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## Microcirculation and multi-organ failure in patients with sepsis

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With great interest, we read the article by Trzeciak et al. who made a commendable effort to investigate whether an improvement in SOFA score over the first 24 h in patients with sepsis was associated with an increase in sublingual microcirculatory perfusion. The authors demonstrated a significant increase in median microvascular flow index (MFI) for SOFA improvers versus non-improvers (+0.23 vs. -0.05, respectively) [1]. Although we appreciate these interesting findings, we would like to raise several comments.

First, the authors quantified microcirculatory flow using a semi-quantitative method presented previously [2]. Using this method produces a MFI for small (i.e. capillaries, 0–20 µm), medium (20–50 µm) and large (50–100 µm) sized microvessels. Analyses of vessels larger than capillaries (i.e. mainly venules) is of limited interest, but experts in the field of microcirculation research recently advised that venular perfusion should also be reported as a quality control index

[3]. However, the authors only mentioned a single MFI per time point. Did they produce an averaged MFI for all micro-vessels in a certain video-microscopic image? Since capillaries are the vessels that are impaired most in sepsis [2, 4], calculation of an averaged MFI for all microvessels would definitely restrain any changes in observed microvascular perfusion.

Second, individual patient data for MFI in the electronic supplementary material show a clear difference in change of MFI between both sub-groups. However, we would like to learn whether median MFI at visit 2 was statistically different between SOFA improvers versus non-improvers (in contrast with the almost equal values of MFI at baseline). Although we can imagine that a trend in perfusion over time might be more important than single values, a single-value threshold, indicating whether microcirculation is either preserved or impaired at a certain moment, would have considerable practical advantages over the continuous monitoring of trends.

Finally, the authors demonstrated that there is an association between early increases in microcirculatory perfusion and multi-organ failure. However, it will be very hard to visualize the modest changes, as presented by the authors, in individual patients at the bedside and the clinical value of a change in MFI of 0.23 points may be very difficult to interpret. In order to implement a future microcirculation-directed-approach to our patients with sepsis, additional research is necessary.

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