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EDITORIAL

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Mean systemic pressure: we can now estimate it, but for what?

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There has been much controversy about the reality of the Guyton's model of circulation [1, 2]. According to this model, systemic venous return is proportional to the pressure gradient for venous return divided by the resistance to venous return. The pressure gradient for venous return is the difference between the mean systemic pressure (Pms) and the right atrial pressure (Pra). The Psm, which is a virtual pressure considered to lie at the level of the venules [3], is positively related to stressed blood volume and negatively related to vascular compliance. The stressed blood volume, which represents 30–40 % of the total blood volume, is hemodynamically active and thus participates in venous return through its impact on Pms. The unstressed blood volume, which represents 60–70 % of the total blood volume, is hemodynamically inactive and serves as a blood reservoir that can be mobilized by venoconstriction and can be converted to stressed blood volume under some critical conditions [4]. Since Pms is a marker of effective blood volume, its measurement would be important to obtain at the bedside in order to better characterize a patient's cardiovascular status and its response to therapies. Until recently, the Pms could not be measured routinely in patients. According to the Guyton's theory, the Pms is the vascular pressure existing at zero flow conditions (Fig. 1) and its measurement requires the physician to stop the circulation and wait for equilibrium between the arterial pressure and the venous pressure. Obviously, this is feasible only in experimental conditions in animals [5] or during cardiac arrest in humans [6]. Recently, Maas et al. [3] proposed an elegant method to estimate Pms in intact conditions in mechanically ventilated patients. This method consists of simultaneously measuring central venous pressure (CVP) and cardiac output (CO) during inspiratory-hold maneuvers at four different plateau pressures. A set of four CVP–CO data pairs can thus be obtained. Considering that CVP is a surrogate of Pra and that CO is equal to venous return in apneic steady-state conditions, a set of four Pra-venous return data pairs is thus obtained and can be fitted by linear regression to define the venous return curve. The estimated Pms is defined as the extrapolation of this linear regression to zero flow (Fig. 1). Using this method, Maas and coworkers [3] found that fluid loading increases the estimated Pms and that a 30° head-up position decreases the estimated Pms, all findings consistent with what it is expected from Guyton's theory. Thereafter, a derived method to estimate Pms was proposed by Persichini and coworkers [7]. This method consists of performing two consecutive sets of four ventilatory-hold maneuvers (inspiratory and expiratory holds, both performed at two levels of positive end-expiratory pressure) resulting in eight CVP–CO data pairs [7]. By doing so in 16 septic patients receiving norepinephrine, a very close linear relationship (average $r^2 = 0.71$) between CO and CVP was found in every patient at baseline and after norepinephrine decrease. This strongly argues that Guyton's model of circulation makes sense. The main limitation of the ventilatory-hold methods to

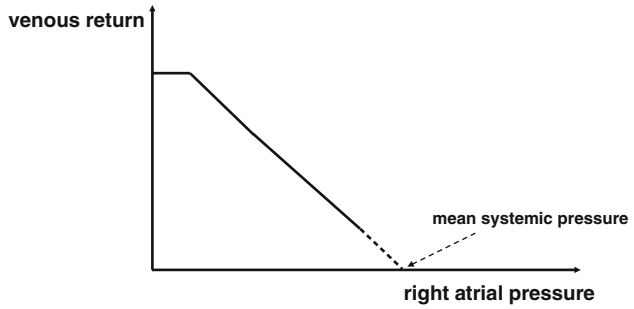

Fig. 1 Relationship between right atrial pressure and venous return according to Guyton's model. Note that at low right atrial pressure, the venous return does not increase further probably because of the collapse of the inferior vena cava at the thorax entry

estimate Pms is that it requires a perfect adaptation of the patient to the ventilator. In addition, because it is cumbersome, this technique cannot be used for routine patient management and thus should be reserved for research purposes. Recently, a noninvasive software algorithm has been developed to estimate a Pms analogue (Pmsa) using the mean arterial pressure (MAP), Pra (or CVP), CO and the patient's anthropometric data. This system automatically collects data from standard bedside and cardiac output monitors. The formula that estimates Pms is proprietary and uses Guyton's model. In a previous study, Maas et al. [8], using the inspiratory-hold method as the reference in postoperative cardiac surgery patients, reported a poor agreement between Pmsa and Pms. However, they found that changes in Pmsa and changes in Pms were directionally concordant in response to head-up tilt and volume loading [8]. In this issue of Intensive Care Medicine, Cecconi et al. [9] also assessed the significance of the Pmsa and the difference between Pmsa and CVP (dVR) during a fluid challenge in post-operative surgical intensive care patients. One-hundred and one fluid challenges were performed in 39 patients. Pmsa increased similarly during a fluid challenge in responders and non-responders (3.1 ± 1.9 vs. 3.1 ± 1.8), whereas the dVR increased in responders but remained unchanged in non-responders [9]. They concluded that the changes in Pmsa and dVR measured during a fluid challenge are consistent with the cardiovascular model described by Guyton. This result is not surprising since Pmsa is calculated from MAP, CVP and CO according to the Guytonian model of circulation. This can thus be viewed as an auto-validation of the proprietary algorithm. Nevertheless, this study does not provide a positive answer to the question of the usefulness of Pmsa to guide fluid management. In this regard, Cecconi et al. [9] clearly show that neither Pmsa nor dVR at baseline predicted fluid responsiveness. This is not really a surprise, since Pmsa and dVR are static variables. It was already demonstrated that static measures of preload such as CVP, pulmonary artery occlusion pressure and left ventricular end-diastolic area are not reliable for predicting the CO response to fluid administration [10]. We have now learned that a static measure of the effective blood volume such as Pms cannot serve as a marker of fluid responsiveness. Nevertheless, knowledge of this easy-to-obtain parameter provides clinicians with additional information that should help to get a more comprehensive picture of the patient's cardiovascular status and its response to therapies.

Conflicts of interest The author declares no conflict of interest.

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Geoffrey Parkin

Re: Mean systemic filling pressure: we can now estimate it but for what?

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Dear Editor,
It is a pleasure to respond, as author of the Pms algorithm to which his editorial refers, to Prof. Teboul's provocative title [1].

Refreshingly, we see acceptance of Pms, rather than any preload measure, as the preferred method of evaluating the effective blood volume, definitely a step in the right direction.

So why does Teboul invite such a bleak reply? Why is a Guytonian approach to the circulation only now finding its way into mainstream care?

One answer, we agree, is that Pms is not easy to measure repeatedly using inspiratory hold or arm compression [2]. We have demonstrated [3] that a useful Pms analogue, Pmsa, can be calculated using

$$\text{Pmsa} = 0.96 * \text{RAP} + 0.04 * \text{MAP} + c * \text{CO} \quad (1)$$

where "c" is an anthropometrically based variable ($0.3 < c < 1.2$) with the dimensions of resistance. This approach allows for the confounding effect of unmeasurable venous resistance change upon measurement of the apparent volume state. Therein lie some of the reasons for "poor agreement" (Editorial) between dynamic Pmsa and static Pms (and by extension, Maas). Our article cautioned against numerical comparison with static Pms for just this reason.

Since (Guyton)

$$\text{CO} = \text{VR} = (\text{Pmsa} - \text{RAP})/\text{RVR} \quad (2)$$

the role of the heart in determining CO may be seen as keeping RAP below Pms. A dimensionless heart variable E_h

$$E_h = (\text{Pmsa} - \text{RAP})/\text{Pmsa}\ 0 \le E_h \le 1) \quad (3)$$

is thus a very useful static descriptor of the global performance of the heart.

Using the SVR (for all its shortcomings) as a resistance measure, Pmsa, E_h and SVR calculated for the present and target circulations permit precise graphical vector guidance for the direction and priority of volumetric, cardioactive and vasoactive therapies.

In a closed loop study, for example [4], volume replacement was targeted to a clinician-prescribed Pmsa. In 601 h of CVVHD in ten subjects using a "bang bang" controller, 409 litres were replaced with a loss of 417 litres with no microcontroller 'knowledge' of the gains and losses. Cardiovascular stability exceeded controls.

In measuring volume responsiveness (Vr) we are interested in the change in CO and therefore Δ (Pmsa-RAP) (Eq. 2) produced by a volume change ΔPms, [5] i.e. [cf. (3) above]

$$\text{Vr.} = \Delta(\text{Pmsa} - \text{RAP})/\Delta\text{Pmsa}\ (0 \le \text{Vr} \le 1) \quad (4)$$

Cecconi et al. [6] have carefully documented these changes showing how they are easily measured.

In their experiments, RVR changed minimally.

We agree that static measures do not predict volume responsiveness. Our dynamic dimensionless measure accurately records volume responsiveness every time the volume state is changed. It does not require positive pressure ventilation, a regular heart rate or other preconditions. It is particularly suitable as is most of the above to closed loop systems of care.

Knowing the volume state, measuring heart performance, quantitating volume responsiveness and achieving vector guidance should we believe start to answer the good professor's "but for what?" challenge.

Conflicts of interest Dr. Parkin is a director and shareholder of Applied Physiology, an Australian medical software house.

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Mean systemic filling pressure: we can now estimate it, but for what? Response to comment by Parkin

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Dear Editor,

I read with interest the letter by Dr. Parkin [1], who raised several points that are in full agreement with what I wrote in my editorial [2]. Dr. Parkin must be respected for having, in the past, elegantly proposed an estimation of the mean systemic pressure (P_{ms}) from an equation that includes mean arterial pressure (MAP), central venous pressure (CVP), and cardiac output (CO) according to a Guytonian model of the circulation. I agree with him that such estimation seems to be valid. However, in his letter Dr. Parkin seems a little confused about the definition and clinical application of the concept of volume responsiveness or unresponsiveness. The following sentences are aimed to clarify these important points. For a clinician, there are two different issues to deal with: one is prediction of volume responsiveness/unresponsiveness, and one is assessment of the response to fluid once it has been infused. Predicting volume responsiveness/unresponsiveness is of major importance, since we know that volume overload is deleterious for critically ill patients [3]. In this respect, identifying in advance patients who would not benefit (no significant increase in CO) from volume infusion would avoid overloading them. In the study to which the editorial [2] referred, Cecconi et al. [4] showed that the value of P_{ms} before any fluid infusion cannot predict volume responsiveness at all. This result was not so surprising since, at best, P_{ms} is a static measure of effective blood volume and thus should share with other static hemodynamic variables the disadvantage of being unable to predict volume responsiveness/unresponsiveness [5]. A totally different issue is to assess the actual hemodynamic response to fluid administration, once it has been done. In this situation, the clinician wants to know how much was the actual benefit of fluid administration in terms of increase in CO. In order to do this, nothing is better than a direct measure of systemic blood flow, i.e., CO. By definition, calculation of P_{ms} using the formula developed by Dr. Parkin needs real-time CO measurements. In this situation, where a real-time CO monitor is used, the value of CO is under the eyes of the clinician. Therefore, what could be the interest of looking at the changes in P_{ms} (so-called ΔP_{ms}) after fluid administration rather than looking at the changes in CO, which provide a direct and relevant quantification of the response to fluid administration? In addition, because P_{ms} is calculated from MAP, CVP, and CO, it must cumulate the potential errors of measurements of each of these hemodynamic variables. So, why complicate what one can do simply? This is the reason why, in terms of clinical practice, the "so what?" question that I mentioned in the title of my editorial deserves to be asked without any kind of provocation.

Conflicts of interest The author has no conflict of interest related to this manuscript.

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