Understanding Guyton’s venous return curves

Daniel A. Beard1 and Eric O. Feigl2

1Department of Physiology, Biotechnology and Bioengineering Center, Medical College of Wisconsin, Milwaukee, Wisconsin; and 2Department of Physiology and Biophysics, University of Washington, Seattle, Washington

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The imaginary mean systemic pressure that would exist at the instant when flow is stopped in the systemic circulation without a change in resistance or capacitances (mmHg)

PMS

Cardiac output; mathematical modeling; vascular function curve

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Glossary

CA Arterial capacitance (liter/mmHg)
CV Venous capacitance (liter/mmHg)
CT Total capacitance in the systemic circulation (liter/mmHg), CT = CA + CV
F Flow, equals cardiac output; equals venous return (liter/min)
PA Mean arterial pressure (mmHg)
PRA Mean right atrial pressure (mmHg)

Address for reprint requests and other correspondence: D. A. Beard, Medical College of Wisconsin, Biotechnology and Bioengineering Ctr., 8701 Watertown Plank Rd., Milwaukee, WI 53226 (e-mail: dbeard@mcw.edu).

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In the 1950s, Guyton and coworkers (9–12) analyzed compliant-circuit models of the systemic circulation to reveal an approximately linear relationship between systemic venous return (cardiac output) and right atrial pressure. Although the mathematical analysis was straightforward and flawless, Guyton et al. (9–14) interpreted their derived equation for venous return as a function of right atrial pressure to imply that right atrial pressure exerts a backward force that impedes venous return to the right atrium. Furthermore, the Guyton model has been interpreted to reveal that the veins exert an elastic force driving blood flow to the heart (16). The concepts that right atrial pressure represents a back pressure limiting venous return and that elastic recoil of the veins does work to produce flow continue to confuse investigators and clinicians, despite detailed and careful explanations, notably by Grodins et al. in 1960 (8), Levy in 1979 (15), Sheriff et al. in 1993 (29), Tyberg in 2002 (31), Brengelmann in 2003 (2), and Reddi and Carpenter in 2005 (25). The continuing controversy is documented by a Point-Counterpoint debate in 2006 (3, 16), with the ensuing letters (1, 4, 5, 17, 18, 21, 23, 24, 28, 32), and a teaching article in 2007 (7). The debates continued in 2009 with more commentary (6, 19, 20). The intent of the present essay is to restate the previous criticisms in a simple manner, emphasizing the cause-and-effect relationship between changes in arterial pressure and concomitant changes in right atrial pressure predicted by the Guyton model.

The systemic circulation consists of distributed resistances and capacitances. If systemic blood volume is constant, then blood shifts between the arterial and venous compartments (segments) when flow through the circulation changes. Guyton and coworkers studied the behavior of the systemic circulation in a series of experiments where the right atrial pressure was varied with the height of a Starling resistor (collapsible tube). Varying the height of the Starling resistor had the effect of variably restricting the inflow to an artificial pump, replacing the right ventricle that delivered flow from the right atrium to the pulmonary artery (9–14). The steady-state experimental measurements of the pump output (equal to left ventricular cardiac output) versus right atrial pressure were plotted as Guyton’s well-known venous return curve (Fig. 1) and interpreted to demonstrate that right atrial pressure represents an effective back pressure limiting venous return.

However, in Guyton’s model (and in the systemic circulation), the steady-state flow (cardiac output = venous return)
determines the right atrial pressure, not the other way around (see APPENDIX for mathematical details). Although right atrial pressure was varied by the elevation of the Starling resistor in Guyton’s experiments, the true independent variable was the flow (cardiac output) through the systemic circulation provided by the artificial pump. The use of a Starling resistor by Guyton et al. to vary the artificial pump output (= cardiac output) has confused readers. The investigators could have used an adjustable tubing clamp arrangement or, more simply, manually controlled the pump speed. This point is confirmed by Grodins et al. (8) who did a similar experiment with similar results using a variable speed pump without a Starling resistor in the experimental preparation, clearly identifying cardiac output as the causal variable.

One of the equations that can be obtained from Guyton’s simple model (Fig. 2) predicts that flow is proportional to mean systemic pressure of the systemic circulation (not arterial pressure) minus right atrial pressure divided by “the resistance to venous return” (Eq. A2 in the APPENDIX). The mean systemic pressure is the hypothetical pressure in the systemic circulation that would be observed if the heart were stopped and pressure equilibrated from aorta to right atrium. It is a reflection of how tightly the blood volume fills the venous and arterial capacitors, as reviewed by Rothe (27). With cardiac output flowing through the systemic circulation, there will be a point where the blood pressure equals the theoretical mean systemic pressure (probably in small veins), but this anatomical point is not fixed if cardiac output changes. What Guyton termed “the resistance to venous return” is the sum of the venous resistance plus the arterial resistance, multiplied by the ratio of arterial capacitance, divided by the total of arterial plus venous capacitances ($R_{VR} = R_V + R_A C_A/C_T$; see APPENDIX). There is no easy intuitive representation of the “resistance to venous return.” In particular it is not equal to the venous resistance in the model and differs by a factor of 2.5 to 74 from the venous resistance, depending on the value $C_A/C_T$ that is used (see APPENDIX).

If one treats flow (left ventricular cardiac output) as the independent variable for the systemic circulation, as emphasized by Levy (15), then Guyton’s data may be plotted in the conventional manner where the causal independent variable (flow) is plotted on the abscissa and the response variable (right atrial pressure) is plotted on the ordinate as in Fig. 3. Figure 3 also shows the arterial pressure in response to forcing flow through the systemic circulation as determined by Guyton’s model (Fig. 2). Although Guyton never reported the changes in arterial pressure that occur with changes in cardiac output in his experiments, arterial pressure is a key variable missing from Guyton’s venous return graphs that aids in understanding the behavior of the systemic circulation. Specifically, Guyton’s data and model demonstrate that as flow through the systemic circulation increases, right atrial pressure falls because of a shift in blood from the venous to the arterial capacitance. Increasing cardiac output is associated with increasing arterial pressure, which is accompanied with increasing the blood volume in the arterial capacitor. Recall that Guyton’s model assumes that blood volume in the systemic circulation remains constant. Specifically, there is no net flow into or out of the systemic circulation from the pulmonary or cardiac blood volumes. Because total blood volume in the systemic circulation is constant, the augmented arterial blood volume must come from the capacitance of the venous circulation; hence, venous and right atrial distending pressure decrease as cardiac output increases. In other words, right atrial pressure is not an independent variable determining flow in this closed system.

Note that Figs. 1 and 3 illustrate the steady-state behavior of the system when, by definition, venous return equals cardiac output and when systemic resistances and capacitances are constant. During transitions between steady states when blood volume is shifting among compartments, venous return and cardiac output will transiently be unequal, as elegantly described by Brengel-
Remembering that PMS and PRA is determined by the flow. This causal relationship can be seen by rearranging Eq. A2 from Guyton’s model to yield $P_{MS} - P_{RA} = FR_{VR}$, where $F$ is the flow. Reordering $P_{MS}$ and $R_{VR}$ constant, right atrial pressure is revealed as a function of flow. Thus right atrial pressure is not an independent “back pressure” limiting venous return.

Another confusing interpretation of the Guyton model is that vascular capacitors produce an elastic “recoil” pressure that drives venous return (equal to cardiac output) as reflected by the mean systemic pressure (Eq. A7). Recall that Guyton’s data and model are only valid for steady-state conditions, where the volumes in the elastic capacitors are constant. The left ventricle generates both the pressure and flow that fills the capacitors (26). Even when passive compliant vessels are filling and emptying in a pulsatile manner, averaged over multiple heartbeats they do not supply energy to move the blood through the circulation. Thus these passive elements cannot do mechanical work on the system.

The utility of Guyton’s model is that steady-state thought experiments may be done where variables are changed one at a time while holding other factors constant. For example, Fig. 4 illustrates what happens in Guyton’s model of systemic circulation when arterial resistance is varied. As arterial resistance is increased, arterial pressure increases and right atrial pressure declines. Again, the explanation is that with an increase in arterial pressure, there will be a shift in blood volume to the arterial side from the venous side of the systemic circulation. Note that in this simulation flow (cardiac output) is held constant.

At this point the knowledgeable reader has probably become impatient. This is not how the cardiovascular system behaves. For example, during exercise there is a decrease in systemic vascular resistance, an increase in cardiac output, and a redistribution of cardiac output (22, 30). Thus a simple series model is inadequate.

Guyton used right atrial pressure as the preload for cardiac function in invoking the Frank-Starling mechanism of cardiac contraction. The associated relationship between right atrial pressure and cardiac output is plotted as a second line in the venous return graph and the intersection of the two lines named the equilibrium point. Such a graph with two lines reminds the reader that the cardiovascular system contains both a heart and a circulation but does not tell the whole story of how the system behaves. For example, heart failure will depress the Frank-Starling curve.
and the equilibrium point will shift to a higher right atrial pressure. Thus the venous return curve (or “vascular function” curve) illustrates how decreased flow through the systemic circulation leads to an elevation in right atrial pressure. But it does not show how this pressure increase is a consequence of blood accumulating on the inlet side of the failing pump. Nor does it demonstrate other key physiological changes associated with heart failure, such as an increase arterial resistance, a redistribution of cardiac output among the various vascular beds, and the retention of salt and water. Thus the application of Guyton’s venous return analysis may hide more than it reveals. Furthermore, while Guyton’s model has served to introduce the function of the systemic circulation, it is inadequate to model the cardiovascular changes that occur during exercise, thermal stress, changes in posture, shock, heart failure, etc.

In summary, the equations of Guyton’s model fit his data. However, Guyton’s interpretation is mechanistically (physiologically) flawed. The misleading interpretation of Guyton’s experiments and model has led to the false conclusion that right atrial pressure represents an effective back pressure impeding venous return and cardiac output. This leads to confused thinking about the cardiovascular system. For example, it follows from Guyton’s interpretation that in a case of compromised cardiac output, a clinician should withhold intravenous fluids to keep right atrial pressure low to avoid compromising venous return. The mechanistically appropriate interpretation is shown in Fig. 3, in which the right atrial pressure is revealed as a function of flow.

Because Guyton’s venous return curves have generated much confusion and little clarity, we suggest that the concept and previous interpretations of venous return be removed from educational materials.

APPENDIX

The circuit model of Guyton et al., representing the circulation as two serial lumped arterial and venous segments, is illustrated in Fig. 2. An arterial resistance and compliance, \( R_A \) and \( C_A \), are associated with the arterial segment; venous resistance and compliance, \( R_V \) and \( C_V \), are associated with the venous segment. The pressure of the blood leaving the left side of the heart is denoted \( P_A \) (for aortic pressure) and the right-side filling pressure \( P_{RA} \) (for right atrial pressure). It is assumed that the pulmonary circulation is noncompliant (nondistensible), and, therefore, when we ignore the relatively small temporal variations in volume of blood in the heart, the total volumes in both circulations (systemic and pulmonary) remain constant. The elements labeled \( C_A \) and \( C_V \) in Fig. 2 are compliant elements that model the elastic distensibility of the arterial and venous segments of the circulation. Guyton’s model invokes a simple linear assumption that the volume of blood in each compartment is proportional to its compliance value \( (C_A \) and \( C_V \) multiplied by the transmural pressure from the inside of the compartment to the outside. A linear Ohm’s Law relationship is associated with the resistance elements labeled \( R_A \) and \( R_V \). This means that the pressure drop across the resistance element can be computed as flow multiplied by resistance. For example, the pressure labeled \( P_V \) is computed \( P_V = P_{RA} + FR_V \), where \( F \) is the flow through the resistor. Similarly, summing the pressure drop across both resistances, \( P_A = P_{RA} + FR_A + FR_V \), or as follows:

\[
F = \frac{P_A - P_{RA}}{R_A + R_V} = \frac{P_A - P_{RA}}{R_T} \tag{A1}
\]

which equates the pressure drop across the circuit with the flow times the total resistance. Additional similar expressions for flow may be obtained, such as

\[
F = \frac{P_{MS} - P_{RA}}{R_{VR}} \tag{A2}
\]

and

\[
F = \frac{P_{RA} - P_{MS}}{R_A(C_V/C_T)} \tag{A3}
\]

where \( R_{VR} \) (the resistance to venous return) and \( P_{MS} \) (the mean systemic filling pressure) are defined below. Following Guyton’s example, we might term the denominator \( R_A (C_V/C_T) \) in Eq. A3, the “resistance to cardiac output.” Equations A1–A3, while correct, may be misleading since they suggest that the distributed resistances and pressures mechanistically determine the flow through the systemic circulation. Alternatively, one may express Eq. A2 as follows:

\[
P_{RA} = P_{MS} - FR_{VR} \tag{A4}
\]

Equation A4 is more straightforward to interpret because right atrial pressure is shown to depend on the flow pushed through the systemic circulation by the heart (or an artificial pump).

Combining the equations for the pressures with the linear volume-pressure relationship, we have the following:

\[
V_A = P_A C_A = [P_{RA} + (F(R_A + R_V))C_A \tag{A5}
\]

\[
V_V = P_V C_V = [P_{RA} + F R_V] C_V \tag{A6}
\]

for the volumes in the arterial and venous compartments, respectively. We next introduce the mean systemic filling pressure, \( P_{MS} \), which is defined as the total blood volume of the circuit divided by the total compliance:

\[
P_{MS} = \sum V / \sum C = \frac{[P_{RA} + F(R_A + R_V)]C_A + (P_{RA} + F R_V)C_V}{C_T} \tag{A7}
\]

where \( C_T = C_A + C_V \) is the total compliance of the network. It is useful to introduce the quantity \( P_{MS} \) because an algebraic manipulation of Eq. A7 yields Eq. A4 when one defines \( R_{VR} = R_V + R_A C_V/C_T \), the resistance to venous return. The relative importance of \( R_V \) in determining \( R_{VR} \) is magnified by the fact that \( C_A \) is substantially smaller than \( C_T \).

The assumptions invoked by the Guyton model and used in the analysis of the Guyton model are summarized as follows:

1) The system operates in the steady state, where venous return equals cardiac output. Pressure and flow variables represent mean values averaged over many cardiac cycles. Pulsations are not considered.

2) The cardiovascular system is a closed system, with blood volume in the systemic circulation remaining constant. There is no shift of blood volume into or out of the systemic circulation from the pulmonary circulation or the heart.

3) The effects of gravity are ignored; the cardiovascular system is horizontal.

4) The effects of intrathoracic pressure are ignored; the chest is open.

5) There is no peripheral muscle pumping as occurs with skeletal muscle contraction during exercise.

6) Circuit elements (resistors and capacitors) behave linearly.

7) \( P_A \): With one exception, Guyton never published arterial pressures from his experiments on venous return. The exception was an arterial pressure of 112 mmHg when cardiac output was 1.176 l/min and right atrial pressure was 0 (12). These data allow us to compute a total resistance of \( R_T = R_V + R_A = 95.2 \text{ mmHg} \cdot \text{min-liter}^{-1} \).

8) \( C_V/C_A \): Guyton et al. (10) published data that the venous capacitance is 18–30 times greater than the arterial capacitance. The value 18 is used here because this is the value Guyton used in subsequent publications (13, 14).
9) $R_A$ and $R_V$: Guyton never published resistance values, but these may be calculated from a single instance where cardiac output and arterial pressure are provided when right atrial pressure was 0 (12). Specifically, from the fit to the data in Fig. 1,

$$R_{VR} = R_V + \frac{C_V}{C_T} R_A = 5.08 \text{mmHg} \cdot \text{min} \cdot \text{liter}^{-1} \quad (A8)$$

From no. 8 above, we have $C_V/C_T = 1/19$. In addition, from no. 7 above, we have

$$R_T = R_V + R_A = 95.2 \text{mmHg} \cdot \text{min} \cdot \text{liter}^{-1} \quad (A9)$$

Solving Eqs. A8 and A9 for $R_A$ and $R_V$, we obtain $R_A = 95.2 \text{mmHg-min-lit}^{-1}$ and $R_V = 0.0690 \text{mmHg-min-lit}^{-1}$. For this set of parameter values, the major contributor to $R_{VR}$ is the term associated with the arterial resistance. (Alternatively, setting $C_A/C_T = 1/31$ yields $R_A = 93.2 \text{mmHg-min-lit}^{-1}$ and $R_V = 2.073 \text{mmHg-min-lit}^{-1}$; in this case the contributions to $R_{VR}$ from the arterial and venous resistances are roughly equal.)

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