IN REPLY

In reply: Why goal-directed hemodynamic therapy is often ineffective and how can we try to improve the results

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To the Editor,

We would like to respond to the three authors' letters^{1–3} that disagreed with our presentation of the regulation of cardiac output based on the venous return principles of Guyton.⁴ Much of the criticism was directed toward our proposed interactions between the stressed and unstressed venous volumes (V_s and V_u). While we recognize these authors' expertise in hemodynamic physiology, we would like to emphasize that the focus of our article was to provide clinicians with the physiologic basis to better understand goal-directed hemodynamic therapy (GDHT) and suggest some actions to possibly increase its effectiveness. The arguments of Dr. Brengelmann are well known, but they do not fundamentally discredit Guyton's principles.¹ Long before Brengelmann, Dr. Levy raised similar arguments in an enlightening paper (with an accompanying editorial by Guyton).^{5,6} A discussion of this dispute is well beyond the scope and space allowed for this letter and would distract from the main purpose of our article.

Concerning our suggestion that V_s and V_u can simultaneously exist in the same vein, there are at least two mechanisms facilitating the constant mixing, or rather converting, of V_u into V_s and V_s into V_u by changing the transmural pressure. One is the periodic constriction and relaxation of smooth muscle within the venous wall; this

mechanism works even when the heart is stopped, even just briefly. Accordingly, one can imagine a vein with no flow in it; at that moment, the blood is all V_u . Smooth muscle in the venous wall then contracts, increasing the transmural pressure; at that moment, part of V_u becomes V_s . This happens because of a change in pressure and compliance in the vascular segment, exactly as Dr. Brengelmann suggests.¹ Thus, we added the V_s/V_u link to the chain of events; this does not negate the role of pressure and compliance changes.

Another mechanism is pulsatile arterial flow—i.e., every stroke volume is associated with an increase in arterial blood volume and a compression of veins. The resulting rhythmic compressions and decompressions facilitate the venous flow. Although unable to generate significant flow, they constantly convert V_u into V_s (and V_s into V_u) within the veins. This might mean that a situation of cardiac arrest is not associated with a complete “no flow” phenomenon, and some movement of blood within the veins can still occur.

Dr. Galetti focuses on the role of energy expenditure of the heart muscle in the regulation of cardiac output.³ We do not have any disagreement with her beautiful physiologic analysis. Instead, our paper presents the work of the heart as contractility according to Starling. The Starling principle of the heart, similarly to Guyton's principle of venous return, has certainly been criticized over the years (now measured in centuries), but it is a way to express the energy expenditure of the heart muscle as it is most commonly used and understood clinically. Although relating physiologic principles, our review is written with the clinician (not engineer) as the intended reader, and the language and explanation are thus adjusted accordingly.

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Dr. Dalmau argues that hydraulic isolation of the arterial and venous systems has no physical or physiologic basis.² We argue that this is not entirely accurate, particularly as the high arterial resistance isolates the low pressure venous system from that high pressure arterial system. This is why high arterial pressure does not significantly affect the venous hemodynamics, including venous pressure. A decrease in arterial resistance may affect venous pressure, as discussed in our article (page 305).⁴

Dr. Brengelmann criticizes our view of V_s and V_u as “separate entities” moving according to a “mysterious shifting about of unstressed and stressed bits”.¹ In his physiologic analysis of V_s and V_u , he ignores our discussion about the effects of regional changes of venous resistance on venous return and cardiac output. From this discussion, we derived the idea of a dynamic change of blood volumes from unstressed to stressed, and vice versa. Dynamic changes of regional blood volumes occur all the time in humans and animals (e.g., hypovolemia and shock). Understanding the dynamic relationship between V_s and V_u may provide a clue about the ineffectiveness of a fluid challenge—i.e., the infused fluid may increase the V_u without a hemodynamic effect at that time point, which may later result in overloading the patient. A decrease in V_u

at the time of fluid infusion by appropriate pharmacologic intervention may turn out to be an effective way to improve GDHT, as we suggested at the end of our article (pages 305-6).⁴

Conflicts of interest No conflicts of interest.

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