

Prognostic significance of central venous-to-arterial carbon dioxide difference during the first 24 hours of septic shock in patients with and without impaired cardiac function

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Abstract

Objective: To investigate the prognostic significance of central venous-to-arterial carbon dioxide difference (cv-art CO₂ gap) during septic shock in patients with and without impaired cardiac function.

Methods: We performed a prospective cohort study in 10 French intensive care units. Patients suffering from septic shock were assigned to the impaired cardiac function group ('cardiac group', n=123) if they had atrial fibrillation (AF) and/or left ventricular ejection fraction (LVEF) <50% at study entry and to the non-cardiac group (n=240) otherwise.

Results: Central venous and arterial blood gases were sampled every 6 h during the first 24 h to calculate cv-art CO₂ gap. Patients in the cardiac group had a higher cv-art CO₂ gap [at study entry and 6 and 12 h (all P<0.02)] than the non-cardiac group. Patients in the cardiac group with a cv-art CO₂ gap >0.9 kPa at 12 h had a higher risk of day 28 mortality (hazard ratio=3.18; P=0.0049). Among the 59 patients in the cardiac group with mean arterial pressure (MAP) ≥65 mm Hg, central venous pressure (CVP) ≥8 mm Hg and central venous oxygen saturation (ScvO₂) ≥70% at 12 h, those with a high cv-art CO₂

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gap (>0.9 kPa; $n=19$) had a higher day 28 mortality (37% vs. 13%; $P=0.042$). In the non-cardiac group, a high cv-art CO_2 gap was not linked to a higher risk of day 28 death, whatever the threshold value of the cv-art CO_2 gap.

Conclusion: Patients with septic shock and with AF and/or low LVEF were more prone to a persistent high cv-art CO_2 gap, even when initial resuscitation succeeded in normalizing MAP, CVP, and ScvO_2 . In these patients, a persistent high cv-art CO_2 gap at 12 h was significantly associated with higher day 28 mortality.

Key words: blood gas analysis; septic shock; central venous-arterial CO_2 difference

Editor's key points

- The difference between venous and arterial pCO_2 can reflect the adequacy of cardiac output and tissue perfusion and has been associated with worse outcomes in sepsis, but the influence of co-existing cardiac dysfunction is unknown.
- In this study of patients with sepsis, the veno-arterial pCO_2 difference was higher in those with cardiac dysfunction and persisted despite resuscitation.
- Despite restoration of other cardiovascular variables, a high veno-arterial pCO_2 difference at 12 h was associated with increased mortality.
- In contrast, the veno-arterial pCO_2 difference was lower in patients without overt cardiac dysfunction and there was no relationship to outcome.
- The prognostic significance of a high veno-arterial pCO_2 difference may depend on cardiac function.

The veno-arterial difference in partial pressure of carbon dioxide (pCO_2), either calculated using mixed (mv-art CO_2 gap) or central venous blood (cv-art CO_2 gap), grossly reflects the veno-arterial difference in CO_2 content (v-art CCO_2 gap).^{1,2} This difference is inversely related to cardiac output (CO) and with tissue oxygen delivery and perfusion in case of normal or high CO .^{3,4} Interestingly, in the context of septic shock and its accompanying microcirculatory shunts,⁵ a high v-art CCO_2 gap (or mv-art CO_2 gap or cv-art CO_2 gap) may unmask tissue hypoperfusion.^{1,3,4,6,7} High values of mv-art CO_2 gap or cv-art CO_2 gap^{2,8} seem associated with poor outcome in septic shock. However, this is not yet definitely established,⁶ perhaps because these variables are imperfect surrogates for v-art CCO_2 gap and/or are worse performing than the ratio of mv-art CO_2 gap to arteriovenous difference in oxygen content [C(a-v)O_2] in detecting anaerobic metabolism.¹

An alternative explanation may lie in the well-known inverse relationship between mv-art CO_2 gap or cv-art CO_2 gap and CO: patients with impaired cardiac function are logically more prone than others to exhibit increased mv- or cv-art CO_2 gap values in stressful situations such as septic shock.⁹ However, studies that have investigated the mv- or cv-art CO_2 gap outcome relationship in septic shock patients^{3,4,7} rarely report the patients' cardiac status (e.g. a history of chronic cardiac failure).

Accordingly, our aim was to compare the temporal course and relationship to outcome of the cv-art CO_2 gap during the first 24 h of septic shock in cardiac and non-cardiac subsets of patients.

Methods

This prospective, multicentre study was a planned companion study of a previously published cohort analysis focused on

central venous oxygen saturation (ScvO_2) in septic shock carried out in 10 French medical-surgical intensive care units (ICUs).¹⁰ The Ethics Committee of the teaching hospital of Limoges, France, approved the protocol for all involved hospitals (agreement number 65-2011-11) and waived the need for prior informed consent.

Consecutive adult patients with circulatory failure of septic origin (i.e. with either severe sepsis plus hypotension, or septic shock) were included within 12 h after ICU admission as soon as they had an intra-arterial and superior vena cava (internal jugular or subclavian) catheter [see Supplementary Table S1 (available at *British Journal of Anaesthesia* online) for detailed inclusion criteria].

Measurements and data collection

Blood gas and lactate measurements were performed as soon as possible (time defined as H0) by sampling blood simultaneously from the superior vena cava through the central venous catheter and then every 6 h during a 24-h period (i.e. at H6, H12, H18 and H24) and from arterial blood at each time point.

Besides underlying chronic diseases, severity scores, and survival status at day 28, a number of clinical and laboratory variables were recorded at each time point (see the complete list in Supplementary Table S2). In addition, we collected the patient's left ventricular ejection fraction (LVEF) if measured by ultrasonography during the first 24 h of the study. No study-specific instructions were given to the clinicians regarding when to perform echocardiographic examination or how to measure LVEF.

Patients' management

Patients were managed following international and national guidelines. None of the participating ICUs had implemented systematic treatment algorithms based on ScvO_2 monitoring.

Definitions

Septic shock and severe sepsis were defined according to the definitions available at the time of the study.¹¹

To classify the patients into cardiac and non-cardiac groups we took into account only objective variables: a patient was considered as belonging to the cardiac group (i.e. as having a suspected or known impaired systolic function) if he/she had atrial fibrillation (AF) at study entry and/or a decreased LVEF $\leq 50\%$ either previously known or as observed on echocardiography (if performed) during the first 24 h of admission.

We calculated the cv-art CO_2 gap as the difference between the central venous and arterial CO_2 partial pressures measured on blood samples drawn simultaneously.

We calculated the cv-art CO_2 gap: C(a-cv)O_2 ratio in patients with available blood haemoglobin measurement and used it as

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