JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 10, NO. 7, 2017

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcin.2017.02.032

EDITORIAL COMMENT

Coincidental Significant Tricuspid Regurgitation at the Time of Right Ventricle–to–Pulmonary Artery Conduit Intervention

Should We Address it, Ignore it, or Take a More Nuanced Approach?*

Camden L. Hebson, MD,[a,b] Georges Ephrem, MD, MSc,[a] Fred H. Rodriguez III, MD[a,b]

Since its inception nearly 2 decades ago, transcatheter pulmonary valve replacement (TPVR) has brought on a paradigm shift in the approach to patients with significant right ventricle-to-pulmonary artery (RV-PA) conduit dysfunction (1). Excellent immediate-, short-, and medium-term outcomes are well documented, no matter if the primary disease is pulmonary stenosis (PS), pulmonary regurgitation (PR), or a combination of the 2 (2–4). Tricuspid regurgitation (TR) is a frequent associated finding in patients being considered for TPVR; indeed, 10% to 35% of congenital heart patients (tetralogy of Fallot, pulmonary atresia, etc.) are reported to have coincidental moderate to severe TR (5,6). No singular mechanism of TR is present, and instead annular dilation (especially in the context of significant PR and right ventricular dilation), congenital dysplasia, pacemaker lead perturbation, and post-surgical disruption (ventricular septal defect patch tethering or valve takedown during ventricular septal defect exposure) have all been described as causes (7,8). Regardless of the reason, the presence of significant TR is thought to mitigate the impact of intervention on PS or PR by perpetuating right ventricular volume overload. Adult congenital and valvular heart disease guidelines reflect this belief and suggest a surgical approach to PS or PR when significant TR is present and thus needs to be concomitantly addressed (9,10). However, newer studies have called this belief into question (8); specifically, can TR be reduced by intervening solely on a dysfunctional pulmonary valve? This has significant implications for the role of TPVR in treating these patients.

SEE PAGE 701

With this in mind, in this issue of *JACC: Cardiovascular Interventions*, Tanase et al. (11) investigated the impact of moderate or severe TR on right ventricular remodeling after TPVR into RV-PA conduits. The investigators conducted a matched cohort study comparing patients with significant TR with those without significant TR. The principal variables of interest were RV size as assessed by cardiac magnetic resonance imaging (CMR) and exercise performance. Severity of TR by echocardiographic assessment was also reported. Data were obtained at baseline (pre-intervention) and 6 months post-implantation, and then echocardiographic assessment of TR severity was also tracked for a median of 6.5 years thereafter. The key patient data included the following: 1) the study group (those with moderate to severe TR at the time of TPVR) represented 13% of all TPVR patients over the study period; 2) mean patient age was 22 ± 8 years, patients with PS, PR, and mixed disease were all represented, and the main anatomic

*Editorials published in *JACC: Cardiovascular Interventions* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Interventions* or the American College of Cardiology.

From the [a]Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia; and the [b]Division of Pediatric Cardiology, Department of Pediatrics, Emory University School of Medicine, Atlanta, Georgia. All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

diagnoses were tetralogy of Fallot (50% of patients) and pulmonary atresia with or without ventricular septal defect (28%); 3) CMR imaging-derived median right ventricular end-diastolic volume index (RVEDVi) was 100 ml/m^2; and 4) the mechanism of TR was not explicitly defined, but the investigators note that upon review of pre-study imaging, TR slowly developed in all patients, thus implying an absence of anatomic or primary pathological cause. The key findings include the following: 1) at 6-month follow-up, there was no statistical difference in decrease in RVEDVi or improvement in exercise parameters between the study groups (regardless of the presence of significant TR); 2) TR itself improved by at least 1 qualitative severity grade in more than 80% of the patients with "significant TR" by 6-month follow-up; 3) at a median of 6.5 years, none of the patients with "significant TR" still had significant TR. The investigators thus conclude that TPVR improves not only RV-PA conduit dysfunction but also meaningful variables such as right ventricular size and exercise performance, regardless of the presence of moderate to severe TR. Furthermore, TR itself steadily improves after TPVR. Thus, significant TR should not preclude TPVR use for RV-PA conduit dysfunction, and instead the decision as to when to intervene on the tricuspid valve should wait until after TPVR.

Tanase et al. (11) should be commended on addressing such a pertinent question: the management of congenital heart patients with RV-PA conduit dysfunction and concomitant moderate to severe TR. The investigators hypothesized that positive right ventricular remodeling and improved clinical status after TPVR would be present regardless of TR severity and furthermore that tricuspid valve function itself would improve in the wake of improved hemodynamic status. Support for the second hypothesis is found in both similar (7,8) and dissimilar patient populations. Specifically, as pointed out by the investigators, "secondary" TR can improve following mitral valve surgery (12), atrial septal defect closure (13), and surgical pulmonary valve replacement (7). Although our group (7) and Jones et al. (8) both addressed the problem of TR associated with pulmonary valve disease, neither study contained vital information on the mechanism of TR due to study design limitations. In contrast, this study does address mechanism, noting that all patients developed TR gradually over many years, and no patients had significant TR at medium-term follow-up, thus implying that a secondary cause (annular dilation, right ventricular enlargement) was present. With this in mind, the reported improvement in TR, as the right ventricle remodels, does seem logical. However, readers should also note the limits of generalizability. This study does not speak to the expected course of TR in the setting of a congenitally dysplastic valve or an iatrogenic cause. It is rational to expect a significantly regurgitant tricuspid valve to remain dysfunctional, even in the context of favorable right ventricular remodeling, if the regurgitation is due to intrinsic problems such as hypoplastic chordae, valve thickening or prolapse, surgical or pacemaker lead trauma, and so on.

It should be pointed out that the median RVEDVi of this study's patient cohort was less than that published in other series and CMR Imaging guidelines (14–16). The investigators note that differences in CMR imaging measuring techniques might contribute to this finding, although the presence of a heterogeneous mixture of patients, including those with primarily PS, likely factors in as well. Regardless, if right ventricular dilation is less severe before intervention on the RV-PA conduit, could this be a confounding reason for lack of statistical difference in post-intervention right ventricular size (i.e., less room for TR to affect remodeling)? We are unable to answer this question on the basis of the data presented here and in the published research at large; in case series in which much larger median RVEDVi values are present, change in right ventricular volume stratified by severity of TR was not included as a subanalysis (14,15).

When deciding on intervention for a dysfunctional RV-PA conduit, does TR matter at all? Tanase et al. (11) seem to argue against its importance, highlighting the similar clinical and imaging results among the cohorts. Others, however, have published contentious findings. Bokma et al. (17) argued that severe pre-operative TR is itself associated with adverse late outcomes, including arrhythmias, heart failure, and mortality. The group then advocates for tricuspid valve repair in those with significant TR at time of PVR and furthermore that pulmonary valve replacement should be pursued before to the development of severe TR if possible. Surgical tricuspid valve intervention is not without risk, however. As stated by Kogon et al. (7), tricuspid valve repair or replacement, when added to pulmonary valve replacement, correlates with prolonged cardiopulmonary bypass time, length of hospital stay, risk for surgical complications such as heart block, and might not even make a difference in TR severity in the long term. When compelling arguments are made on both sides of such a debate, the need for further studies becomes clear.

Overall, the results of this study are exciting to providers caring for adults with congenital heart

disease. When determining the best approach for patients with RV-PA conduit dysfunction, transcatheter options are attractive given the expected faster patient recovery and avoidance of a sternotomy and dissection (and the implications for the next time surgery is needed). If concomitant TR can be addressed without surgery, more options are available to our patients. As is true in most aspects of adult congenital cardiology, however, this decision is more complex than it might seem. From the data available to date, it is safe to say that a singular approach to this issue is inadequate. Instead, we would advocate for nuance. Specifically, the first step in the evaluation of moderate to severe TR associated with RV-PA conduit dysfunction should be evaluating the mechanism of the TR itself. In those with primary pathology, surgical intervention at time of surgical pulmonary valve replacement should be considered. In those with secondary TR, TPVR would seem to be the best approach. In those patients who are difficult to categorize, we would advocate to do as Tanase et al. (11) did: go back to previous echocardiograms, look at changes over time, and add to this the description of the anatomy gleaned from previous operative reports to make the best determination possible. At the very least, this subtlety should be incorporated into patient counseling; if further procedures might soon be needed, one would do well to let patients know the risk.

ADDRESS FOR CORRESPONDENCE: Dr. Camden L. Hebson, Emory University School of Medicine, Department of Medicine, Division of Cardiology, 101 Woodruff Circle, Suite 319, Atlanta, Georgia 30322. E-mail: chebson@emory.edu.

REFERENCES

1. Bonhoeffer P, Boudjemline Y, Saliba Z, et al. Percutaneous replacement of pulmonary valve in a right ventricle to pulmonary artery prosthetic conduit with valve dysfunction. Lancet 2000;356:1403–5.

2. Armstrong AK, Balzer DT, Cabalka AK, et al. One-year follow-up of the Melody transcatheter pulmonary valve multicenter post-approval study. J Am Coll Cardiol Intv 2014;7:1254–62.

3. Borik S, Crean A, Horlick E, et al. Percutaneous pulmonary valve implantation: 5 years of follow-up: does age influence outcomes? Circ Cardiovasc Interv 2015;8:e001745.

4. Cheatham JP, Hellenbrand WE, Zahn EM, et al. Clinical and hemodynamic outcomes up to 7 years after transcatheter pulmonary valve replacement in the US Melody Valve Investigational Device Exemption Trial. Circulation 2015;131:1960–70.

5. Mahle WT, Parks WJ, Fyfe DA, et al. Tricuspid regurgitation in patients with repaired tetralogy of Fallot and its relation to right ventricular dilatation. Am J Cardiol 2003;92:643–5.

6. Hoashi T, Kagisaki K, Kitano M, et al. Late clinical features of patients with pulmonary atresia or critical pulmonary stenosis with intact ventricular septum after biventricular repair. Ann Thorac Surg 2012;94:833–41.

7. Kogon B, Mori M, Alsoufi B, Kanter K, Oster M. Leaving moderate tricuspid regurgitation alone at the time of pulmonary valve replacement: a worthwhile approach. Ann Thorac Surg 2015;99:2117–22.

8. Jones TK, Rome JJ, Armstrong AK, et al. Transcatheter pulmonary valve replacement reduces tricuspid regurgitation in patients with right ventricular volume/pressure overload. J Am Coll Cardiol 2016;68:1525–35.

9. Nishimura RA, Otto CM, Bonow RO, et al. 2104 AHA/ACC guideline for the management of patients with valvular heart disease: an 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.

10. Baumgartner H, De Groot NM, de Haan F, et al. ESC guidelines for the management of grown-up congenital heart disease. Eur Heart J 2010;31:2915–57.

11. Tanase D, Ewert P, Georgiev S, et al. Tricuspid regurgitation does not impact right ventricular remodeling after percutaneous pulmonary valve implantation. J Am Coll Cardiol Intv 2017;10:701–8.

12. Yilmaz O, Suri RM, Dearani JA, et al. Functional tricuspid regurgitation at the time of mitral valve repair for degenerative leaflet prolapse: the case for a selective approach. J Thorac Cardiovasc Surg 2011;142:608–13.

13. Toyono M, Krasuski RA, Pettersson GB, Matsumura Y, Yamano T, Shiota T. Persistent tricuspid regurgitation and its predictor in adults after percutaneous and isolated surgical closure of secundum atrial septal defect. Am J Cardiol 2009;104:856–61.

14. Oosterhof T, van Straten A, Vliegen HW, et al. Preoperative thresholds for pulmonary valve replacement in patients with corrected tetralogy of Fallot using cardiovascular magnetic resonance. Circulation 2007;116:545–51.

15. Frigiola A, Tsang V, Bull C. Biventricular response after pulmonary valve replacement for right ventricular outflow tract dysfunction: is age a predictor of outcome? Circulation 2008;118 Suppl:S182–90.

16. Geva T. Repaired tetralogy of Fallot: the roles of cardiovascular magnetic resonance in evaluating pathophysiology and for pulmonary valve replacement decision support. J Cardiovasc Magn Reson 2011;13:9.

17. Bokma JP, Winter MM, Oosterhof T, et al. Severe tricuspid regurgitation is predictive for adverse events in tetralogy of Fallot. Heart 2015;101:794–9.

KEY WORDS congenital heart disease, tetralogy of fallot, tricuspid regurgitation