

Correlation between Central Venous - Arterial Carbon Dioxide Tension Gradient and Oxygen Delivery Changes Following Fluid Therapy

Alexandre Yazigi*, Hicham Abou-Zeid, Fadia Haddad, Samia Madi – Jebara, Gemma Hayek and Khalil Jabbour

Department of anesthesia and surgical intensive care, Hotel-Dieu de France hospital, Saint-Joseph University, Beirut, Lebanon

Abstract

Background: Central venous-arterial carbon dioxide (CVA-CO₂) tension gradient was related to low cardiac output after coronary surgery. The objective of this study was to assess the correlation between CVA-CO₂ tension gradient and oxygen delivery (DO₂) changes following fluid therapy in coronary surgery.

Methods: A prospective interventional study was conducted in a cardiac surgery intensive care unit. Forty consecutive sedated and mechanically ventilated adult patients, with a cardiac index < 2.3 L/min/m² and a pulmonary artery occlusion pressure ≤ 12 mmHg following coronary surgery, were included. All patients received a 500 ml bolus of an isotonic crystalloid solution over 20 min. Concomitant hemodynamic parameters, arterial and central venous blood gases were measured before (T₀) and after (T₁) volume loading. Means were compared by Student's test and correlations by Spearman coefficient. P ≤ 0.05 was considered to be significant.

Results: CVA-CO₂ gradient decreased (12.6 ± 3.0 vs 10.2 ± 3.7 mmHg; p = 0.01) and DO₂ increased (312 ± 57 vs 357 ± 81 l/min/m²; p = 0.001) significantly from T₀ to T₁. The correlation between CVA-CO₂ gradient changes and DO₂ changes was negative and statistically significant (r = -0.38; p=0.015).

Conclusion: CVA-CO₂ gradient and DO₂ changes were inversely and significantly correlated in patients receiving fluid therapy following coronary surgery. In this context, CVA-CO₂ gradient changes could be used as an indicator to guide volume loading and to assess its effect on DO₂.

Keywords: Central venous carbon dioxide tension; Central venous-arterial carbon dioxide tension gradient; oxygen delivery; fluid therapy; coronary surgery

Introduction

Venous hypercapnia during circulatory failure is attributed to reduction in oxygen delivery and impairment of tissue carbon dioxide clearance [1]. Several studies in animal models showed that mixed venous - arterial carbon dioxide (MVA-CO₂) tension gradient was increased when oxygen delivery to tissues (DO₂) was experimentally diminished by positive end expiratory pressure, cardiac tamponade or bleeding [2,3,4]. Bakker et al reported that septic patients with a MVA-CO₂ tension gradient above 6 mmHg had a significantly lower DO₂ [5]. Brandt et al showed an inverse correlation (r = -0.74) between DO₂ and MVA-CO₂ tension gradient in acutely ill post surgical patients [6]. DO₂ was also reported as a factor correlated with MVA-CO₂ tension gradient following coronary surgery under cardiopulmonary bypass [7]. These data suggest that MVA-CO₂ gradient is clinically useful in assessing oxygen delivery to tissues. However, MVA-CO₂ tension gradient measurement is obtained only from a correctly positioned pulmonary artery catheter. The insertion of these catheters is associated with significant risks, increased health care costs and its risk / benefit ratio is a matter of debate [8,9,10].

Central venous CO₂ tension, obtained in a less risky and costly manner from a central venous catheter, may be an interesting alternative to mixed venous CO₂ tension measurement. Substantial differences between central venous and arterial CO₂ (CVA-CO₂) tension were found in critically ill patients [11,12] as well as during cardiopulmonary resuscitation in a canine model [13] and in humans [14,15]. However, the correlation between CVA-CO₂ tension gradient and DO₂ has not been assessed yet. A significant correlation between the changes of CVA-CO₂ tension gradient and DO₂ would make CVA-CO₂ gradient a valuable indicator to guide volume loading and to

assess its impact on DO₂ following coronary surgery. The aim of this study was to analyze the correlation between CVA-CO₂ tension gradient and DO₂ changes in patients receiving fluid therapy following coronary surgery.

Methods

This prospective observational study was approved by our institutional review board and all participants gave an informed written consent. Two hundred sixty adult patients underwent elective coronary surgery in our department over a period of 6 months. Anesthesia was induced and maintained using etomidate 0.3 mg/kg, pancuronium 0.2 mg/kg, midazolam 0.1 mg/kg/h, fentanyl 5µg/Kg/h and isoflurane up to 1 minimum alveolar concentration. Invasive hemodynamic monitoring was achieved with a 20 gauge radial artery catheter (Plastimed, Saint-Lieu-la-Forêt, France) and a 7.5 Fr 2nd pulmonary artery catheter (Edwards Lifesciences, Irvine, CA, USA) with a proximal port positioned in the superior vena cava. Cardiopulmonary bypass was performed under hemodilution and mild hypothermia, using a membrane oxygenator primed with a

***Corresponding author:** Alexandre Yazigi, Department of anesthesia and surgical intensive care, Hotel-Dieu de France hospital, Saint-Joseph University, Beirut, Lebanon, Tel: 961-3-440721; E-mail: ritalama@idm.net.lb

Received November 14, 2010; **Accepted** December 09, 2010; **Published** December 13, 2010

Citation: Yazigi A, Abou-Zeid H, Haddad F, Madi-Jebara S, Hayek G, et al. (2010) Correlation between Central Venous - Arterial Carbon Dioxide Tension Gradient and Oxygen Delivery Changes Following Fluid Therapy. J Anesth Clin Res 1:110. doi:10.4172/2155-6148.1000110

Copyright: © 2010 Yazigi A, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



crystalloid solution. Myocardial preservation was achieved with a cold cardioplegia solution containing 30 mM of potassium per litre. Coronary anastomoses were performed under total aortic cross clamping.

At the end of surgery, the intraoperative anesthetic perfusion regiments of midazolam, fentanyl and vecuronium were maintained and patients were transferred to the cardiac surgery unit. Arterial, pulmonary artery and central venous pressures were displayed on an electronic monitor (Hellige SMU 611, Freiburg, Germany) and measured at end-expiration. Cardiac output was obtained by the thermodilution technique. Cardiac index was computed by averaging 3 consecutive measurements of cardiac output divided by the patient body surface area. The position of the proximal and distal ports of the pulmonary artery catheter was confirmed by the transduced waveforms and by chest radiography. Patients were consecutively included in the study if they had, at the time of admission in the cardiac surgery unit, a cardiac index < 2.3 L/min/m² associated with a pulmonary artery occlusion pressure and a central venous pressure ≤ 12 mmHg. Exclusion criteria were: a left ventricular ejection fraction $\leq 40\%$, intracardiac shunting, valvular disease, active bleeding, inotropic drugs or hemodynamic mechanical assistance. Patients included in the study received a 500 ml bolus of an isotonic crystalloid solution administrated over 20 min. Fluid therapy was stopped if pulmonary artery occlusion pressure reached 18 mmHg.

Concomitant hemodynamic and blood gases measurements were recorded immediately before starting fluid therapy (T0) and repeated at the end of the loading manoeuvre (T1). Blood samples of 2 ml were simultaneously obtained from the radial artery catheter and from the central venous catheter after withdrawal of dead space blood and flushing fluid. All samples were withdrawn over 30 sec, using a low-negative pressure technique. Samples were immediately analyzed for blood gas variables, using a blood gas analyzer (ABL, Radiometer, Copenhagen, Denmark) calibrated according to standards supplied by the manufacturer. Hemodynamic measurements included cardiac index (CI), stroke volume index (SVI), mean arterial pressure (MAP), mean pulmonary artery pressure (MPAP), central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP) and systemic vascular resistance index (SVRI). Concomitant arterial hemoglobin concentration (Hg) and rectal temperature were also recorded. At the 2 measurement times T0 and T1, DO₂ was calculated as: $DO_2 \text{ (ml/min/m}^2\text{)} = CI \times 10 \times (Hg \times SaO_2 \times 1.36 + PaO_2 \times 0.003)$. During the study period, patients were sedated with midazolam 0.1 mg/Kg/h and paralyzed with vecuronium 0.02 mg/Kg/h. Mechanical ventilation was provided with a tidal volume of 10 ml / kg, a FIO₂ of 60 % and a respiratory rate of 12 / min. Body temperature was maintained with a warming blanket.

On the basis of a preliminary investigation that showed a correlation coefficient of 0.4 between CVA-CO₂ gradient and DO₂ changes following fluid therapy, it was determined that a sample of 36 patients is needed to demonstrate a significant correlation, with a power of 80 % and an α coefficient of 0.05, between the 2 primary evaluated parameters in our study. All data were checked for normal distribution by One-Sample Kolmogorov-Smirnov test and are presented as mean $\pm$ standard deviation unless otherwise indicated. Variables were compared by paired Student's t test and Wilcoxon Signed test by ranks, as needed. The changes in individual values of CVA-CO₂ tension gradient and DO₂ were recorded as Δ CVA-CO₂ gradient and Δ DO₂. The association between Δ CVA-CO₂ gradient and Δ DO₂ was evaluated by Spearman correlation coefficient. The changes in individual values of mean arterial pressure and central

venous pressure from T0 to T1 were expressed as Δ MAP and Δ CVP. The correlations between Δ DO₂ and Δ MAP or Δ CVP were also evaluated by Spearman correlation coefficient. Statistical evaluations were performed using the SPSS (version 13.0) statistical package. $P \leq 0.05$ was considered to be statistically significant.

Results

Forty consecutive adult patients, 25 male and 15 female, requiring fluid therapy upon their admission in CSU, were included in this study. Acute physiology and chronic health evaluation II (APACHE) score ranged between 12 and 16. All patients responded to volume loading by increasing CI above 15 % of its base line value without raising pulmonary artery occlusion pressure over 18 mmHg. Hemodynamic parameters, rectal temperature and arterial haemoglobin concentration at T0 and T1 are presented in (Table 1). Cardiac index, central venous pressure and pulmonary artery occlusion pressure were higher at T1 compared to T0. Systemic vascular resistance index and arterial hemoglobin concentration were lower at T1 compared to T0.

	T0	T1	p
CI (l/min/m ²) SVI (ml/m ²)	1.8 $\pm$ 0.2 21 $\pm$ 2.5	2.2 $\pm$ 0.3 26 $\pm$ 3	0.001 0.02
MAP (mmHg)	80 $\pm$ 11	85 $\pm$ 12	0.580
PAOP (mmHg)	8.0 $\pm$ 3.0	10.3 $\pm$ 2.9	0.001
PVC (mmHg)	5.2 $\pm$ 3.0	7.1 $\pm$ 3.2	0.001
SVRI (dyne.sec.cm ⁵ .m ²)	3015 $\pm$ 634	2580 $\pm$ 605	0.001
HR (beats / min)	85 $\pm$ 11	92 $\pm$ 8	0.138
Temperature(°C)	36.0 $\pm$ 0.8	36.2 $\pm$ 0.7	0.158
Hemoglobin (g/dl)	11.7 $\pm$ 1.4	11.0 $\pm$ 1.2	0.016

Data expressed in mean $\pm$ standard deviation; T0 = before fluid therapy; T1 = after fluid therapy. CI = cardiac index. SVI = stroke volume index. MAP = mean arterial pressure. PAOP = pulmonary artery occlusion pressure. CVP = central venous pressure. SVRI = systemic vascular resistance index. HR = heart rate.

Table 1: Hemodynamic parameters, rectal temperature and arterial haemoglobin concentration at T0 and T1.

	T0	T1	p
PaO ₂ (mmHg)	200 $\pm$ 80	220 $\pm$ 85	0.311
PaCO ₂ (mmHg)	34.1 $\pm$ 3.6	34.5 $\pm$ 4.1	0.819
PcvO ₂ (mmHg) ScvO ₂ (%)	30.1 $\pm$ 4.8 53 $\pm$ 8	31.5 $\pm$ 5.0 58 $\pm$ 9	0.10 0.01
PcvCO ₂ (mmHg)	46.8 $\pm$ 4.4	44.6 $\pm$ 5.3	0.03
CVA-CO ₂ tension gradient (mmHg)	12.6 $\pm$ 3.0	10.2 $\pm$ 3.7	0.01

Data expressed in mean $\pm$ standard deviation; T0 = before fluid therapy; T1 = after fluid therapy. CVA-CO₂ tension = central venous-arterial carbon dioxide tension.

Table 2: Arterial and central venous oxygen and carbon dioxide tension at T0.

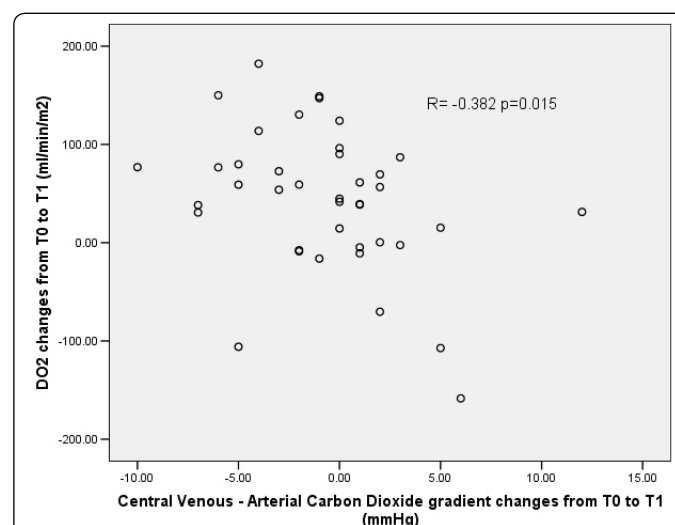


Figure 1: The correlation between CVA-CO₂ tension gradient and DO₂ changes from T0 to T1.

Arterial and central venous oxygen and carbon dioxide tension at T0 and T1 are presented in (Table 2). There was a significant decrease of CVA-CO₂ tension gradient at T1 compared to T0. Oxygen delivery increased significantly from T0 to T1 (312 ± 57 ml/min/m² vs 357 ± 81 ml/min/m²; $p = 0.001$). The negative correlation between Δ CVA-CO₂ gradient and Δ DO₂, shown in (Figure 1), was moderate but statistically significant ($r = -0.38$; $p = 0.015$). Changes in DO₂ did not correlate with CVP ($r = 0.1$; $p = 0.4$) or with Δ MAP ($r = 0.05$; $p = 0.6$).

Discussion

The current study assessed CVA-CO₂ tension gradient and DO₂ in patients presenting a low cardiac index and filling pressures following coronary artery bypass grafting. This hemodynamic scenario is common after cardiac surgery and is caused, at least in part, by a reduced vascular volume and blood sequestration into the venous compartment [16]. The management of this hemodynamic scenario usually includes fluid therapy to expand the intravascular compartment and increase venous return [16]. Our study found a CVA-CO₂ tension gradient of 12.6 ± 3 mmHg in patients with a low CI following coronary surgery. This gradient was larger than physiological venous-arterial CO₂ tension differences [1] and was previously reported in several categories of critically ill patients [11,12,17,18]. The gradient decreased after fluid therapy and its changes correlated moderately with DO₂ changes.

The large CVA-CO₂ tension gradient in our study population may be explained by two mechanisms related to circulatory failure: 1- hydrogen ions generated by anaerobic lactic acidosis are buffered by bicarbonate and lead to an increased CO₂ production; 2- reduced pulmonary blood flow is associated, in ventilated patients and according to the Fick equation, to a decreased PaCO₂, a diminished venous CO₂ clearance and an increased venous CO₂ tension. A widened CVA-CO₂ tension difference was documented in several categories of critically ill patients [11,12,17,18]. The effect of cardiopulmonary bypass on CVA-CO₂ gradient was not reported. Takami et al measured mixed venous - arterial carbon dioxide tension gradient following cardiopulmonary bypass in 140 adult patients and found a range between 7.7 and 15.7 mmHg [7]. Furthermore, mixed venous- arterial carbon dioxide gradient was significantly linked to bypass duration [7].

Our study showed a negative and statistically significant correlation coefficient between Δ CVA-CO₂ tension gradient and Δ DO₂ following fluid therapy. Oxygen delivery is a compound parameter related to cardiac index and arterial oxygen content. Previous studies showed that CVA-CO₂ tension gradient inversely correlate with cardiac index [17-20]. Cuschieri et al reported, in 83 consecutive intensive care unit patients, a negative correlation coefficient of 0.89 between CVA-CO₂ gradient and cardiac index [19]. Ho et al obtained a correlation coefficient of -0.38 between CVA-CO₂ gradient and cardiac index in 16 patients in circulatory failure [20]. Cardiac index and CVA-CO₂ gradient were also found to be inversely correlated ($r = -0.57$) in 50 consecutive septic shock patients [17]. Venous-arterial CO₂ tension difference is not significantly affected by arterial oxygen content, the second component of tissue oxygen delivery. It was shown, in an in situ vascularly isolated dog limb, that venous-arterial CO₂ tension difference remains stable following arterial oxygen desaturation [21]. Dubin et al reported, in another animal model, that mixed venoarterial and mesenteric venoarterial CO₂ tension gradients did not change significantly when DO₂ was decreased by hemodilution [22]. The correlation between CVA-CO₂

tension gradient and DO₂ changes in our study was only moderate because venous-arterial CO₂ tension gradient depends on a number of other factors than tissue perfusion. These factors include CO₂ production and CO₂ haemoglobin dissociation curve which is affected by acidosis, temperature and the Halden effect [23,24]. Ho et al reported that cardiac index accounted for only 21% of the CVA-CO₂ gradient variability [20].

The results of the current study have clinical implications. An insufficient increase of DO₂ following fluid therapy may perpetuate low tissue perfusion [16]. In a resource limited context where monitoring techniques as pulmonary artery catheters, oesophageal Doppler or pulse pressure variation recording might not be available, measurement of Δ CVA-CO₂ gradient can be used as an alternative to assess the impact of volume loading on DO₂. Its ability as a marker of volume responsiveness is higher than classic hemodynamic parameters as MAP or CVP. An insufficient decrease in CVA-CO₂ tension gradient after volume expansion may indicate the need of additional fluid or alternative therapies as inotropic drugs. The clinical setting of our investigation was limited to cardiosurgical patients. More studies are needed to evaluate how Δ CVA-CO₂ gradient could be used to assess the impact of hemodynamic therapeutic modalities in various types of critically ill patients. Recently, Vallée et al showed that in resuscitated septic shock patients, the persistence of a CVA-CO₂ tension gradient above 6 mmHg indicated the need of further therapies [17].

The major limitation of the current study is that CVA-CO₂ tension gradient decreased but remained high following the fluid challenge. This may be related to the fact that patients received a single fluid bolus of 500 ml and that their cardiac index was not completely corrected. CVA-CO₂ tension gradient changes from T0 to T1, although statistically significant, were narrow and with limited clinical relevance. It would be useful to determine a cut off point of CVA-CO₂ gradient changes that predict a significant increase in DO₂ above 15 % of its base line value. Giraud et al recently reported central venous oxygen saturation (ScvO₂) changes threshold of 4% to be a marker of fluid responsiveness [25]. The design of our investigation and the narrow changes in CVA-CO₂ tension gradient did not allow this type of accurate assessment. Further researches are needed to find which CVO₂-CO₂ gradient change value will predict most accurately a significant increase in DO₂. Our study has other limitations. First, it was undertaken in sedated, paralysed and ventilated patients with a stable arterial blood gases, oxygen consumption and carbon dioxide production. As venous-arterial carbon dioxide tension gradient is partially related to carbon dioxide production and to the Halden effect on CO₂ haemoglobin dissociation curve [24], our results may not be valid in awake and spontaneously breathing patients. Second, this study was based on one set of measurements per patient receiving a single fluid bolus. Repeated measurements following several fluid boluses would provide a more accurate assessment of the correlation between CVA-CO₂ tension gradient and oxygen delivery changes after volume loading. Finally, this study did not clarify if Δ CVA-CO₂ gradient monitoring during fluid therapy was of outcome benefit in the specific context of cardiac surgery. It was shown, in septic shock patients that a CVA-CO₂ tension gradient inferior to 6 mmHg predict a high lactate clearance and a better SOFA score [17]. Bakker et al reported that non survivors had a significantly higher mixed venous-arterial carbon dioxide gradient than survivors following septic shock [5].

We conclude that, in patients receiving fluid therapy following coronary surgery, Δ CVA-CO₂ tension gradient and Δ DO₂ were inversely and moderately correlated. These data indicate that, in the

absence of a pulmonary artery catheters or an oesophageal Doppler, measurement of $\Delta\text{CVA-CO}_2$ gradient can be used to guide volume loading and to assess its effect on DO_2 . Further studies are needed to evaluate, in the context of cardiac surgery, whether CVA- CO_2 tension gradient is useful to monitor hemodynamic resuscitation and to improve clinical outcome.

References

- Johnson BA, Weil MH (1991) Redefining ischemia due to circulatory failure as dual defects of oxygen deficits and of carbon dioxide excesses. *Crit Care Med* 19:1432-1438.
- Groeneveld AB, Vermeij CG, Thijs LG (1991) Arterial and mixed venous blood acid-base balance during hypoperfusion with incremental positive end-expiratory pressure in the pig. *Anesth Analg* 73: 576-582.
- Zhang H, Vincent JL (1993) Arteriovenous differences in PCO_2 and pH are good indicators of critical hypoperfusion. *Am Rev Respir Dis* 148: 867-871.
- Van der Linden P, Rausin I, Deltell A, Bekrar Y, Gilbert E, et al (1995) Detection of tissue hypoxia by arteriovenous gradient for PCO_2 and pH in anesthetized dogs during progressive hemorrhage. *Anesth Analg* 80: 269-275.
- Bakker J, Vincent JL, Gris P, Leon M, Coffernils M, et al. (1992) Venous-arterial carbon dioxide gradient in human septic shock. *Chest* 101: 509-515.
- Brandi LS, Giunta F, Pieri M, Sironi AM, Mazzanti T (1995) Venous-arterial PCO_2 and pH gradients in acutely ill postsurgical patients. *Minerva Anestesiol* 61: 345-350.
- Takami Y, Masumoto H (2005) Mixed venous-arterial CO_2 tension gradient after cardiopulmonary bypass. *Asian Cardiovasc Thorac Ann* 13: 255-260.
- Weil MH (1998) The assault on the Swan-Ganz catheter: a case history of constrained technology, constrained bedside clinicians, and constrained monetary expenditures. *Chest* 113: 1379-1386.
- Kelso LA (1997) Complications associated with pulmonary artery catheterization. *New Horiz* 5: 259-263.
- Djaiani G, Karski J, Yudin M, Hynninen M, Fedorko L et al. (2006) Clinical outcomes in patients undergoing elective coronary artery bypass graft surgery with and without utilization of pulmonary artery catheter-generated data. *J Cardiothorac Vasc Anesth* 20: 307-310.
- Malinoski DJ, Todd SR, Slone S, Mullins RJ, Schreiber MA (2005) Correlation of central venous and arterial blood gas measurements in mechanically ventilated trauma patients. *Arch Surg* 140: 1122-1125.
- Adrogué HJ, Rashad MN, Gorin AB, Yacoub J, Madias NE (1989) Assessing acid-base status in circulatory failure. Differences between arterial and central venous blood. *N Engl J Med* 320: 1312-1316.
- Martin GB, Carden DL, Nowak RM, Tomlanovich MC (1985) Comparison of central venous and arterial pH and PCO_2 during open-chest CPR in the canine model. *Ann Emerg Med* 14: 529-533.
- Nowak RM, Martin GB, Carden DL, Tomlanovich MC (1987) Selective venous hypercarbia during human CPR: implications regarding blood flow. *Ann Emerg Med* 16: 527-530.
- McGill JW, Ruiz E (1984) Central venous pH as a predictor of arterial pH in prolonged cardiac arrest. *Ann Emerg Med* 13: 684-687.
- Bojar RM, Douglas JM, Kenneth GW (1994) Manual of perioperative care in cardiac and thoracic surgery. (2th ed), Blackwell Science, Cambridge, Massachusetts.
- Vallée F, Vallet B, Mathe O, Parraguette J, Mari A et al (2008) Central venous-to-arterial carbon dioxide difference: an additional target for goal-directed therapy in septic shock? *Intensive Care Med* 34: 2218-2225.
- Sutton RN, Wilson RF, Walt AJ (1967) Differences in acid-base levels and oxygen-saturation between central venous and arterial blood. *Lancet* 2: 748-751.
- Cuschieri J, Rivers EP, Donnino MW, et al (2005) Central venous-arterial carbon dioxide difference as an indicator of cardiac index. *Intensive Care Med* 31: 818-822.
- Ho KM, Harding R, Chamberlain J (2007) A comparison of central venous-arterial and mixed venous-arterial carbon dioxide tension gradient in circulatory failure. *Anaesth Intensive Care* 35: 695-701.
- Vallet B, Teboul JL, Cain S, Curtis S (2000) Venoarterial CO_2 difference during regional ischemic or hypoxic hypoxia. *J Appl Physiol* 89: 1317-1321.
- Dubin A, Estenssoro E, Murias G, Pozo MO, Sottile JP et al (2004) Intramucosal-arterial PCO_2 gradient does not reflect intestinal dysoxia in anemic hypoxia. *J Trauma* 57: 1211-1217.
- Lamia B, Monnet X, Teboul JL (2006) Meaning of arterio-venous PCO_2 difference in circulatory shock. *Minerva Anestesiol* 72: 597-604.
- Giovannini I, Chiarla C, Boldrini G, Terzi R (1999) Quantitative assessment of changes in blood CO_2 tension mediated by the Haldane effect. *J Appl Physiol* 87: 862-66.
- Giraud R, Siegenthaler N, Gayet-Ageron A, Combescure C, Romand JA, et al. (2010) ScvO_2 as a marker to define fluid responsiveness. *J Traum* 27.