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Pitfalls in the assessment of ventriculo-arterial coupling from peripheral waveform analysis in septic shock. Comment on *Br J Anaesth* 2020; 125: 1018–1024

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Editor—We read with interest the paper by Morelli and colleagues[1] on the ability of the systolic-dicrotic notch pressure (SDP) difference to predict the response to esmolol infusion in septic shock patients with persistent tachycardia despite 24 h of haemodynamic optimisation. The message delivered by this *post hoc* analysis[2] is that since ventriculo-arterial (V-A) coupling is a function of both arterial elastance (Ea) and contractility ($_{art}dP/dt_{max}$), and the former decreases with HR, the effects of beta-blockade on cardiovascular efficiency depend essentially on the behaviour of contractility. On this basis, the authors divided patients according to the response of $_{art}dP/dt_{max}$ to esmolol infusion (preserved *vs* decreased); they found that the SDP difference calculated from a *peripheral* arterial waveform (i.e. the radial artery) was the only variable capable of differentiating the two groups both before and after beta-blockade. This parameter was consequently proposed for an overall assessment of cardiovascular efficiency.

The authors should be congratulated for their effort in bringing rather complicated concepts such as V-A coupling to the bedside. We believe that adding a more physiological point of view to the limitations listed in their papers[1,2] may facilitate the external applicability of their findings. While the time-dependency of elasticity in arteries (especially large elastic arteries) is not a novel finding,[3] the use of peripheral SDP difference as a marker of V-A coupling has received little attention so far and definitely deserves further discussion.

Morelli and colleagues[1] claim that '*…a delayed aortic valve closure is indicated by lower dicrotic notch pressure, thus increased SDP difference…*'. While this is certainly true at the aortic level, caution should be paid when analysing peripheral arterial waveforms: the dicrotic notch on a peripheral arterial wave is often considered a surrogate of the *aortic incisura*, but more than mere terminology separates the two.[4] The *incisura* and the following dicrotic wave reflect, respectively, aortic valve closure and rebound of the aortic root at the termination of retrograde flow; they both become less evident distally from the ascending aorta and disappear on arterial signals recorded 35–40 cm from it.[4] The appearance of one (sometimes multiple) late dicrotic notch and wave on peripheral arterial waveforms may not represent aortic valve closure, but rather the impact of backward waves reflected at the arterio-arteriolar junction.[4,5] In young healthy individuals, the timing of wave reflection almost coincides with the beginning of diastole to facilitate coronary perfusion (Fig. 1). Recent animal models have shown that the effect of reflected waves on V-A coupling is actually negligible in normal conditions.[6] If, however, the physical characteristics of the arterial system are altered by aging or disease, reflected waves may change in both amplitude and position,[7] reaching the aortic root during systole and adding complexity to the model[6] (Fig. 1). The architecture of the arterial tree of the fluid-resuscitated septic shock patient (as in Morelli and colleagues[1]) has been investigated in animal models[8] and it is characterised by peripheral vasodilation, aortic wall stiffness with oedema, and low compliance of muscular arteries. In such a deranged arterial tree, propagation of backward waves to the aorta is not predictable from analysis of a peripheral arterial waveform, thus we believe that conclusions about V-A coupling should be drawn with caution under these circumstances.

The authors suggest that '*…increased SDP difference reflects a lower afterload, increased myocardial contractility, or both…*' thus '*…the SDP difference can be proportional to the degree of V-A coupling*'.[1] We were surprised by this statement since it is

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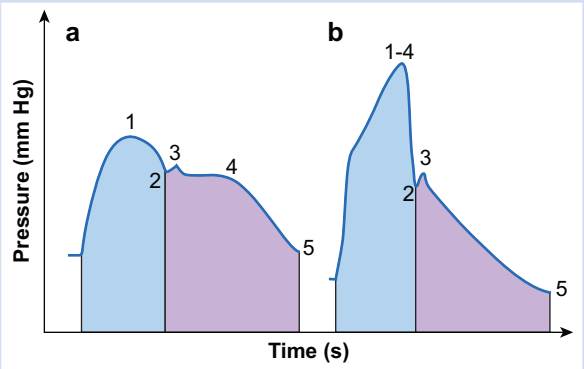

Fig 1. Aortic pressure waveforms in conditions of (a) normal and (b) altered coupling of the cardiovascular system. Normal coupling is reflected by a lower aortic systolic dicrotic pressure difference, that is a smaller difference between mean pressure during systole (light red area), and mean pressure during diastole (light blue area). 1: systolic pressure; 2: dicrotic notch; 3: dicrotic wave; 4: reflected wave; 5: diastolic pressure.

widely accepted that a lower difference between mean systolic and mean diastolic pressure in the aorta reflects better cardiovascular efficiency[9] (Fig. 1). Moreover, the authors seem here to contradict a statement in their previous paper: '*...In healthy subjects the value of MAP − P_{dic} is very low. By contrast, in septic shock MAP − P_{dic} is high ...*'[2] where P_{dic} is the dicrotic pressure. Septic shock is indeed associated with V-A decoupling despite low Ea,[10] thus we do expect a higher SDP difference in this condition. However, SDP difference should decrease if coupling improves after esmolol infusion, as opposed to what the authors suggest.[1]

This apparent paradox is not easily explained since too many factors play a role in the physiology of SDP difference to assume a simple linear relationship with V-A coupling. However, we believe that considering *aortic* and *peripheral* SDP difference separately might be of assistance. Indeed, *aortic* SDP difference reflects V-A coupling, but more likely in the direction suggested by the authors in their first paper[2] (the lower the difference, the better the coupling, as generally accepted[9]), while the *peripheral* SDP difference should be discussed in terms of reflected waves and distance from the aorta. On this basis, the lower *peripheral* SDP difference observed by Morelli and colleagues[1] in patients who do not benefit from HR reduction may be explained by another mechanism often associated with this finding, that is an increased vascular tone (see Fig. 9[5]). The radial artery is a middle-size muscular artery, and its elasticity is not significantly affected by HR reduction in the high HR range of patients studied by Morelli and colleagues.[3] Increased tone at this level could then coexist with a more pronounced increased elasticity of larger elastic arteries explaining the global decrease in Ea when HR is reduced.[1] Ea is, in fact, an overall indicator of afterload, but it does not allow evaluation of its individual components that play a role in wave speed and reflection, such as total peripheral resistance and compliance of muscular and elastic arteries. The seemingly lower pulse pressure before esmolol administration and the lower reduction in Ea after beta-blockade in patients who do not benefit from HR reduction in Morelli and colleagues[1] both support the hypothesis of a higher peripheral vascular tone in this group. This might reflect a baroreflex response to lower contractility.

Although use of peripheral waveform analysis to guide beta blockade in septic shock is intriguing, the physiology behind the SDP difference is too complex to assume a linear relationship with V-A coupling. Further investigation is warranted before the preliminary findings of Morelli and colleagues[1] can be generalised and considered applicable at the bedside.

Declarations of interest

The authors declare that they have no conflicts of interest.

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