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## Physiology and technology hand in hand for clinical imaging of the microcirculation

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Sir: Given the growing interest in the study of microcirculation, we believe that an editorial comment [1] about our article [2] should be welcome. Unfortunately, we feel that the editorialists failed to understand our findings.

Drs. Takala and Jakob raise some specific issues. First, they emphasize the high susceptibility of the model to hemorrhage, already addressed in the manuscript. Unfortunately, they fail to realize that reductions of 24% in cardiac output (CO) only marginally increased lactate ( $1.6 \pm 0.3$  to  $2.4 \pm 0.6$  mmol/l) and had no effects on systemic and intestinal oxygen consumptions, blood pressure or base excess, while provoking clear microcirculatory changes. These, however, could be tracked non-invasively in the sublingual mucosa, rendering it a potential area for the clinical monitoring of hypoperfusion.

The editorialists' statement about microcirculatory changes being less prominent than those of CO because of the lower percent reduction of red blood cell velocity (RBCV) is misleading. For example, during the first bleeding step, when CO fell by 24%, RBCV decreased by 10%, but capillary density (CD) reduction was 26%, and heterogeneity increased several times in ileal mucosa. Indeed,

microcirculation was more severely affected than CO.

We feel that to conceive of microcirculatory perfusion as only dependent on RBCV is conceptually incorrect. Microcirculation changes should not only be assessed in terms of convective oxygen transport, but also as alterations in diffusional mechanisms. Thus, a similar percent reduction of CO and CD might have the same significance in terms of blood flow, but the reduction in CD could threaten oxygenation by increasing diffusional distances and reducing the exchange area. Lastly, increased heterogeneity acts as a further challenge to oxygenation [3].

With regard to flow quantification, the strong correlations between the RBCV and microvascular flow index, as well as their parallel decrease during the step-wise bleeding, show that they both track the changes in perfusion adequately.

Finally, the editorialists do not understand why RBCV was measured in fewer vessels in ileal mucosa than in sublingual/serosal areas. This was related to the software performance in the circulatory villi network; see ESM [2].

Recently, the editorialists published a study showing the limitations of the OPS to detect mesenteric hypoperfusion [4]. They admit, however, that the poor quality of their images and their method of evaluation were potential explanations for their negative findings. In contrast, we demonstrate, with an improved technology, that the use of adequate images, together with a comprehensive and quantitative analysis, provides valuable information about the microcirculation.

We agree with Drs. Takala and Jakob that an adequate use of the technology is critical for the assessment of the microcirculation. Otherwise, the situation could be like that with the pulmonary artery

catheter: routine use without adequate training and physiological insight was not able to improve clinical outcomes. A deep knowledge about the underlying physiology must go hand in hand with adequate skills for the use of new technology. Only then, as recently pointed out by Dr. Weil, can a new era of hemodynamic monitoring be welcome where the macro- will be expanded to the microcirculation [5].

**Conflict of interest statement** The author has not disclosed any potential conflicts of interest.

## References

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