Critical Care

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The elusive relationship between cardiac filling and fluid responsiveness

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Editor:

Munoz et al. [1] have recently published an important pilot study in *Critical Care*. In 90 mechanically ventilated patients with circulatory failure who were admitted to the intensive care unit (ICU) for less than 24 h, four measures of 'venous congestion' (VC) were related to fluid responsiveness (F_R) or unresponsiveness (F_{UR}). To score VC, each patient received 1 point for any of the following: (1) a central venous pressure (CVP) > 12 mmHg; (2) a lung ultrasound score (LUS) > 10; (3) a venous excess ultrasound score (VExUS) > 1; and (4) a lateral E/e' > 10 for the left ventricle. Additionally, F_R was measured pragmatically based on either pulse pressure variation, stroke volume variation, passive leg raising, or end expiratory occlusion test (considering the presence of arrhythmias, spontaneous ventilation, and the availability of monitoring devices). The authors hypothesized that F_R patients would have fewer VC signals than F_{UR} patients. Contrary to these expectations, there was no statistically significant difference between F_R and F_{UR} patients with respect to number of VC signals. Fifty-three percent of F_R patients had at least one VC signal; only slightly more (57%) of F_{UR} showed at least one VC signal. From this, the authors correctly concluded that VC is present in a clinically significant fraction of F_R patients and clinicians should, therefore, be wary when resuscitating based only upon measures of F_R. However, we note that their results are equally true in the reverse sense which brings to mind the fundamental relationship between surrogates of cardiac filling (e.g., VC or lack thereof) and the response to additional preload (i.e., F_R). For example, the frequently used strategy of prescribing fluids based on a lower CVP or flat IVC [2].

Though not explicitly mentioned by Munoz and colleagues, of equal importance in their data is the high fraction of patients without VC (i.e., normal venous measures) who were, nonetheless, F_{UR}. Specifically, 43% of patients with *normal venous measures* were predicted to *not* increase stroke volume with another fluid bolus. The takeaway from this observation is that deciding to give IV fluid based only upon venous measures is also problematic. This is even more striking when looking only at VExUS score, which all 90 patients had calculated (supplemental data). For those patients who were F_R, approximately 97% had a VExUS score of zero or 1. However, roughly 87% of patients who were F_{UR} also had a VExUS score of zero or 1; thus, the specificity of a VExUS of zero or 1 for detecting F_R is only 13%!

How do we make sense of these findings? One approach is to return to basic cardiac physiology and consider the shape of the Frank–Starling curve as it relates cardiac filling on the x-axis and stroke volume on the y-axis (see Fig. 1) [3–5]. If the entire population of patients had normal, upright cardiac function curves that flatten out at higher filling pressure, then normal/low venous measures would associate with F_R (i.e., ascending curve) and VC

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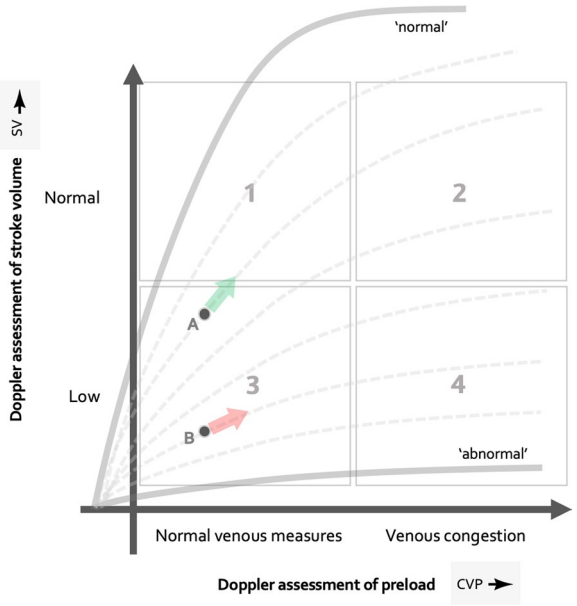

Fig. 1 The Doppler starling curve. The four hemodynamic phenotypes (1–4) are generated by combinations of normal and low stroke volume on the *y*-axis and normal or congested venous measures on the *x*-axis. The family of Starling curves (dotted lines) shows that a patient can have normal venous measures and be responsive (patient A, green) or unresponsive (patient B, red). If a population is studied with cardiac dysfunction, more patient B physiology will be observed

with F_{UR} (i.e., flat curve), as hypothesized by Munoz and colleagues. However, if greater numbers of patients with flattened cardiac function curves are studied, then being F_{UR} and having normal venous measures will necessarily be more common. We have recently described this physiology in terms of a 'Doppler Starling curve' where normal venous measures (i.e., VExUS zero or 1) and F_{UR} may be observed in hemodynamic 'quadrants' (Q_x) Q_1 and Q_3 (and theoretically more common in Q_3 than Q_1, see Fig. 1). In a pilot study using simultaneous common carotid artery and internal jugular Doppler ultrasonography in emergency department (ED) patients deemed to require intravenous fluid expansion we, like Munoz and colleagues, observed a high proportion (i.e., 67%) of F_{UR} assessments with jugular venous Doppler morphologies consistent with low preload (i.e., normal venous measures) [4]. On the other hand, like Munoz et al., we observed that a clinically significant (i.e., 14%) fraction of F_R assessments occurred when there was a pulsatile, congested jugular venous Doppler morphology. Within the Doppler Starling curve framework, this constellation is seen in Q_2 and Q_4 with the proportion determined by the severity of cardiac dysfunction in the population studied (see Fig. 1). Taken together, the poor relationship between venous measures and the presence or absence of F_R speaks to the diversity of cardiac function curves in the ICU. Importantly, neither ejection fraction [6], nor LV fractional shortening (as observed by the authors) can accurately determine the slope of the Frank–Starling curve—it demands a dynamic assessment! Deciding IV fluids based only on F_R/F_{UR} or based only on venous measures (e.g., VExUS) carries equal risk—both the *x*- and *y*-axes of the Frank–Starling relationship should be serially measured during resuscitation to best tailor IV fluid therapy.

In summary, Munoz and colleagues have published an influential pilot investigation, executed with rigor. We should continue to anticipate little relation between venous measures and fluid responsiveness, especially with impaired cardiac function. Doppler phenotyping could be useful to better delineate the safety profile of IV fluids throughout the course of illness.

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JESK is cofounder and chief medical officer of Flosonics Medical, a start-up working to commercialize a wearable Doppler ultrasound.

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