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EDITORIAL

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The elusive microcirculation

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In the current issue of Intensive Care Medicine, Bracht and colleagues present a study in sheep intestines where they investigate the response of the microcirculation to ischemia as measured by two techniques aimed at the microcirculation: OPS imaging and laser Doppler flowmetry [1]. Their goal was to investigate how sensitive the two techniques aimed at the microcirculation were able to detect a progressive flow reduction to the intestines. To this end they applied a tourniquet around the superior mesenteric artery and progressively restricted arterial blood flow to the intestine. The results of their study showed that the laser Doppler signal deviated at less arterial flow reduction (45%) than did microcirculatory flow as detected by direct observation of capillary red blood cell flow using OPS imaging. Alterations in capillary red blood cell flow could not be detected until an arterial flow reduction of 75 % had been reached. Because of this difference they concluded that OPS imaging was insensitive in being able to detect gut ischemia.

What makes this paper of special interest is that it can be regarded from two points of view. One would be from a technical point of view, where two techniques, purportedly measuring the same physiological compartment, are compared to each other in terms of specificity and sensitivity. Alternatively one can interpret the results as reflecting physiological phenomena associated with progressive arterial occlusion. Reflecting from both points of view allows interesting and import conclusions to be drawn concerning the study of the microcirculation in critical illness.

The first issue which has to be considered is whether the two techniques are measuring the same physiological compartment. OPS imaging provides precise (given that the image quality is of sufficient standard) and direct visualization of the flowing cells in the microcirculation of the outer most cellular layer of the surface of the intestinal villi. This is more difficult for the laser Doppler signal where all movement (e.g. in arterioles, capillaries and venules) in an unknown layer of the mucosa is being measured. This affect is exacerbated if the laser Doppler signal used is red light, since this light penetrates deeper into tissue. In this way, laser Doppler would measure a deeper compartment than the green light used in OPS imaging which only penetrates the immediate surface and where only capillary vessels are seen. If indeed OPS imaging would be sensing flow in the outer layer of the villi and the laser Doppler in the deeper layer then an interesting observation arises from this paper. Namely, that the microcirculation in the tip of the villi (being observed by OPS imaging) is able to sustain its flow (presumably by the action of control mechanisms) at the expense of the flow of the deeper mucosal layer (being measured by the laser Doppler technique). Redistribution of blood flow within the intestines is well known. In this light, their findings have identified the value of the critical cut-off point for arterial occlusion for the two compartments as being different. This being respectively 45 and 75% flow reduction for the outer and inner microcirculatory layers of the mucosal villi. One could argue that monitoring the microcirculation of the mucosa using OPS imaging is most relevant because it identifies, almost by definition, the

critical arterial flow reduction value which comprimizes the most important microcirculatory compartment for the barrier function of the gut, mainly the microculatory bed closest to the lumen of the gut. Well, is there evidence that the mucosa is more resilient to ischemia and shock than the deeper layers of the intestines? Well, yes. In fact, several animal studies have shown that during ischemia and shock mucosal blood flow and oxygen tension is preserved in the mucosa at the expense of the serosa (e.g. [2]).

The second aspect of the paper by Bracht et al. [1] that requires consideration are the technical methodologies for assessment of the microcirculation. In assessing the microcirculation three phases should be distinguished, each of which should be performed with great care: 1) optimal microcirculatory image acquisition; 2) image analysis; and 3) microcirculatory scoring. Firstly, it is of major importance that high quality images are acquired in the microcirculatory region of interest. This means that the capillaries with (flowing) red blood cells should be clearly visible on a monitor and that images must be recorded and stored digitally to avoid any image compression-induced quality loss. If microcirculatory images do not meet the required standard, then disparity can occur in the subsequent microcirculatory evaluation. That this may have been a problem in the present study is illustrated by the somewhat unclear images OPS images shown in Fig. 4a, b, where capillaries can hardly be identified. This lack of resolution is further amplified by the large discrepancy found between the vessel densities scored by the two investigators (Fig. 1). Indeed, the authors point out that sub optimal images may have been a problem and that improved image quality and a solution to movement of the images could have benefitted their results. Such improvements have recently been introduced in the form of a novel optical modality called SDF imaging and specialized image processing and analysis software to correct for image movement [3–5]. Secondly, the acquired images must be analyzed quantitatively for physical microcirculatory parameters, such as capillary diameter and length and red blood cell velocities. This relies heavily on the preceding image acquisition step, i.e., with suboptimal images, the image analysis will be inaccurate and unreliable. Thirdly, and ultimately, the analyzed microcirculatory images must be scored for relevant functional parameters like capillary density and microvascular flow index [6]. The authors have chosen to apply a semi-quantitative scoring method which mainly discriminates between stagnant and flowing cells, a specific characteristic of microcirculatory alterations in sepsis for which this score was specifically developed [6]. A more appropriate and probably more sensitive method for detecting and quantifying the presumably step-wise reduction of microcirculatory blood flow following progressive arterial blood flow restriction, would have been direct determination of capillary red blood cell velocities measured by the use of space-time diagrams [5, 7]. If one or more of the above-mentioned steps are performed inadequately, unreliable conclusions could be drawn from the microcirculatory measurements, which in turn could lead to inter-observer bias and inconclusive results.

In conclusion, considering and reflecting on this paper by Bracht et al. has allowed many aspects in the assessment and (patho) physiology of microcirculatory alterations during ischemia and shock, to be considered. Discussions such as these can be expected to provide important contributions to optimize the assessment and interpretation of microcirculatory alterations during critical illness.

Conflict of interest I am, besides my affiliations listed above, chief scientific officer of a company called MicroVision Medical. MicroVision Medical is a university-based company dedicated to the development of optical spectroscopic tools for study of the microcirculation and tissue oxygenation. In this context I hold patents and shares.

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