

Venous return and clinical hemodynamics: how the body works during acute hemorrhage

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Shen T, Baker K. Venous return and clinical hemodynamics: how the body works during acute hemorrhage. *Adv Physiol Educ* 39: 267–271, 2015; doi:10.1152/advan.00050.2015.—Venous return is a major determinant of cardiac output. Adjustments within the venous system are critical for maintaining venous pressure during loss in circulating volume. This article reviews two factors that are thought to enable the venous system to compensate during acute hemorrhage: 1) changes in venous elastance and 2) mobilization of unstressed blood volume into stressed blood volume. We show that mobilization of unstressed blood volume is the predominant and more effective mechanism in preserving venous pressure. Preservation of mean circulatory filling pressure helps sustain venous return and thus cardiac output during significant hemorrhage.

hemorrhage; venous return; circulation; Guyton

The vein is one whole, which is divided into as many main branches as there are principal places which it has to nourish.

Leonardo Da Vinci (1452–1519)

THE VENOUS SYSTEM plays a central role in the regulation of the circulation. In this article, we review the concepts of venous elastance, unstressed blood volume, and stressed blood volume. We show how the venous system physiologically adapts to maximally preserve venous pressure and thus cardiac output during acute hemorrhage. We also review the effects of vasoconstrictors such as norepinephrine on the venous system.

The Venous System

Approximately 70% of the systemic blood volume is located in veins (23). Venous return is necessary for cardiac output, and venous return is enhanced as venous tone increases. Thus, alterations in venous vasomotor tone can provide rapid and significant compensations for changes in circulating volume. The classic venous return and cardiac output curves were constructed by Guyton and colleagues over 50 yr ago (Fig. 1) (11). In normal humans, cardiac output is strongly governed by the amount of blood flowing into the heart (i.e., venous return). During this inflow, right atrial pressure (RAP) rises. Instantaneous RAP also represents the prevailing effective downstream pressure that influences the rate at which blood flows back to the heart. The circulation is at steady state when venous return equals cardiac output. Venous return, at any given moment, is determined by the difference between mean systemic pressure [MSP; the capacitance-weighted mean pressure of the entire circulation (10)] and RAP. Normal resting MSP is estimated at 8–12 mmHg and RAP

is ~2–3 mmHg. Thus, the gradient for venous return is ~5–10 mmHg (7, 9). MSP can be effectively measured when the circulation ceases and all the vascular pressures equalized; this was first done by Starr in 1940 (28). The importance of the venous return and its regulation can be summarized by the axiom that a heart cannot pump more than it receives.

Filling the Venous System

To understand how the venous system adapts to hemorrhage, it is instructive to first review how veins fill. The dynamics of the venous system can be appreciated by realizing that the total venous volume consists of two hypothetical components: unstressed blood volume and stressed blood volume (Fig. 2). Imagine an empty vein beginning to be filled with blood. When blood is first placed in the empty vessel, there is essentially no pressure exerted on the vessel wall despite the presence of increasing amounts of volume. Since this initial volume of blood exists at negligible pressure, it is termed the “unstressed blood volume.” Once sufficient unstressed blood volume is placed into the vessel, any additional volume will begin to produce a measurable distending pressure in the vessel. This additional volume is termed the “stressed blood volume” because it stresses the vessel wall and generates measurable pressure. Importantly, it is only the stressed blood volume that is hemodynamically active (it largely determines MSP and thus venous return). The initial blood placed in the vein, the unstressed blood volume, is physiologically inert and does not influence hemodynamics. The final intravascular pressure within the vein is determined by two factors: the amount of stressed volume placed in the vessel and the elastance of the vessel, a point we return to shortly. In human and animal studies, the stressed blood volume amounts to ~25–30% of the total blood volume (~20 ml/kg), leaving a large reservoir of unstressed volume available for mobilization (7, 16). Indeed, one of the most important aspects of the venous system is its ability to shift blood from unstressed to stressed and thereby maintain filling pressures.

Another factor that affects venous pressure during changes in venous blood volume is venous elastance. Elastance refers to the change in pressure that results when there is a change in stressed blood volume (elastance = dP/dV , where P is pressure and V is volume). Thus, elastance is a slope. A vessel with a higher elastance would have a greater pressure rise when additional stressed blood volume is placed into the vein compared with a vessel with a lower elastance. Elastance is the mathematical reciprocal of compliance, which describes the change in volume with a change in pressure (compliance = dV/dP). Elastance can be measured at different venous volumes and may vary as a function of the volume in the vein.

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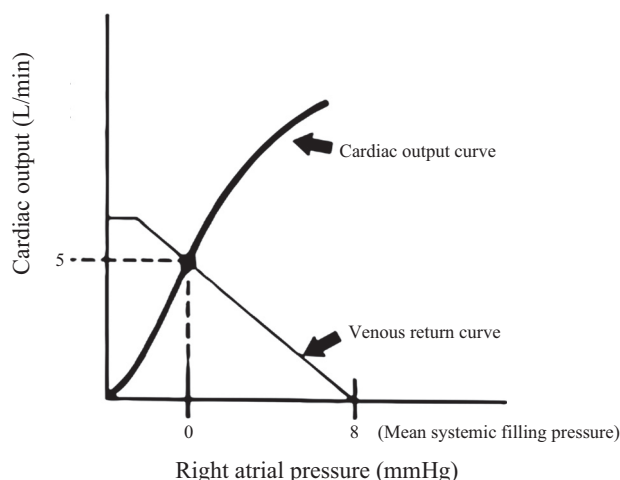


Fig. 1. Coupling of cardiac and venous return curves. The intersection represents the steady-state operating point of the circulatory system.

This variability occurs because the distensibility of a blood vessel may differ with its fullness and is not linear over the entire pressure-volume relation (23).

If we kept the total blood volume constant and were interested in increasing venous pressure, we could achieve this through two potential mechanisms: 1) an increase in venous elastance or 2) an increase in the amount of stressed blood volume.

Hemorrhage Reveals How the Venous System Adjusts to Maintain Pressure

Consider an extremely rapid hemorrhage of 1.5 liters (nearly the entire stressed blood volume). This will reduce the pressure in the veins to near zero. As a result, MSP would fall to near zero and venous return would also abruptly decrease to near zero. Fortunately, almost immediately, various compensatory reflex mechanisms would be activated. For example, both systemic and intracardiac baroreceptor systems will act to attempt to restore MSP and thus arterial pressure (21, 23). There are three potential physiological adjustments that the venous system might invoke to cope with this hemorrhagic insult:

1. No change in venous elastance or unstressed blood volume (Fig. 3A). With no change in venous elastance or unstressed blood volume, blood loss would cause venous pressure to fall along the pressure-volume curve. Thus, as blood was lost, the stressed blood volume would directly decrease and the overall venous pressure would fall. A clinical example of this would be hemorrhage in the face of total spinal shock or during a high-spinal anesthetic.

2. A simple change in venous elastance (Fig. 3B). If the body used an increase in venous elastance as a compensatory mechanism, then this would be reflected in a steeper slope of the pressure-volume relationship as hemorrhage proceeded. If elastance increased as the hemorrhage progressed, then venous pressure could be maintained at a lower total blood volume until the elastance approached infinity (when the pressure-volume slope approached vertical). This physiological strategy would limit the maximum tolerable blood loss to the stressed blood volume in the system. Any bleeding beyond this volume would cause an abrupt drop in venous pressure to near zero; the

gradient for venous return would abruptly disappear, and cardiac output would cease. Experiments in animals (27) and humans (6) have demonstrated negligible changes in venous elastance after hemorrhage. The administration of sympathomimetics (epinephrine) or sympatholytics (ganglionic blocker) also seems to have little or no effect on venous elastance (5, 26, 27). Thus, from available clinical data, it appears that changes in elastance play a small role in compensating for blood loss.

3. Converting unstressed blood volume to stressed blood volume (Fig. 3C). If the venous system were to convert unstressed blood volume to stressed blood volume during an acute hemorrhage, then a large reservoir of unstressed blood volume would be available for recruitment into stressed blood volume. Graphically, this is reflected in a simple left shift of the pressure-volume relation. Simple conversion of unstressed to stressed blood volume does not alter the elastance of the vein (as reflected by the constant slope of the pressure-volume relationship). However, it significantly reduces the capacitance of the venous system. Experimentally, near-maximal venoconstriction with norepinephrine can shift nearly 15–20 ml/kg of blood volume (nearly 1.5 liters in adults) (5, 22, 24) from being unstressed to stressed. This allows the venous pressure to be maintained at near normal levels despite significant blood loss. The molecular mechanism that underlies the vein's transition to a smaller container but one that has similar distensibility characteristics (i.e., elastance) remains unknown. A combination of a substantial decrease in unstressed blood volume and a slight increase in elastance is the most likely scenario that

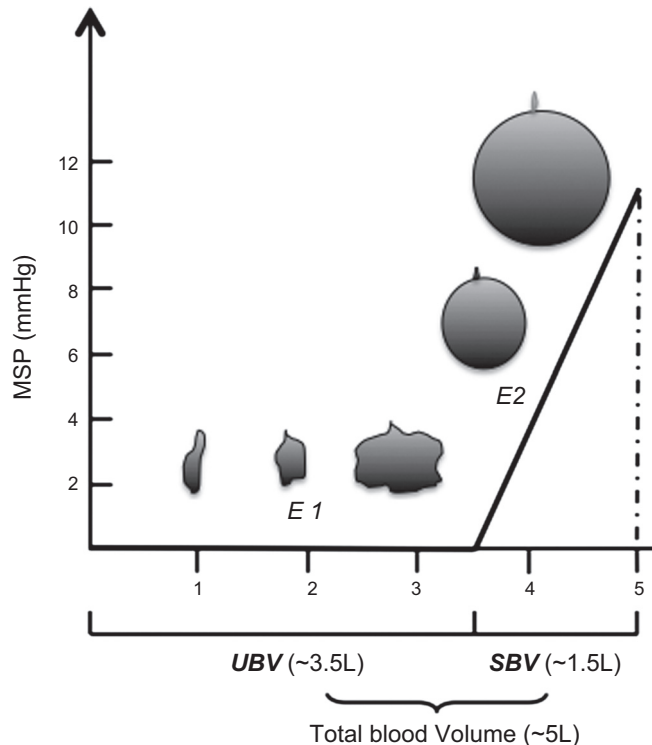


Fig. 2. Pressure-volume relationship demonstrating that total blood volume consists of two hypothetical components: unstressed blood volume (UBV) and stressed blood volume (SBV). UBV produces no pressure, whereas SBV produces stretch on the vessel wall and contributes to mean systemic pressure (MSP). E1 and E2 represent the elastance of each type of virtual volume. The balloons (from empty to full) demonstrate the concept of blood volume before and after it causes wall tension.

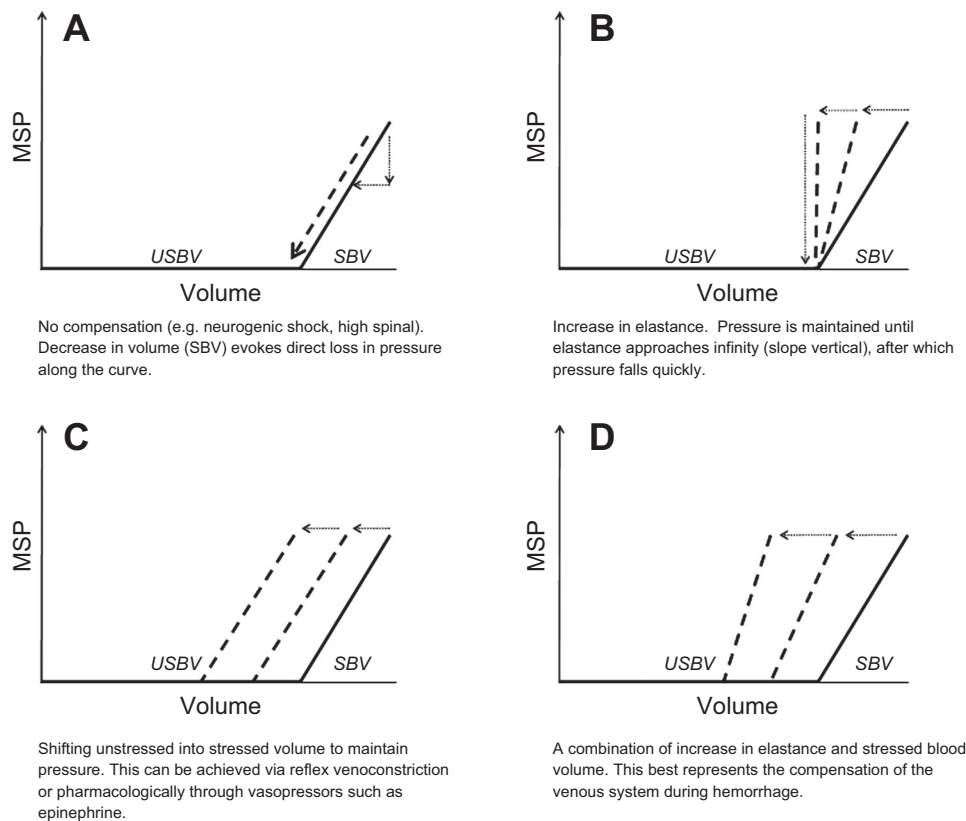


Fig. 3. Hypothetical responses of the venous system during acute hemorrhage. *A*: no compensation. *B*: increase in elastance. *C*: shifting unstressed into stressed volume to maintain pressure. *D*: combination of increase in elastance and stressed blood volume.

occurs in nature to maintain venous pressures during a hemorrhagic insult (Fig. 3D) (3, 30). The dominant compensatory mechanism, however, is the conversion of unstressed to stressed blood volume (5).

Thus, the venous system is a high-capacitance system whose large reservoir of unstressed volume is available for mobilization during an acute hemorrhage. This compensatory mechanism helps explain why many patients maintain their hemodynamics during the early phases of a significant hemorrhage (up to 10–15% of their circulatory volume) without much alteration in their cardiac output. Such compensation indicates successful conversion of unstressed blood volume to stressed blood volume during the bleed, which preserves the venous pressure, MSP, venous return, and thus cardiac output. However, once all available unstressed blood volume has been converted to stressed blood volume, any additional bleeding results in rapid loss of venous pressure and cardiac output. The ability of the body to carry out this compensation is decreased under the vasodilating effects of general and neuraxial anesthesia but is greatly augmented with vasopressors such as norepinephrine (8) or epinephrine (30). These drugs directly convert unstressed blood volume to stressed blood volume while maintaining nearly normal venous elastance.

An important implication of these adjustments in the venous system is that cardiac output, together with venous and arterial pressures, can be maintained in the face of significant blood loss without any overt signs of hypovolemia. The traditional teaching of circulatory physiology has focused on the performance of the left heart as a pump that itself regulates the cardiac output. In contrast, the venous return model emphasizes that cardiac output is equal to and regulated by the

amount of blood flowing into the heart. During hemorrhage, as long as venous inflow is preserved through maintenance of the stressed blood volume (and thus MSP), measured parameters such as heart rate, central venous pressure, and systemic blood pressure may remain largely unchanged and significant hypovolemia can be effectively masked (Fig. 4) (20). Compensated hypovolemia, which occurs in early hemorrhage, has negative

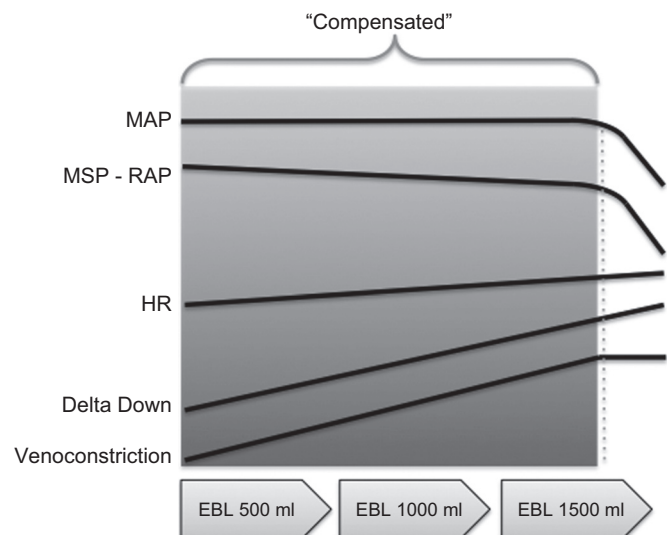


Fig. 4. Schematic of progressive hemorrhage showing that mean arterial pressure (MAP), heart rate (HR), and venous return [MSP-right atrial pressure (RAP)] are preserved during early hemorrhage due to compensatory mechanisms. However, as the extent of hemorrhage approaches UVB, the filling pressure drops, as does systemic blood pressure. EBL, estimated blood loss.

consequence as blood flow to less essential vascular beds (e.g., splanchnic and cutaneous circulation) is diverted centrally (7, 19), rendering these areas at risk for ischemia. The venous return model also has implications for the action of vasopressor drug use during hemorrhage. During decompensated hypovolemia, it is common to use vasopressors to increase arterial blood pressure. However, the unseen action of vasopressors during hemorrhage is to cause significant venoconstriction (thereby maintaining stressed blood volume, venous return, and cardiac output) in addition to arterial vasoconstriction (which increases systemic vascular resistance and afterload) (4, 15, 29). Thus these drugs can restore systemic and venous pressures to normal while the patient remains hypovolemic. The effects of venoconstriction are limited by the amount of unstressed blood volume available for conversion. Thus, use of vasopressors during hemorrhage should be recognized as only a temporizing measure rather than the principle method of achieving the desired systemic pressure. Indeed, use of any vasopressors in the bleeding patient should raise the suspicion of underlying hypovolemia (15).

Accurate assessment of the intravascular volume status of a hemodynamically unstable patient is often challenging. The use of dynamic parameters such as “delta down” (a decrease in systolic arterial pressure due to cardiopulmonary interactions that occur shortly after a positive-pressure breath is delivered to an intubated patient) and pulse pressure variation in mechanically ventilated patients appear helpful in detecting volume responsiveness (12, 17). However, their sensitivity for hypovolemia is greatly reduced by any use of vasopressors that shift unstressed to stressed blood volume, making volume assessment inconclusive (4, 18). Thus, if a patient has significant delta down while on vasopressors, then they are very likely hypovolemic; however, if the patient does not have significant delta down, they may still be hypovolemic.

Although venous return theory provides an understanding of the critical pathophysiology of the circulation during acute hemorrhage, the clinical utility of this theory has lagged. Recently, Maas et al. (13) have worked toward measuring MSP at the bedside using minimally invasive monitors in ventilator-dependent patients using inspiratory hold maneuvers. The same group has measured MSP peripherally through vascular occlusion of the arm and determined stressed blood volume through stepwise intravenous fluid administration in adult patients (14). These methods give a preliminary forecast into the possibility of more practical applications of the venous return model, whereby patient management decisions may be based on actually measuring the MSP, stressed blood volume, and venous elastance.

Finally, it is important to note that our description of the circulation and the venous system here is a simplified treatment. For example, we did not address passive recoil effects, nonsteady state effects, volume transfers between the peripheral and central compartments, or the fact that the human circulation has numerous vascular compartments working in parallel. The interested reader is directed to more complete descriptions (23, 25), including some current controversies regarding the venous return theory (1, 2). Nevertheless, our simplified treatment does not alter the central message that human veins primarily adjust capacity and not elastance during hemorrhage. In conclusion, during initial acute hemorrhage in humans, the venous return, and thus cardiac output, is impor-

tantly supported by the venous system converting unstressed to stressed blood volumes.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: T.S. and K.B. conception and design of research; T.S. prepared figures; T.S. drafted manuscript; T.S. and K.B. edited and revised manuscript; T.S. and K.B. approved final version of manuscript.

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