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**EDITORIAL COMMENT**

# The fastest way to the heart is through the veins: towards a better understanding of congestion

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**This article refers to 'Changes in inferior vena cava area represent a more sensitive metric than changes in filling pressures during experimental manipulation of intravascular volume and tone' by J.B. Ivey-Miranda *et al.*, published in this issue on pages 455–462.**

Congestion is a hallmark feature of heart failure (HF) and is associated with organ dysfunction and impaired prognosis.[1] As such, acquiring an adequate 'decongestive' state is the goal in every HF patient. However, the assessment of congestion can be challenging. The gold standard remains invasive measurement of right atrial pressures (RAP) and pulmonary capillary wedge pressures (PCWP). This involves deep venous puncture and advancing a pulmonary artery catheter through the right heart and pulmonary circulation, which may come with a risk of complications and is a relatively time consuming procedure. Furthermore, this cannot routinely be performed in every patient in whom the congestion status is questioned. Guidelines recommend to monitor pulmonary artery pressure (PAP) using a wireless haemodynamic monitoring system in symptomatic patients with HF in order to improve clinical outcomes (class IIb).[2] However, most clinicians rely on signs (e.g. oedema, pulmonary rales, S3 sound, elevated jugular venous pressure) and symptoms (e.g. dyspnoea, orthopnoea) as a surrogate for invasive haemodynamic assessment. Despite their widespread use, these signs and symptoms lack specificity and sensitivity to be used as reliable measures to quantify congestion.[3] Echocardiography is the most used non-invasive alternative to estimate filling pressures and quantify congestion, but this requires time, resources and expertise. Other non-invasive ultrasound measures such as lung ultrasound, internal jugular vein ultrasound, renal venous Doppler and inferior vena cava (IVC) ultrasound may be easier and faster alternatives.[4] The IVC is of particular interest as measuring its diameter and collapsibility to estimate RAP is recommended during echocardiography by American and European societies.[5] However, these recommendations are based upon limited evidence and only allow to distinguish between normal and elevated RAP, but do not allow to quantify pressures.[6]

In this issue of the Journal, Ivey-Miranda and colleagues report on a novel wireless implantable IVC sensor that allows repeated measurements of the cross-sectional IVC area.[7] The sensor is a 'passive' device, resonating at a certain frequency when activated by the detection system, which consists of a belt and a hardware unit. Changes in IVC area translate in changes in detected frequency and can thus be monitored. This resonance technique is not new and is already used in the aforementioned PAP sensors that are available in clinical practice.[8,9] As there is no need for a battery within the implanted sensor, battery life-span is not an issue. The authors first provided evidence that the sensor can accurately measure IVC area both *ex vivo* (in tubes with known area) and *in vivo* in sheep (using intravascular ultrasound as reference). Next, they studied the behaviour and accuracy of the IVC area as an estimate for RAP with different haemodynamic manipulations in nine sheep under general anaesthesia and positive pressure ventilation. Nitroglycerine was infused at a constant rate, inducing venodilatation. Nitroglycerine increases venous capacitance leading to increased venous pooling of blood and reduces effective circulating volume. Nitroglycerine infusion decreased IVC area, RAP and mean PAP (mPAP), but the change in IVC area was of greater magnitude than that observed in the other variables. In another experiment, rapid right ventricular pacing was applied to induce diastolic and systolic dysfunction. The IVC area, RAP and mPAP increased, but again the change in IVC area was most pronounced.

The most important and insightful part of the study was the manipulation of volume. After draining blood to an RAP of 2 mmHg, the authors gradually reinfused a 1:1 mixture of hydroxyethyl starch and blood. Importantly, the IVC area already increased

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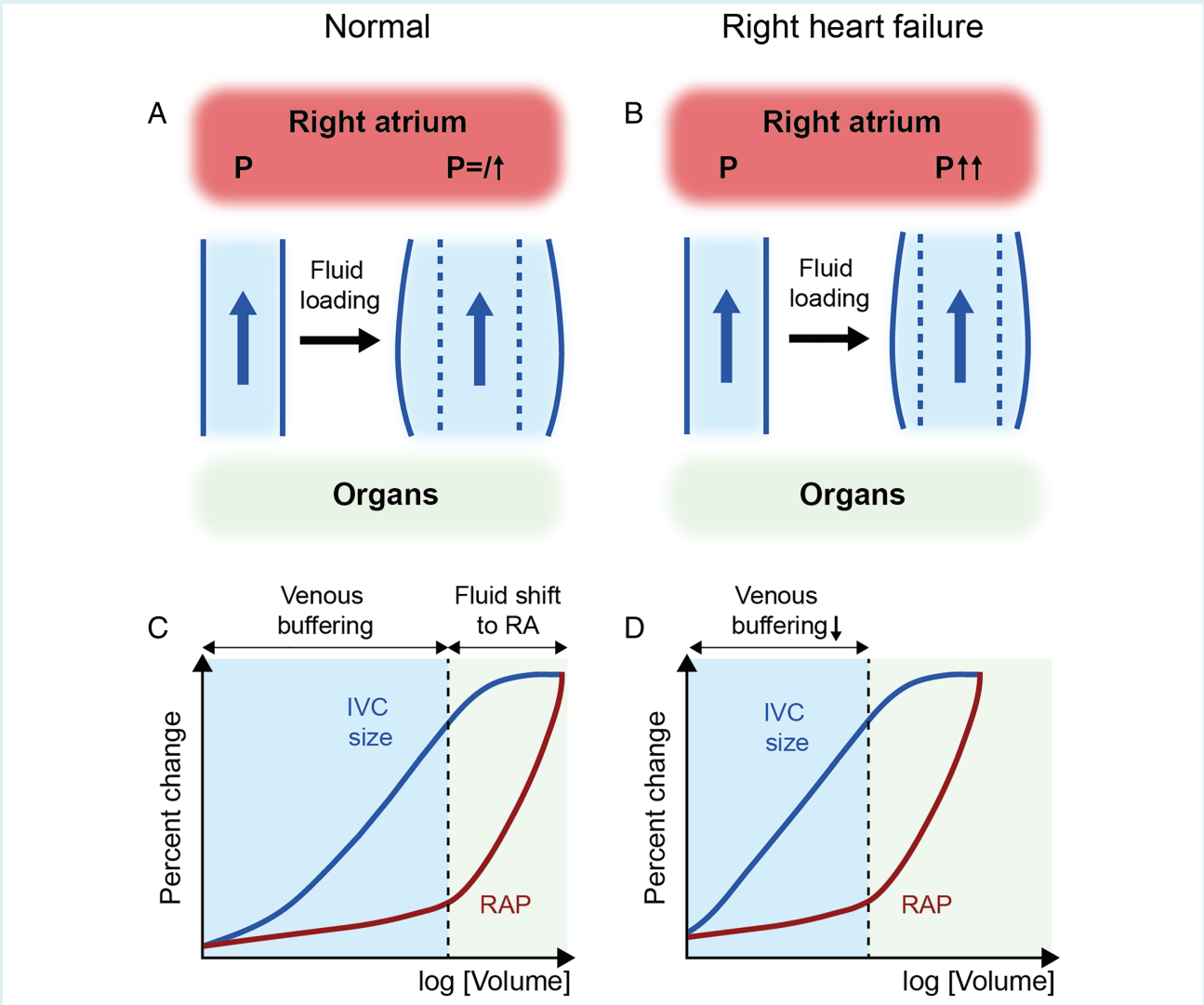


**Figure 1** The central role of the venous system in congestion. Fluid loading in healthy individuals is largely buffered by the venous system in highly compliant capacitance vessels, storing blood and only modestly increasing effective circulating volume. Panels *A* and *B* represent the venous flow (arrow) from the organs (bottom) through the veins (middle) to the right atrium (RA) (top). (*A*) Fluid loading distends venous capacitance vessels in which blood is stored. The flow towards the RA results in a minor increase in filling pressures. (*B*) In case of reduced venous capacitance, as in heart failure, fluid loading can only partially be buffered by the venous system. The effective circulating volume and flow towards the RA increase more significantly which might also lead to a more pronounced increase in filling pressures, especially if the heart cannot accommodate this increased preload as is the situation with heart failure. (*C*) During volume loading, inferior vena cava (IVC) size increases gradually in a first phase. Volume is buffered by the venous system and filling pressures increase only minimally. When this buffering capacity is exhausted, further volume loading increases the effective circulating volume and flow towards the RA, leading to an increase in RA pressures (RAP). (*D*) In heart failure, venous capacitance is reduced and venous buffering capacity is decreased, shifting the IVC size and RAP curve to the left. P, filling pressure.

early on during volume loading while only minimal changes in RAP or PCWP were noted. Only after a large amount of blood was reinfused, RAP and PCWP started to increase significantly. In addition, when more blood was infused, a plateau was observed for IVC area (maximal dilatation) while RAP and PCWP continued to increase.

What should we conclude from this exciting pathophysiological, yet very clinically relevant, study? First, there is a potential new kid on the block. This 'passive' IVC area sensor seems to reliably quantify venous blood volume in the IVC as a surrogate for congestion, at least in a small group of anaesthetized sheep. Currently, the CardioMEMS® system (Abbott, Sylmar, CA, USA) is the only commercially available device remotely monitoring intravascular pressures, specifically PAP. Tailoring therapy based upon PAP measurements decreased the risk of HF hospitalizations.[8,10] This IVC area sensor might offer new opportunities as it uses another

measurement concept (venous distention instead of pressures) and monitors right-sided congestion in contrast to left-sided congestion with PAP sensors. However, a lot of questions need to be answered before we can implement the device in clinical practice: Can the device safely be implanted in humans? Does it reliably measure IVC area in humans? How do we define normal and abnormal IVC area, and does this threshold need to be personalized to each patient? And finally, can management guided by IVC area improve outcomes?

Second, these findings support the use of IVC distention on echocardiography as a measure of venous congestion, for which there is, surprisingly in light of its generalized use, only limited evidence to date.[6] Larger IVC diameters have previously been shown to be associated with worse outcomes in both outpatients[11] as well as patients with acute HF[12] in small observational studies. However, there are no data yet on longitudinal changes in IVC, its use to guide therapy and its correlation with outcomes. The ongoing randomized multicentre CAVA-ADHF (Ultrasound evaluation of the inferior vena CAVA in addition to clinical assessment to guide decongestion in Acute Decompensated Heart Failure) study[13] is investigating if decongestion guided by IVC ultrasound measurements is more effective in acute HF than usual care. It will provide more evidence on the role of IVC measurements in guiding treatment in acute HF.

Third, this study provides important insights in how pressure and volume relate (*Figure 1*). From a pathophysiological standpoint, we believe that this paper clearly shows that the key is in the veins. Indeed, changes in IVC were observed far before changes were observed in filling pressures in the experiments conducted in the paper commented herein. The venous system contains approximately 70% of the total blood volume and acts as a reservoir with so-called 'capacitance' vessels.[14] Most blood is pooled in the splanchnic circulation which drains through the liver into the IVC. In essence, the IVC is a highly compliant large conduit vessel transferring blood from organs below the diaphragm (including the splanchnic circulation) to the right heart. Adrenergic stimuli can decrease venous capacitance, reducing the venous blood pool and increasing the effective circulating blood volume. What happens when volume increases? The increased blood volume is first buffered by the highly compliant capacitance vessels so that there is only a modest increase in effective circulating volume. The IVC gradually dilates with increasing volumes. Because of this venous buffering, filling pressures only increase minimally. When the maximal buffering capacity of the venous system is approached, all extra volume is directly shifted to the right heart, leading to a fast increase in RAP and subsequently PCWP especially in HF patients who cannot handle the extra volume. Of note, venous capacitance is reduced in patients with HF because of increased neurohumoral stimulation.[14] Importantly, both modifications of ventricular function and venous capacitance influence this pressure–volume relationship shifting it left or right and this clarifies why changes in IVC area can be larger than changes in filling pressures (*Figure 1*). This also explains why elevated pulmonary pressures can be seen in patients with very different overall volume status: patients with poor venous capacitance can develop elevated pulmonary pressure for normal or minimally elevated blood volumes.[15]

Overall, this study emphasizes the central role of the venous system as an essential part of the pathophysiology of congestion in the setting of fluid overload. Indeed, the fastest way to the heart is through the veins.

**Conflict of interest**: none declared.

## References


1. Harjola VP, Mullens W, Banaszewski M, Bauersachs J, Brunner-La Rocca HP, Chioncel O, et al. Organ dysfunction, injury and failure in acute heart failure: from pathophysiology to diagnosis and management. A review on behalf of the Acute Heart Failure Committee of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). *Eur J Heart Fail*. 2017;**19**:821–36.
2. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur J Heart Fail*. 2022;**24**:4–131.
3. Gheorghiade M, Follath F, Ponikowski P, Barsuk JH, Blair JEA, Cleland JG, et al. Assessing and grading congestion in acute heart failure: a scientific statement from the Acute Heart Failure Committee of the Heart Failure Association of the European Society of Cardiology and endorsed by the European Society of Intensive Care Medicine. *Eur J Heart Fail*. 2010;**12**:423–33.
4. Pellicori P, Platz E, Dauw J, ter Maaten JM, Martens P, Pivetta E, et al. Ultrasound imaging of congestion in heart failure: examinations beyond the heart. *Eur J Heart Fail*. 2021;**23**:703–12.
5. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging*. 2015;**16**:233–71.
6. Beigel R, Cercek B, Luo H, Siegel RJ, Angeles L. Noninvasive evaluation of right atrial pressure. *J Am Soc Echocardiogr*. 2013;**26**:1033–42.
7. Ivey-Miranda JB, Wetterling F, Gaul R, Sheridan S, Asher JL, Rao VS, et al. Changes in inferior vena cava area represent a more sensitive metric than change in filling pressures during experimental manipulation of intravascular volume and tone. *Eur J Heart Fail*. 2022;**24**:455–62.
8. Abraham WT, Stevenson LW, Bourge RC, Lindenfeld JA, Bauman JG, Adamson PB. Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: complete follow-up results from the CHAMPION randomised trial. *Lancet*. 2016;**387**:453–61.
9. Mullens W, Sharif F, Dupont M, Rothman AMK, Wijns W. Digital health care solution for proactive heart failure management with the Cordella Heart Failure System: results of the SIRONA first-in-human study. *Eur J Heart Fail*. 2020;**22**:1912–9.
10. Lindenfeld J, Zile MR, Desai AS, Bhatt K, Ducharme A, Horstmanshof D, et al. Haemodynamic-guided management of heart failure (GUIDE-HF): a randomised controlled trial. *Lancet*. 2021;**398**:991–1001.
11. Pellicori P, Carubelli V, Zhang J, Castiello T, Sherwi N, Clark AL, et al. IVC diameter in patients with chronic heart failure: relationships and prognostic significance. *JACC Cardiovasc Imaging*. 2013;**6**:16–28.
12. Cubo-Romano P, Torres-Macho J, Soni NJ, Reyes LF, Rodríguez-Almodóvar A, Fernández-Alonso JM, et al. Admission inferior vena cava measurements are associated with mortality after hospitalization for acute decompensated heart failure. *J Hosp Med*. 2016;**11**:778–84.
13. Jobs A, Vonthein R, König IR, Schäfer J, Nauck M, Haag S, et al. Inferior vena cava ultrasound in acute decompensated heart failure: design rationale of the CAVA-ADHF-DZHK10 trial. *ESC Heart Fail*. 2020;**7**:973–83.
14. Fudim M, Hernandez AF, Felker GM. Role of volume redistribution in the congestion of heart failure. *J Am Heart Assoc*. 2017;**6**:e006817.
15. Miller WL, Sorimachi H, Grill DE, Fischer K, Borlaug BA. Contributions of cardiac dysfunction and volume status to central haemodynamics in chronic heart failure. *Eur J Heart Fail*. 2021;**23**:1097–105.