Editorial

Right ventricular-pulmonary artery coupling—an emerging perspective in transcatheter aortic valve replacement

Sameer Arora[1], Nikita Patil[2], John Vavalle[1]

[1]Division of Cardiology, University of North Carolina, Chapel Hill, NC, USA; [2]Department of Internal Medicine, Cape Fear Valley Medical Center and Campbell University School of Osteopathic Medicine, Fayetteville, NC, USA

Correspondence to: Sameer Arora, MD. Division of Cardiology, University of North Carolina, 160 Dental Circle, Chapel Hill, NC 27599, USA. Email: saror@email.unc.edu.

Comment on: Sultan I, Cardounel A, Abdelkarim I, *et al.* Right ventricle to pulmonary artery coupling in patients undergoing transcatheter aortic valve implantation. Heart 2019;105:117-21.

Submitted Nov 06, 2018. Accepted for publication Nov 20, 2018.
doi: 10.21037/jtd.2018.11.92
View this article at: http://dx.doi.org/10.21037/jtd.2018.11.92

Since its approval in 2011 in high and prohibitive-surgical-risk patients, transcatheter aortic valve replacement (TAVR) has expanded its indication to intermediate-surgical-risk patients (1,2). Studies are underway to investigate its potential as a modality in low-surgical risk patients and establish an all-risk indication for TAVR for treatment of patients with severe symptomatic aortic stenosis. During this journey, TAVR has crossed many hurdles through refinements in risk stratification, operator experience, and technological advancements. Risk stratification techniques have played a major role in attempting to identify patients who may or may not be suited to TAVR as an intervention. With rapid dissemination of TAVR, even a small risk of adverse outcomes could translate into a high absolute number of affected patients. Therefore, it is critical to continue to investigate these poor predictive indicators for better risk stratification and better patient selection to improve outcomes.

In a recent study by Sultan *et al.*, the investigators evaluated the impact of noninvasively measured tricuspid annular plane systolic excursion (TAPSE)-pulmonary artery systolic pressure (PASP) ratio as an estimate of right ventricle (RV) to pulmonary artery (PA) coupling on TAVR outcomes (3). This was a single-tertiary-care-center-based retrospective observational cohort analysis of 457 patients with native severe aortic stenosis who underwent successful TAVR with either balloon-expandable or self-expanding valves. The researchers found an association between baseline TAPSE/PASP ratio and all-cause mortality after TAVR. TAPSE was estimated using the apical four-chamber view in transthoracic echocardiogram (TTE) while PASP was computed using the maximum tricuspid regurgitant jet velocity from continuous wave Doppler and the right atrial pressure from inferior vena cava measurements. The results of a subset study demonstrated a good reproducibility in terms of intra- and inter-observer reliability. Patients with higher TAPSE/PASP ratio indicative of a better RV-PA coupling had a lower STS-PROM score and were less often found to have multivessel coronary disease requiring coronary artery bypass grafting. Conversely, those with a lower TAPSE/PASP score signifying worse RV-PA uncoupling had more left-sided chamber remodeling, lower LVEF, lower stroke volume index and a higher prevalence of at least moderate mitral and tricuspid regurgitation. Around 97% of patients in the study had NYHA functional class III/IV. A higher TAPSE/PASP ratio (implying better RV-PA coupling) was associated with a favorable survival even after a meticulous adjustment for relevant baseline clinical and echocardiographic characteristics and was found to be a better predictor than other individual prognostic factors such as TAPSE, PASP or the STS-PROM risk assessment tool (3).

Despite their limitations, TAPSE derived from echo as a measure of right ventricular systolic function and PASP estimated from doppler echo are easily available parameters by noninvasive techniques (4). The prognostic ability of TAPSE/PASP ratio has been studied in heart failure (5,6). A 2013 study by Guazzi

et al. explored the significance of TAPSE-PASP ratio as a physiologically more relevant parameter (as a measure of right ventricular function in relation to right ventricular afterload) as a prognostic tool in patients with heart failure. In this study of 293 heart failure patients, a lower TAPSE/PASP ratio was associated with a worse NYHA functional class and higher mortality; and was found to have a better prognostic ability than either TAPSE and PASP alone; independent of the nature of heart failure (5). Similarly, a cohort study of Asian population with heart failure found an association between the TAPSE/PASP ratio and a composite end-point of all-cause mortality and heart failure hospitalization, independent of LV function (6).

Heart failure is common in patients with AS who qualify for valve replacement. About 97% of patients in the study by Sultan *et al.* had NYHA functional class III/IV. In the PARTNER 2 trial investigating patients at intermediate-risk for surgery, 77% of those who underwent TAVR had NYHA functional class III or IV at baseline (2). Notably, Sultan *et al.* in their study found a lower TAPSE/PASP ratio to be associated with higher all-cause mortality even after adjusting for baseline characteristics such as LVEF, stroke volume index and STS-PROM score (3) supporting an independent association between the right cardiopulmonary functional entity and mortality in patients undergoing TAVR. Furthermore, a recent work from the Atherosclerosis Risk in Communities (ARIC) study found RV-PA uncoupling to be associated with increased incidence of heart failure or death even among elderly persons free of heart failure, implying a role for RV-PA uncoupling to detect occult RV dysfunction (7) in elderly persons. The findings by Sultan *et al.* illustrating the importance of TAPSE/PASP ratio as a prognostic factor (3) will be a great asset in risk prediction models looking at TAVR outcomes.

There is evidence supporting the role of assessments of TAPSE, PASP and TAPSE/PASP ratio in pulmonary hypertension (8-12). Pulmonary hypertension is common in patients undergoing TAVR and about 42% of patients in the TAVR arm of the PARTNER trial (13) had baseline pulmonary hypertension. In a study of 290 patients with pulmonary arterial hypertension, TAPSE/PASP ratio was found to be associated with hemodynamics, functional class as well as mortality (8). In a study of 277 patients undergoing TAVR, elevated PASP was associated with an adverse prognosis (9). Additionally, persistent pulmonary hypertension after TAVR, estimated by PASP by echo, has been found to be associated with lower survival in other studies as well (10,11). In an interesting study of 617 patients undergoing TAVR in Germany, investigators found a strong correlation between a reversal of pulmonary hypertension post-TAVR and a favorable survival up to a 5.9-year follow-up (12), a finding supported by another study (11). Findings by Sultan *et al.* elucidating TAPSE/PASP ratio as a measure of RV-PA coupling in evaluating outcomes after TAVR (3) opens up several new avenues for research. It will be interesting to investigate, for example, if there is an incremental improvement in the right-sided hemodynamics in patients with better RV-PA coupling post-TAVR, and whether this translates into favorable outcomes incremental to those with reversible pulmonary hypertension. The effect of the reversal of pulmonary hypertension on RV reverse remodeling has been previously studied in patients with chronic thromboembolic pulmonary hypertension, wherein reverse remodeling with a reduction in afterload via pulmonary endarterectomy was noted to improve RV-arterial coupling and RV function (14). Moreover, a better baseline RV-PA coupling was recently found to be associated with better LV-reverse remodeling and prognosis after cardiac resynchronization therapy (15). These findings offer several plausible physiological explanations for better post-TAVR outcomes in patients with better RV-PA coupling as determined by TAPSE/PASP ratio in the study by Sultan *et al.* (3). Concurrently, they also support a need to study reversibility of RV-PA coupling after TAVR and its effect on outcomes in order to determine if and how the RV-to-PA coupling should guide risk stratification of patients with symptomatic AS under consideration for TAVR.

Few studies have investigated the role of isolated TAPSE and RV dysfunction in TAVR patients as well (16,17). A study by Griese *et al.* investigating 702 patients undergoing TAVR between 2009 and 2014 utilized TAPSE as a measure of RV function and found lower TAPSE <14 mm to be associated with increased rate of renal failure requiring dialysis (16). Furthermore, they found the RV systolic function to be an independent determinant of late mortality in this study (16). Another study investigated a potential prognostic role of tricuspid regurgitation and RV dysfunction (estimated by TAPSE) in TAVR patients and only RV dysfunction, and not tricuspid regurgitation was found to be associated with higher mortality post-TAVR (17). The utilization of TAPSE, however, as a tool for assessment of RV dysfunction is limited by the changes in the pattern of the right ventricular contraction after cardiac surgery (18,19), and alternative methods for non-invasive measurements of RV-PA coupling need to be

studied and validated in this study population.

As our knowledge of the RV-PA coupling evolves, more comprehensive noninvasive measures of the RV reserve are expected to emerge, particularly involving the assessment of dynamic RV reserve with its relation to exercise. A study of chronic pulmonary hypertension in a porcine model found RV contractile reserve (as measured by dobutamine pharmacological stress response) to be strongly associated with ventricular-arterial coupling (20). A small pilot translational study suggested a link between resting RV dysfunction (determined by RV-PA coupling) and RV maladaptation to exercise in chronic thromboembolic pulmonary vascular disease (21). The assessment of RV exercise contractile reserve and exercise RV-to-PA coupling for various strata of baseline TAPSE/PASP ratios in heart failure patients suggested a role of exercise RV testing in additional risk-stratification (22). Perhaps with the advancements in the field of stress echo (23), research determining RV contractile exercise reserve and integrating the TAPSE/PASP ratio may better inform risk-stratification. Other advanced techniques involving cardiac magnetic resonance, resting and exercise right heart catheterization parameters and cardiopulmonary exercise testing are also emerging (24).

Until such studies are concluded and the relevant technology becomes readily available, the TAPSE/PASP ratio as a surrogate marker of the adaptability of the right cardiopulmonary functional entity is a simple, noninvasive, resource-sensitive, feasible and reproducible measure (3) that needs to be confirmed in other large studies, diverse patient populations and hospital settings; and validated in prospective studies as a convenient risk stratification tool in TAVR. The effect of this parameter on other outcome measures than survival also needs to be investigated.

This study by Sultan *et al.* (3) is commendable in its elucidation of the role of TAPSE/PASP ratio as a readily available measure in the prognosis of patients undergoing TAVR; and to our knowledge, is the first study to explore its impact on mortality after TAVR. Future studies should also evaluate the utility of this tool in other valvular heart diseases and disease processes that share the common features of heart failure, pulmonary hypertension, and RV dysfunction.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2438-88.
2. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients. N Engl J Med 2016;374:1609-20.
3. Sultan I, Cardounel A, Abdelkarim I, et al. Right ventricle to pulmonary artery coupling in patients undergoing transcatheter aortic valve implantation. Heart 2019;105:117-21.
4. Rudski LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 2010;23:685-713; quiz 786-8.
5. Guazzi M, Bandera F, Pelissero G, et al. Tricuspid annular plane systolic excursion and pulmonary arterial systolic pressure relationship in heart failure: an index of right ventricular contractile function and prognosis. Am J Physiol Heart Circ Physiol 2013;305:H1373-81.
6. Bosch L, Lam CS, Gong L, et al. Right ventricular dysfunction in left-sided heart failure with preserved versus reduced ejection fraction. Eur J Heart Fail 2017;19:1664-71.
7. Nochioka K, Querejeta Roca G, Claggett B, et al. Right Ventricular Function, Right Ventricular-Pulmonary Artery Coupling, and Heart Failure Risk in 4 US Communities: The Atherosclerosis Risk in Communities (ARIC) Study. JAMA Cardiol 2018;3:939-48.
8. Tello K, Axmann J, Ghofrani HA, et al. Relevance of the TAPSE/PASP ratio in pulmonary arterial hypertension. Int J Cardiol 2018;266:229-35.
9. Bishu K, Suri RM, Nkomo VT, et al. Prognostic impact of pulmonary artery systolic pressure in patients undergoing transcatheter aortic valve replacement for aortic stenosis.

Am J Cardiol 2014;114:1562-7.
10. Masri A, Abdelkarim I, Sharbaugh MS, et al. Outcomes of persistent pulmonary hypertension following transcatheter aortic valve replacement. Heart 2018;104:821-7.
11. Sinning JM, Hammerstingl C, Chin D, et al. Decrease of pulmonary hypertension impacts on prognosis after transcatheter aortic valve replacement. EuroIntervention 2014;9:1042-9.
12. Alushi B, Beckhoff F, Leistner D, et al. Pulmonary Hypertension in Patients With Severe Aortic Stenosis: Prognostic Impact After Transcatheter Aortic Valve Replacement: Pulmonary Hypertension in Patients Undergoing TAVR. JACC Cardiovasc Imaging 2018. [Epub ahead of print].
13. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364:2187-98.
14. Rolf A, Rixe J, Kim WK, et al. Right ventricular adaptation to pulmonary pressure load in patients with chronic thromboembolic pulmonary hypertension before and after successful pulmonary endarterectomy--a cardiovascular magnetic resonance study. J Cardiovasc Magn Reson 2014;16:96.
15. Schmeisser A, Rauwolf T, Ghanem A, et al. Right heart function interacts with left ventricular remodeling after CRT: A pressure volume loop study. Int J Cardiol 2018;268:156-61.
16. Griese DP, Kerber S, Barth S, et al. Impact of right and left ventricular systolic dysfunction on perioperative outcome and long-term survival after transcatheter aortic valve replacement. J Interv Cardiol 2017;30:217-25.
17. Schwartz LA, Rozenbaum Z, Ghantous E, et al. Impact of Right Ventricular Dysfunction and Tricuspid Regurgitation on Outcomes in Patients Undergoing Transcatheter Aortic Valve Replacement. J Am Soc Echocardiogr 2017;30:36-46.
18. Raina A, Vaidya A, Gertz ZM, et al. Marked changes in right ventricular contractile pattern after cardiothoracic surgery: implications for post-surgical assessment of right ventricular function. J Heart Lung Transplant 2013;32:777-83.
19. Okada DR, Rahmouni HW, Herrmann HC, et al. Assessment of right ventricular function by transthoracic echocardiography following aortic valve replacement. Echocardiography 2014;31:552-7.
20. Guihaire J, Haddad F, Noly PE, et al. Right ventricular reserve in a piglet model of chronic pulmonary hypertension. Eur Respir J 2015;45:709-17.
21. Axell RG, Messer SJ, White PA, et al. Ventriculo-arterial coupling detects occult RV dysfunction in chronic thromboembolic pulmonary vascular disease. Physiol Rep 2017;5.
22. Guazzi M, Villani S, Generati G, et al. Right Ventricular Contractile Reserve and Pulmonary Circulation Uncoupling During Exercise Challenge in Heart Failure: Pathophysiology and Clinical Phenotypes. JACC Heart Fail 2016;4:625-35.
23. Rudski LG, Gargani L, Armstrong WF, et al. Stressing the Cardiopulmonary Vascular System: The Role of Echocardiography. J Am Soc Echocardiogr 2018;31:527-50.e11.
24. Kubba S, Davila CD, Forfia PR. Methods for Evaluating Right Ventricular Function and Ventricular-Arterial Coupling. Prog Cardiovasc Dis 2016;59:42-51.

Cite this article as: Arora S, Patil N, Vavalle J. Right ventricular-pulmonary artery coupling—an emerging perspective in transcatheter aortic valve replacement. J Thorac Dis 2019;11(2):345-348. doi: 10.21037/jtd.2018.11.92

