cardiac index (Ci), and arterial and venous blood gas levels were measured before and after FC. VO_2 and CO_2-O_2 derived variables were calculated. VO_2 responders were defined as patients showing more than a 15% increase in VO_2. Of the 92 FC responders, 43 (46%) were VO_2 responders. At baseline, pCO_2 gap, C(a-v)O_2 were lower in VO_2 responders than in VO_2 non-responders, and central venous oxygen saturation ($ScvO_2$) was higher in VO_2 responders. FC was associated with an increase in MAP, SV, and CI in both groups. With regard to $ScvO_2$, FC was associated with an increase in VO_2 non-responders and a decrease in VO_2 responders. FC was associated with a decrease in $pvCO_2$ and pCO_2 gap in VO_2 non-responders only. The pCO_2 gap/C(a-v)O_2 ratio and C(a-v)CO_2 content /C(a-v)O_2 content ratio did not change with FC. The CO_2 gap content/C(a-v)O_2 content ratio and the C(a-v)CO_2 content /C(a-v)O_2 content ratio did not predict fluid-induced VO_2 changes (area under the curve (AUC) [95% confidence interval (CI)] = 0.52 [0.39–0.64] and 0.53 [0.4–0.65], respectively; p = 0.757 and 0.71, respectively). $ScvO_2$ predicted an increase of more than 15% in the VO_2 (AUC [95%CI] = 0.67 [0.55–0.78]; p<0.0001).

applied to the collection, storage, and use of personal data. As the database of this study was authorized by the CNIL, we cannot make available data without prior agreement of the CNIL. Requests may be sent to: elisabeth.laillet@chu-dijon.fr.

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Conclusions

Our results showed that the ratios of central venous to arterial carbon dioxide content and tension to arteriovenous oxygen content were not predictive of VO_2 changes following fluid challenge in postoperative cardiac surgery patients.

Introduction

Fluid challenge (FC) is the most frequently performed bedside haemodynamic intervention in perioperative care. This procedure is usually used to increase cardiac output (CO) so that oxygen delivery (DO_2) matches oxygen consumption (VO_2) [1, 2]. After FC, VO_2 can either increase (if there is an oxygen debt) or remain unchanged [2]. In recent years, several studies have focused on parameters that are able to accurately track VO_2/DO_2 dependency [3–7]. Although the blood lactate concentration was initially described as a surrogate marker of VO_2/DO_2 dependency, an elevated lactate value may not necessarily reflect anaerobic metabolism [8]. Although $ScvO_2$ might be indicative of DO_2, its significance may be diminished during distributive shock with alteration of the oxygen extraction ratio (O_2ER)—even after cardiac surgery [5, 9, 10]. It was recently suggested that the veno-arterial carbon dioxide tension gradient (pCO_2 gap) and the pCO_2 gap/$C(a\text{-}v)O_2$ ratio are more sensitive indices of anaerobic metabolism and the VO_2 increase upon FC [5, 11–14]. These parameters were developed and validated in ICU patients with sepsis, in whom they accurately predict an increase in VO_2 with FC.

In clinical practice, the difficulty is to identify hemodynamic and/or oxygenation parameters that are clinically relevant to become endpoints for titration of interventions. Increasing DO_2 is an accepted goal for optimization following cardiac surgery [15, 16] which is considered as a major surgery associated with high incidence of postoperative complications. Thus, predicting VO_2 responsiveness can identify the patients for which DO_2 increase is most beneficial [15, 16]. To date, these parameters have not been extensively studied in non-septic or postoperative patients. A few studies of postoperative cardiac surgery patients have shown that in contrary to the situation in patients with sepsis, pCO_2 gap is poorly correlated with perfusion variables [17, 18].

The present study aims at investigating the ability of the pCO_2 gap/$C(a\text{-}v)O_2$ ratio and the $C(a\text{-}v)CO_2$ content/$C(a\text{-}v)O_2$ content ratio to predict a VO_2 increase upon FC in postoperative cardiac surgery patients.

Material and methods

Ethics

The study was approved by the independent ethics committee at Amiens University Hospital (Amiens, France). Because the protocol study is considered as observational and part of routine clinical practice, the French law did not require written consent. According to ethics committee, all patients received written information on the study. Oral consent was obtained from patient or subject's next of kin. The capacity to consent was checked by excluding confusion in awake patient who were not sedated. Confusion was assessed by clinical examination based on confusion assessment method for the intensive care unit. In case of confusion, the consent was obtained from subject's of kin. The consent was noted on study observation book. The present manuscript was drafted in compliance with the STROBE checklist for cohort studies [19].

Patients

This observational study was performed in the cardiothoracic ICU at Amiens University Hospital (Amiens, France) between 2014 and 2017. Some of the patients were previously included in a study that evaluate association between end tidal carbon dioxide pressure and oxygen extraction [7]. The main inclusion criteria were as follows: age 18 or over, controlled positive ventilation, and a clinical decision to perform FC for volume expansion. The indications for FC were arterial hypotension (a systolic arterial pressure (SAP) below 90 mmHg and/or a mean arterial pressure (MAP) below 65 mmHg), a stroke volume (SV) variation of more than 10% during a passive leg raising manoeuver and/or clinical signs of hypoperfusion (skin mottling, and a capillary refill time of more than 3 sec). The non-inclusion criteria were permanent arrhythmia, heart conduction block, a pacemaker, poor echogenicity, aortic regurgitation, spontaneous ventilation, ongoing haemorrhage, and right heart dysfunction.

Haemodynamic parameters

Transthoracic echocardiography (with the CX50 ultrasound system and an S5-1 Sector Array Transducer, Philips Medical System, Suresnes, France) was performed by a physician who was blinded to the study outcomes. The left ventricular ejection fraction was measured using Simpson's biplane method with a four-chamber view. The aortic surface area (SAo, in cm^2) was calculated as $\pi\times$(diameter of the left ventricular outflow tract)^2/4. The aortic velocity-time integral (VTIAo), was measured with pulsed Doppler at the LVOT on a five-chamber view. The SV (mL) was calculated as VTIAo×SAo. Cardiac output (CO) was calculated as SV×heart rate (HR) (ml min^{-1}) and was expressed as an indexed CI, i.e. CO/body surface area (ml min^{-1} m^2). Mean echocardiographic parameters were calculated from five measurements (regardless of the respiratory cycle) and analysed off lines.

Oxygenation parameters

We recorded the ventilator settings (tidal volume, plateau pressure and end-expiratory pressure) at baseline. All blood gas parameters were measured with arterial and central venous catheters. Arterial and venous blood gas levels, the blood lactate level, the blood haemoglobin (Hb) concentration and oxyhaemoglobin saturation were measured using an automated analyser (ABL800 FLEX, Radiometer, Bronshoj, Denmark). Arterial oxygen content (CaO_2) and venous oxygen content (CvO_2) were calculated as follows: $CaO_2 = 1.34 \times Hb \times SaO_2 + 0.003 \times PaO_2$; $CvO_2 = 1.34 \times Hb \times ScvO_2 + 0.003 \times PvO_2$, where Hb is the haemoglobin concentration (g.dl^{-1}), PaO_2 is the arterial oxygen pressure (mmHg), SaO_2 is the arterial oxygen saturation (%), PvO_2 is the venous oxygen pressure (mmHg), $ScvO_2$ is the central venous oxygen saturation (in%), and 0.003 is the solubility coefficient of oxygen [14]. pCO_2 gap was calculated as follows: pCO_2 gap = $PcvCO_2$ –$PaCO_2$ (mmHg). C(a-v)O_2 was calculated as CaO_2 minus CvO_2 (ml) [14]. DO_2 and VO_2 were calculated from arterial and central venous blood gas measurements as follows: DO_2 (ml min^{-1} m^{-2}) = (CaO_2 x 10 x CO)/body surface area; VO_2 (ml min^{-1} m^{-2}) = the arteriovenous difference in oxygen content (C(a-v)O_2 x CO x 10)/body surface area. Arterial and venous CO_2 contents ($CaCO_2$, $CvCO_2$) were calculated according to the Douglas formula [14, 20]. The C(a-v)CO_2 content was calculated as $CvCO_2$ minus $CaCO_2$ (ml).

Protocol

During the study period, the patients were mechanically ventilated in volume-controlled mode, with a tidal volume set to 7–9 ml kg^{-1} ideal body weight, and a positive end-expiratory pressure (PEEP) of 5–8 cmH_2O. The patients were sedated with propofol, with a target Ramsay

score >5. The ventilator settings (oxygen inspired fraction, tidal volume, respiratory rate, and end positive pressure) were not modified during the study period.

The following clinical parameters were recorded: age, gender, weight, ventilation parameters, and primary diagnosis. After an equilibration period, HR, SAP, MAP, diastolic arterial pressure, central venous pressure (CVP), SV, CO, and arterial/venous blood gas levels were measured at baseline. In the present study, FC always consisted of a 10-minute infusion of 500 ml of Ringer's lactate solution. Immediately after FC, a second set of measurements was made.

Statistical analysis

The variables' distribution was assessed using a Shapiro-Wilk test. Data were expressed as the number, proportion (in percent), mean ± standard deviation (SD) or the median [interquartile range (IQR)], as appropriate. Patients were classified as fluid responders or non-responders as a function of the effect of FC on the SV. An FC response was defined as an increase of more than 15% in the SV after FC [21]. Patients were classified as VO_2 responders or non-responders as a function of the effect of FC on VO_2. A VO_2 response was defined as an increase of more than 15% in the VO_2 after FC [7]. The non-parametric Wilcoxon rank sum test, Student's paired t test, Student's t test, and the Mann-Whitney test were used to assess statistical significance, as appropriate. Linear correlations were tested using Pearson's or Spearman's rank method. A receiver-operating characteristic curve was used to establish the ability of $ScvO_2$, pCO_2 gap/$C(a\text{-}v)O_2$ ratio or the $C(a\text{-}v)CO_2$ content/$C(a\text{-}v)O_2$ content ratio to predict an increase of more than 15% in VO_2 [7, 14]. Assuming that 60% of patients would be fluid responders and that 20 to 30% of fluid responders would be VO_2 responders, we calculated that a sample of 105 patients was sufficient to demonstrate that the pCO_2 gap/$C(a\text{-}v)O_2$ ratio predict an increase in VO_2 upon FC with an area under the curve (AUC) greater than 0.80, a power of 80%, and an alpha risk of 0.05. Taking the exclusion criteria and incomplete data in account, the sample size was set to 115 participants. The threshold for statistical significance was set to $p<0.05$. SPSS software (version 24, IBM, New York, NY, USA) was used for all statistical analyses.

Results

Patients

All patients had undergone cardiovascular surgery with cardiopulmonary bypass Table 1, Fig 1. Of the 115 included patients, five were excluded (Fig 1), and so the final analysis covered 110 patients. Of these, 92 (84%) were classified as FC responders, and 43 (47%) were classified as VO_2 responders.

Effect of FC on haemodynamic and oxygenation parameters in the population as a whole

FC was associated with increases in MAP, CVP, SV, CO, DO_2, and VO_2, and decreases in HR, and pCO_2 gap Table 2. At baseline, the arterial lactate concentration was not correlated with $ScvO_2$ (r = -0.044, p = 0.650), pCO_2 gap/$C(a\text{-}v)O_2$ ratio (r = 0.052, p = 0.587), or $C(a\text{-}v)CO_2$ content /$C(a\text{-}v)O_2$ content ratio (r = 0.019, p = 0.841).

Differences between VO_2 responders and VO_2 non-responders among fluid responders

Of the 92 FC responders, 43 (46%) were VO_2 responders (Fig 1). All VO_2 responders were FC responders Table 2. FC increased MAP, SV, and CI in the two groups Table 2.

Table 1. Characteristics of the study participants on inclusion.

Variables	Overall population (n = 110)
Age (mean (SD), years)	69 (11)
Gender (F/M)	32 /78
Surgery, n (%)	
Valvular	55 (50)
CABG	30 (27)
Combined surgery	15 (14)
Other	6 (9)
SAPS 2	40 (13)
Respiratory parameters	
Tidal volume (ml kg^{-1} of predicted body weight, mean (SD),	7.8 (0.6)
Total PEEP (cmH_2O, mean (SD))	6 (1)
Number of patients treated with norepinephrine (n, %)	25 (25)
Median dose (gamma Kg^{-1} min^{-1})	0.7 (0.5 to 1.4)
Number of patients treated with dobutamine (n, %)	4 (5)
Median dose (gamma Kg^{-1} min^{-1})	5 (5 to 7)
LVEF (%, mean (SD))	49 (11)

Values are expressed as the mean ± SD or the number (%). CABG: coronary artery bypass graft.

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At baseline, pCO_2 gap and $C(a\text{-}v)O_2$ were lower in VO_2 responders than in VO_2 non-responders, and $ScvO_2$ was higher Table 3. The arterial lactate concentration did not differ when comparing the two groups, and did not change upon FC. Furthermore, FC increased $ScvO_2$ in VO_2 non-responders and decreased $ScvO_2$ in VO_2 responders. FC decreased $pvCO_2$ and pCO_2 gap in VO_2 non-responders only Table 3. The pCO_2 gap/$C(a\text{-}v)O_2$ ratio and the $C(a\text{-}v)CO_2$ content/$C(a\text{-}v)O_2$ content ratio did not change upon FC.

The FC-induced changes in the $C(a\text{-}v)CO_2$ content/$C(a\text{-}v)O_2$ content ratio and the pCO_2 gap/$C(a\text{-}v)O_2$ ratio were associated ($r = 0.499$, $p<0.0001$), but neither was correlated with

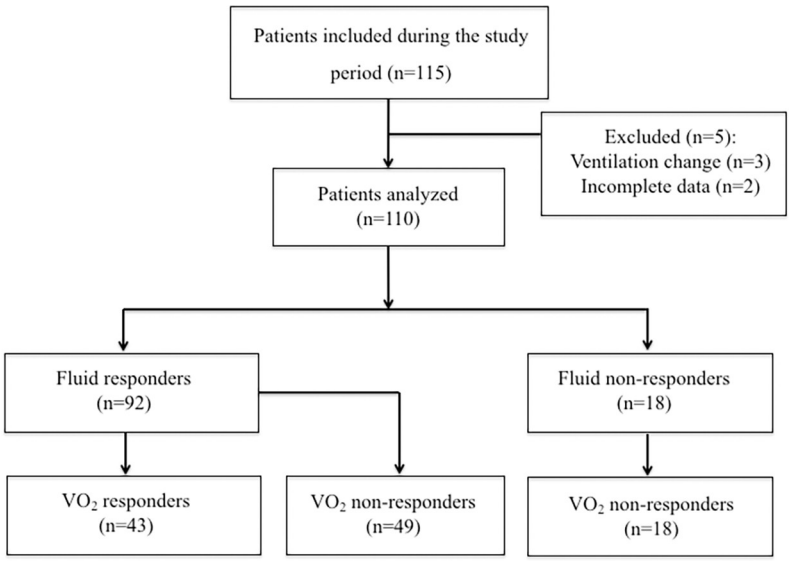

Fig 1. Flow chart diagram of the study.

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Table 2. Comparison of haemodynamic parameters according to response of VO_2.

Hemodynamic variables	VO_2 responders (n = 43)	VO_2 non responders (n = 49)	*p value*
Respiratory minute ventilation (l min^{-1})	**8.2 (1.3)**	**8 (1)**	***0.290***
Body temperature (°C)	**36.3 (1.7)**	**36.6 (0.4)**	***0.273***
Capillary refill time (sec)			
Pre-FC	**3.6 (1.5)**	**3.6 (1.3)**	***0.908***
Post-FC	**3.2 (1.2)** [a]	**2.9 (1.4)** [a]	***0.289***
Haemoglobin (g dl^{-1})			
Pre-FC	**11.4 (1.6)**	**11.2 (1.4)**	***0.518***
Post-FC	**11.2 (1.7)** [a]	**10.8 (1.4)** [a]	***0.210***
HR (bpm)			
Pre-FC	**82 (22)**	**85 (19)**	***0.574***
Post-FC	**78 (21)** [a]	**81 (16)** [a]	***0.404***
MAP (mmHg)			
Pre-FC	**74 (14)**	**70 (12)**	***0.140***
Post-FC	**84 (16)** [a]	**82 (12)** [a]	***0.472***
SV (ml)			
Pre-FC	**44 (15)**	**42 (15)**	***0.652***
Post-FC	**60 (18)** [a]	**55 (21)** [a]	***0.263***
CI (ml min^{-1} m^{-2})			
Pre-FC	**1.7 (0.6)**	**1.8 (0.7)**	***0.524***
Post-FC	**2.3 (0.7)** [a]	**2.2 (0.9)** [a]	***0.921***
DO_2 (ml min^{-1} m^{-2})			
Pre-FC	**269 (103)**	**274 (95)**	***0.811***
Post-FC	**339 (124)** [a]	**319 (119)** [a]	***0.428***
VO_2 (ml min^{-1} m^{-2})			
Pre-FC	**75 (34)**	**100 (39)**	***0.002***
Post-FC	**115 (37)** [a]	**93 (31)**	***0.007***

Values are expressed as the mean (SD) or the median [interquartile range]. **CI**, indexed cardiac output; ***DO_2***, oxygen delivery; **FC**, fluid challenge; **HR**, heart rate; **MAP**, mean arterial pressure; **SV**, stroke volume; ***VO_2***, oxygen consumption

[a]: $p<0.05$ within groups (pre-/post-FC).

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changes in VO_2 (r = -0.092, p = 0.337 and r = -0.05, p = 0.957) or arterial lactates (r = 0.129, p = 0.18 and r = -0.10, p = 0.916). The FC-induced changes in VO_2 and $ScvO_2$ were associated (r = 0.61, p = 0.0001).

Ability of overall perfusion parameters to predict an increase in VO_2

With an AUC [95% confidence interval (CI)] of 0.52 [0.39–0.64] and 0.53 [0.4–0.65], respectively; p = 0.757 and 0.71, respectively, the $C(a\text{-}v)CO_2$ content /$C(a\text{-}v)O_2$ content ratio and the pCO_2 gap/$C(a\text{-}v)O_2$ ratio did not predict FC-associated changes in VO_2. Baseline $ScvO_2$ was poorly predictive of an increase of more than 15% in the VO_2, with an AUC [95%CI] of 0.67 [0.55–0.78] ($p<0.0001$).

Discussion

Our study produced several relevant results. The pCO_2 gap/$C(a\text{-}v)O_2$ ratio and the $C(a\text{-}v)CO_2$ content /$C(a\text{-}v)O_2$ content ratio did not predict increase in VO_2 in postoperative cardiac surgery patients. $ScvO_2$ was poorly predictive of an FC-associated increase in VO_2. The arterial

Table 3. Comparison of perfusion parameters according to response of VO_2.

Variables	VO_2 responders (n = 43)	VO_2 non responders (n = 49)	*p value*
Arterial pH			
Pre-FC	**7.35 (0.07)**	**7.38 (0.2)**	***0.447***
Post-FC	**7.38 (0.05)** [a]	**7.39 (0.2)**	***0.667***
Venous pH			
Pre-FC	**7.32 (0.05)**	**7.33 (0.2)**	***0.751***
Post-FC	**7.32 (0.06)**	**7.33 (0.2)**	***0.728***
Oxygen arterial saturation (%)			
Pre-FC	**97.6 (1.2)**	**97.7 (1.7)**	***0.679***
Post-FC	**97.4 (1.7)**	**97.6 (1.4)**	***0.628***
$ScvO_2$ (%)			
Pre-FC	**67.7 (12)**	**60.8 (10)**	***0.003***
Post-FC	**62.8 (9)** [a]	**68.4 (10)** [a]	***0.005***
$PaCO_2$ (mmHg)			
Pre-FC	**38.4 (5)**	**36.4 (5)**	***0.068***
Post-FC	**37.3 (4)**	**36.7 (5)**	***0.510***
$PvCO_2$ (mmHg)			
Pre-FC	**46.7 (6.1)**	**46.6 (5.4)**	***0.942***
Post-FC	**46.5 (5.4)**	**44.7 (5.3)** [a]	***0.104***
pCO_2 gap (mmHg)			
Pre-FC	**8.3 (3.7)**	**10 (3.3)**	***0.020***
Post-FC	**9.2 (3.8)**	**8 (3.6)** [a]	***0.143***
CaO_2 (ml)			
Pre-FC	**15.4 (2.2)**	**15.1 (2)**	***0.555***
Post-FC	**15 (2.2)** [a]	**14.4 (1.9)** [a]	***0.171***
CvO_2 (ml)			
Pre-FC	**10.8 (2.7)**	**9.5 (2.1)**	***0.009***
Post-FC	**9.7 (2.2)** [a]	**10.2 (2.2)** [a]	***0.285***
$C(a\text{-}v)O_2$ (ml)			
Pre-FC	**4.5 (1.8)**	**5.6 (1.6)**	***0.003***
Post-FC	**5.3 (1.2)** [a]	**4.2 (1.9)** [a]	***0.002***
$CaCO_2$ (ml)			
Pre-FC	**51.2 (7)**	**48.3 (7.9)**	***0.034***
Post-FC	**52.1 (5.9)**	**49.8 (5.1)** [a]	***0.052***
$CvCO_2$ (ml)			
Pre-FC	**57.3 (5.8)**	**55.6 (5.4)**	***0.052***
Post-FC	**56.9 (6.3)**	**53.2 (5.9)** [a]	***0.004***
$C(a\text{-}v)CO_2$ content (ml)			
Pre-FC	**5.8 (2.9–7.4)**	**6.8 (4.5–7.4)**	***0.239***
Post-FC	**5.3 (3.5–7.3)**	**2.9 (1.6–6.1)** [a]	***0.023***
pCO_2 gap/$C(a\text{-}v)O_2$ ($mmHg\ ml^{-1}$)			
Pre-FC	**1.93 (1.36–2.29)**	**1.89 (1.42–2.)**	***0.710***
Post-FC	**1.82 (1.39–2.21)**	**1.86 (1.36–2.29)** [a]	***0.863***
$C(a\text{-}v)CO_2$ content /$C(a\text{-}v)O_2$ content ratio			
Pre-FC	**0.98 (0.43–2.06)**	**1.1 (0.86–1.85)**	***0.625***
Post-FC	**0.96 (0.59–1.39)**	**0.81 (0.46–1.15)** [a]	***0.109***
Arterial lactates ($mmol\ l^{-1}$)			

(*Continued*)

Table 3. (Continued)

Variables	VO_2 responders (n = 43)	VO_2 non responders (n = 49)	*p value*
Pre-FC	**1.8 (0.9)**	**1.9 (0.7)**	***0.590***
Post-FC	**1.8 (0.9)**	**2 (0.8)**	***0.251***

Values are expressed as the mean (SD) or the median [interquartile range]. **FC**, fluid challenge; ***VO_2***, oxygen consumption

[a]: $p<0.05$ within groups (pre-/post-FC).

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lactate level was not associated with VO_2 changes. These results suggest that physician should take in account the population studied before analysing oxygen derivate parameters and predicting VO_2 dependency.

The pCO_2 gap/C(a-v)O_2 ratio and the C(a-v)CO_2 content/C(a-v)O_2 content ratio are known to be associated with anaerobic metabolism, lactate clearance, and mortality in ICU patients with sepsis [11, 12, 14]. The present study is the first to have specifically focused on postoperative patients. Our present results did not suggest that the above-mentioned ratios are of value in non-septic patients. There are several possible explanations for our findings. Most of these are probably related to the difference between the various study populations (i.e. sepsis vs cardiac surgery), which may alter the significance of and relationships between systemic parameters related to oxygen and carbon dioxide [9, 22].

In the present study, the relationship between FC and changes in arterial and venous carbon dioxide content/tension differed to that observed in patients with sepsis [6, 12, 14]. Baseline pCO_2 gap was higher after cardiac surgery in VO_2 non-responders, and decreased only in VO_2 non-responders. In the context of sepsis, pCO_2 gap is higher in VO_2 responder patients, and decreases only in VO_2 responder patients. We did not demonstrate differences in FC-induced changes in O_2-derived parameters, relative to those observed in patients with sepsis. C(a-v)O_2 decreased in VO_2 non-responders (due to an increase in CvO_2) and increased in VO_2 responders (due to a decrease in CvO_2). The physiological relationships that allow the pCO_2 gap/C(a-v)O_2 ratio and the C(a-v)CO_2 content/C(a-v)O_2 content ratio to be used as indicators of anaerobic metabolism are probably altered by the inability of pCO_2 gap to adequately reflect tissue CO_2 production and elimination [17]. Our group has already studied pCO_2 gap as a prognostic factor for the postoperative course in cardiac surgery [17]. Even though pCO_2 gap was poorly correlated with tissue perfusion parameters, we did not demonstrate an association between pCO_2 gap and outcomes.

The divergence between sepsis and post-operative situations might be due to several factors. The extent of microcirculation alterations caused by sepsis or surgery/cardiopulmonary bypass may differ [23, 24]. It has been demonstrated that sepsis is systematically associated with the disruption of microcirculatory regulation, i.e. a decrease in the functional capillary index, absent/intermittent capillary flow, increased heterogeneity in the perfusion index, arteriovenous shunting, and cellular hypoxia [25]. Cardiac surgery with cardiopulmonary bypass is associated with a wide range of microcirculatory alterations, including a decrease in microvascular perfusion, increased heterogeneity in the perfusion index and red blood cell velocity, and arteriovenous shunting [23, 26]. These changes are associated with alterations in the arteriovenous oxygen difference, systemic oxygen consumption, and CO_2 and O_2 diffusion [27]. Moreover, cardiac surgery microcirculatory alterations may be induced by (amongst other factors) cardiopulmonary bypass haemodilution and temperature changes during the operative period. Haemodilution was demonstrated to alter the relationship between CO_2 pressures and CO_2

contents, which do not alter pCO_2 gap in the same way as haemorrhage [28]. It was also demonstrated that anaesthetic agents alter regional critical DO_2 and microcirculation by changing the peripheral vascular resistance [29]. When considering the above-mentioned arguments and data as a whole, the pCO_2 gap/C(a-v)O_2 ratio and the C(a-v)CO_2 content/C(a-v) O_2 content ratio do not reflect complex, inconsistent alterations in regional VO_2, DO_2 and the latter's interrelationships after cardiac surgery.

Our results confirmed those report by Fischer et al., who demonstrated that only $ScvO_2$ was associated with VO_2 dependency in postoperative patients after maximization of the SV by FC [30]. Nevertheless, $ScvO_2$ remains poorly predictive of VO_2 changes [10]. Our results and those of Fischer et al. confirm previous demonstrations of $ScvO_2$'s poor ability to track VO_2 changes [10]. Likewise, arterial lactate was not associated with VO_2 changes in Fischer et al.'s study and in the present study. Arterial lactate is known to be a complex variable that may be not always be associated with tissue hypoxia/hypoperfusion and anaerobic metabolism [8]. At present, no clinical parameter has demonstrated its superiority to predict VO_2 dependency. Only goal directed hemodynamic optimisation protocols have demonstrated a decrease of post-operative complications due to a maximisation of DO_2. Further research is needed to identify and describe new indicators of VO_2 dependency in non-septic patients. In this way, ventriculo-arterial coupling and mitochondrial PO_2 may be of interest [31, 32].

The present studies had several limitations. The fact that pCO_2 gap was measured in central venous blood (rather than mixed venous blood) might have underestimated CO_2 exchange from splanchnic territories. However, other studies have used central venous blood to calculate VO_2- and CO_2-derived parameters [14]. The observed changes in O_2- and CO_2-derived parameter were small and reproducible [33]. We assessed VO_2 using the Fick method, which may not be reliable in ICU patients. Nevertheless, previous studies have used the Fick method to calculate VO_2 [6, 14]. The latter results were similar to those previously demonstrated to be predictive of VO_2 changes. Lastly, we performed a single-centre study; however, our results are in line with those reported in Fischer et al.'s study [28].

Conclusions

Our present results did not demonstrate the ability of the pCO_2 gap/C(a-v)O_2 ratio and C(a-v) CO_2 content/C(a-v)O_2 content ratio to predict VO_2 dependency in postoperative cardiac surgery patients. The present finding demonstrated that the population studied should be consider at bedside when assessing VO_2 dependency with oxygen derivate parameters. The effect of cardiac surgery and/or cardiopulmonary bypass on the relationship between CO_2 content and CO_2 partial pressure may explain in part this finding.

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