Can (and should) the venous tone be monitored at the bedside?

Hollmann D. Aya[a,b] *and Maurizio Cecconi*[a,b]

Purpose of review
Most of our blood volume is contained in the venous compartment. The so-called 'compliant veins' are an adjustable blood reservoir, which is playing a paramount role in maintaining haemodynamic stability. The purpose of this study is to review what is known about this blood reservoir and how we can use this information to assess the cardiovascular state of critically ill patients.

Recent findings
The mean systemic filling pressure (Pmsf) is the pivot pressure of the circulation, and a quantitative index of intravascular volume. The Pmsf can be measured at the bedside by three methods described in critically ill patients. The Pmsf can be modified by the fluid therapy and vasoactive medications.

Summary
The Pmsf along with other haemodynamic variables can provide valuable information to correctly understand the cardiovascular status of critically ill patients and better manage the fluid therapy and cardiovascular support. Future studies using the Pmsf will show its usefulness for fluid administration.

Keywords
central venous pressure, fluid therapy, mean systemic filling pressure, systemic compliance, venous tone

INTRODUCTION

The venous system plays an important role in cardiovascular homeostasis. It is not merely a conduct of blood to the heart. It serves as an adjustable blood reservoir to maintain blood flow constant in changing situations. Veins contain 70% of total blood volume whereas arteries contain only 13–18%, and capillaries 7% [1,2]. Venous walls are thin, although muscular enough to contract or expand, depending on the needs of the circulation. During hypovolaemia, sympathetic nervous reflexes cause venoconstriction, sending blood back to the central circulation. Actually, even after 20% of the total blood volume has been lost, the circulatory system functions almost normally because of this variable reservoir function of veins [1]. Similarly, when a person is standing absolutely still, the pressure in the veins of the feet is about 90 mmHg, simply because of the gravitational effect of the blood in veins. This effect could actually be life threatening, if there was no compensatory reflex. Hainsworth [3] pointed out that almost all the possible reflex venoconstriction is used to maintain cardiac output (*CO*). Venous tone is thus very important in haemodynamic haemostasis.

Certain parts of the venous system are particularly compliant. These include the spleen, the liver, the large abdominal veins and the venous plexus beneath the skin. Splanchnic and cutaneous veins have a high population of $\alpha 1$ and $\alpha 2$-adrenergic receptors, so they are very sensitive to adrenergic stimulation, contrary to skeletal and muscle veins [4].

Given that the heart pumps blood continuously into the aorta, the mean pressure in the aorta remains high, averaging 80–100 mmHg. As the blood flows into the systemic circulation, the mean pressure falls progressively as low as the level of the right atrial pressure (RAP). When the heart stops, the arterial pressure falls down and the RAP progressively increases. At a certain point, blood will not be flowing, and the pressure will be the same in all parts of the circulatory system. This is called the mean systemic filling pressure (Pmsf). The Pmsf was described by Bayliss and Starling [5], and they

[a]General Intensive Care Unit, St. Georges Healthcare NHS Trust and [b]Cardiovascular Sciences Institute, St George's University of London, London, UK

Correspondence to Maurizio Cecconi, MD, MD(UK), General Intensive Care Unit, First Floor, St James Wing, St. Georges Healthcare NHS Trust, London, UK. Tel: +44 208 725 0879; e-mail: m.cecconi@nhs.net

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KEY POINTS

- The venous system serves as a blood reservoir adjustable to the blood flow requirements.
- The Pmsf is a quantitative measurement of the volume status and represents a measurement of the venous reservoir tone.
- The Pmsf can be measured at the bedside by using inspiratory hold manoeuvres, by using a stop-flow arterial–venous equilibrium pressure or using a computerized mathematic algorithm.
- Although very little evidence is available, the Pmsf monitoring has a lot of potential. The Pmsf can provide important information when a clinician wants to challenge the system using a bolus of fluids or a PLR test. The Pmsf can also guide decisions regarding the use of further fluid or vasoconstrictors.
- The understanding of the Pmsf has allowed us to better integrate *CO* and CVP monitoring at the bedside.

figured that somewhere in the circulation there must be a point where the pressure is not changing when the heart stops. Actually, during a cardiac arrest, the pressure in the small veins (< 1 mm) and venules does not change substantially; they are the 'pivoting point' of the system (Fig. 1). The Pmsf is less than the capillary pressure, close to the portal venous pressure and greater than the RAP. Its anatomic location is not necessarily at the same venous branching level in the various organs. The importance of the pivotal pressure, rather than its anatomical location, is that it provides a quantitative measurement of the intravascular filling status independent from cardiac function. Its value is equal to the Pmsf.

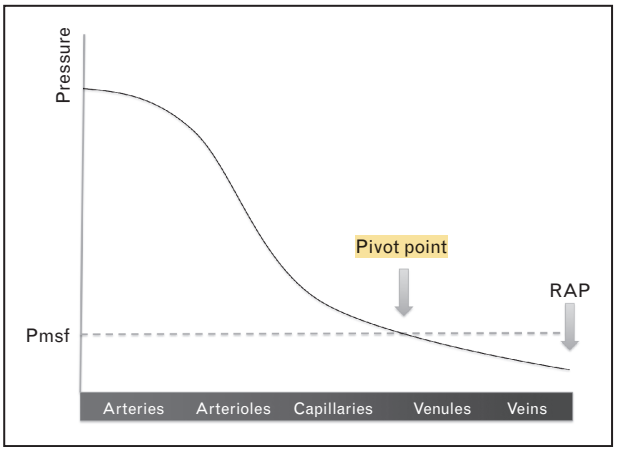

FIGURE 1. Pressures across cardiovascular system. Pmsf is the mean systemic filling pressure. Pmsf is the pressure at all points in the cardiovascular system when the heart stops. During normal circulation, there is a point (pivot point) where the pressure equals the Pmsf. At that point, the pressure is independent of flow, and theoretically localized at the venule territory. Previously published by Rothe *et al.* [6].

Let us imagine the 'blood reservoir' as a distensible compartment. The volume required to fill a distensible tube, such as a tyre or a blood vessel, with no pressure rise is called the 'unstressed' volume (V_o). Further volume expansion will imply necessarily a pressure rise and an elastic distension of the wall of the tube, which depends on the compliance (C) of the wall (Fig. 2). This volume is the 'stressed' volume (V_s) and is related to the pressure as shown in the following equation:

$$\text{Pmsf} = V_s/C,$$

Guyton *et al.* [6,7] realized that it is actually the difference in pressure between two points, not any single pressure at any point of the cardiovascular system, which determines the rate of flow. Given

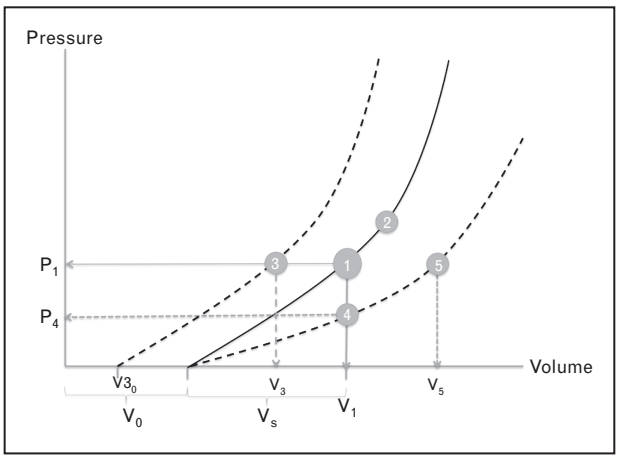

FIGURE 2. Volume–pressure relationship in the venous compartment. The point 1 represents the total blood volume at the mean systemic filling pressure P_1. For this point, the volume at 0 pressure is the unstressed volume (V_0) and the difference between the total volume (V_1) and V_0 is the stress volume (V_s). The continuous black line represents the baseline compliance. The point 2 represents a change in pressure induced by a change in intravascular volume. When a certain amount of blood is removed from the venous system, point 1 can move forward point 3. The system contains now less blood (V_3) at the same pressure given that some unstressed volume (now $V3_0$) was recruited into stressed volume. However, the system can maintain the pressure–volume relationship (parallel dashed line). This means that the capacity of the system was reduced but not the compliance. When the system suffers an increased compliance, the same total volume is displaced from point 1 to point 4, as it is not able to generate the same amount of pressure (P_4). To return to P_1, volume must be expanded (V_5) unless compliance is corrected.

that most of the blood is in the venous reservoir, the pressure at this point is particularly interesting. Guyton pointed out that venous return must be defined by using the three parameters, which are as follows: the Pmsf, the RAP and the resistance to venous return (RVR). This can be also mathematically represented as follows:

$$\text{Venous return} = \frac{(\text{Pmsf} - \text{RAP})}{\text{RVR}}.$$

Guyton [8] drew venous return curves in recently dead dogs. The author replaced the heart with a pump and controlled the RAP by increasing or decreasing the minute capacity of the pump. He also controlled the Pmsf by increasing or decreasing the total quantity of blood. From these curves one can spot that, for any given RAP, the greater the Pmsf, the greater the venous return is. Importantly, under isovolumetric conditions, the greater is the RAP, the lower is the venous return. During steady conditions, *CO* and venous return are equal, the Pmsf plays an important role on the regulation of *CO*.

MEASUREMENT OF VENOUS TONE: YES, WE CAN!

The challenge of measuring the venous tone is that the Pmsf is not easy to measure in patients with an intact circulation. Schipke *et al.* [9] performed a fibrillation–defibrillation sequence in 82 patients to measure the Pmsf over 13 s. A true equilibrium pressure was not achieved, and the arterial–central venous pressure difference was 13.2 ± 6.2 mmHg.

Pinsky [10] proposed a model in animals with an intact circulation to construct venous return curves, observing the relationship between instantaneous changes in right ventricular *CO* and RAP during intermittent positive pressure recruitment manoeuvres, and then extrapolating the RAP value to zero *CO*. The Pmsf calculated was similar to the Pmsf measured during circulatory arrest. Other studies [11–13] have confirmed this linear relationship between venous return and central venous pressure (CVP) and derived Pmsf from the regression equation in animal models with intact circulation. Maas *et al.* [14] applied the same rationale to study the effect of a 12-s inspiratory hold manoeuvre to three different steady-state levels on CVP and blood flow (CO) measured via the pulse contour method during the last 3 s in mechanically ventilated postoperative cardiac patients. This interesting study again showed a linear relationship between CVP and CO, and importantly, the Pmsf could be estimated in intensive care patients with an intact circulation. Obviously, this technique is only feasible in fully sedated patients under mechanical ventilation. This method was also used by Keller *et al.* [15] to assess the changes of passive leg raising (PLR) on venous return. They observed nine postoperative cardiac patients at baseline during PLR and after the volume expansion (500 ml of hydroxyethyl starch). They reported the Pmsf at baseline of 19.7 mmHg. This only increased to 22 mmHg after PLR and to 26.9 mmHg after the volume expansion. Although *CO* increased after PLR and the volume expansion, the gradient of pressure of venous return (difference between the Pmsf and CVP) increased by 2 mmHg after PLR and by 5.8 mmHg after the volume expansion. This could explain why a PLR test does not systematically increase *CO* in fluid responsive patients [16], or even for a fluid challenge, the increase in the Pmsf is an essential condition to effectively test the cardiac response.

Parkin and Wright [17] described a method for estimating a Pmsf analogue (Pmsa) using the mean arterial pressure (MAP), RAP, *CO* and anthropometric data. The calculation of Pmsa was fully described in other publications [18]. In essence, they used a mathematical algorithm to build a cardiovascular model using the patient's data. The clinical validity of this approach was tested in 10 patients in acute renal failure receiving continuous vein–venous hemofiltration [19]. Fluid replacement therapy was electro-mechanically controlled to a target value of Pmsa. Despite some limitations of this study, this approach supports the concept of using Pmsa as a quantitative parameter of the intravascular volume status. This method was used to analyse haemodynamic changes after a fluid challenge (250 ml of colloids or crystalloids in five minutes) in patients admitted to intensive care [20▪▪]. Pmsa increased similarly in responders and nonresponders as expected, but interestingly CVP increased more in nonresponders, neutralizing the changes in the gradient of pressure of venous return as described by Guyton.

Recently, Gupta *et al.* [21] used Pmsa to investigate the performance of cardiac power (defined as the product of arterial pressure and *CO*) relative to Pmsa (CP_{vol}). CP_{vol} represents a measurement of cardiac performance adjusted to the vascular tone. According to the authors, values below 0.047 of CP_{vol} have a high sensitivity (97%) and not so high specificity (57.5%) to predict fluid responsiveness.

Anderson [22] proposed a noninvasive technique to measure Pmsf by a rapid occlusion of the circulation in the arm (Pmsf-arm). Once the arterial (Pa) and venous pressures (Pv) in the arm equilibrate, the pressure measured would be the Pmsf.

Maas *et al.* [23] compared these three methods in 11 postoperative cardiac surgery patients. Bland–

Altman analysis for the difference between Pmsf-arm and Pmsf showed a bias of −1.0 (±3.1) mmHg ($P = 0.06$) and a coefficient of variation of 15%. Although there was a nonsignificant bias, one may think that this is actually quite significant considering the small sample size of this study. Regarding the difference between the Pmsf and Pmsa, there was a bias of −6.0 (±3.1) mmHg ($P < 0.001$) and a coefficient of variation of 17%. The three methods were useful to track changes after the volume expansion.

SHOULD THE VENOUS TONE BE MONITORED AT THE BEDSIDE?: PRACTICAL IMPLICATIONS

Unfortunately, despite the importance of venous tone on the maintenance of cardiovascular stability, there is still very little evidence about the impact of this information on the management of critically ill patients.

Rangappa *et al.* [24] investigated the potential of a computerized decision-support system (Navigator, Applied Physiology, Sidney, Australia) to improve consistency of haemodynamic evaluation and treatment decisions by intensive care unit clinical staff with different levels of expertise and experience in 20 patients admitted after elective cardiac surgery. The study showed that Pmsa was commonly underestimated by all categories of ICU staff, and that this system may improve consistency in decision making.

Sondergaard *et al.* [25▪] carried out a small pilot clinical trial in 27 postoperative patients, requiring goal-directed therapy to evaluate the efficiency of the Navigator system in achieving haemodynamic targets (measuring the percentage time in target zone and the averaged standardized distance from the centre of the target and time to achieve targets) and the level of concordance between the therapy suggested by the system and an expert clinician. The mean percentage time in the target zone was 36.7% for control and 36.5% for intervention and the averaged standardized distance was 1.5 in control and 1.6 in intervention (no *P* value was reported). There was a high level of concordance between decision-support recommendation and anaesthetist action (84.3%). The authors concluded that the treatment recommended by the Navigator system mirrored that of a senior anaesthetist in the achievement of therapeutic goals. Unfortunately, this study is probably underpowered to show differences in the efficiency measurements, fluid balance or vasoactive medications. In addition, it is quite interesting that in both cases the percentage of time in the target zone was so low.

However, some interesting studies demonstrated that some useful information could be obtained by observing the Pmsf. The current consensus on circulatory shock and haemodynamic monitoring states that even in the context of fluid responsive patients, fluid management should be carefully titrated, especially in the presence of elevated intravascular filling pressures [26]. A similar principle applies to the Pmsf. A fluid challenge should be used to assess fluid responsiveness particularly in the presence of high Pmsf values. In addition, a fluid challenge can be used not only to test fluid responsiveness but also, as spotted by Maas *et al.* [27], to assess systemic compliance. Given that the Pmsf is the pressure at the pivot point, which is located at the venule territory, this may represent an estimation of the venous reservoir compliance. In this study, systemic compliance is reported from 15 postoperative cardiac surgery patients around 64 ml/mmHg. Systemic venous compliance could be very useful information to prioritize treatment: a high compliance after a fluid challenge may indicate the use of vasopressors instead of infusion of a large amount of fluids. Another study [28] showed that administration of noradrenaline increased *CO* in preload responsive patients. Noradrenaline increased the Pmsf either by reducing venous compliance or by venoconstriction (reduction of venous capacity and shifting unstressed volume to stressed compartment, see Fig. 2). Unfortunately, the authors did not assess the effect of noradrenaline on venous compliance. In the rest of the patients, noradrenaline had predominantly an arterial vasoconstrictive effect, increasing cardiac afterload. This study stressed the importance of monitoring venous tone and *CO* when using vasopressors.

As venous return equals *CO*, in real-life practice *CO* and CVP changes can provide most of the information about the Guytonian view of the circulation. However, without the understanding of how the venous tone works, understanding how to use CVP can be difficult. Proof of this is the number of studies that looked at the CVP as a preload index [29]. CVP performs as the meeting point between the Pmsf and cardiac function: a high CVP can be related to a high Pmsf or a low cardiac function or both. Thus, knowing the Pmsf would help clinicians to better understand the haemodynamic status of critically ill patients at the bedside.

CONCLUSION

The venous system plays an important role in the haemodynamic stability. Most of the blood volume is stored and regulated in the venous territory. The

Pmsf can now be measured and it is the pressure of the pivot point of the circulation where the pressure is independent of blood flow. This pressure is the driving pressure of the circulation and affects, along with the cardiac function, venous return. Three methods have been described to measure the Pmsf at the bedside, in patients with intact circulation. This variable must now be integrated as another piece of information, which helps to understand patients' conditions and to guide haemodynamic therapy.

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Conflicts of interest

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