

## **Chapter 31: Cardiac imaging for TPVr: evaluation, planning, and intra-procedural use**

*Zachary L. Steinberg, MD<sup>1</sup>, Rose Tompkins, MD<sup>2</sup>, and Doff B. McElhinney, MD<sup>2</sup>*

<sup>1</sup>University of Washington

<sup>2</sup>Stanford University, Lucile Packard Children's Hospital Stanford

Since the first reported transcatheter pulmonary valve replacement (TPVR) by Bonhoeffer et al. in 2000(1), thousands of patients have undergone TPVR worldwide (2). The Melody valve, a valved segment of bovine jugular vein sewn inside of a platinum-iridium stent, is the most commonly implanted valve in the United States, having received US Food and Drug Administration (FDA) approval under Humanitarian Device Exemption in 2010 and full premarket approval in 2015. Although TPVR using the Melody valve has had a major impact on the management of patients with obstruction or regurgitation of a surgical right ventricular outflow tract (RVOT) conduit or bioprosthetic pulmonary valve (BPV), many patients are not candidates for TPVR due to the Melody valve's size limitation to conduits  $\leq 24$  mm in diameter. Therefore, there has been a growing interest in alternative transcatheter valves to increase the number of eligible congenital heart disease patients. With an external maximum diameter of 29 mm, the Edwards Sapien transcatheter aortic valve is sometimes used in larger right ventricular to pulmonary artery (RV-PA) conduits throughout Europe and is currently under trial in the United States. Additionally, a number of self-expanding stented valves designed for the native or patched RVOT are under investigation, and are expected to further increase the number of patients eligible for TPVR over the next decade. Regardless of valve type, successful TPVR hinges on high quality multi-modality imaging for appropriate patient selection, pre-procedural planning, intra-procedural valve implantation in some cases, and assessment of intra- or post-procedural complications.

### **Patient Selection**

Currently, there are no published guidelines providing a comprehensive set of indications for TPVR; however, the US Melody Valve Trial has provided a framework for patient selection(3). In brief, the trial permitted valve implantation in symptomatic patients with at least moderate conduit stenosis or regurgitation. Valve implantation in asymptomatic patients required severe conduit stenosis, severe conduit regurgitation, or depressed right ventricular (RV) systolic function (**Table 1**). In practice, it is generally accepted that asymptomatic patients with either severe RVOT obstruction or pulmonary regurgitation (PR) who also demonstrate either declining ventricular function, objective worsening of functional capacity, or severe and progressive RV enlargement are considered for TPVR. Many of these criteria are based on indications for surgical PVR and extrapolated to the TPVR population. Furthermore, it is important to assess for concomitant hemodynamically significant lesions, which might lead to additional percutaneous interventions (e.g. branch pulmonary artery stenosis) or, alternatively, lead to consideration for surgical intervention (e.g. aortic/mitral valve pathology). However, it should be noted that as experience with TPVR continues to increase, our understanding of criteria that better identifies appropriate patients, as well as, optimal timing of TPVR implantation will continue to improve. Therefore, pre-procedural imaging techniques will likely continue to evolve as well.

**Table 1: Indications for Melody implantation as defined by the US Melody Valve Trial**

<b>Conduit-specific inclusion criteria for the US Melody Valve Trial</b>	
<b>In patients with NYHA Class I symptoms</b>	<b>In patients with NYHA Class II-IV symptoms</b>
Conduit diameter between 16 and 22 mm RVOT conduit dysfunction Mean gradient $\geq$ 40 mmHg Severe PR* RV fractional shortening $<$ 40%	Conduit diameter between 16 and 22 mm RVOT conduit dysfunction Mean gradient $\geq$ 35 mmHg Moderate PR**

\*Color Doppler jet width  $>$  40% of the width of the valve annulus or diastolic flow reversal extending into the proximal branch pulmonary arteries

\*\*Color Doppler jet width 20-40% of the width of the valve annulus or diastolic flow reversal extending into distal main pulmonary artery

### **Pre-Procedure Imaging: Echocardiography**

Transthoracic echocardiography is the first-line imaging modality for pre-TPVR patient selection as it remains the most common and readily available imaging tool for following patients with RV-PA conduit or BPV. Complete intracardiac assessment of biventricular and valvular function, as well as, evaluation of branch pulmonary artery and aortic anatomy should be the first step in pre-TPVR assessment. Particular attention should be focused on severity of conduit regurgitation and/or stenosis, in addition to RV size and function, to help determine patient appropriateness per the above-mentioned criteria.

#### Assessment of conduit pulmonary valve function

Complete two-dimensional, as well as, color and spectral Doppler should be performed of the RV-PA conduit or BPV. The severity of RVOT obstruction is determined from continuous wave spectral Doppler aligned parallel to the right ventricular outflow tract (RVOT) to assess maximum velocity and mean gradient across the conduit or valve. The mean RVOT gradient is determined by tracing the border of the Doppler recording and integrating the area under the curve. Per the US Melody Valve Trial, an average of at least 3 Doppler tracings were used for patients in sinus rhythm or at least 5 for those not in sinus rhythm. A mean gradient  $\geq$  40 mmHg was classified as severe stenosis. The degree of PR should be determined by assessing the width of the regurgitant jet relative to the width of the conduit by color Doppler and assessing for reversal of flow in the main and branch pulmonary arteries using pulse wave spectral Doppler. Severe PR will be associated with a wider regurgitant jet, holodiastolic flow reversal in the main and branch pulmonary arteries, and early diastolic equalization of pressures between the RV and PA as assessed by spectral Doppler (**Figure 1**).

Studies using exercise stress echocardiography have found that, among patients with conduit or BPV stenosis referred for TPVR, RVOT gradients increase with exercise, and more dysfunctional ventricles have a reduced ventricular reserve during exercise as compared to patients with less ventricular dysfunction at rest. In a small group of patients evaluated after TPVR, the relative change in RVOT gradient with exercise was similar to pre-TPVR (approximately 70% increase in peak RVOT gradient both pre and post-TPVR)(4). The value of such evaluations is not yet established in patients considered

for TPVR, but they may prove to be useful in patients with apparent mismatch between resting hemodynamic and symptomatic status. For example, they may help clarify exertional hemodynamics and impaired ventricular reserve in symptomatic patients without a significant resting gradient, or alternatively, unmask symptoms or impaired RV stress reserve in otherwise asymptomatic patients, which may influence patient referral for TPVR.

#### Assessment of RV function

RV function as determined by echocardiography was not used as a criterion for TPVR in the US Melody Valve Trial per se, but often aids in patient selection for TPVR, especially for asymptomatic patients. Per the US Melody Valve Trial, RV function was determined quantitatively using the fractional area change (FAC) method, where area tracings of the RV were obtained from end-diastole and end-systole in the apical four-chamber view utilizing the formula  $FAC = [end\ diastolic\ area - end\ systolic\ area] / end\ diastolic\ area \times 100$ (5). An RV FAC <35% generally indicates RV systolic dysfunction and has been shown to correlate reasonably well with cardiac magnetic resonance imaging (CMR) derived RV ejection fraction, although in structurally normal hearts(6). For the US Melody Trial specifically, a cut-off value for FAC < 40% was used as a criterion for asymptomatic, New York Heart Association class I patients. On review of echocardiographic assessment of RV systolic function compared to CMR, there was only a fair correlation among this patient population, thus suggesting that CMR is likely more useful than echocardiography if patient candidacy is weighing more heavily on RV function(5).

Other echocardiographic techniques that are used for quantitative estimation of RV function include 3-D echocardiography and strain imaging. 3-D echocardiography is increasingly being utilized for more quantitative assessment of RVEF but has been shown to underestimate RV volumes and hence the calculation of RVEF compared to CMR derived volumes. Both strain and strain rate imaging are being investigated in this population and may identify patients with early RV systolic or diastolic dysfunction that is not yet reflected by a significant decline in calculated RVEF. Although there are no established criteria for the incorporation of these techniques into pre-TPVR evaluation, they may be used more routinely in the future as experience increases (7).

#### Assessment of RV size and RV systolic pressure

RV size should be quantitatively assessed as imaging quality allows per standard methods as described in American Society of Echocardiography guidelines(6). In addition, estimation of RV systolic pressure should also be performed utilizing the maximum velocity of tricuspid regurgitant jet and inferior vena cava diameter.

#### **Pre-Procedural Imaging: Cross-Sectional Imaging**

While Doppler derived mean RVOT pressure gradients and RV systolic pressures correlate closely with invasive hemodynamic measurements, echocardiography is often less accurate in estimating the severity of PR and RV size and function relative to the gold standard of CMR(5). Thus, in patients with predominant PR, CMR is generally an important component of pre-procedural evaluation. Additionally, complete evaluation of branch pulmonary artery, aortic, and coronary anatomy is insufficient with transthoracic imaging alone. Given that patients with an RV-PA conduit or BPV can

harbor concomitant disease such as branch pulmonary artery stenosis, or have higher risk anatomical features for TPVR such as a coronary artery in close proximity to the RVOT, adequate imaging of these other structures is helpful in preprocedural planning. As such, cross-sectional imaging is an important adjunctive imaging modality in select cases when there is sufficient concern for supravalvar pulmonary stenosis, ascending aortic enlargement, aortic coarctation, or at-risk anatomy for coronary artery compression.

In most TPVR candidates, CMR is the cross-sectional imaging modality of choice given that it spares the patient radiation and has the ability to accurately assess RV size and function, severity of PR, and differential pulmonary artery blood flow (**Figure 2**). In addition, CMR provides clear imaging of the RVOT, branch pulmonary arteries, and aorta for more accurate assessment of significant dilation or stenosis (**Figure 3**). Typically, coronary artery origin and course are adequately seen, however, cardiac computed tomographic angiography (CCTA) provides a more detailed coronary artery assessment relative to CMR and may be recommended in select cases where coronary artery anatomy is less clear on CMR.

CCTA should also be considered in those patients with a contraindication to CMR (such as non-MR compatible permanent pacemaker or internal cardiac defibrillator) or for patients with prior RVOT or branch pulmonary artery stents given that CMR imaging is susceptible to device artifact. CCTA can provide quantitative ventricular volumes and function, as well as, excellent detail of the branch pulmonary arteries, aorta, and coronary arteries but at the expense of radiation exposure to the patient (**Figure 4**). Unlike CMR, CCTA is unable to provide quantitative flow data including PR fraction or differential pulmonary blood flows, but RV size and function can often be determined from volumetric data.

As the technology advances for TPVR in the native or patched RVOT, we anticipate an increased need for cross-sectional imaging to provide more accurate measurements of RVOT dimensions as part of pre-procedural planning. As some of these devices are still under investigation, including the Medtronic Harmony valve, there are no published criteria on how to obtain these measurements or what values would be inclusive or exclusive.

Ultimately, no patient should be turned down from consideration of TPVR due to lack of cross-sectional imaging, as much of the data can be obtained from a transthoracic echocardiogram and any necessary additional information can be acquired during cardiac catheterization, either prior to or at the time of the planned intervention. However, whenever possible, it is our practice to obtain cross-sectional imaging to aid in procedural planning.

### **Intra-Procedural Imaging: Angiography**

Following appropriate patient selection, intra-procedural angiographic assessment of the RVOT is necessary in order to ensure a safe and effective outcome. We recommend biplane (as opposed to single plane) fluoroscopy with anterior-posterior (AP) and lateral cameras adjusted to projections that optimize imaging of the RVOT, PA bifurcation, and coronary-conduit relationship. Prior to intervention, angiographic assessment should be performed with injections in the RV, RVOT, and/or conduit, with the aim of understanding the level and appearance of the RVOT, including subvalvar obstruction if appropriate. The AP and lateral cameras should be adjusted to profile the intended implant location, to

understand the PA bifurcation, and to characterize the relationship between the RVOT and the coronary arteries (see below). The projections may be fairly standard or variable degrees of obliqueness, depending on the RVOT orientation, which can be highly variable in these patients. Angiographic measurements of the conduit should be performed in both imaging planes to determine appropriate conduit size in preparation for balloon angioplasty and stent deployment (**Figure 5**). Additional assessment of the distal conduit and branch pulmonary artery anatomy should be performed at this time to ensure that all hemodynamically significant lesions have been identified.

Next, coronary artery angiography is performed to assess the likelihood of coronary artery compression during conduit angioplasty. It is common practice to engage each coronary artery selectively and perform angiograms with the cameras orientated to understand the relationship between the conduit and the coronary arteries. In many cases, this can be achieved, this can be achieved with the AP camera in a steep caudal projection, such that the conduit is visualized on-end, and the lateral camera in a 90-degree LAO projection, but it should be individualized on a patient-by-patient basis (**Figure 6**). Aortic root angiography is also reasonable prior to or in lieu of selective coronary angiography if both coronaries are well opacified. If, following coronary angiography, the likelihood of coronary artery compression remains even a remote concern, we recommend proceeding with coronary artery compression testing, the technique for which has been detailed extensively by Morray et al. (8). High-risk patients who should always undergo coronary artery compression testing include those with tetralogy of Fallot with an anomalous left coronary artery arising from the right sinus, a Ross procedure, or D-transposition of the great arteries, regardless of the type of corrective surgery (either atrial or arterial switch)(8).

If balloon compression testing is performed, it is important to choose a balloon diameter that closely approximates or even exceeds the size of desired RVOT stent to ensure adequate conduit dilation has been performed. Following maximal inflation of the RVOT balloon, coronary angiography is performed with evaluation of contrast flow to the distal myocardium. Once again, the camera angles are optimized to profile the plane between the conduit and the at-risk coronary artery, in order to identify even modest compression or distortion. If coronary compression is witnessed, the TPVR should not be implanted.

Additional consideration may be given to ascending aortography during RVOT balloon compression testing as distortion of the ascending aorta can result from RVOT stent implantation resulting in aortopulmonary fistulae, aortic regurgitation, and proximal kinking of a coronary artery (**Figure 7**). Patients with high-risk anatomy for aortic distortion include those with a history of either a Ross procedure or an arterial switch operation(9-12).

Following RVOT stenting and Melody valve implantation, conduit angiography is repeated to ensure a competent valve and to exclude the presence of conduit disruption or distal pulmonary vascular injury. In patients with concern for coronary artery or aortic compression, or in whom there is high PA pressure after TPVR, ascending aortic angiography may be helpful to assess for aortic regurgitation, aortopulmonary fistula, or coronary compression. If arterial closure devices are considered, common femoral artery angiography should be performed to confirm a sheath insertion site above the level of the femoral artery bifurcation and to rule out the presence of an arterial dissection.

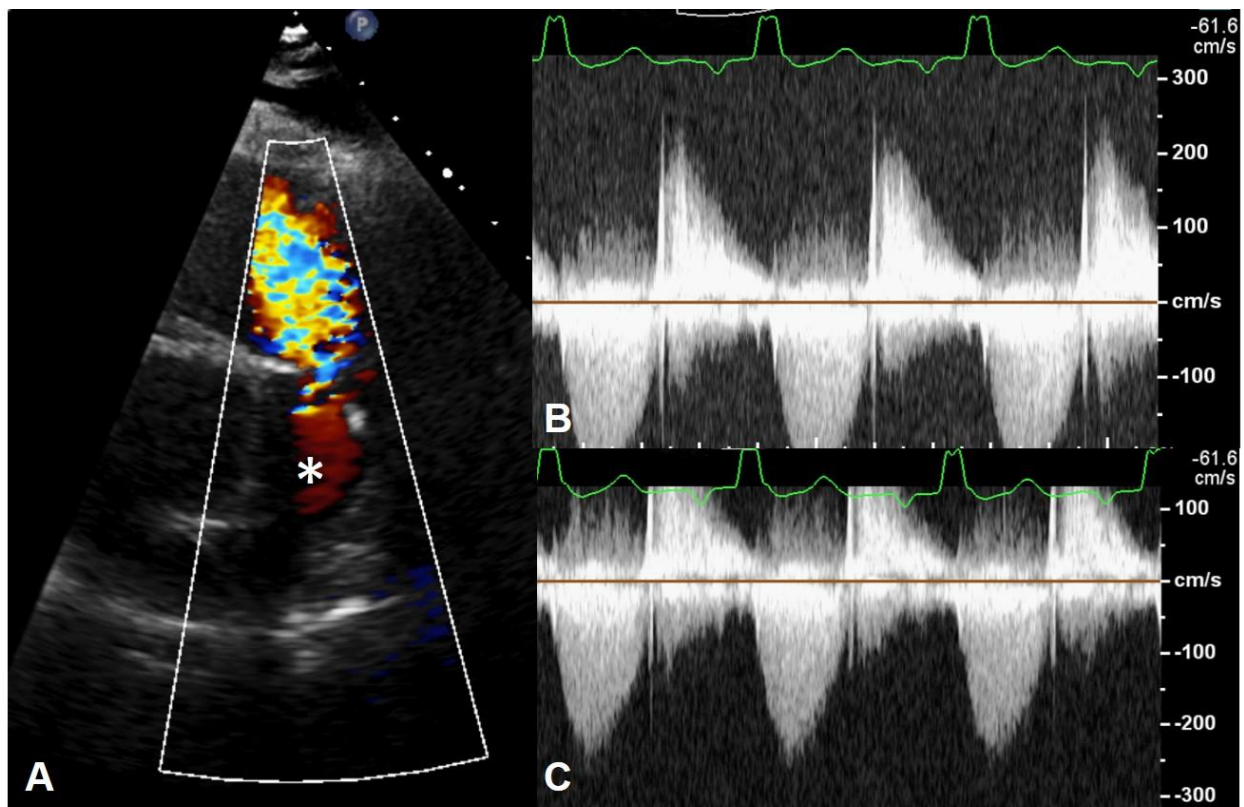
## **Additional Imaging Considerations**

The use of three-dimensional (3D) rotational pulmonary angiography during TPVR is on the rise with limited data suggesting its use may limit total contrast load and radiation exposure(13). In our experience, 3D rotational pulmonary angiography is most useful when complex conduit or branch pulmonary artery anatomy is present. In some cases, a benefit of 3D rotational angiography is the ability to determine optimal fluoroscopic angles for conduit stenting and branch pulmonary artery interventions using image-processing software.

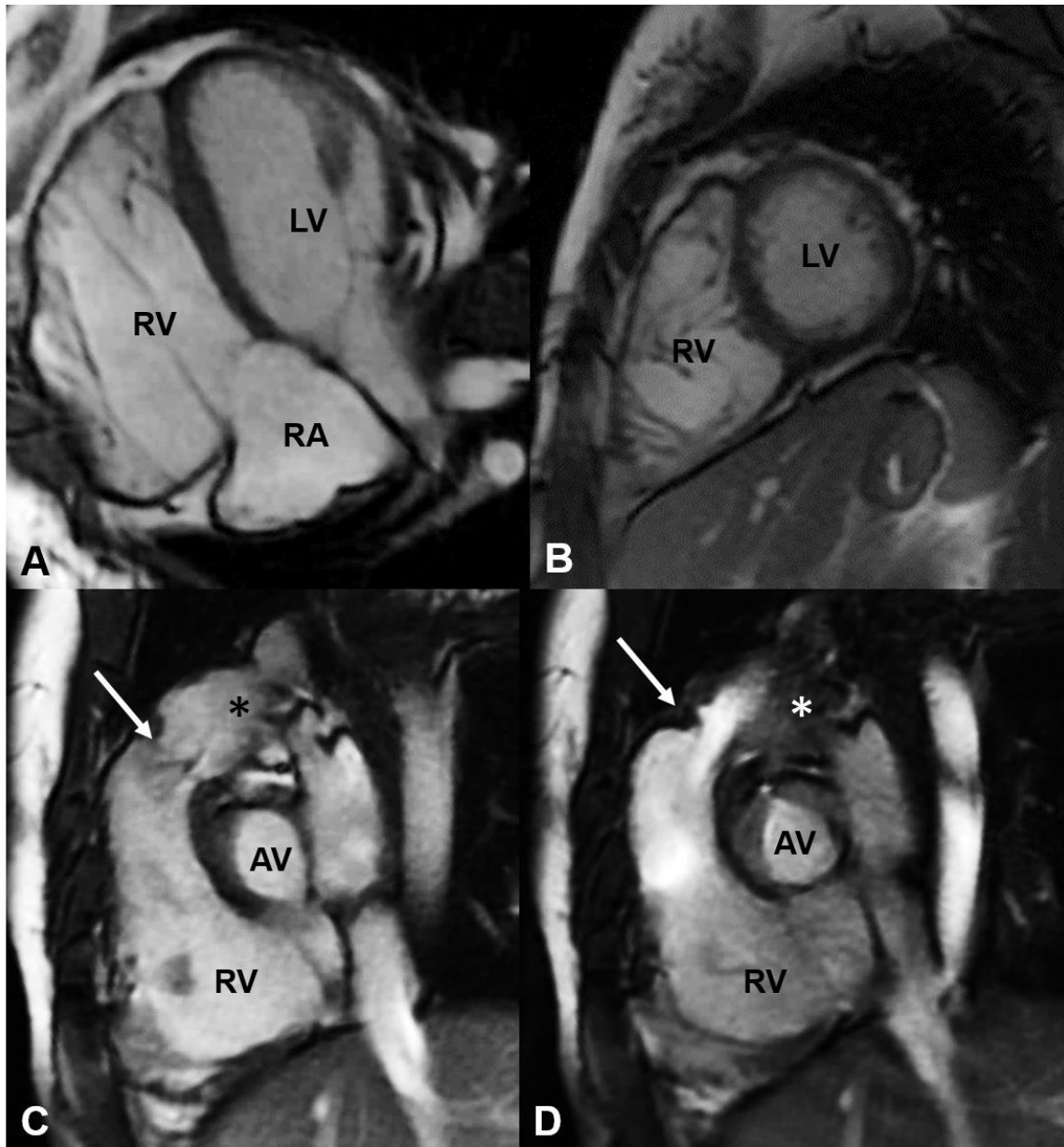
An additional consideration in patients undergoing TPVR is the use of intracardiac echocardiography (ICE) to assess valve competence or paravalvar leak (which is very uncommon) post-implantation, although it is not clear that this practice has an impact on outcomes of clinical management(14,15). However, if significant PR is suspected based on angiography shortly following device implantation, ICE imaging may help to demonstrate the mechanism of failure and aid in the decision to perform additional interventions.

**Figures:**

**Figure 1. Transthoracic echocardiographic assessment of a RV-PA conduit.** **A)** Short axis view at the level of the aortic valve allowing visualization of the RV-PA conduit (**asterisk**). Color flow Doppler demonstrates moderate-severe pulmonary regurgitation with a jet width almost equal to the width of the RVOT. **B)** Continuous wave spectral Doppler through the RV-PA conduit showing rapid deceleration of the pulmonary regurgitant flow and near equalization of RV and PA pressures prior to the end of diastole consistent with moderate-severe regurgitation. **C)** Continuous wave spectral Doppler through the RV-PA conduit demonstrating only mild pulmonic stenosis. Measured peak and mean pressure gradients of 27 and 16 mmHg, respectively.

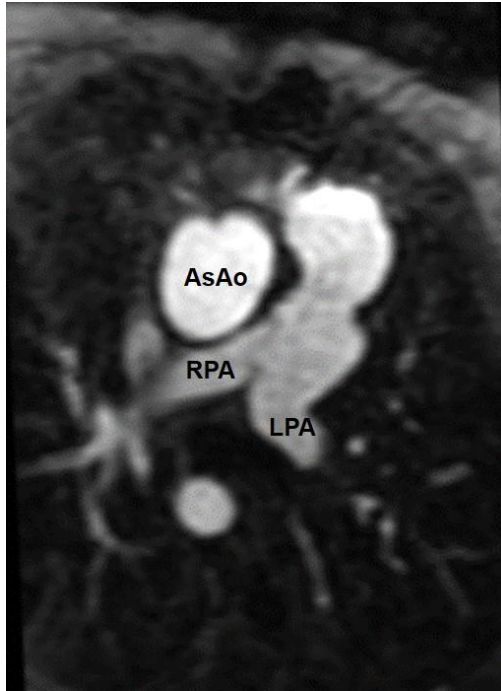


**Figure 2. Cardiac magnetic resonance images (CMR) of a patient with a RV-PA conduit, moderate-severe pulmonary regurgitation, and moderate pulmonic stenosis.** A) Apical four chamber image demonstrating significant RV dilation relative to the LV. B) Short axis image again showing the significant dilation of the RV relative to the LV. Indexed RV end-diastolic volume measured 168 mL/m<sup>2</sup>, which is consistent with severe dilation. C) Sagittal image during diastole showing the RVOT and its connection to the RV-PA conduit (asterisk is within the conduit). Valve leaflets of the bioprosthetic pulmonary valve at the proximal end of the conduit are visible (arrow). D) Sagittal image of the RVOT during systole showing significant de-phasing of flow across the bioprosthetic pulmonary valve consistent with moderate stenosis. RV: right ventricle, LV: left ventricle, RA: right atrium, AV: aortic valve.

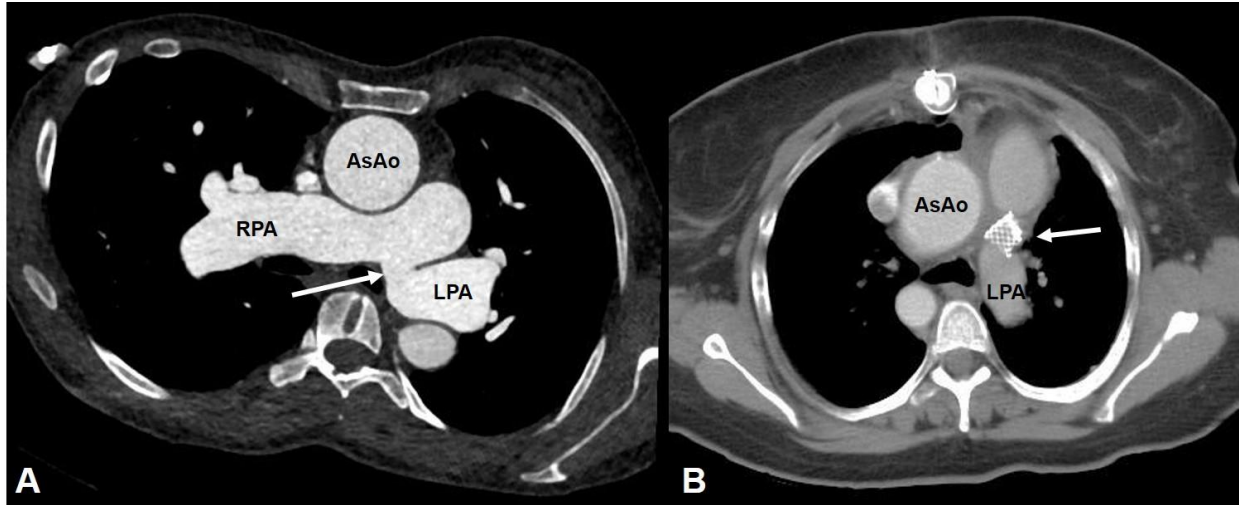




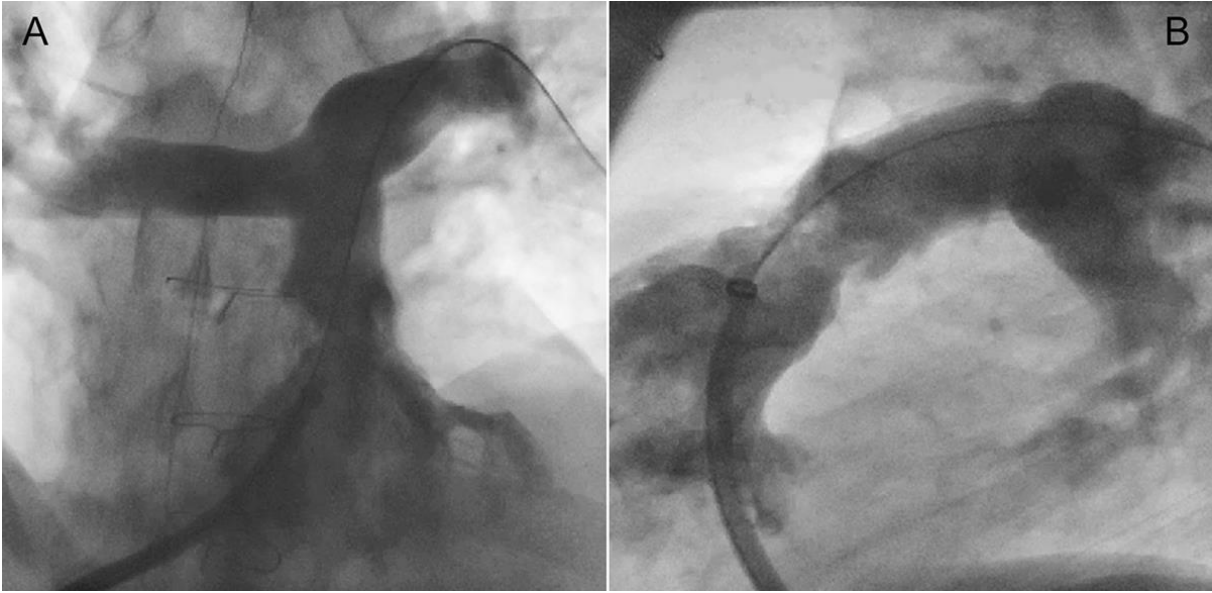
**Figure 3. Axial cross-sectional magnetic resonance angiogram (MRA) image at the level of the ascending aorta and pulmonary artery.** This patient has a RV-PA conduit that is connected just proximal to the branching of the pulmonary arteries. MRA imaging allows clear visualization of the branch pulmonary arteries to ensure no other level of obstruction as part of pre-TPVR planning. AsAo: ascending aorta, RPA: right pulmonary artery, LPA: left pulmonary artery



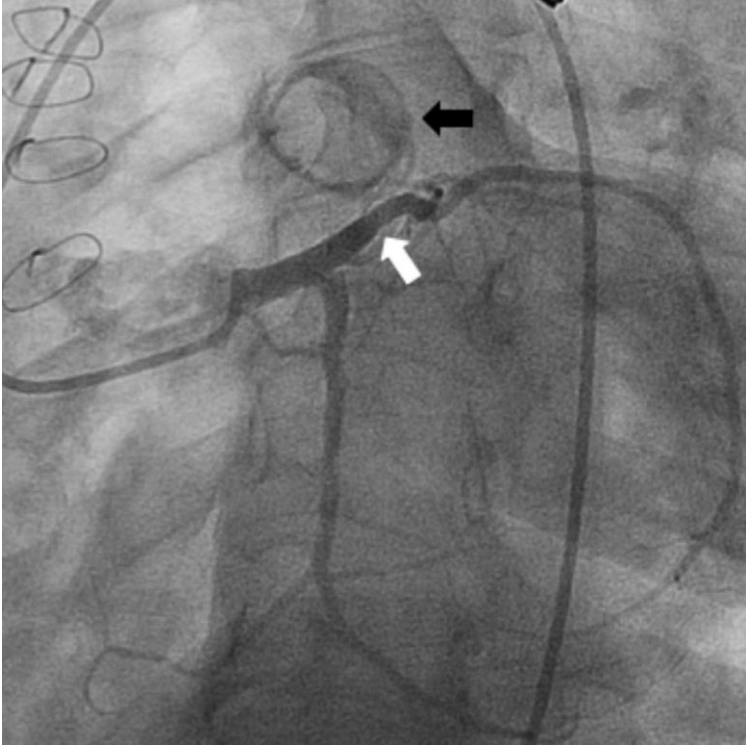
**Figure 4. Axial computed tomography angiogram (CTA) of the chest at the level of ascending aorta and pulmonary artery.** A) An example of left pulmonary artery stenosis (arrow) noted during a pre-TPVR evaluation. B) Patient with a previously placed stent (arrow) in the proximal left pulmonary artery with relative stenosis. Minimal artifact on CT allows better visualization of stents within the branch pulmonary arteries relative to CMR. AsAo: ascending aorta, RPA: right pulmonary artery, LPA: left pulmonary artery



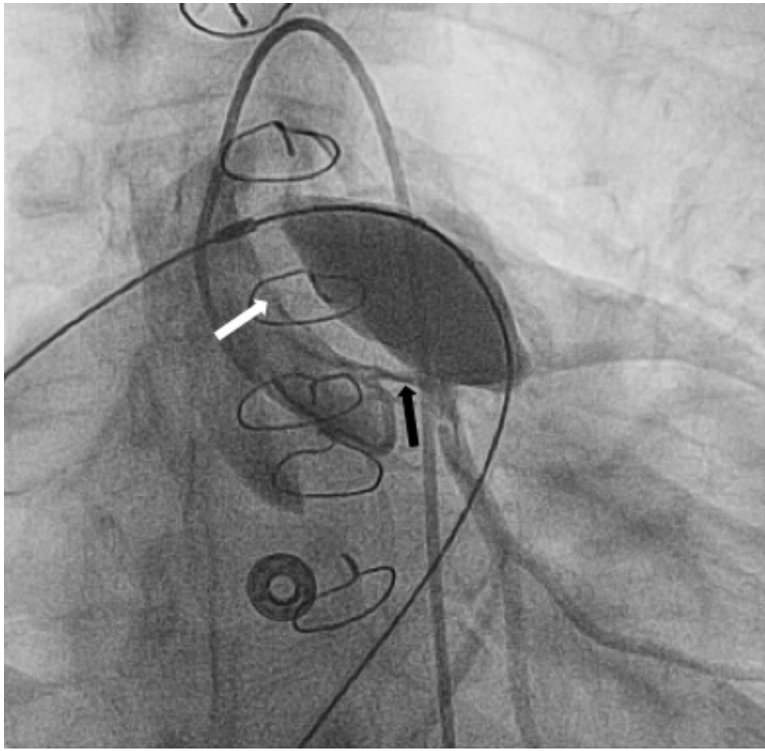
**Figure 5.** Right ventricular outflow tract angiography in AP cranial (A) and lateral (B) projections in preparation for TPVR.



**Figure 6.** Coronary angiography in the left anterior oblique caudal projection in which the calcified RV-PA conduit (black arrow) is visualized on-end and the left anterior descending artery (white arrow) is seen coursing directly inferior to the conduit.



**Figure 7.** Aortic root compression (white arrow) during RVOT balloon angioplasty leading to kinking of the left main coronary artery (black arrow).



#### 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. Hijazi ZM, Ruiz CE, Zahn E et al. SCAI/AATS/ACC/STS operator and institutional requirements for transcatheter valve repair and replacement, part III: Pulmonic valve. *The Journal of thoracic and cardiovascular surgery* 2015;149:e71-8.
3. Zahn EM, Hellenbrand WE, Lock JE, McElhinney DB. Implantation of the melody transcatheter pulmonary valve in patients with a dysfunctional right ventricular outflow tract conduit early results from the u.s. Clinical trial. *Journal of the American College of Cardiology* 2009;54:1722-9.
4. Hasan BS, Lunze FI, Chen MH, Brown DW, Boudreau MJ, Rhodes J, McElhinney DB. Effects of transcatheter pulmonary valve replacement on the hemodynamic and ventricular response to exercise in patients with obstructed right ventricle-to-pulmonary artery conduits. *JACC Cardiovascular Interventions* 2014;7:530-42.
5. Brown DW, McElhinney DB, Araoz PA et al. Reliability and accuracy of echocardiographic right heart evaluation in the U.S. Melody Valve Investigational Trial. *Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography* 2012;25:383-392.e4.

6. Lang RM, Badano LP, Mor-Avi V 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. *Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography* 2015;28:1-39.e14.
7. Tretter JT, Friedberg MK, Wald RM, McElhinney DB. Defining and refining indications for transcatheter pulmonary valve replacement in patients with repaired tetralogy of Fallot: the role of anatomical and functional imaging. *Interventional Journal of Cardiology* 2016;221:916-25.
8. Morray BH, McElhinney DB, Cheatham JP et al. Risk of coronary artery compression among patients referred for transcatheter pulmonary valve implantation: a multicenter experience. *Circulation Cardiovascular Interventions* 2013;6:535-42.
9. Torres AJ, McElhinney DB, Anderson BR et al. Aortic Root Distortion and Aortic Insufficiency During Balloon Angioplasty of the Right Ventricular Outflow Tract Prior to Transcatheter Pulmonary Valve Replacement. *Journal of interventional cardiology* 2016;29:197-207.
10. Torres A, Sanders SP, Vincent JA et al. Iatrogenic aortopulmonary communications after transcatheter interventions on the right ventricular outflow tract or pulmonary artery: Pathophysiologic, diagnostic, and management considerations. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions* 2015;86:438-52.
11. Taggart NW, Hagler DJ, Connolly HM. Melody valve erosion into the ascending aorta. *Congenital heart disease* 2013;8:E64.
12. Kenny D, Holoshitz N, Turner D, Hijazi ZM. Aortopulmonary fistula after transcatheter pulmonary valve replacement. *Circulation Cardiovascular interventions* 2013;6:e67-8.
13. Goreczny S, Moszura T, Dryzek P et al. Three-dimensional image fusion guidance of percutaneous pulmonary valve implantation to reduce radiation exposure and contrast dose: A comparison with traditional two-dimensional and three-dimensional rotational angiographic guidance. *Netherlands heart journal : monthly journal of the Netherlands Society of Cardiology and the Netherlands Heart Foundation* 2017;25:91-99.
14. Awad SM, Masood SA, Gonzalez I et al. The use of intracardiac echocardiography during percutaneous pulmonary valve replacement. *Pediatric cardiology* 2015;36:76-83.
15. Whiteside W, Pasquali SK, Yu S, Bocks ML, Zampi JD, Armstrong AK. The Utility of Intracardiac Echocardiography Following Melody Transcatheter Pulmonary Valve Implantation. *Pediatric cardiology* 2015;36:1754-60.