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### The effects of hyperoxia on sublingual microcirculation: An unsolved puzzle

We thank Dr. Damiani and colleagues for their insightful comments about our study [1]. We believe they point out the present uncertainties about the effects of hyperoxia on microcirculation and about the acquisition and analysis of sublingual videos.

Dr. Damiani et al. speculate that the failure to identify detrimental effects of hyperoxia on sublingual microcirculation in our study might be related to methodological issues. We agree with the concept that a continuous measurement in a single site could produce different results when compared to intermittent evaluations performed in different places. This does not imply that continuous measurements are superior to intermittent measurements. Single-spot measurement might be particularly useful to monitor the response of single vessels to a therapeutic intervention. Continuous measurements, however, are focused on a single zone. Thus, they might fail to notice regional heterogeneities in the response to hyperoxia. Conversely, intermittent and multiple measurements could give a more comprehensive panorama. Since regional heterogeneities within the sublingual mucosa might be present, the assessment of at least three videos is required to reach a complete picture of the microcirculation [2]. Moreover, continuous and prolonged measurements are more prone to compression artifacts.

In a study quoted and performed by the authors of the letter, a similar reduction in total and perfused vascular density was described by continuous measurements at 2 min and by intermittent measurement at 2 h [3]; they found that the proportion of perfused vessels (PPV) was decreased at 2-min but not at 2-h. Therefore, the type of measurement produced different values of PPV but similar changes in densities. An experimental study of hyperoxia carried out in rabbits failed to notice changes in the PPV, even when continuous measurements were performed in individual vessels [4]. In accordance with these results, there is no reason to ascribe our findings of unchanged densities to intermittent measurements.

In our publication, we comprehensively discuss the conflicting results about the effects of hyperoxia on sublingual microcirculation [1]. These range from severe alterations to lack of detrimental effects. Likewise, we found a beneficial effect of hyperoxia in septic patients, consisting in a decreased heterogeneity flow index (HFI). Donati et al. found that after 2-h of hyperoxia, there were subtle decreases in microvascular densities, but PPV and microvascular flow index (MFI) remained stable [3]. However, HFI increased. This is difficult to explain,

given that HFI is calculated from MFI, which did not change during the study.

Damiani and colleagues also arise the hypothesis of the microvascular dysfunction as a possible explanation for the lack of vasoconstrictory response to hyperoxia in our patients with septic shock. Although this interpretation is interesting, it does not explain why in healthy volunteers, like in septic patients, microcirculation is not compromised during hyperoxia.

Overall, it is apparent that information is controversial, not only between but also within studies. The underlying explanations might reside in the different populations studied, but also in the difficulties for assessing the microcirculation (video acquisition and analysis). Although clinical studies clearly establish the risks of hyperoxia, physiological studies failed to show that the sublingual mucosa is a suitable window to monitor the effects of hyperoxia on microcirculation.

### References

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