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EDITORIAL COMMENT

Pressure-Volume Loop Analysis in Tricuspid Valve Intervention

Are We There Yet?!*

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Pressure-volume loop (PVL) analysis is the gold standard for assessing ventricular function (1,2). For decades, PVL research was limited to animal studies or ex-vivo experiments (1,3). Having undergone significant advancement in the PVL conductance catheter technology, this system can be used in clinical practice (4,5). The introduction of transcatheter heart valve (THV) technology has uncovered the knowledge gap of our understanding of cardiovascular physiology beyond conventional echocardiography or standard hemodynamic assessment in the catheterization laboratory. Historically, right ventricle (RV) physiology research has been less intensely investigated in comparison with the left ventricle (LV) (2). Some challenges of RV performance are addressed by the introduction of 3-dimensional echocardiography and cardiac MRI (CMR) (6,7). Nevertheless, the fundamental understanding of RV function, especially in isolated tricuspid regurgitation (TR), is yet to be further discovered.

In this issue of *JACC: Case Reports*, van den Enden et al (8) demonstrate an elegant application of PVL in an 84-year-old woman with isolated severe TR and NYHA function class IV, no longer responding to optimal medical therapy. There was no left-sided heart disease, and the RV ejection fraction (EF) was normal. THV intervention by transcatheter edge-to-edge tricuspid repair (TEETR) with TriClip XT (Abbott) was proposed to the patient. Despite normal RVEF and LVEF, the baseline hemodynamic studies demonstrated severely reduced cardiac output. The post-TEETR hemodynamic parameters improved after successful TR reduction. The patient had an immediate increase in cardiac output by nearly 17%. Nevertheless, the more striking findings in this case report are in the PVL indices and PVL curves, rather than reduction of color Doppler jet or modestly augmented cardiac output.

The PVL analysis demonstrated a marked reduction of total RV pressure-volume area (PVA), while the LV PVA increased. PVA is a strong surrogate for the total mechanical energy of that beat of the ventricle (9). Stroke work (SW) is the amount of external (efficient) work of the ventricle. Therefore, the SW to PVA ratio (SW/PVA) is a more reliable index of ventricular function. Post TEETR, the SW/PVA increased from 0.54 to 0.68, suggesting recovered RV performance, with no significant change in LV SW/PVA notwithstanding a modest increase in LV PVA. These findings highlight the improvement of bioenergetics of both ventricles, albeit with a reduction of RVEF resulting from higher RV afterload. Ventriculoarterial coupling measures forward flow with minimal energy cost for the ventricle (10). Studies of LV-aorta coupling have shown a virtually perfect correlation between the ratio of end-systolic elastance (E_{es}) to arterial elastance (E_a). Most studies have applied a similar relationship of the E_{es}/E_a ratio for RV-PA coupling. This index is a more sensitive marker of RV function and detects changes of the RV function earlier than hemodynamic changes or echocardiographic measurements. The normal value of the E_{es}/E_a ratio for the RV is between 1.5 and 2 (11). After THV intervention in this patient, RV-PA coupling substantially increased, with

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pre-TEETR: 0.43 to post-TEETR: 0.98. The ventriculoarterial coupling recovery demonstrates the immediate improvement of the RV function, despite a mild reduction in RVEF, also highlighting the discordance of myocardial performance and EF.

The synchronous ventricle follows a reduction of ventricular volume during systole, whereas it does not occur with a dyssynchronous ventricle, at least in some segments of the PVL (12). Thus, the more dyssynchronous the ventricle functions, the more energy loss occurs (12). There was a marked reduction of intraventricular dyssynchrony after TEETR, highlighting enhanced RV and LV performance. Intraventricular dyssynchrony measurement by conductance catheter is an invaluable measured index, validated by tissue Doppler imaging (13).

An interesting observation of the LV PVL curve is the reformed lusitropy, as demonstrated by the improvement of the LV end-diastolic pressure-volume relationship (EDPVR) (14). One might consider several mechanistic possibilities:

- Reduced intraventricular dyssynchrony
- Increased preload to the LV, hence optimizing the Frank-Starling curve
- The reduced shift of the interventricular septum to the LV (i.e., D-shaped septum)

Concurrently, it appears that the lusitropy of the RV function has slightly decreased, i.e., less compliant RV after TEETR. This finding may be related to the elevated right-sided filling pressure or the acute changes of the geometry of the tricuspid annulus by the TriClip insertion, which may acutely change the RV-EDPVR. Whether RV-EDPVR recuperates in time remains unknown.

A few words of caution are noteworthy. As the investigators pointed out, the cardiac output measurement by thermodilution in severe TR is often inaccurate. The ideal cardiac output measurement is the Fick method, by real-time total body oxygen consumption measurement. However, the special equipment is often not available in most catheterization laboratories. Either CMR or echocardiography imaging modalities may be helpful in such clinical scenarios. It is self-evident that CMR applies only before and after the TEETR procedure, not in real time. Nevertheless, imaging modalities are usually operator dependent, minimizing the reproducibility of such studies. Moreover, the PVL values of stroke volume and cardiac output are the average values of PVL from beat to beat, especially in the presence of atrial fibrillation, as in this index case. Finally, as noted, the RV-PA coupling ratio is used akin to LV assessment by the E_{es}/E_a ratio (11,15). Brener et al (11) have elegantly questioned the accuracy of this oversimplified formula for the RV-PA coupling. Although we are confident that RV-PA coupling has improved, the absolute value may be slightly different.

We congratulate the investigators for their futuristic approach to understanding the RV function beyond the conventional measurements. When combined with hemodynamics, flow-dynamic studies add a new horizon to cardiovascular pathophysiology. Furthermore, the PVL analysis may demonstrate fundamental distinctions in different treatment modalities, such as in the outcomes in patients undergoing valve repair versus replacement. By providing a large-scale international registry, we may develop predictive models for better treatment strategies. Artificial intelligence may also mitigate some of the challenges of extensive data acquisition and interpretation. Currently, there are only a handful of published case reports of PVL in structural heart disease. We hope to observe large-scale studies with PVL as one of the primary endpoints in future clinical trials.

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