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LETTER TO THE EDITOR

Estimating the effective arterial elastance at bedside: a reply to a rebuttal

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We are sorry to report that we do not find Monge Garcia et al. rebuttal [1] to our letter [2] convincing. Some of their points seem warranted, but so many of their claims demand challenge and are not evidence-based.

Claim 1 "Ignoring stroke volume, any peripheral estimation of Ea [the effective arterial elastance] will be valid as long as the arterial surrogate is close to Pes [the left ventricular end-systolic pressure LVESP]. In this regard, MAP [the mean arterial pressure], dicrotic notch pressure and 90% of aortic systolic pressure offer similar performance. But *aortic*, not femoral or radial pressure [1]". As far as aortic pressure is concerned, this claim is not evidence-based. The opposite has been documented by two independent studies using high-fidelity pressure recordings and showing that MAP markedly underestimates LVESP while 90% aortic systolic arterial pressure (SAP) matches LVESP [3, 4] (Table 1). The important point is that in humans, particularly those with stiff or hypertensive vasculature exhibiting a widened aortic pulse pressure, MAP and LVESP may deviate substantially [2–4]. For sake of clarity, we will not discuss here the issue of aortic dicrotic notch pressure because dicrotic notch pressure was not an issue that was discussed in our letter [2], and also because the discussion and conclusion of the related article [5] focused on the estimation of Ea based on the MAP/SV ratio (where SV is stroke volume).

Claim 2 "Moreover, if arterial stiffness increases, the arterial pulse wave velocity will increase boosting the impact of arterial wave reflections on peripheral pressure measurements. If this is the case, peripheral SAP will significantly overestimate Pes [LVESP] [1]". This claim is not evidence-based. As far as the amplification of SAP from aorta to the brachial artery is concerned, the opposite is in fact universally admitted. Indeed, the brachial SAP is close to aortic SAP in subjects with increased arterial stiffness, including elderly subjects and hypertensive patients, due to the mild amount of systolic pressure amplification [6–9]. In these subjects, due to high pulse wave velocity, the reflected pressure wave is increased and anticipated, thus adding up to the incident aortic pressure wave in systole, instead of adding up in early diastole, as observed in young healthy subjects. Thus, in subjects with increased arterial stiffness, the estimation of LVESP based on 90% brachial SAP is expected to be especially accurate; this is less verified at the radial artery level given the significant amplification of SAP from brachial to radial artery [6–9]. There is also an overestimation of LVESP (and thus Ea) if one applies the 90% SAP approximation in peripheral arteries of subjects exhibiting a potentially marked SAP amplification from aorta to periphery, such as young healthy subjects in whom the pulse wave velocity is normally low given their highly compliant arteries. However, this limitation may be minimized by using arterial sites where pulse wave amplification is lesser, namely the brachial or femoral sites rather than the radial site [6–10]. Moreover, because peripheral MAP markedly underestimates LVESP, further studies are needed to compare the respective value of the 90% SAP/SV ratio and of the MAP/SV ratio for estimating Ea at bedside, especially in young, healthy subjects.

Claim 3 "If we look carefully to Fig. 1 in their comment, even if MAP overestimate(s) Pes [LVESP], this difference

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Table 1 Performance of the estimates of left ventricular end-systolic pressure (LVESP) in high-fidelity pressure studies [3, 4]

	Kelly et al. study [3] High preload	Kelly et al. study [3] Low preload	Chemla et al. study [4] Control subjects	Chemla et al. study [4] Hypertensive patients
N	10	10	20	46
SAP (mmHg)	142.0 ± 24.9	104.6 ± 24.5	132 ± 7	182 ± 12
LVESP (mmHg)	137.4 ± 24.59	98.6 ± 24.8	117 ± 10	164 ± 9
MAP (mmHg)	111.4 ± 15.97	85.68 ± 19.8	94 ± 6	126 ± 10
(MAP–LVESP) difference (mmHg)	− 26.0	− 12.92	− 23	− 38
(MAP–LVESP) difference, % LVESP	− 19	− 13	− 20	− 23
(90% SAP–ESP) difference (mmHg)	− 9.6	− 4.46	+ 1.8	− 0.2
(90% SAP–ESP) difference, % LVESP	− 7	− 4.5	+ 1.5	− 0.1

Mean values (SD) of LVESP, mean aortic pressure (MAP), and systolic aortic pressure (SAP) are indicated as published. The same 10 subjects (6 older subjects with and history of systemic hypertension, and 4 younger normotensive subjects) were investigated under high and low preload in the Kelly et al. study [3]. We also calculated the mean differences and the mean percentages, as indicated. The MAP markedly underestimated LVESP in both studies and in all groups under study while 90% SAP provided a reasonably good estimate of LVESP. The authors' claim [1] that MAP and 90% SAP offer similar performance as surrogates of LVESP was clearly ruled out. One implication is that the MAP/SV ratio markedly underestimates Ea [2–4]

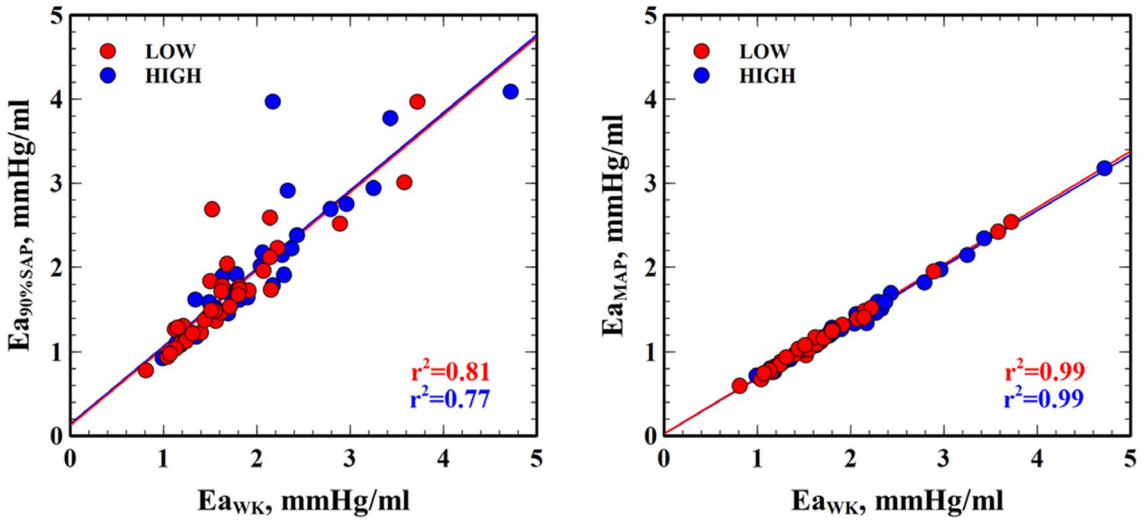

Fig. 1 Peripheral estimates were compared with the reference effective arterial elastance calculated using a three-element Windkessel model derived Ea (Ea-wk) during an incremental change in noradrenaline dose in 37 septic shock patients. LOW and HIGH refer to the lowest and highest dose of noradrenaline. Peripheral estimates were either the ratio of 90% radial systolic arterial pressure (SAP) over stroke volume (SV) (left panel) or the mean arterial pressure (MAP) over SV ratio (right panel). Note that the former estimate was close to the identity line (left panel) while the later estimate markedly and systematically underestimated Ea-wk (right panel). Drawings are as published in this figure of Ref. [1], with data points and calculations having been obtained from Ref. [11]

will be always less than for the 90% of SAP. [1]" This is a wrong statement as MAP always underestimates LVESP [3, 4] (Table 1).

We concentrated on baseline values of various estimates of Ea as their reliability is a prerequisite before discussing any dynamic change [2]. Our concerns were also based on a thorough analysis of the authors' recent experimental data [5]. Instead of sticking to these data, the authors mainly based their rebuttal on reasoning on another study in which they have calculated Ea using the complex, empirical equation derived from the three-element Windkessel model (Ea-wk) [11]. This is not standard practice. However, we are prepared to also extend our comments to that study [11]. Let us examine the related claim [1]:

Claim 4 "According to our analysis, the relationship of MAP estimates of Pes [LVESP] was better than for 90% SAP estimates for both Ea [Ea-dicrotic notch] and Eawk, and the limits of agreements narrower (Figs. 1, 2). [1]" As far as Eawk is concerned, the reader may easily conclude the opposite, namely that the peripheral MAP/

SV ratio systematically underestimates Ea-wk while the linear relationship between 90% SAP/SV and Ea-wk is close to the identity line (Fig. 1). We note that the two peripheral estimates of Ea were not compared in terms of mean bias and 95% confidence interval. This is the best way to compare various estimates of a given variable. The better correlation coefficient observed with one estimate versus the other (Fig. 1) simply shows stronger correlation, but it does not show accuracy for clinical purposes [12]. According to our own calculation based on Table 2 from Ref 11 and on Fig. 1, the peripheral MAP/SV ratio underestimates Ea-wk by approximately 35–40% in both the noradrenaline lowest-dose group and highest-dose group. We hope the reader will admit that this is an unacceptable underestimation. Conversely, if one looks at Fig. 1, the mean bias related to the 90% SAP/SV estimate of Ea-wk is likely to be very mild given the balanced position of the data points around and close to the identity line. It is interesting to note that we recently documented that the 90% SAP/SV ratio at the femoral level only slightly overestimates the central Ea (carotid LVESP/SV) by $8 \pm 8\%$ in 50 hemodynamically stable, critically ill patients [10]. We will not discuss the issue of estimating Ea by using peripheral dicrotic notch pressure [1, 5], because, according to our daily practice, the precise determination of peripheral notch pressure may be especially difficult in numerous patients, including critically ill patients.

Finally, we note that the authors have not answered the following questions clearly raised in our commenting letter [2]. If the MAP/SV ratio is really a robust and preferable estimate of Ea, what is the added value of Ea over total peripheral resistance (MAP/SV = total peripheral resistance × heart rate)? For a given inotropic state and heart rate, are we prepared to support that the LV-arterial coupling only depends on total peripheral resistance? And are we prepared to support that there is no need to take into account the role arterial stiffness on the LV-arterial coupling? After having read their rebuttal [1], these questions remain unanswered. As extensively documented by others [9], we support a significant pathophysiological role of the pulsatile component of arterial load.

In conclusion, our disagreement with Monge Garcia et al. is substantial and we maintain our previous remarks. The MAP/SAV ratio is simply the product of total peripheral resistance multiplied by heart rate, and its added value is thus questionable. This approximation of Ea must be especially avoided in a general population in which elderly or hypertensive subjects are included. If one wants to calculate Ea for studying the LV-arterial coupling at bedside, the 90% SAP/SV ratio is a validated estimate that takes into account the steady and pulsatile components of the LV afterload, and the brachial or femoral sites must be favored over the radial site given the less marked SAP amplification from central aorta to periphery. Further clinical studies are needed to solve the present controversy.

Compliance with ethical standards

Conflict of interest None declared for all authors in the subject matter (pathophysiology).

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