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Combination of venoarterial PCO_2 difference with arteriovenous O_2 content difference to detect anaerobic metabolism in patients

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Abstract *Objective:* Under conditions of tissue hypoxia total CO_2 production (VCO_2) should be less reduced than O_2 consumption (VO_2) since an anaerobic CO_2 production should occur. Thus the VCO_2/VO_2 ratio, and hence the venoarterial CO_2 tension difference/arteriovenous O_2 content difference ratio ($\Delta PCO_2/C_{(a-v)}O_2$), should increase. We tested the value of the $\Delta PCO_2/C_{(a-v)}O_2$ ratio in detecting the presence of global anaerobic metabolism as defined by an increase in arterial lactate level above 2 mmol/l (Lac^+). *Design and setting:* Retrospective study over a 17-month period in medical intensive care unit of a university hospital. *Patients:* We obtained 148 sets of measurements in 89 critically ill patients monitored by a pulmonary artery catheter. *Results:* The $\Delta PCO_2/C_{(a-v)}O_2$ ratio was higher in those with increased (n=73) than in the normolactatemic group (2.0±0.9 vs. 1.1±0.6, p<0.0001). Among all the O_2- and CO_2-derived parameters the $\Delta PCO_2/C_{(a-v)}O_2$ ratio had the highest correlation with the arterial lactate level (r=0.57). Moreover, for a threshold value of 1.4 the $\Delta PCO_2/C_{(a-v)}O_2$ ratio predicted significantly better than the other parameters (receiver operating characteristic curves) the presence of hyperlactatemia (positive and negative predictive values of 86% and 80%, respectively). The overall survival estimate at 1 month was greater when the $\Delta PCO_2/C_{(a-v)}O_2$ ratio was less than 1.4 on the first set of measurements (38±10% vs. 20±8%, p<0.01). *Conclusion:* The $\Delta PCO_2/C_{(a-v)}O_2$ ratio seems a reliable marker of global anaerobic metabolism. Its calculation would be helpful for a better interpretation of pulmonary artery catheter data.

Keywords Anaerobic metabolism · Venoarterial carbon dioxide tension difference · Lactate · Tissue hypoxia

Introduction

The diagnosis of global tissue hypoxia has important implications in the management of critically ill patients. These patients are frequently equipped with a pulmonary artery catheter that allows measurements of mixed venous blood oxygen (O_2) and carbon dioxide (CO_2) tensions. Unfortunately, neither O_2- nor CO_2-derived parameters have been shown to be of great value in detecting and monitor global tissue hypoxia [1, 2, 3, 4]. However, considering both O_2- and CO_2-derived parameters could be of particular interest. Under conditions of tissue hypoxia a decrease in global O_2 consumption is associated with a decrease in aerobic CO_2 production while an anaerobic production of CO_2 should occur, mostly through buffering the excess of protons by bicarbonate ions [5]. Thus the total CO_2 production (VCO_2) should be less reduced than the O_2 consumption (VO_2). In other words, the VCO_2/VO_2 ratio (respiratory quotient) should increase. According to the Fick equation, VO_2 is equal to the product of cardiac output and arteriovenous O_2 content difference ($C_{(a-v)}O_2$). Similarly, VCO_2 is equal to the

product of cardiac output and venoarterial CO_2 content difference. Therefore the respiratory quotient is equal to the venoarterial CO_2 content difference/$C_{(a-v)}O_2$ ratio. Over the physiological range of CO_2 contents CO_2 tension is linearly related to CO_2 content (steep part of the dissociation CO_2 curve) [6]. Therefore venoarterial CO_2 tension difference (ΔPCO_2) could be used as a surrogate for the difference between mixed venous and arterial CO_2 contents. In this connection, under anaerobic metabolism conditions, the increase in respiratory quotient should be reflected by the increase in $\Delta PCO_2/C_{(a-v)}O_2$ ratio.

The aim of our study was to test the hypothesis that the $\Delta PCO_2/C_{(a-v)}O_2$ ratio better detects global anaerobic metabolism in critically ill patients than the other standard parameters provided by the pulmonary artery catheter. Despite the potential difficulties of interpretation of increased blood lactate level in critically ill patients especially with sepsis [7, 8, 9], we defined the presence of anaerobic metabolism by an increase in arterial lactate level above 2 mmol/l.

Materials and methods

Patients

We retrospectively reviewed hemodynamic data obtained in 89 critically ill patients hospitalized between September 1998 and March 2000 in our institution. These patients underwent pulmonary artery catheterization for bedside hemodynamic monitoring. At the time of the study all patients were receiving mechanical ventilation and sedative drugs (midazolam and fentanyl). There were 58 men and 39 women, with a median age of 63±7.4 years. The patients illnesses were adult respiratory distress syndrome or acute lung injury (n=30), septic shock (n=47), and cardiogenic shock (n=12). Mortality rate at 1 month was 71±7%.

Measurements

Methods

All patients underwent systemic and pulmonary arterial catheterization. The systemic arterial catheter was inserted into the radial or the femoral artery. The pulmonary artery catheter (Baxter Edward's Critical-Care, Irvine, Calif, USA) was inserted via the jugular or the subclavian vein. Cardiac output was calculated as the mean of four measurements obtained by injecting 10 ml cooled saline solution. Immediately after measuring cardiac output arterial and mixed venous blood samples were withdrawn simultaneously for determination of the following variables: arterial oxygen tension (P_aO_2), arterial carbon dioxide tension (P_aCO_2), mixed venous oxygen tension (P_vO_2), mixed venous carbon dioxide tension (P_vCO_2), arterial oxygen saturation (S_aO_2) and mixed venous oxygen saturation (S_vO_2; IL BG3 Cooximeter, Instrumentation Laboratories, Paris, France). Hemoglobin concentration (Hb) was also measured. The arterial oxygen content (C_aO_2), mixed venous oxygen content (C_vO_2), arteriovenous oxygen content difference ($C_{(a-v)}O_2$), oxygen delivery (DO_2), oxygen consumption (VO_2), oxygen extraction ratio (O_2ER), and venoarterial CO_2 tension difference (ΔPCO_2) were calculated using the following formulas:

- $C_aO_2=(1.34\times S_aO_2\times Hb)+(0.003\times P_aO_2)$
- $C_vO_2=(1.34\times S_vO_2\times Hb)+(0.003\times P_vO_2)$
- $C_{(a-v)}O_2=C_aO_2-C_vO_2$
- $DO_2=10\times CI\times C_aO_2$
- $VO_2=10\times CI\times(C_aO_2-C_vO_2)$
- $O_2ER=(C_aO_2-C_vO_2)/C_aO_2$
- $\Delta PCO_2=P_vCO_2-P_aCO_2$

Cardiac index (CI) was calculated as the cardiac output divided by the body surface area. Arterial blood lactate concentration was measured using an enzymatic method (Lactate PAP, Biomerieux, Lyon, France).

Data selection and analysis

This retrospective study considered only sets of measurements which include arterial blood lactate level, hemodynamic and blood gas measurements simultaneously obtained. A total of 148 sets of hemodynamic, blood gas and lactate measurements were obtained. Hemodynamic sets of measurements were separated into two subgroups according to the lactate level: those with lactate level was 2 mmol/l or higher (Lac^+; n=73) and those with lactate level less than 2 mmol/l (Lac^-; n=75).

Statistics

Hemodynamic data were reviewed retrospectively. Continuous variables were expressed as the mean ±standard deviation and were compared using an unpaired the two-tailed t test. A statistical correlation was examined between arterial lactate level and each studied O_2- or CO_2-derived parameter by using a linear regression test. The value of S_vO_2, ΔPCO_2, $C_{(a-v)}O_2$, and the $\Delta PCO_2/C_{(a-v)}O_2$ ratio to predict the existence of increased arterial lactate concentration (>2 mmol/l) was analyzed using receiver operating characteristic (ROC) curves. The area under the ROC curve (±SE) for each parameter was calculated and compared [10, 11]. Survival data were analyzed with standard Kaplan-Meier technique for estimation of survival probabilities and were compared using the log-rank test. A two-tailed p value of less than 0.05 was taken to indicate statistical significance.

Results

The main hemodynamic and blood gas results of the two groups are presented in the Table 1. Mean arterial pressure was significantly lower in the Lac^+ group than in the Lac^- group (69±13 vs. 79±11 mmHg, p<0.001) and heart rate significantly higher (112±21 vs. 104±20 beats/min, p<0.02). CI and pulmonary artery occlusion pressure were similar in the two groups. VO_2 was lower in the Lac^+ group than in the Lac^- group (109±41 vs. 127±32, p<0.01). There was no significant difference between the two groups with regard to S_vO_2, DO_2, $C_{(a-v)}O_2$, or O_2ER. The ΔPCO_2 was higher in the Lac^+ group than in the Lac^- group (3.8±2.0 vs. 6.1±2.7; p<0.001). $\Delta PCO_2/C_{(a-v)}O_2$ ratio was greater in the Lac^+ group than in the Lac^- group (2.0±0.9 vs. 1.1±0.6, p<0.0001).

Arterial lactate level was significantly (p<0.01) but poorly correlated to $C_{(a-v)}O_2$ and ΔPCO_2 (r=0.26 and r=0.28, respectively). By contrast, a good correlation

Table 1 Main hemodynamic parameters and blood gases (n=148) ($\Delta PCO_2/C_{(a\text{-}v)}O_2$ venoarterial carbon dioxide tension difference/ arteriovenous oxygen content difference)

	Arterial blood lactate concentration		
	<2 mmol/l (n=75)	≥2 mmol/l (n=73)	p
Heart rate (beats/min)	104±20	112±21	0.04
Mean arterial pressure (mmHg)	79±11	69±13	<0.0001
Pulmonary artery occlusion pressure (mmHg)	12±5	14±6	0.14
Cardiac index (l min^{-1} m^{-2})	3.7±1.2	3.6±1.3	0.60
Arterial hemoglobin concentration (g/dl)	9.8±1.4	9.4±1.8	0.31
Arterial oxygen saturation (%)	95±4	94±5	0.11
Mixed venous oxygen saturation (%)	69±9	69±11	0.69
Oxygen delivery (ml min^{-1} m^{-2})	471±149	427±167	0.10
Arteriovenous oxygen content difference	3.6±1.0	3.3±1.4	0.09
Oxygen consumption (ml min^{-1} m^{-2})	127±32	109±41	<0.01
Oxygen extraction ratio (%)	28±8	27±10	0.61
Arterial carbon dioxide tension (mmHg)	43±9	43±15	0.97
Mixed venous carbon dioxide tension (mmHg)	47±9	49±15	0.29
Venoarterial carbon dioxide tension difference (mmHg)	3.8±2.0	6.1±2.7	<0.0001
$\Delta PCO_2/C_{(a\text{-}v)}O_2$	1.1±0.6	2.0±0.9	<0.0001
Arterial pH	7.36±0.06	7.24±0.11	<0.0001
Lactate (mmol/l)	1.3±0.4	6.4±6.1	<0.0001

Table 2 Correlation between O_2- and CO_2-derived parameters and arterial lactate concentration ($\Delta PCO_2/C_{(a\text{-}v)}O_2$ venoarterial carbon dioxide tension difference/ arteriovenous oxygen content difference)

Parameter	Correlation coefficient (r)	p
Arterial oxygen saturation	–0.01	0.94
Mixed venous oxygen saturation	0.14	0.09
Oxygen delivery	–0.13	0.10
Arteriovenous oxygen content difference	–0.26	0.01
Oxygen consumption	–0.35	<0.0001
Oxygen extraction ratio	–0.16	0.05
Arterial carbon dioxide tension	–0.26	<0.01
Venoarterial carbon dioxide tension difference	0.28	<0.01
Mixed venous carbon dioxide tension	–0.20	0.01
$\Delta PCO_2/C_{(a\text{-}v)}O_2$	0.57	<0.0001

was obtained between $\Delta PCO_2/C_{(a\text{-}v)}O_2$ ratio and arterial lactate level (r=0.57, p<0.0001). Table 2 summarizes the correlation coefficients between the main O_2- and CO_2-derived parameters and arterial lactate levels.

Figure 1 shows the ROC curves for the $\Delta PCO_2/C_{(a\text{-}v)}O_2$ ratio, ΔPCO_2, S_vO_2, and $C_{(a\text{-}v)}O_2$, constructed to test the value of each parameter to predict hyperlactatemia. The area under the ROC curves was 0.85±0.03, 0.75±0.04, 0.49±0.05, and 0.38±0.05 for $\Delta PCO_2/C_{(a\text{-}v)}O_2$ ratio, ΔPCO_2, S_vO_2, and $C_{(a\text{-}v)}O_2$, respectively. The area for $\Delta PCO_2/C_{(a\text{-}v)}O_2$ ratio was significantly greater than that for each other parameter (p<0.05). From the ROC curve an optimal cutoff value of 1.4 was determined for $\Delta PCO_2/C_{(a\text{-}v)}O_2$ ratio to predict the presence of hyperlactatemia. Using this threshold value of 1.4 the $\Delta PCO_2/C_{(a\text{-}v)}O_2$ ratio predicted the presence of hyperlactatemia with a sensitivity of 79%, a specificity of 84%, a positive predictive value of 86%, and a negative predictive value of 80%.

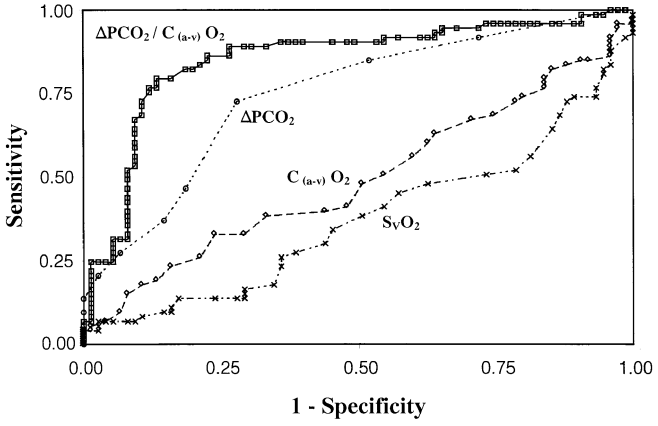

Fig. 1 Receiver operating characteristic curves of the studied O_2- and CO_2-derived parameters for the prediction of hyperlactatemia (arterial lactate level ≥2 mmol/l)

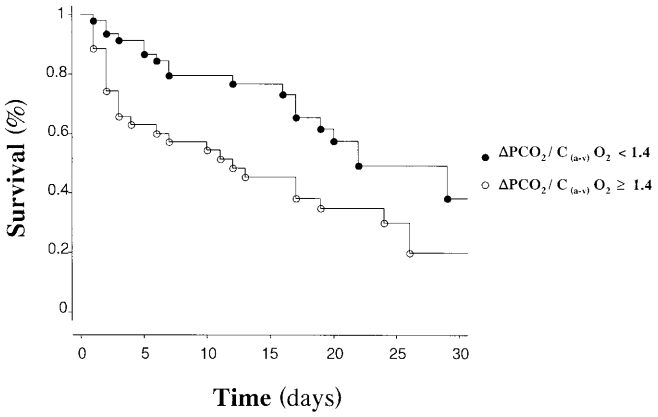

Fig. 2 Kaplan-Meier estimates for 1-month overall survival in patients with venoarterial carbon dioxide tension difference/arteriovenous oxygen content difference ratio ($\Delta PCO_2/C_{(a-v)}O_2$) <1.4 and patients with $\Delta PCO_2/C_{(a-v)}O_2$ ratio ≥1.4 on the first set of measurements

When we considered only the first set of measurements obtained in each of the 89 patients after inserting the catheter, we found that the arterial lactate level was 2 mmol/l or greater in 42 patients and lower than 2 mmol/l in 47. All the 42 patients with increased arterial lactate received vasoactive drugs (dopamine or norepinephrine and/or dobutamine). Of the 47 patients with normal arterial lactate 38 received vasoactive drugs. The mortality rate was higher in the Lac^+ group (32/42 patients) than in the Lac^- group (20/47 patients; 76% vs. 42%, p=0.002).

Still considering only the first set of measurements (n=89), we found the following: (a) $C_{(a-v)}O_2$ and ΔPCO_2 were significantly but poorly correlated to the arterial lactate level (r=0.26 and r=0.22, respectively), while a very significant (p<0.0001) correlation was still obtained between the $\Delta PCO_2/C_{(a-v)}O_2$ ratio and the arterial lactate level (r=0.48). (b) A $\Delta PCO_2/C_{(a-v)}O_2$ ratio greater than 1.4 predicted the existence of increased arterial lactate concentration (>2 mmol/l) with a sensitivity of 74%, a specificity of 85%, a positive predictive value of 82% and a negative predictive value of 78%. In terms of prognostic correlates, we found that (a) the arterial lactate level was lower in 30-day survivors (2.0±1.5 mmol/l) than in nonsurvivors (5.4±6.1 mmol/l, p<0.01), and (b) there were no significant differences between 30-day survivors (n=37) and nonsurvivors (n=52) with regard to ΔPCO_2 (5.1±6.9 vs. 4.8±7.1 mmHg, p=0.61) and $C_{(a-v)}O_2$ (3.6±0.9 vs. 3.3±1.9, p=0.21), while the $\Delta PCO_2/C_{(a-v)}O_2$ ratio tended to be higher in 30-days nonsurvivors than in survivors (1.7±1.0 vs. 1.3±0.5; p=0.07). The Kaplan-Meier overall survival estimate at 1 month was significantly greater for patients with a $\Delta PCO_2/C_{(a-v)}O_2$ ratio lower than 1.4 on the first set of measurements (38±10%) than for patients with a $\Delta PCO_2/C_{(a-v)}O_2$ ratio of 1.4 or higher (20±8%, p<0.01; Fig. 2).

Discussion

Oxygen-derived parameters are poorly correlated with anaerobic metabolism [12, 13], and therefore they cannot be used as prognostic indicators in critically ill patients [14]. Indeed, other important determinants such as metabolic needs and O_2 extraction capabilities interfere with tissue hypoxia. This leads to difficulty in interpreting O_2-derived parameters, particularly in detecting global tissue hypoxia. For instance, a low VO_2 can be due either to tissue hypoxia whatever its mechanism (e.g., sepsis, heart failure, hypovolemia) or to a reduced O_2 demand without hypoxia. Low values of S_vO_2 can be associated either with global tissue hypoxia when cardiac output and/or hemoglobin concentration are acutely reduced or with aerobic conditions if compensatory mechanisms of O_2 extraction had time to occur as in chronic low cardiac output syndrome [15]. On the other hand, normal or even high values of S_vO_2 can be associated with profound tissue hypoxia related to severe impairment of O_2 extraction capabilities [12, 13]. Similar conclusions can be drawn for O_2ER and $C_{(a-v)}O_2$. Accordingly, we did not find significant differences between the Lac^+ and Lac^- groups with regard to S_vO_2, DO_2, $C_{(a-v)}O_2$, or O_2ER. Furthermore, correlation coefficients between these O_2-derived parameters and arterial lactate concentration were all very low (<0.25; Table 2). Only VO_2 was lower in the Lac^+ group than in the Lac^- group (Table 1). This could be explained by VO_2/DO_2 dependence which was likely to occur in the Lac^+ group, although O_2 conformance cannot be excluded in these severely ill patients [16]. It is unlikely that the difference in VO_2 between the two groups could be explained by drug-induced differences in O_2 demand, since (a) sedative drugs which are able to decrease O_2 demand were given to all patients and not only to the most severe ones, and (b) catecholamines which increase O_2 demand were given to almost patients and particularly to those in the Lac^+ group.

As an approximate of the difference between venous and arterial CO_2 contents, ΔPCO_2 is proportional to CO_2 production and inversely related to cardiac output (Fick equation). Anaerobic CO_2 production is thought to occur when tissue hypoxia is present, mostly because of buffering of bicarbonate ions by the protons produced in excess secondary to the hydrolysis of adenosine triphosphate [5]. Therefore ΔPCO_2 has been proposed as a marker of tissue hypoxia [17, 18]. In this regard, Van der Linden et al. [19] in an animal model of acute hemorrhage found a significant correlation between blood lactate levels and ΔPCO_2 during the bleeding protocol (r=0.84, p<0.001). Marked and progressive increases in

ΔPCO_2 were observed during the VO_2/DO_2 dependent period in another experimental model of progressive blood flow reduction [20]. During human cardiac arrest and cardiopulmonary resuscitation high values of ΔPCO_2 have also been reported [17, 21]. However, in all these studies tissue hypoxia was secondary to the reduction in blood flow. Considering the Fick equation, low blood flow can result in a widening of ΔPCO_2 even if no additional CO_2 production occurs. This is explained by the CO_2-stagnation phenomenon [22]. Because of the slowing of transit time a greater than normal addition of CO_2 per unit of blood traversing the efferent microvessels tends to generate hypercapnia in the venous circulation. In this regard, increased values ΔPCO_2 have been reported in patients with low cardiac output without global tissue hypoxia as demonstrated by VO_2/DO_2 independence and normal blood lactate levels [23]. This point emphasizes the lack of specificity of ΔPCO_2 in detecting tissue hypoxia. In the present study 11 patients exhibited normal lactate levels but higher than normal (>6 mmHg) ΔPCO_2 values. On the other hand, normal ΔPCO_2 can be associated with global tissue hypoxia in normo- or hyperdynamic shock states, as evidenced by several clinical studies [2, 3, 4]. This is explains by the fact that high venous blood flow is sufficiently high to clear the CO_2 produced by the hypoxic cells, even if the production of CO_2 is higher than normal because of occurrence of anaerobic CO_2 generation [22]. This point was recently demonstrated in an isolated limb dog model [24]. In that study hypoxic conditions were created either by reducing flow ("ischemic" hypoxia) or by reducing FIO_2 while maintaining a constant flow [24]. Interestingly, ΔPCO_2 increased only in the "ischemic" hypoxia group [24]. In the other group ΔPCO_2 did not change despite induction of profound tissue hypoxia, probably because of the maintained flow [24]. This finding emphasizes the poor sensitivity of ΔPCO_2 in detecting tissue hypoxia.

In the present study we postulated that the ratio of VCO_2/VO_2 and thus its surrogate, the ratio of $\Delta PCO_2/C_{(a-v)}O_2$, would detect global tissue hypoxia. Indeed, under these conditions VO_2 should decrease, and thus aerobic CO_2 production should also decrease. Because of the anaerobic generation of CO_2, global CO_2 production should decrease less than VO_2, and the ratio of $\Delta PCO_2/C_{(a-v)}O_2$ should therefore increase. Findings from experimental studies are consistent with this hypothesis [25, 26]. Groeneveld et al. [25] reported a lower decrease in VCO_2 (by 21±2%) than in VO_2 (by 27±2%) after reduction in cardiac output following positive end-expiratory pressure in pigs. Cohen et al. [26] demonstrated in an experimental graded hemorrhage in swine that the airway respiratory quotient (VCO_2/VO_2) increased from 0.87±0.07 to 1.16±0.07 at the peak hemorrhage because of a smaller reduction in VCO_2 than of VO_2 [26]. After restitution of blood the airway respiratory quotient returned to its baseline value [26].

In our study we used the $\Delta PCO_2/C_{(a-v)}O_2$ ratio as a surrogate of the respiratory quotient by assuming that ΔPCO_2 is proportional to the venoarterial CO_2 difference. This assumption is reasonable over the usual range of the CO_2 contents for which the relationship between PCO_2 and CO_2 content is linear [27]. Despite this approximation and the potential error of measurement of PCO_2 (±1 mmHg) [28], our results are quite consistent with our hypothesis. Indeed the $\Delta PCO_2/C_{(a-v)}O_2$ ratio was higher in the Lac^+ group than in the Lac^- group, and there was a good correlation between $\Delta PCO_2/C_{(a-v)}O_2$ ratios and arterial lactate levels. In addition, a value of the $\Delta PCO_2/C_{(a-v)}O_2$ ratio above 1.4 predicted an increased arterial lactate level with high positive and negative predictive values. None of the other O_2- or CO_2-derived parameters obtained from the pulmonary artery catheter reached the same degree of prediction of hyperlactatemia. Finally, from our data the $\Delta PCO_2/C_{(a-v)}O_2$ ratio seems to have a better prognostic value than ΔPCO_2 or $C_{(a-v)}O_2$ when considered separately

From our hypothesis $\Delta PCO_2/C_{(a-v)}O_2$ ratio is assumed to indicate the presence of anaerobic CO_2 generation and thus the occurrence of anaerobic metabolism, whatever the blood flow conditions. However, we found a good (r=0.57) but not an excellent correlation between $\Delta PCO_2/C_{(a-v)}O_2$ ratio and arterial lactate concentration. This can be explained by at least three reasons: (a) The measurement of PCO_2 may suffer from potential risks of error [28]. (b) Our assumption of the linearity but difference between ΔPCO_2 and CO_2 contents could be erroneous in some cases. First, the dissociation curve of CO_2 is not strictly linear but rather curvilinear, although much more linear than the oxygen dissociation curve [6]. Second, this relationship can also be influenced by the oxygen saturation of blood so that the lower the saturation of hemoglobin with oxygen the larger the CO_2 content for a given PCO_2 (Haldane effect). In this extent, as stressed by Jakob et al. [29], changes in ΔPCO_2 might not parallel changes in CO_2 contents differences under conditions of very low values of SvO_2 (<30%). However, although the Haldane effect could be significant in some areas with low local venous oxygen saturation, it is unlikely that it would play a major role at the level of mixed venous blood where oxygen saturation is rarely extremely low. In our study SvO_2 was never observed below 40% in our patients. (c) Increased arterial lactate level may not reflect tissue hypoxia in critically ill patients. Indeed, arterial lactate concentration is the result of lactate production – thought to indicate the presence of anaerobic metabolism – and lactate clearance that can be slower in patients with sepsis [7] and in those with liver and/or kidney dysfunction [8, 9]. This last point may account for the slow response of arterial lactate level to significant hemodynamic changes frequently observed in critically ill patients. Moreover, in septic patients increased arterial lactate could be sec-

ondary to sepsis-induced dysfunction of pyruvate dehydrogenase even in the absence of significant anaerobic metabolism [9, 30].

Finally, we must underline out that the retrospective nature of this study may in itself represent a methodological limitation in interpreting the data. This point should incite investigators to undertake further prospective studies to well delineate the field of clinical use of the $\Delta PCO_2/C_{(a-v)}O_2$ ratio in critically ill patients.

Conclusion

The $\Delta PCO_2/C_{(a-v)}O_2$ ratio seems to be a more reliable marker of global anaerobic metabolism than the other O_2- and CO_2-derived parameters obtained invasively. Its simple calculation would be useful for clinicians while interpreting pulmonary artery catheter data. Whether clinicians could more rapidly adapt a patient's therapy on the basis of the course of $\Delta PCO_2/C_{(a-v)}O_2$ ratio than by monitoring arterial lactate levels requires further studies.

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