The relationship of CO2 metabolism to tissue perfusion, microcirculation, and treatment response in shock and sepsis
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SUMMARY AND CONCLUSIONS

The monitoring of CO₂ may give meaningful information about the systemic blood flow and tissue perfusion. In this thesis we show:

1. Cardiac output and end-tidal PCO₂ (PETCO₂) are strongly correlated in a logarithmic fashion.

2. Alveolar CO₂ elimination, and consequently PETCO₂, depend on CO₂ production, alveolar ventilation, and pulmonary perfusion (cardiac output). If the first two variables are maintained constant, reductions in PETCO₂ reflect decreases in cardiac output. Critical reductions in cardiac output, however, also decrease CO₂ production and change the slope of the PETCO₂/cardiac output relationship. This phenomenon is associated with an increased respiratory quotient. Therefore, PETCO₂ may be useful for the monitoring of pulmonary blood flow and as a warning of ongoing anaerobic metabolism.

3. The development of intramucosal acidosis—i.e., an increase in intramucosal-arterial PCO₂ difference (ΔPCO₂)—precedes the reduction in systemic and intestinal oxygen consumption. Thus, ΔPCO₂ is a sensitive marker of hypoperfusion.

4. Venoarterial and intramucosal-arterial PCO₂ gradients are the result of interactions between changes in aerobic and anaerobic CO₂ production, the CO₂ dissociation curve, and blood flow to tissues. During oxygen supply dependence, opposite changes in aerobic and anaerobic CO₂ production are present: aerobic CO₂ production decreases as a consequence of depressed aerobic metabolism, but anaerobic CO₂ production appears because of the bicarbonate buffering of anaerobically generated protons. Despite the fall in total CO₂ production, there is an increase in the respiratory quotient, as O₂ consumption decreases even more. This relative increase in VCO₂ to VO₂ might generate tissue and venous hypercarbia only in lowflow states, where there is diminished CO₂ removal. Consequently, CO₂ gradients are poor indicators of tissue dysoxia in conditions with preserved tissue perfusion such as hypoxic and anemic hypoxia.

5. Tissue and venous hypercarbia is a universal occurrence. Regional heterogeneities, however, may occur not only during hypoperfusion but after the resuscitation.

6. The increase in blood flow through volume expansion or a vasoactive drug may recruit the microcirculation and avoid the development of intramucosal acidosis in experimental endotoxemia. Nevertheless, the effects of vasoactive drugs may be inconsistent. Levosimendan prevents the appearance of increased ΔPCO₂, but side effects related to excessive vasodilation may occur according to the dosage. Dobutamine, the drug that more predictably increases mucosal gut PCO₂, fails to do so in our model.
7. Intestinal intramucosal acidosis depends on villi hypoperfusion. In endotoxemic shock, microvascular abnormalities are present in different territories. The normalization of systemic and intestinal hemodynamics by means of fluid resuscitation corrects some of these disorders but is unable to improve intramucosal acidosis related to persistent villi hypoperfusion.

8. In hemorrhage, there are also microcirculatory alterations that are more extensive than the changes in cardiac output. As an expression of heterogeneity, these alterations are more evident in the intestinal mucosa than in the intestinal serosa and the sublingual mucosa.

9. The magnitude of microcirculatory perfusion may be adequately evaluated by the semiquantitative microvascular flow index, which parameter strongly correlates with the actual red blood cell velocity as measured by software.

10. The optimal perfusion pressure for sublingual microcirculation is dependent on its basal state. Patients with severely compromised perfused capillary density show increases when arterial blood pressure is elevated from 65 to 85 mm Hg with norepinephrine. Conversely, patients with relatively preserved microcirculation show a decreased perfused capillary density when blood pressure is increased. The conclusion is that the titration of vasopressors to reach an optimal perfusion pressure should be done on the basis of an evaluation of the microcirculation in each individual.

11. The choice of fluid for resuscitation could be a relevant therapeutic issue. Despite the lack of clinical studies focussed on the effects of different fluids on the microcirculation of septic patients, research performed in relevant experimental models has shown beneficial effects of starches. Starch solutions might improve the microcirculation because of their effects on different mechanisms such as the interaction between endothelial cells and leukocytes, regional alterations in nitric-oxide production, red blood cell deformability and aggregability, coagulation and fibrinolysis, glycocalyx, and inflammatory injury. The results of our randomized controlled pilot study show that patients resuscitated with 6% hydroxyethyl starch 130/0.4 (HES) have a better sublingual microcirculation than do those in the saline solution group. These results suggest that early goal-directed therapy may allow a better recruitment of the microcirculation when 6% HES 130/0.4 is used for the expansion of intravascular volume compared to saline solution.