Review Article

Transcutaneous PCO_2 monitoring in critically ill patients: update and perspectives

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Abstract: The physiology of venous and tissue CO_2 monitoring has a long and well-established physiological background, leading to the technological development of different tissue capnometric devices, such as transcutaneous capnometry monitoring (TCM). To outline briefly, measuring transcutaneous PCO_2 ($tcPCO_2$) depends on at least three main phenomena: (I) the production of CO_2 by tissues (VCO_2), (II) the removal of CO_2 from the tissues by perfusion (wash-out phenomenon), and (III) the reference value of CO_2 at tissue inlet represented by arterial CO_2 content (approximated by arterial PCO_2, or $artPCO_2$). For this reason, there are, at present, roughly two clinical uses for $tcPCO_2$ measurement: a respiratory approach where $tcPCO_2$ is likely to estimate and non-invasively track $artPCO_2$; and a hemodynamic under-estimate use where $tcPCO_2$ can reflect tissue perfusion, summarized by a so-called "tc-art PCO_2 gap". Recent research shows that these two uses are not incompatible and could be combined. The spectrum of indications and validation studies in ICUs is summarized in this review to give a survey of the potential applications of TCM in critically ill patients, focusing mainly on its potential (micro)circulatory monitoring contribution. We strongly believe that the greatest benefit of measuring $tcPCO_2$ is not to only to estimate $artPCO_2$, but also to quantify the gap between these two values, which can then help clinicians continuously and noninvasively assess both respiratory and hemodynamic failures in critically ill patients.

Keywords: Transcutaneous capnometry; carbon dioxide monitoring; intensive care; microcirculation; shock

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Introduction

The measurement of oxygen (O_2) and carbon dioxide (CO_2) gas tension via a transcutaneous route which could non-invasively assess arterial blood gas pressures ($artPO_2$ and $artPCO_2$, respectively) was developed in the 1980s (1). For transcutaneous capnometry (measuring transcutaneous carbon dioxide gas pressure, $tcPCO_2$), sensors are based on chemical electrodes, which Dr. Severinghaus adapted for use in blood gas analysis (2-4). In respiratory failure, the evaluation of adequacy of alveolar ventilation with $artPCO_2$ remains a routine challenge. With consideration of some technical or device-related cautions, relevant interpretation of $tcPCO_2$ measurement is plausible, and can lead to reliable $artPCO_2$ estimation with transcutaneous capnometry monitoring (TCM) while limiting blood gas analysis and arterial puncture (5). Importantly, $tcPCO_2$ is also by nature and physiology a circulatory variable which is dependent on systemic and local cutaneous perfusion conditions. During circulatory failure, decoupling between $artPCO_2$ and $tcPCO_2$ occurs, leading to tissue hypercarbia unrelated to arterial PCO_2 (6-8). Interestingly, this mismatch, with

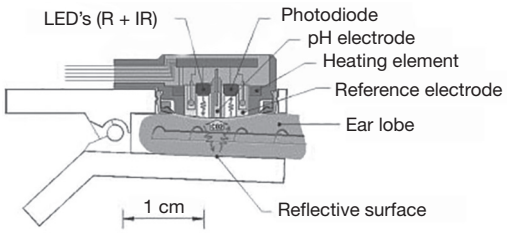

Figure 1 A transcutaneous PCO_2 sensor at the ear lobe using Stow-Severinghaus technology, from Eberhard *et al.* (2,9).

a strong physiological and clinical background, offers potential perspectives for peripheral tissue perfusion monitoring in the critically ill patient (9). Although this approach has been investigated since the 1980s, adherence remains low in daily clinical practice. Updated technology and recent clinical reports of innovative modifications including measurement at low temperature (37 ℃) and/or with thermal challenge (electrode heated from 37 ℃ to 42 ℃) have yielded promising results that may provide crucial support for the use of this tool in the field of peripheral tissue perfusion monitoring (1,10,11).

The body of indications and validation studies in ICUs are summarized in this review to give a panorama of potential applications of TCM in critically ill patients.

$tcPCO_2$ technology

Dr. Severinghaus was the first to describe the measurement of PCO_2 on human skin surfaces (3). Transcutaneous measurement of PCO_2 is based on the phenomenon of CO_2 gas diffusing very easily throughout the body tissue and skin, and can thus be detected by a sensor on the skin surface. CO_2 is measured by determining the pH of an electrolyte solution separated from the skin by a highly permeable membrane. A change in the pH is then proportional to the logarithm of PCO_2 change (*Figure 1*). By heating the skin, vasodilation with local hyperemia is produced which increases the diffusion of CO_2 and increases the delivery of arterial blood to the dermal capillary area beneath the sensor. Most of the time, the sensor is heated between 42 ℃ and 44 ℃ to create the "arterialization" of the tissue (by small arteriole and capillary dilatation) leading to an increase of arterial contribution in the signal. Overall, transcutaneous PCO_2 measurements correlate fairly well with the corresponding arterial PCO_2 values, even after applying a correcting algorithm to take into consideration the physico-chemical modifications after elevating the temperature of the sensor (2).

This electrochemical method has proven to be accurate and reliable but requires an *ex vivo* "calibration period" before placing the sensor on the skin, and a subsequent *in vivo* "equilibration period" to obtain a stable value. It should be noted that the position of the sensor at the earlobe shortens this equilibration time due to its rich vascularization and thus decreases the time response and analytic inertia during acute changes. This technical limitation has hindered the development and use of $tcPCO_2$ monitoring as a surrogate of $artPCO_2$ in current practice (1). A technology based on obtaining $tcPCO_2$ by infrared light is currently being developed to try to increase the ease and reactivity of bedside measurement (2).

$tcPCO_2$ monitoring: physiological overview

Physiology of tissue and cutaneous carbon dioxide monitoring has a long and well-established physiological background, which has been the foundation for the development of different mucosal and cutaneous capnometric devices, extensively described in recent quality reviews (1,6,9). At its core, the measurement of $tcPCO_2$ is dependent on three main phenomena:

(I) The production of CO_2 by the tissues (VCO_2);
(II) The removal of CO_2 from the tissues by perfusion (so-called "washout-out" phenomenon);
(III) The reference value of CO_2 at tissue inlet represented by arterial CO_2 content ($CaCO_2$).

For this reason, there are, at present, roughly two clinical uses for $tcPCO_2$ measurement: a respiratory use where $tcPCO_2$ is likely to non-invasively estimate and track $artPCO_2$, and a hemodynamic use where $tcPCO_2$ could reflect tissue perfusion by an evaluation of the difference between $tcPCO_2$ and $artPCO_2$, so-called "gap CO_2". The simplified physiology of TCM and the main clinical scenario reflecting these two indications are schematically illustrated in *Figure 2* (respiratory use *Figure 2A,B*, hemodynamic use *Figure 2C,D,E,F*). Additionally, we have depicted three frequent and relevant clinical issues and described them according to whether the monitoring of $tcPCO_2$ is performed with a sensor at 37 ℃ or a heated sensor at 42 ℃ to 44 ℃ (11,12). The three clinical hemodynamic situations are the following:

(I) A stable circulatory state with almost preserved tissue perfusion conditions, when $tcPCO_2$ can be interpreted as an $artPCO_2$ surrogate;

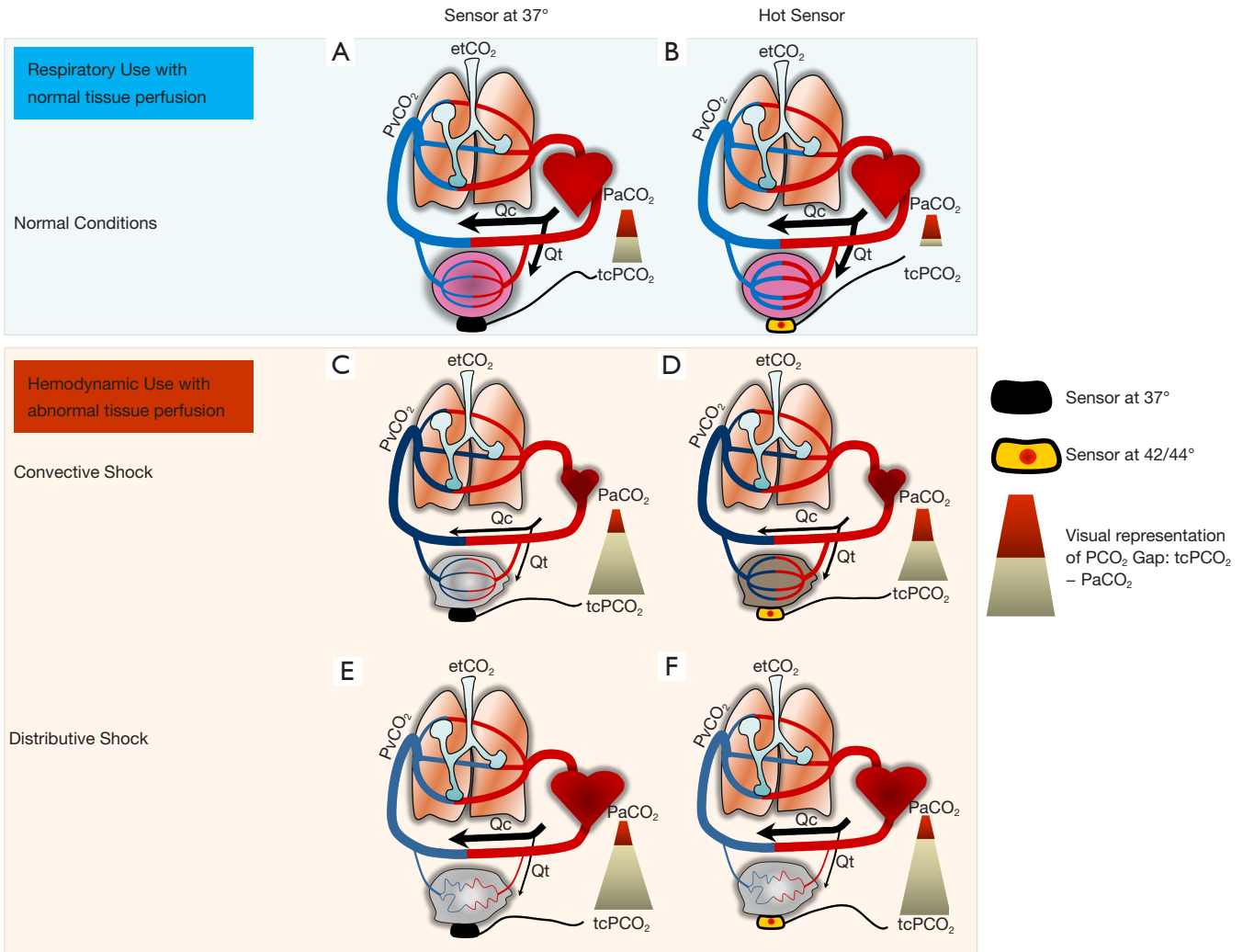

Figure 2 Pathophysiological patterns describing transcutaneous capnometry during respiratory and hemodynamic issues, resumed in schematic vignettes or panels (n=6). See text for extensive description and commentary. Qc, cardiac output; Qt, regional or tissue flow; Pa CO_2 or artPCO$_2$, arterial CO_2 tension; $PvCO_2$ or cvPCO$_2$, central-venous CO_2 tension; tcPCO$_2$, transcutaneous CO_2 tension; etCO$_2$, end-tidal CO_2 tension.

(II) An overt shock state with low cardiac output or low O_2 delivery called "convective shock", for and corresponding to core pathophysiological patterns of hypovolemic, hemorrhagic or cardiogenic shock;

(III) A "distributive shock" corresponding to a resuscitated septic shock with restored cardiac output but with an alteration of peripheral microperfusion.

Moreover, as warming the skin impacts tcPCO$_2$ value and local cutaneous blood flow, behavior of tissue hypercarbia depends on locally applied electrode temperature (1,2). For this reason, interpretation of tcPCO$_2$ measurements must take into account the temperature level (i.e., normothermia at 37 ℃ *vs.* heated conditions at 42–45 ℃) (11). The authors propose this graphic representation in order to illustrate and clarify these six "clinical and measurement situations" based on robust physiological concepts and the results of their recent work. Each illustration will be developed in more detail in the sections to follow.

tcPCO$_2$ monitoring as a surrogate of artPCO$_2$

TCM to track artPCO$_2$ variations: remind the basics

Cutaneous PCO$_2$ represents a mixture of venous, capillary, and arterial CO_2 tension values. In normal conditions,

tissue metabolism (VCO_2) is coupled with tissue perfusion. When metabolism increases, all the CO_2 produced is washed out so that the PCO_2 gap between $tcPCO_2$ and $artPCO_2$ ($_{tc\text{-}art}\Delta PCO_2$) remains constant at around 5 mmHg (*Figure 2A*) (8,9). Heating the skin from 37 ℃ to 45 ℃ increases the skin blood flow by three to four times and enhances the contribution of arterial blood flow by opening the precapillary sphincter arterioles (1,3). Also, in preserved circulatory conditions, $tcPCO_2$ with heated electrodes (42–45 ℃) will closely approximate $artPCO_2$, as heat produces the so-called "arterialization" of local blood flow in the cutaneous area where the sensor is applied (*Figure 2B*) (13-15). Two correcting factors are then applied to bring the $tcPCO_2$ value close to the value of $artPCO_2$: (I) a fixed correction is removed from the crude $tcPCO_2$ value, as an "aerobic factor", and, as a consequence, that tissue PCO_2 is always physiologically higher than the arterial PCO_2 regardless of the quality of tissue arterialization (4.5 mmHg/℃); (II) a Severinghaus constant is applied, due to the increase of $tcPCO_2$ responds to the CO_2 production induced by the heat of the sensor, also called the "metabolic constant", ranging from 5 to 10 mmHg depending on the type of device (2).

Summary of the clinical evidence for $tcPCO_2$ as a reliable $artPCO_2$ surrogate

As the main purpose of this issue concerning CO_2-related variables is to focus on hemodynamic management, we will briefly relate and summarize the main clinical data available on TCM for respiratory use.

We can reasonably state that TCM may be useful for non-invasively and continuously estimating actual arterial PCO_2, which can be of critical importance during respiratory pump failure leading to alveolar hypoventilation with hypercapnic issues. This tool could prevent the need to perform iterative blood gas analysis and could help to monitor the course of $artPCO_2$ with populations in whom estimates of $artPCO_2$ may guide therapeutic interventions. Different pathophysiological disorders are likely to promote an increase of $artPCO_2$: low alveolar ventilation (with related respiratory acidosis), increased dead space (anatomic or functional), depressed respiratory drive, or bronchial obstructive diseases as acute exacerbation of chronic obstructive pulmonary disease (COPD), especially whose receiving NIV.

While monitoring $tcPCO_2$ is considered as a valid method in routine respiratory care practice for assessing the adequacy of ventilation (16), and the cumulative data available in the specific setting of critically ill patients appears to be substantial, the precision of the technique as an $artPCO_2$ surrogate is still disputed (3,5). Examination of the aggregated literature suggests that accuracy and reliability appear good with limits of agreement in a narrow range for most ICU patients (inside ±5 mmHg and almost all values inside ±10 mmHg) (1,5). However, this opinion is debated, as other authors claim that confidence may be insufficient, as around 20% of the values of arterial-to-transcutaneousPCO_2 difference are outside the acceptable range of ±7.5 mmHg (15). There are also numerous reports underscoring the underestimation in the highest $artPCO_2$ values along with other authors who consider the TCM unsuitable or disputable for the emergency room or ICU patients (3,17,18).

As it concerns end tidal CO_2 ($EtCO_2$), pragmatically speaking, the relevance of $tcPCO_2$ could be increased with an initial and punctual concomitant arterial blood gas analysis to estimate initial potential gradient, and repeated sequentially so as to not dismiss the distortion with time. Relating to this, Horvath *et al.* reported good concordance during NIV for ARF and that discordance might have decreased with the initial $_{tc\text{-}art}\Delta PCO_2$ estimate to rule out discrepancy (19). Additionally, Rodriguez *et al.* reported good correlation in PCO_2 data changes (transcutaneous and arterial) over a 17-hour period, and only 20% of the samples had minor changes in opposing directions (13).

Nonetheless, Conway *et al.* recently pooled the available literature on the accuracy and precision of TCM to offer the most complete picture about this issue in a review with extensive meta-analysis (whole pooled population: 7,021 paired measurements, 2,817 patients in 73 studies; ICU patients: 16 studies (22% of 73 reviewed studies) with n=2,128 measurements; acute respiratory failure, 14 studies, n=993 paired measurements). In the whole population, they concluded that there are substantial differences between $tcPCO_2$ and $artPCO_2$ depending on the technical aspects (17,20,21), such as location site or temperature of electrode, and advocated the ear lobe as the site and a heated electrode of more than 42 ℃ for the temperature. However, these authors stated that the available literature attests to TCM being an accurate tool to estimate $artPCO_2$ to a clinically acceptable degree in the adult ICU population (22).

Finally, many factors or limitations should be considered when interpreting $tcPCO_2$-observed values as a surrogate of $artPCO_2$. Hasibeder *et al.* reported that $artPCO_2$ and cardiac output values could only explain 66% of the $tcPCO_2$

value variability, suggesting that many other factors were distorting the concordance between transcutaneous and arterial CO_2 in ICUs (23). In our opinion, it would be interesting to further investigate the role of several factors, especially in most hypercapnic critically ill patients with acidosis, to determine the accuracy of $tcPCO_2$ in outlier ICU patients and help in the interpretation of TCM. The most important factors appear to be the technological concerns relating to device performance and differences between monitors (TCM developed by SenTech© or Radiometer©, fiberoptic sensors etc.), location of sensor for measurement, cutaneous adiposity or edema, and of course, disturbed peripheral perfusion by adrenergic tone, drugs, sepsis, shock, fever, etc. However, the respective contribution of each factor may be difficult to capture in ICUs, as outlined by these authors (13).

To conclude this chapter, and in accordance with abundant concordant literature, we advocate the potential use of TCM in ICUs for ventilator management, because of its non-invasiveness, continuous monitoring, and accuracy of the transcutaneous CO_2 sensor technology (2,5,13,15,22,24-26). For the longitudinal use as a trending monitor, we support the application of iterative punctual invasive $artPCO_2$ measurements with blood gas analysis to recalibrate and rescale the difference between arterial and transcutaneous PCO_2 value, or $_{tc\text{-}art}\Delta PCO_2$ gap (13,22). In this way, TCM could perform an interesting sniffing function over time to track artPCO2 elevation during therapeutic procedures such as prolonged NIV. Finally, in the case of suspected altered tissue perfusion or ongoing shock, $tcPCO_2$ signal may be ambiguous and should be interpreted with caution, as detailed in the next section.

$tcPCO_2$ monitoring as a marker of tissue perfusion

Proof of concept and clinical rationale for use of capnometric data (CO_2 derived parameters) in altered tissue perfusion during macrocirculatory or microcirculatory failure have been extensively demonstrated and described (6-8,27-29). These numerous studies clearly demonstrate that the elevation of tissue CO_2 is ubiquitous throughout the body in shock states, and is closely related to tissue perfusion alteration. This paradigm has been evidenced by monitoring tissue PCO_2 at different clinically available sites including the gastric, buccal, sub-lingual, and thus, the skin level. Schematically, the difference between $tcPCO_2$ and $artPCO_2$ ($_{tc\text{-}art}\Delta PCO_2$ gradient) can increase when circulatory failure or occult microcirculatory shock is ongoing. This may be considered a limitation of the arterial PCO_2 estimation technique, and may give an opportunity for hemodynamic assessment in specific clinical situations.

$tcPCO_2$ in low oxygen delivery situations or convective shocks

Behavior of $tcPCO_2$ during macrocirculatory failure leading to low cardiac output and/or low O_2 delivery (DO_2), referred to as "convective shocks" (cardiogenic or hemorrhagic shock), is depicted in (*Figure 2C*) (12). When circulatory failure occurs, $tcPCO_2$ and $artPCO_2$ mismatch and become decoupled as demonstrated in a famous and seminal clinical study from an L.A. team of Tremper and Shoemaker who monitored the kinetics of $tcPCO_2$ during overt shock states (hemorrhage, heart failure, or the operating room) (*Figure 3*) (30). This figure illustrates the hemodynamic nature of $tcPCO_2$ as we can observe that $tcPCO_2$ values mirror the cardiac output time course, and become dramatically decoupled from $artPCO_2$ kinetics in the clinical case condition of low flow states. In this setting, note that the difference between tissue and arterial PCO_2 is more relevant than the absolute value of $tcPCO_2$ to track local tissue PCO_2 balance (and overcome the influence of arterial CO_2 content and thus $artPCO_2$ on $tcPCO_2$). In this framework, high PCO_2 gap values may be suggestive of flow stagnation by low local perfusion. Many clinical reports, along with robust experimental data, support the notion that hemorrhagic or cardiogenic shocks, together with cardiac arrest, lead to a huge increase in tissue hypercarbia. Of note, some recent additional pre-clinical data reinforce this currently still valid finding (29,31).

$tcPCO_2$ in microcirculatory or distributive shock

According to experts, the gold-standard technique for microcirculatory perturbation assessment remains optical direct sublingual microvideoscopy (SDF-OPS or IDF technologies) (32). However, these tools appear cumbersome, require time-consuming offline analysis, and have not yet reached clinical utility despite over a decade of research and technological advance. Also, a system to assess the microcirculation at the point of care seems highly desirable. On the other hand, the clinical signs of peripheral perfusion impairments (skin mottling, refill capillary time, etc.) are meaningful and informative for microcirculatory derangement but may appear late and be

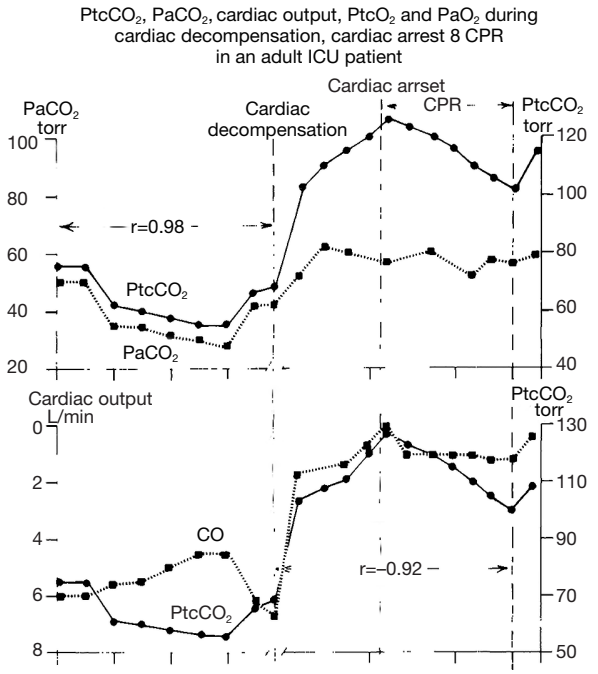

Figure 3 Two-day time course of $PtcCO_2$ and PaO_2, upper section; $PtcCO_2$ and cardiac output (CO plotted inversely i.e., with zero at the top to 8 L/min at the bottom of the scale), lower section. Note during the first day, the close trend of $PtcCO_2$ with $PaCO_2$, while the patient has adequate blood flow (CO >4 L/min). During day 2, the CO drops to below 2 L/min and $PtcCO_2$ rises, and note how $PtcCO_2$ correlates with1/CO (r=–0.92). Also note how $PtcCO_2$ responds to CPR by a decrease of more than 20 torr (upper section). Adapted from (30).

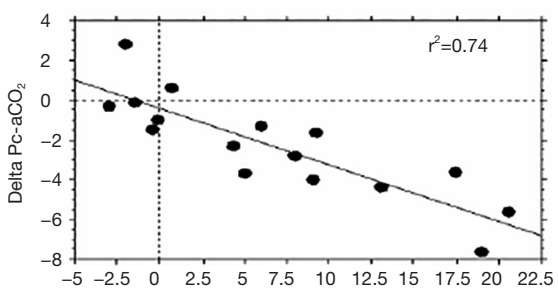

Figure 4 Relation between changes in delta Pc-aCO_2 (as cutaneous-arterial ΔPCO_2) and changes in microcirculatory skin blood flow assessed by laser Doppler flowmetry (delta TPU, variation or tissue perfusion unit, abscissa axis) during 16 fluid challenges. For more details, see (10).

insufficiently sensitive for guiding therapeutics. As outlined by several authors, refined therapeutic tailored management should embrace and target microcirculatory dimensions of shock (33). Tissue capnometry, via gastric or sublingual routes, or more simply with trans-cutaneous monitoring, could aid in this purpose, and offer, as complement, a more sensitive insight than that provided by clinical examination (9-11,27,33).

Gastric tonometry and sublingual capnometry have shown their clinical validity and their relationship to microperfusion, but have not been put into practice at this time due to paradigmatic or technological concerns (6,9). As an alternative, skin monitoring at the earlobe thus seems to be a user-friendly way to monitor tissue CO_2. Indeed, in a previous work, Vallée *et al.* used this device to examine whether cutaneous earlobe $tcPCO_2$ could be used to assess tissue perfusion in septic shock patients. In that study, the sensor was heated at 37 ℃ to limit the impact of arterial PCO_2 on cutaneous PCO_2 due to the arterialization of the blood being minimal compared with when the sensor is warming to 42 ℃ (10). They found that a threshold value of 16 mmHg for the gradient between the earlobe $tcPCO_2$ and arterial PCO_2 reliably discriminated between those patients with septic shock and tissue hypoperfusion from those patients in the control group, with a sensitivity of 83% and a specificity of 90%. Furthermore, it was found that the fluid challenge induced a decrease in the earlobe to-arterial PCO_2 gradient in parallel with the improvement of the microcirculatory blood flow in the earlobe (*Figure 4*). Interestingly, where a significant reduction in earlobe-to-arterial PCO_2 gradient was observed in survivors compared to non-survivors, no significant changes were found with the traditional macrocirculatory parameters (cardiac output and central venous oxygen saturation). Interestingly, these authors confirmed the microcirculatory nature of $tcPCO_2$ signal as demonstrated by the correlation between laser-Doppler flowmetry investigation and $tcPCO_2$ values (*Figure 5*). $tcPCO_2$ at 37 ℃ at the earlobe, therefore, seems to be a plausible tool to continuously and non-invasively estimate tissue perfusion in shock patients in ICUs.

$tcPCO_2$ monitoring with variations of sensor temperature: insights from a heat challenge

We have seen that the $tcPCO_2$ can be monitored at 37 ℃ with a heated sensor. The dynamic change in the

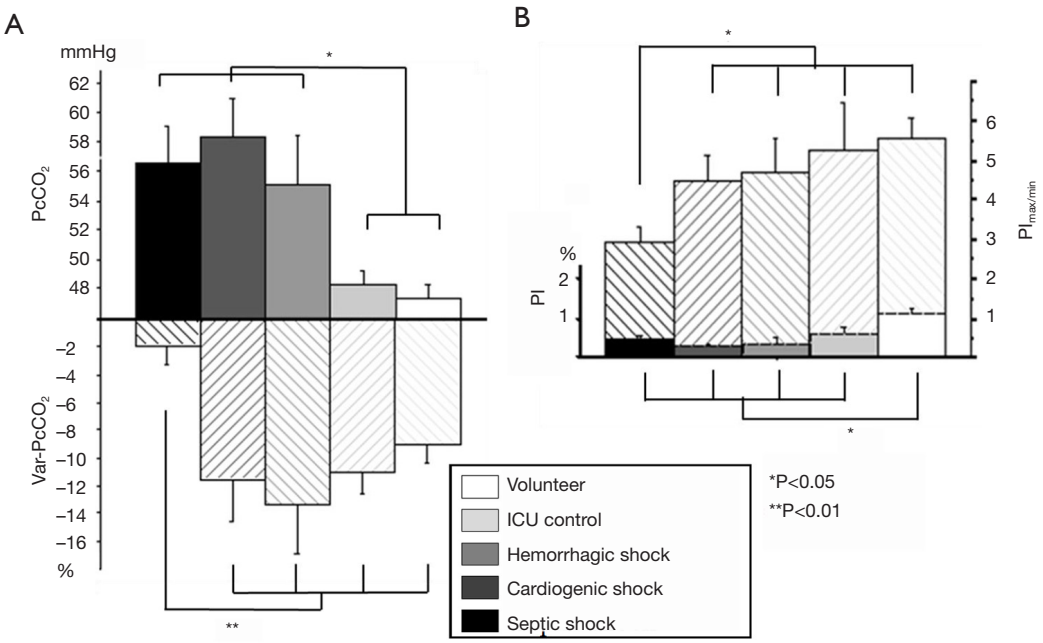

Figure 5 Results of the heating challenge at baseline in the different groups (volunteers, ICU control, hemorrhagic shock, cardiogenic shock, septic shock). (A) Baseline $tcPCO_2$ (or $PcCO_2$) measured at 37 ℃ (solid bars), and tc-art$\Delta PcCO_2$ ($\Delta PcCO_2$) (hashed bars). (B) Baseline plethysmographic perfusion index (PI) measured at 37 ℃ (solid bars) and $PI_{max/min}$ (hashed bars). For more details, see reference (11).

temperature may therefore appear as a dynamic test to evaluate tissue perfusion during shock. Heat challenge may be added to track microcirculatory failure and reversibility. This concept of studying the variations of cutaneous capnometry during a heating challenge was recently described (*Figure 6*) (11). The same paradigm has been used in a recent study by the De Backer team with a laser-Doppler flowmetry device, adding external validity for heat or thermal challenge with TCM (34). Schematically, a crude estimate with no heated electrode (standardized normothermia) together with a functional provocative test (as a thermal or heating challenge) could be useful or informative on peripheral perfusion to evaluate tissue hypercarbia related to low flow states or altered microcirculation with loss of "hemodynamic coherence", as recently conceptualized as occurring during sepsis and "microcirculatory shock" (35). For example, in the case of convective shock, without functional microcirculatory damage, the heat challenge will induce vasodilation which can lead to a decrease in $tcPCO_2$ by a recruited flow (or washout phenomenon) (*Figure 2D*). This is conceptually more hazardous in the case of a longstanding distributive shock where the constitutive alteration of the microcirculation (shunt, micro-thrombi, etc.) is not even slightly sensitive to vasodilation induced by the local increase in the temperature of the sensor (*Figure 2F*). Thus, a heat challenge (*Figure 2D*), which is likely to recruit a microvascular contingent with preserved vasoreactivity, could help to confirm hemodynamic coherence (intact macro-microcirculatory coupling) and/or to diagnose the reversibility of local peripheral hypoperfusion and anticipate targeted therapies (11). From this perspective, the combined monitoring of the perfusion index (PI) from the photoplethysmography signal also allows a good reflection of the quality of vasodilation and "arterialization" induced by the local heating of the sensor (*Figure 5*).

$tcPCO_2$ monitoring: personal perspectives and unanswered questions

We promote the graphical conceptual framework depicted in *Figure 2* to describe two possible uses of TCM in ICUs. The first, and most commonly proposed utility, is when TCM is used to estimate $artPCO_2$ for respiratory issues (*Figure 2A,B*); the second is when TCM is used to estimate tissue perfusion in shock states (*Figure 2C,D,E,F*). We believe that these two approaches are not conflicting, but it seems necessary to consider the limitations and specific

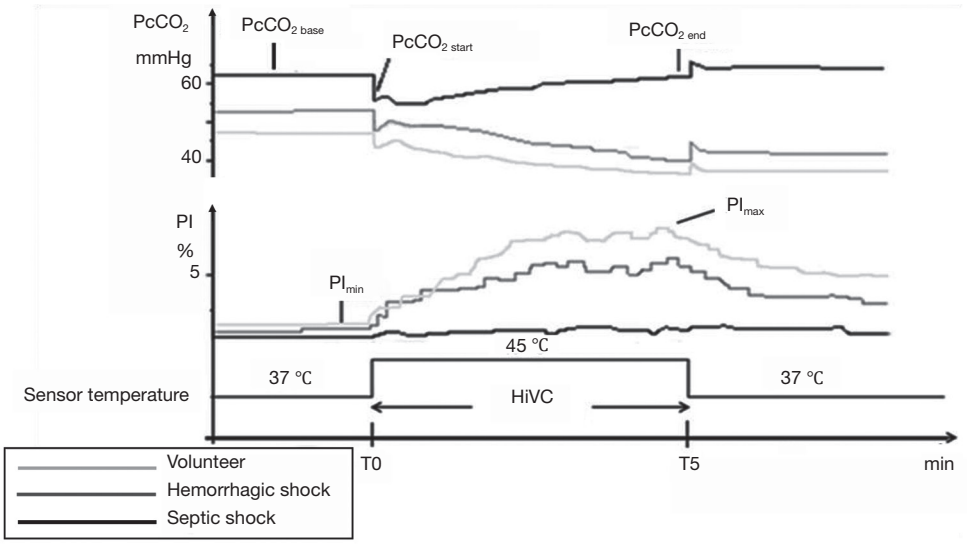

Figure 6 Stereotypical examples of the heating challenge performed in a healthy volunteer (light grey), non- septic shock (hemorrhagic in this example, medium grey), and septic shock patient (black). For more details, see reference (11). $PcCO_2$ or $tcCO_2$, transcutaneous CO_2 tension; PI%, plethysmographic perfusion index.

conditions for each indication. In doing so, we can obtain the appropriate bedside interpretation and receive the maximum benefit from this currently underused, but non-invasive and continuous type of benign monitoring. Indeed, we believe that a dual approach could allow the clinicians to better capture both the respiratory and hemodynamic status of the most severe patients. For example, a patient under respiratory TCM monitoring who exhibits an unexpected increase in $tcPCO_2$ due to *de novo* or early onset shock, may be misinterpreted as a false positive of a presumed related respiratory issue instead of a tissue perfusion abnormality. For this reason, we might advocate the continuous use of the sensor at low temperature (37 ℃) to thereby limit the risk of skin burns, but with regular heating challenges and a coupled and dynamic analysis of all parameters. Indeed, a "normal" 37°-$tcPCO_2$ value would show that there is no patent tissue perfusion disorder (*Figure 2A*), and then the $tcPCO_2$ value at the end of the heating test would reflect a value close to $artPCO_2$ (*Figure 2B*). Conversely, a high value of $tcPCO_2$ would attempt to show abnormalities in tissue perfusion (*Figure 2C,E*), and the heating test would make it possible to monitor the existence of microcirculation dysfunction and its reversibility, which would be strongly related to the prognosis of a patient in shock (*Figure 2D,F*). We believe that these assumptions would allow for a unique and codified interpretation of TCM. Obviously, additional studies dealing with different clinical situations and populations are mandatory to further support our hypotheses and refine our suggested algorithm. There are also many unanswered questions which include the temperature of the sensor in relation to the skin temperature (iso *vs.* normothermia), the thermal variations and kinetics during a heating test, the position at the earlobe as a reflection of the whole peripheral perfusion, and the variability and reproducibility of the $tcPCO_2$ value mainly in specific clinical situations such as acidosis or hyperoxia (2,13,23). Furthermore, it will be necessary to compare TCM with other devices that estimate the microcirculation, and to ultimately test drugs targeting microcirculatory dysfunction. To conclude, as a next step, we suggest integrating values of the $tcPCO_2$ and tc-$artPCO_2$ gap into holistic therapeutic algorithms, and advocate considering systemic and regional CO_2-related parameters for advanced circulatory monitoring, as recently proposed (36,37).

$tcPCO_2$ monitoring: conclusion

Transcutaneous CO_2 monitoring has been developing for many years, and its utility has been proven in at least two different clinical situations in critically ill patients: arterial PCO_2 estimation and tissue perfusion monitoring. Probably because of this ambivalence, which can be confusing for clinicians, this monitoring has been, in our

opinion, underused thus far. However, recent research has shown that these two aforementioned applications are not irreconcilable and could be combined. We believe that estimating arterial PCO_2 and measuring the $tcPCO_2$ gap between arterial-to-tissue CO_2, in normothermia (37 ℃), combined with the provocative perfusion test as a heat challenge (electrode warmed to 42–44 ℃), would help clinicians to continuously and noninvasively capture both respiratory and hemodynamic failures in critically ill patients. Even preliminary, our data on heat challenge as a way to assess microcirculatory shock has shown potential and may stimulate further investigations in this field. For the future, it would be desirable for $tcPCO_2$ sensors to offer refined technological innovation (with automated temperature tests and manipulation of algorithmic constants) in order to popularize the daily use of this device in different clinical settings.

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None.

Footnote

Conflicts of Interest: A patent application (n° PCT IB2009/006903) is pending on variations of $PcCO_2$ and PI during Heating Challenge. The patent belongs to the Assistance Publique-Hôpitaux de Paris (France). F Vallée and H Nougue received consultant fees from Radiometer. The other authors have no conflicts of interest to declare.

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