splanchnic ischemia is expected to trigger gut cell death,[12] possible translocation of endotoxin from the gut, and eventual multiorgan disease. It follows that the surmise that increased intra-abdominal pressure (whatever the positive effects on mean systemic filling pressure are) is not harmful is incorrect. Most would agree that significant abdominal hypertension calls for only one therapeutic modality: early abdominal decompression.[13] This alone can prevent the downward spiral of organ ischemia, acidosis, and renal failure. Because the analysis of the venous circulation stops at the right atrium, it cannot account for the effects of increased intrathoracic pressures (upward motion of diaphragm with increased intra-abdominal pressure) on the pulmonary vasculature and the downstream consequences on the right heart.

The commentary on the utility or lack thereof of measured central venous pressures is, of course, timely, considering the ever-increasing evidence base of dynamic circulatory indices. However, one might add, almost in requiem, that increased central venous pressure is still a useful clinical tool in the evaluation of right heart or pericardial disease.

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References

1. Gelman S: Venous function and central venous pressure. ANESTHESIOLOGY 2008; 108:735–48
2. Guyton AC, Lindsey AW, Kaufmann BW: Effect of mean circulatory filling pressure and other peripheral circulatory factors on cardiac output. Am J Physiol 1955; 180:463–8
3. Brengelmann GL: Counterpoint: The classical Guyton view that mean systemic pressure, right atrial pressure and venous resistance govern venous return is not correct. J Appl Physiol 2006; 101:1525–6
4. Magder S: Point: The classical Guyton view that mean systemic pressure, right atrial pressure and venous resistance govern venous return is not correct. J Appl Physiol 2006; 101:1523–5
5. Brengelmann GL: A critical analysis of the view that right atrial pressure determines venous return. J Appl Physiol 2003; 84:849–59
6. Schrier RW, Abraham WT: Hormones and hemodynamics in heart failure. N Engl J Med 1999; 341:577–85
7. Balmain S, Padmanabhan N, Ferrell WR, Morton JG, McMurray JJV: Differences in arterial compliance, microvascular function and venous capacitance between patients with heart failure and either preserved or reduced left ventricular systolic function. Eur J Heart Fail 2007; 9:865–71
8. Gelman S: The physiology of aortic clamping and cross clamping. ANESTHESIOLOGY 1995; 82:1026–57
9. Russell JA: Catecholamines and the splanchnic circulation. Crit Care Med 1999; 27:242–3
10. Krejci V, Hiltebrand LB, Jakob SM, Takala J, Sigurdsson GH: Vasopressin in septic shock. Crit Care 2007; 11:R29
11. Humer MF, Phang PT, Friesen BP, Allard MF, Goddard CM, Walley KR: Heterogeneity of gut capillary transit times and impaired gut oxygen extraction in endotoxemic pigs. J Appl Physiol 1996; 81:895–904
12. Hotchkiss RS, Schmieg RA Jr, Swanson PE, Freedman BD, Tinsley KW, Cobb JP, Karl IE, Buchman TG: Rapid onset of intestinal epithelial and lymphocytic apoptotic cell death in patients with trauma and shock. Crit Care Med 2000; 28:3207–17
13. Maerz LJ, Kaplan LJ: Abdominal compartment syndrome. Crit Care Med 2008; 36:S212–5

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Inspiratory Increases in Systolic Blood Pressure ("Delta-up") and Pulse Pressure Are Not Equivalent

To the Editor:—We read with interest the recent review by Dr. Gelman on venous function and central venous pressure. In the paragraph on systolic blood pressure and pulse pressure variations, Dr. Gelman describes the effects of positive-pressure ventilation on ventricular and stroke volumes and states that during inspiration, a temporary increase (as compared with end of expiration) in left ventricular (LV) stroke volume, pulse pressure, and systolic blood pressure occurs.[1] This deflection is called "delta-up" and is usually around 2–4 mmHg.[1] Delta-up has effectively been described as reflecting the inspiratory increase in LV stroke volume.[2] However, delta-up actually quantifies the inspiratory increase in systolic blood pressure[2] and may thus result either from an increase in LV stroke volume or an increase in extramural aortic pressure related to the increase in pleural pressure.[3] Unlike the systolic blood pressure, the pulse pressure is directly proportional to LV stroke volume.[3] It is thus the inspiratory increase in pulse pressure (which could be called "deltaPP-up") that reflects the inspiratory increase in LV stroke volume. No study, however, has investigated whether delta-up and deltaPP-up behave similarly among ventilated patients. We recently reviewed 298 arterial blood pressure curves recorded immediately before or after fluid challenges in 35 mechanically ventilated patients (21 men and 14 women, mean [± SD] age of 55 ± 14 yr) in the intensive care unit (n = 17) or in the operating room (n = 18). Delta-up was measured as previously described (fig. 1).[4] For each patient, the arterial pressure curve recording with the largest delta-up was then selected. In these 35 recordings, pulse pressure and deltaPP-up (the difference between maximal pulse pressure at inspiration and pulse pressure at end-expiratory pause; fig. 1) were then also measured. We found that deltaPP-up (1.6 ± 1.8 mmHg) was smaller than delta-up (5.3 ± 2.4 mmHg; $P < 0.01$ *vs.* deltaPP-up). All 35 patients had a positive delta-up (range, 2–13 mmHg), whereas deltaPP-up ranged between −1 and 8 mmHg and was positive (≥ 1 mmHg) in only 23 patients ($P < 0.01$ *vs.* delta-up). Among the 16 patients where delta-up was 6 mmHg or greater, deltaPP-up was 2 mmHg or less in 12 patients. These data show that inspiratory increases in systolic blood pressure (delta-up) and pulse pressure (deltaPP-up) are not equivalent. Extramural aortic pressure seems to be the primary determinant of delta-up in many patients. Using delta-up as an indicator of inspiration-induced increase in LV stroke volume may thus be misleading. Finally, it has been suggested that the pulse pressure variation, because it includes this inspiratory increase in LV stroke volume that is not related to fluid responsiveness, may falsely predict positive responses to volume expansion.[3,5] In the current study, where the criterion for selection of arterial curves was a large delta-up, deltaPP-up was large enough to potentially result in such false-positive pulse pressure variation in only one patient (deltaPP-up = 8 mmHg [13% of the pulse pressure]; pulse pressure variation = 15%; delta-up = 13 mmHg; delta-down = 3 mmHg). This strongly suggests that this theoretical limitation of pulse pressure variation may be relevant in only a small proportion of patients. In any case, deltaPP-up, but not delta-up, should be measured to detect such occurrence.

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References

1. Gelman S: Venous function and central venous pressure: A physiologic story. ANESTHESIOLOGY 2008; 108:735–48

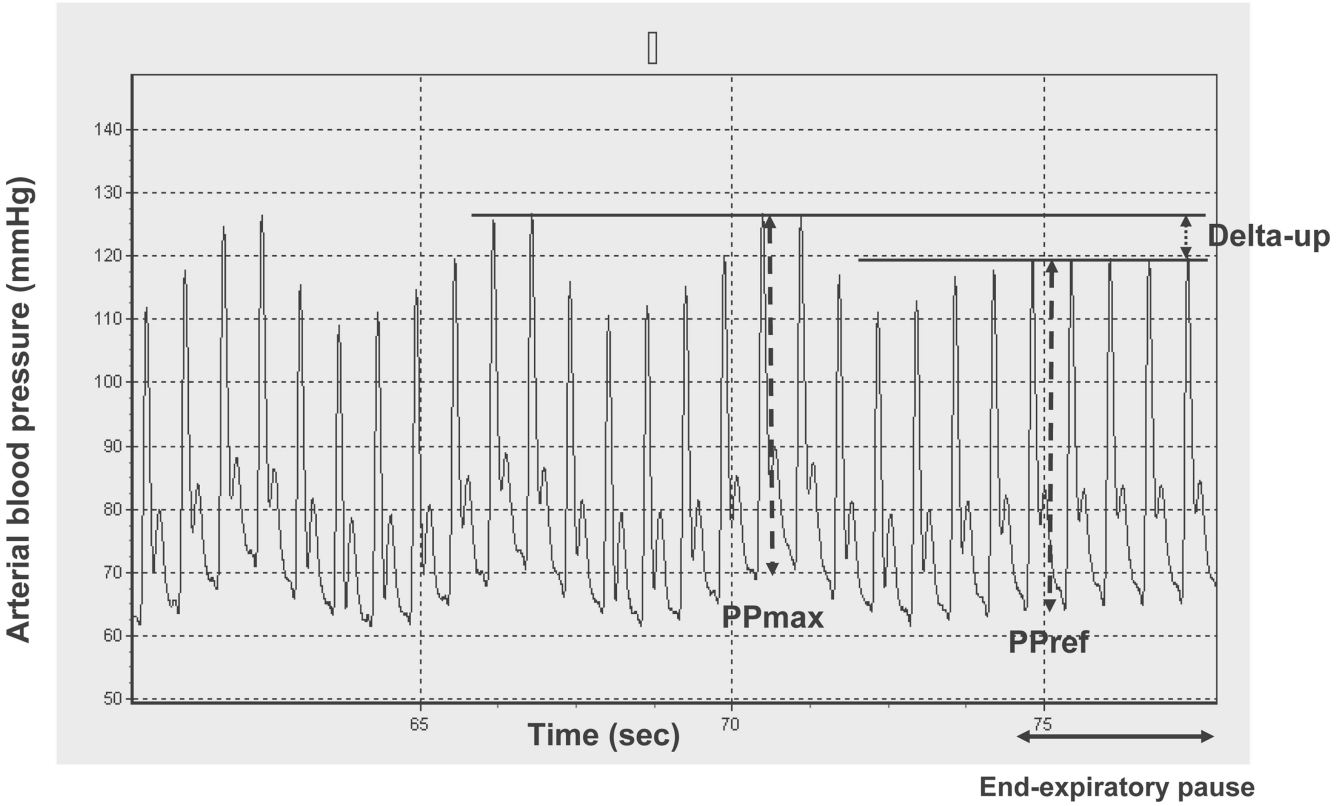

Fig. 1. Respiratory changes in arterial blood pressure in a mechanically ventilated patient. The difference between the maximum systolic blood pressure and the systolic blood pressure during end-expiratory pause (end of recording) defines delta-up. The difference between the maximum pulse pressure (PPmax, with pulse pressure = systolic minus diastolic pressure) and the pulse pressure during end-expiratory pause (PPref) defines deltaPP-up. In this typical example, delta-up = 7 mmHg, whereas deltaPP-up = 1 mmHg.

2. Perel A: Assessing fluid responsiveness by the systolic pressure variation in mechanically ventilated patients. ANESTHESIOLOGY 1998; 89:1309–10

3. Michard F, Teboul JL: Using heart-lung interactions to assess fluid responsiveness during mechanical ventilation. Crit Care 2000; 4:282–9

4. Tavernier B, Makhotine O, Lebuffe G, Dupont J, Scherpereel P: Systolic pressure variation as a guide to fluid therapy in patients with sepsis-induced hypotension. ANESTHESIOLOGY 1998; 89:1313–21

5. Perel A: Automated assessment of fluid responsiveness in mechanically ventilated patients. Anesth Analg 2008; 106:1031–3

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In Reply:—I agree with Dr. Augoustides that my review article[1] "does not detail the role of venous pressure in spinal cord perfusion." The review is focused "on the gross physiologic relation within the venous system."[1 (p735)] Therefore, I did not discuss the role of veins in different organs and systems. Nevertheless, the issue *per se* is quite important. The spinal cord injury during surgical repair of thoracoabdominal aneurysms to a great extent depends on a dramatic decrease in spinal cord perfusion pressure, which is defined as a difference between distal aortic pressure minus cerebrospinal fluid pressure or venous pressure, whichever is higher. It is clear from this simple equation that the higher the central venous pressure (CVP) is, the lower perfusion pressure would be. The work by Etz *et al.*[2] quoted by Dr. Augoustides does not prove but is in agreement with the speculation above. Their and other observations strongly suggest that a high CVP can be dangerous for this patient population. Interestingly, similar situations can be observed in patients undergoing liver transplantation: A high CVP may jeopardize the perfusion of the transplanted liver. Therefore, I agree with Dr. Augoustides that increased intramural and transmural CVP can be detrimental to perfusion of quite a few organs, including the spinal cord. Finally, I thank Dr. Augoustides for high evaluation of my review article.

I am very thankful to Dr. Jayant for bringing to our attention an excellent and innovative work by Brengelmann.[3,4] Compared with the classic work of Guyton, Brengelmann and also Levy[5] have introduced an interesting and important concept emphasizing the role of the heart as a pump and shifts of blood volume within the circulatory system. Regarding the volume shifts, the discussion of the flow–pressure–volume relation in figure 3 of the review[1 (p737)] as well as the two-compartment model[(pp739–41)] address this issue. Regarding pump function, Levy and Brengelmann are correct in that it is crucially important that circulation stop without a pump. The Guyton concept of mean circulatory filling pressure (MCFP) is not necessarily incorrect: Stress volume and pump function are needed to maintain MCFP, and only then (when it is maintained by stress volume and pump function) does MCFP become the driving force for venous return. This is why Rothe[6] declared that the MCFP is the "pivoting pressure," emphasizing the importance of this pressure as a driving force for venous return.

At the end of his first paragraph, Dr. Jayant correctly says that "failure of pump function leads to an assortment of chemical mediators that can . . . affect the venous capacity." I agree. In the second paragraph of the letter, Dr. Jayant expresses the thought that analysis

of the overall circulatory system "that stops at the right atrium is seemingly not complete." I also agree. The review in question focuses only on the venous system,[1] (p735) not on "the overall circulatory system." The fact that the review does not discuss in detail heart and pulmonary circulation should not be construed to say that I do not believe that these parts of the circulation are important. The review describes the venous system itself in more detail than the work by Levy and Brengelmann does; the latter focuses more on the overall cardiovascular system than on the details of the venous system *per se*. If I had introduced the concept described by Brengelmann, I would have had to delete something else that in my mind is more relevant to the focus of the review.

In the third paragraph of his letter, Dr. Jayant says that the two-compartment model described in my review "offers an elegant explanation of the increase in filling pressure with aortic clamping." Then Dr. Jayant says that "as the physiologic setting becomes complex (heart failure . . .) it becomes increasingly difficult to apply." Not at all. As I mentioned in my review,[1] (p737) a decrease in cardiac output due to cardiac failure would decrease flow from the splanchnic arteries, decrease volume within splanchnic veins, and shift this volume to the systemic circulation, increasing preload and recruiting the Frank–Starling mechanism.

A few lines later, I am afraid Dr. Jayant does not properly distinguish the two compartments within the venous system: "working like an arteriovenous fistula" in my example is related to a decrease in arterial resistance in the fast (main) compartment rather than to a decrease in resistance to hepatic outflow (slow compartment). Despite that these specific examples that Dr. Jayant lists in this paragraph fit quite well (and can be easily explained by) the two-compartment model, I agree conceptually that not all physiologic and pathophysiologic observations can fit this model. Models rarely if ever explain everything.

In the same paragraph, Dr. Jayant separates changes in stress volume from the mobilization of this volume; then he says, "This is an either/or function." I disagree. This is the same function: Mobilization of blood volume from the splanchnic system is an increase in stress volume secondary to the shift of blood from unstressed volume.

In the fourth paragraph of his letter, Dr. Jayant writes that "increased intrathoracic pressure increases transmural central venous pressure." This is wrong in most situations and is certainly wrong in the situation when an increase in intrathoracic pressure is due to routine controlled ventilation in a patient with normal heart function and blood volume. In such a situation, transmural CVP does not increase; only intramural CVP does. When intramural CVP is increased, the sympathetic nervous system is moderately activated, leading to an increase in splanchnic arterial resistance (associated with a passive recoil of splanchnic veins) as well as active constriction of the splanchnic veins (veins are much more sensitive to sympathetic stimulation than arteries),[7] working in concert with squeezing the abdominal venous system by the shift of the diaphragm downward and increasing intraabdominal pressure. These responses increase stressed volume and then MCFP, which maintains the baseline pressure gradient for venous return (MCFP − CVP). This does not lead, as Dr. Jayant suggests, to splanchnic ischemia. If it did, we would be dead before we started walking: Every time we stand up, a low degree of sympathetic stimulation occurs, and blood shifts from the splanchnic veins into the systemic circulation to increase stress volume and MCFP, maintaining normal transmural CVP and venous return. Only a high degree of sympathetic nervous tone might lead to severe arterial constriction within the splanchnic vasculature, which might jeopardize blood supply to the gut. Dr. Jayant writes "most would agree that significant abdominal hypertension calls for only one therapeutic modality: early abdominal decompression." I disagree only with the word *most*: I would say that *all* would agree with this notion. Therefore, the whole point here is the degree of increase in sympathetic nervous system discharge: A low degree is absolutely needed for every moment of survival, whereas a high degree is dangerous.[1] (pp739,741,744)

Finally, I am happy that Dr. Jayant, having a very critical mind, agrees with me that "increased central venous pressure is still a useful clinical tool in the evaluation of right heart or pericardial disease"; I say so in the review.(p744) Therefore, I would not think that my review is a requiem to the CVP; it is rather an opera; *opera* in Latin means "labor" or "work produced," where many parts (singing, dancing, visual art, music, and so on) are put together.[8]

We should be thankful to Dr. Tavernier *et al.* for sharing with us their recent observations on the importance of an increase in pulse pressure (deltaPP-up) compared with an increase in systolic pressure (delta-up), mentioned in my review.[1] In the review, I was talking about both systolic pressure variation (SPV) and pulse pressure variation (PPV). I started the description with delta-up; however, just a few lines later I wrote about delta-down, mentioning that it is larger than delta-up and referring to the total SPV: delta-up plus delta-down. In SPV, delta-down plays a more important role than delta-up does, not only because it is larger but also because it reflects the volume status, as was shown by Dr. Tavernier *et al.* a decade ago.[9] Practically, it is much easier to assess SPV than PPV. I agree that PPV is considered to be a more accurate indicator of responsiveness to fluid load than SPV is; however, the differences between them are really minimal.[10] For example, a relatively recent study demonstrated that the coefficients of correlation between stroke volume and SPV or PPV were exactly the same: 0.91.[11]

Other investigators also found that SPV and PPV were the most accurate predictors of fluid responsiveness, even emphasizing that SPV was more independent of the setting of mechanical ventilation.[12] Therefore, mainly based on the simplicity and usefulness of using the SPV, this section of the review[1] addressed the SPV as a total, with the main component of delta-down rather than focusing only on delta-up. Obviously, I would echo the opinion of Dr. Tavernier *et al.* that if one has an opportunity in clinical practice to assess PPV with separation of deltaPP-up and deltaPP-down, it would ensure more accurate assessment of patient's volume status.

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References

1. Gelman S: Venous function and central venous pressure: A physiologic story. Anesth 2008; 108:735–48
2. Etz CD, Luehr M, Kari FA, Bodian CA, Smego D, Plestis K, Griepp RB: Paraplegia after extensive thoracic and thoracoabdominal aortic aneurysm repair: Does critical spinal cord ischemia occur postoperatively? J Thorac Cardiovasc Surg 2008; 135:324–30
3. Brengelmann GL: A critical analysis of the view that right atrial pressure determines venous return. J Appl Physiol 2003; 94:849–59
4. Brengelmann GL: Counterpoint: The classical Guyton view that mean systemic pressure, right atrial pressure and venous resistance govern venous return is not correct. J Appl Physiol 2006; 101:1525–6
5. Levy MN: The cardiac and vascular factors that determine systemic blood flow. Circ Res 1979; 44:739–47
6. Rothe CF: Mean circulatory filling pressure: Its meaning and measurement. J Appl Physiol 1993; 74:499–509
7. Karim F, Hainsworth R: Responses of abdominal vascular capacitance to stimulation of sympathetic nerves. Am J Physiol 1976; 231:434–40
8. The New Shorter Oxford English Dictionary, vol. 2. Oxford, Oxford University Press, 1993, p 2005
9. Tavernier B, Makhotine O, Lebuffe G, Dupont J, Scherpereel P: Systolic pressure variation as a guide to fluid therapy in patients with sepsis-induced hypotension. Anesthesiology 1998; 89:1313–21
10. Perel A: Automated assessment of fluid responsiveness in mechanically ventilated patients. Anesth Analg 2008; 106:1031–3
11. Berkenstadt H, Friedman Z, Preisman S, Keidan I, Livingstone D, Perel A: Pulse pressure and stroke volume variations during severe haemorrhage in ventilated dogs. Br J Anaesth 2005; 94:721–6
12. Preisman S, Kogan S, Berkenstadt H, Perel A: Predicting fluid responsiveness in patients undergoing cardiac surgery: Functional haemodynamic parameters including the respiratory systolic variation test and static preload indicators. Br J Anaesth 2005; 95:746–55

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