JACC: CASE REPORTS VOL. 2, NO. 11, 2020

MINI-FOCUS ISSUE: CONGENITAL HEART DISEASE

INTERMEDIATE

CASE REPORT: CLINICAL CASE

When "Blue Babies" Grow Up

Complications After Surgical Repair of Tetralogy of Fallot

Alexandra M. Sanchez, MD,[a] Matthew R. Lozier, MD,[a] Humberto Rovira Alvardo, MD,[a] Abdullah Sarkar, MD,[a] Jillian M. Smith, ARNP,[b] Samantha Molina, ARNP,[b] Alexander Llanos, MD,[b] Todd Roth, MD,[c] Ami Bhatt, MD[d]

ABSTRACT

Tetralogy of Fallot (TOF) is a complex congenital cardiac defect. Surgical correction is well established as the treatment of choice and has resulted in a rapidly growing group of adults living with TOF. We describe potential complications of patients who have undergone TOF repair and were lost to follow-up. (**Level of Difficulty: Intermediate.**)
(J Am Coll Cardiol Case Rep 2020;2:1723–9) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Tetralogy of Fallot (TOF) is a rare and complex congenital cardiac defect that alters the normal flow of blood through the heart. The 4 main characteristics of TOF are a large ventricular septal defect (VSD), pulmonary stenosis, right ventricular (RV) hypertrophy, and an overriding aorta. These defects must be repaired with open heart surgery soon after birth or relatively early in infancy to allow for increased longevity and survival into adulthood (1,2). Although there have been advances in medical therapy over the last 2 decades, continued lifelong care from specialists is essential because long-term heart problems resulting from the original repair are common (Table 1).

LEARNING OBJECTIVES

- To recognize the importance of long-term surveillance in patients with adult congenital heart disease, such as TOF.
- To identify major long-term complications of TOF.
- To be familiar with guidelines for evaluation and management of TOF.
- To recognize the most common surgical procedures appropriate for management of TOF and symptomatic relief.

HISTORY OF PRESENTATION

A 44-year-old white woman with a history of TOF at birth underwent a left-sided Blalock-Taussig shunt in the neonatal period followed by complete repair at the age of 3 years. She presented to our community-based multidisciplinary adult congenital heart disease clinic to establish care with a local cardiologist after she was noted to have a markedly abnormal electrocardiogram and an enlarged heart on a chest radiograph during an urgent care visit for an upper respiratory infection (Figures 1 and 2). Her cardiac examination revealed a mildly enlarged heart

From the [a]University of Miami Miller School of Medicine, Holy Cross Hospital, Fort Lauderdale, Florida; [b]Department of Cardiology, Holy Cross Hospital Jim Moran Heart and Vascular Research Institute, Fort Lauderdale, Florida; [c]Adult Congenital Heart Center, Memorial Healthcare System, Hollywood, Florida; and the [d]Adult Congenital Heart Disease Program, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts. All authors have reported that they have no relationships relevant to the contents of this paper to disclose. Sarah Moharem-Elgamal, MD, Served as the Guest Editor for this article.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

Manuscript received December 23, 2019; revised manuscript received May 18, 2020, accepted June 23, 2020.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2020.06.023

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

PR = pulmonary regurgitation

PVR = pulmonary valve replacement

RV = right ventricular

TOF = tetralogy of Fallot

TTE = transthoracic echocardiogram

VSD = ventricular septal defect

to palpation with an RV lift. The first heart sound was normal, whereas the second heart sound had a slightly wide split. There was a grade 2/6 short, low-pitched systolic ejection murmur that was loudest at the mid-upper left sternal border with slight radiation to the posterior lung fields, as well as a grade 2/6 low-pitched diastolic murmur in the same region.

PAST MEDICAL HISTORY

The patient is an active smoker who recently relocated. She saw her adult congenital heart disease specialist 3 years earlier and needed to establish care with a local cardiologist. As a child, she was advised to avoid overexertion with physical activities and thus did not participate in competitive sports. However, she otherwise denied any limitations when playing with other children. She gave birth to 1 child without complications.

INVESTIGATIONS

At the time of her initial evaluation within our clinic, she denied any active symptoms. A baseline transthoracic echocardiogram (TTE) was obtained and showed evidence of a VSD repair and a dilated right ventricle with mildly decreased function. There was no evidence of pulmonary hypertension despite mild to moderate tricuspid regurgitation and pulmonary regurgitation (PR). She had done well over the years until she was found to have unprovoked bilateral pulmonary emboli and right lower extremity deep vein thrombosis 2 years after the initial visit with us. Results of an extensive hypercoagulable work-up were negative. As part of her work-up, she underwent an esophagogastroduodenoscopy and colonoscopy along with advanced imaging that demonstrated a mass in the cecum. The patient had subsequent episodes of venous thrombosis and was placed on lifelong anticoagulation with rivaroxaban 20 mg daily. TTE was obtained during her admission, and severe PR and RV dilation were noted. Cardiac magnetic resonance (CMR) confirmed severe PR (regurgitation fraction 46%) and an RV end-diastolic volume index of 218 ml, with an RV ejection fraction of 40% (**Figures 3A to 3D**).

MANAGEMENT

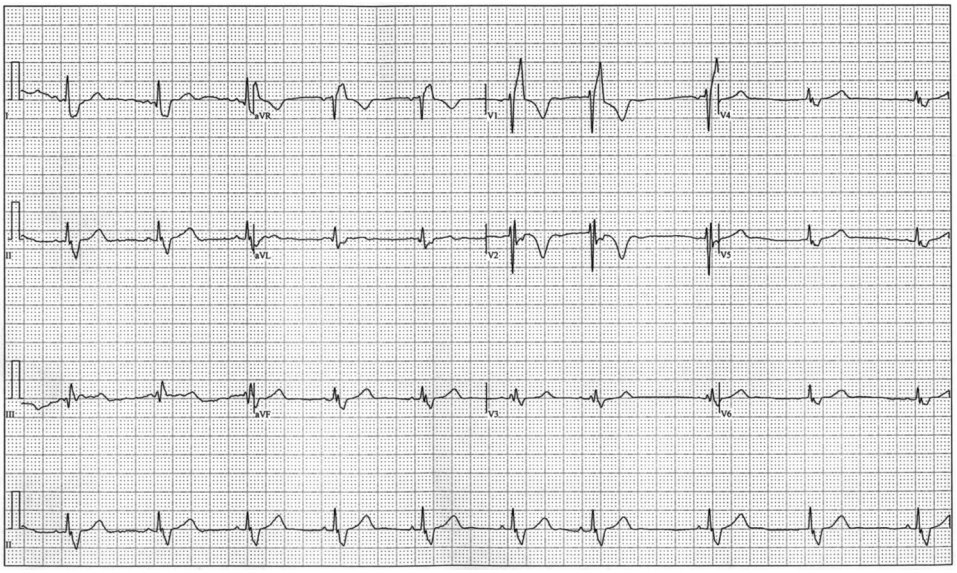
The patient was sent to her pediatric cardiac surgeon because of severe right-sided heart enlargement, moderate tricuspid regurgitation, and severe PR for redo sternotomy with pulmonary valve replacement (PVR) using an Edwards No. 27 Magna-Ease bioprosthetic valve (Edwards Lifesciences, Irvine, California) and tricuspid valve repair using an Edwards No. 32 annuloplasty ring. She had no perioperative or post-operative complications. A repeat TTE post-operatively demonstrated mild PR with normal antegrade flow. The patient was doing well and was asymptomatic for 6 to 9 months post-redo sternotomy with a PVR and tricuspid valve replacement before she started having worsening fatigue, fluid retention, and dyspnea. Post-operative TEE showed thickening and restricted mobility of the medial leaflet of the Magna-Ease valve without significant flow obstruction and a maximal velocity of 2.14 m/s. Repeat cardiac magnetic resonance showed severe PR (regurgitation fraction 45%), an RV ejection fraction of 44%, and an RV end-diastolic volume index of 161 ml. The patient appeared to have rapid deterioration of her bioprosthetic valve, suspected to be secondary to thrombosis caused by a lack of compliance and a questionable coagulopathy (**Figures 4A to 4D**).

TABLE 1 Relevant Guidelines for TOF Recommendation

COR	LOE	Guidelines
I	B-NR	CMR can help quantify ventricular size and function, pulmonary valve function, pulmonary artery anatomy, and left-sided heart abnormalities in patients with repaired TOF.
I	B-NR	PVR (surgical or percutaneous) can relieve symptoms in patients with repaired TOF and moderate or greater PR with unexplained cardiovascular symptoms.
IIb	C-EO	PVR may be considered for preservation of ventricular size and function in asymptomatic patients with repaired TOF and ventricular enlargement or dysfunction with moderate or greater PR.
IIa	B-NR	Surgical PVR may be considered for adults with repaired TOF and moderate or greater PR, with other lesions requiring surgical interventions or ventricular tachyarrhythmias.

CMR = cardiac magnetic resonance; COR = Class of Recommendation; LOE = Level of Evidence; PR = pulmonary regurgitation; PVR = pulmonary valve replacement; TOF = tetralogy of Fallot.

FIGURE 1 Baseline Electrocardiogram Demonstrating Sinus Bradycardia, a Short PR Interval With Rate Variation, and Right Bundle Branch Block



She reported extreme fatigue and dyspnea on minimal exertion. It was believed that the bioprosthetic valve dysfunction was significant enough to recommend placement of a transcatheter valve within the failing bioprosthetic pulmonic valve (**Figure 5**). A Melody valve (Medtronic, Minneapolis, Minnesota) was believed to be preferable because of a better flow profile and possibly less of a tendency to thrombosis. **Table 2** shows the chronological sequence of these complications in a patient post-TOF repair and the subsequent management strategies used.

DISCUSSION

After surgical repair, a marked improvement can be expected in the patient's functional class and quality of life; however, careful follow-up is required to monitor for residual hemodynamic abnormalities (3). Many patients are asymptomatic through early adulthood, and that is why many are lost to follow-up and miss the opportunity to identify and treat long-term complications of TOF before these conditions become irreparable (4). Conversely, a significant number of patients with TOF will develop progressive RV dysfunction from residual pulmonary insufficiency or stenosis (5). It is crucial that primary care physicians and local cardiologists know how to recognize signs and symptoms of a worsening condition and make timely referrals to tertiary adult congenital cardiology clinics for further evaluation and management.

The most frequent problem that occurs after TOF repair is pulmonary backflow (4). This can have detrimental effects on RV function and can lead to irreversible RV decompensation, arrhythmias, and subsequently higher mortality rates (3,4). Patients

FIGURE 2 Baseline Chest Radiograph Showing Cardiomegaly

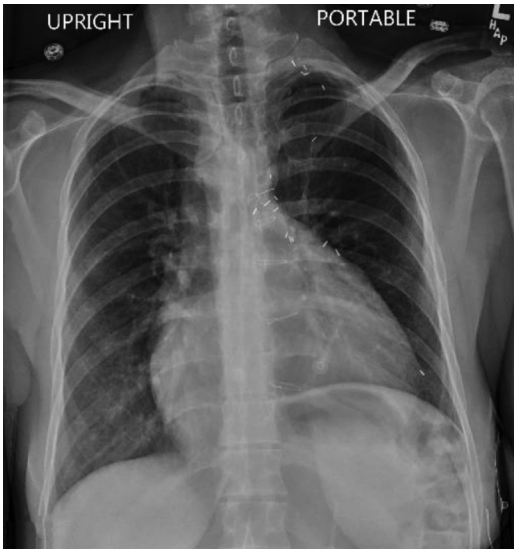
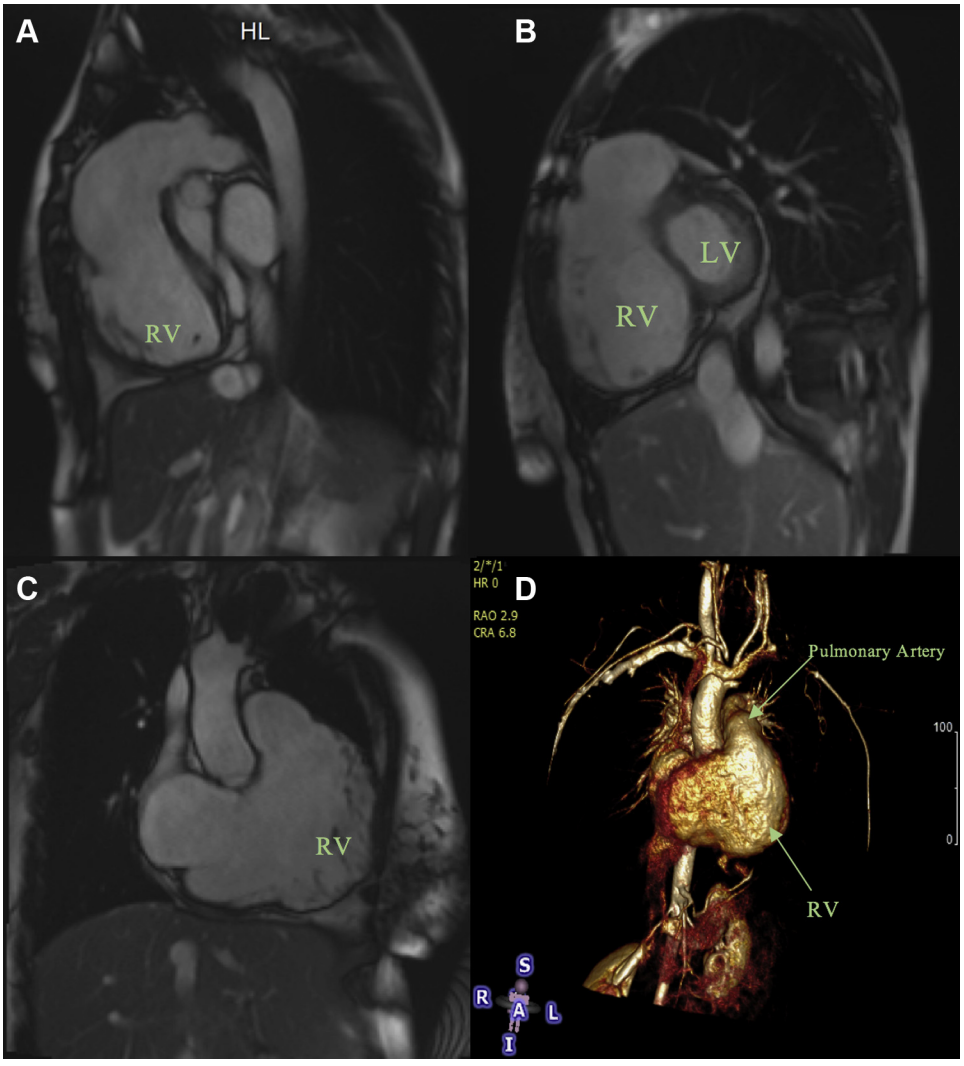


FIGURE 3 CMR Demonstrating Severe Pulmonary Regurgitation

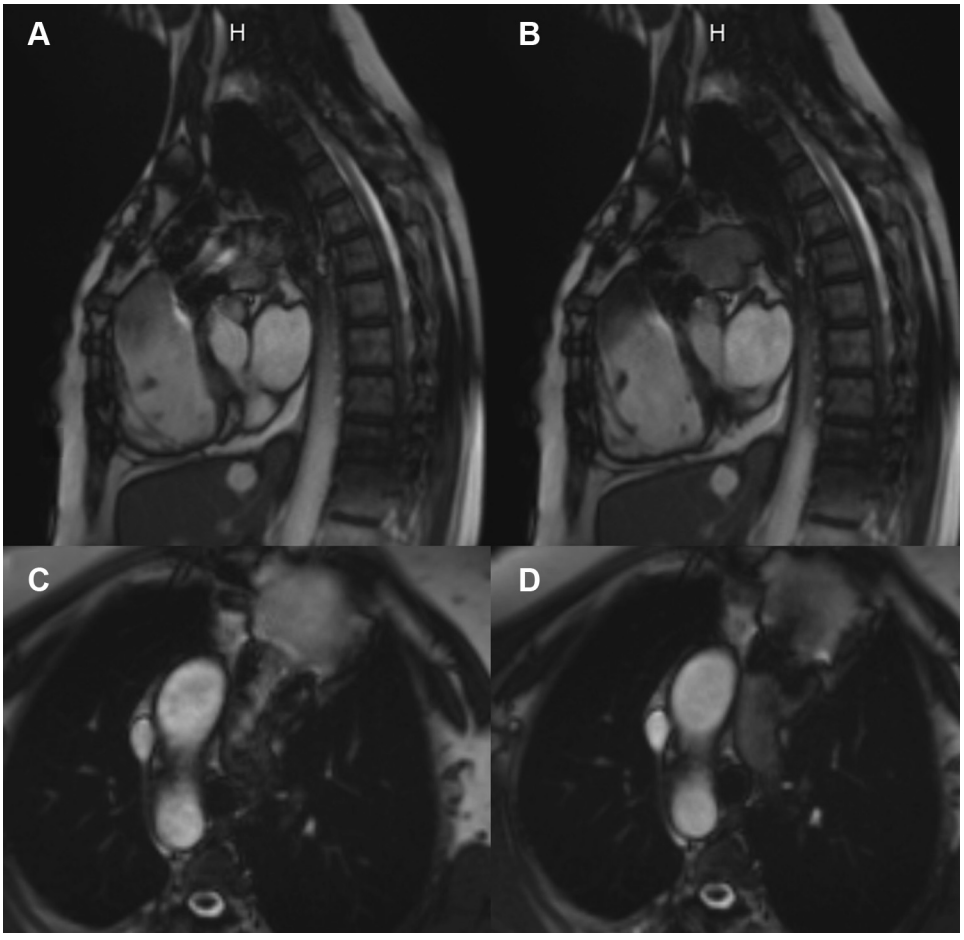


Images showing a regurgitation fraction of 46%, a right ventricular end-diastolic volume index of 218 ml, and a right ventricular ejection fraction of 40%. **(A)** Sagittal view. **(B)** Short-axis view demonstrating large right ventricle. **(C)** Coronal view of pre-operative large right ventricle. **(D)** 3-dimensional cardiac magnetic resonance (CMR) showing a large right ventricle. A = axis; HL = head left obliquity; I = inferior; L = left; LV = left ventricle; R = right; RV = right ventricle; S = superior.

present with palpitations, exertional dyspnea, right-sided heart failure, and syncope during later stages (1,4). A low-pitched diastolic murmur may be heard along with a pansystolic murmur if a residual VSD is present (4). Electrocardiograms commonly show RV hypertrophy with a right bundle branch block (3,4). A larger RV volume and mass are often seen with a longer QRS complex duration, which when longer than 180 ms is strongly associated with ventricular arrhythmias and sudden death (4). Chest radiography will show cardiomegaly and a prominent right ventricle; however, a CMR is the gold standard for evaluating RV size and function, as well as PR (6). Baseline CMR is recommended even for asymptomatic patients (**Table 1**) (4,6).

Our patient required reintervention for severe pulmonary insufficiency. PVR is the standard of care and is expected to decrease both RV end-diastolic

FIGURE 4 **Repeat Cardiac Magnetic Resonance of Post-Operative Complications**



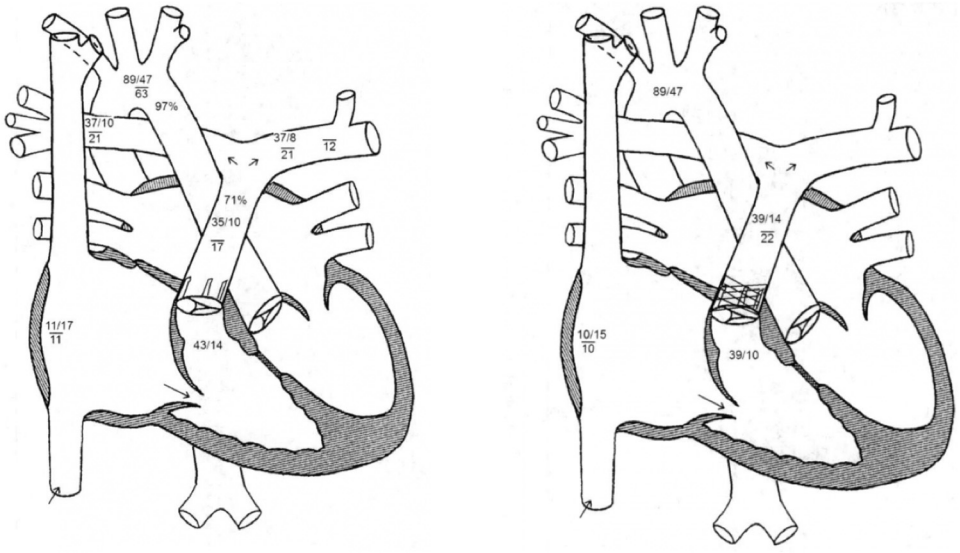
Images showing severe pulmonary regurgitation (regurgitation fraction 45%), right ventricular ejection fraction of 44% and right ventricular end-diastolic volume index of 161 ml. **(A)** Short-axis view in systole. **(B)** Short-axis view in diastole. **(C)** Axial view in systole. **(D)** Axial view in diastole. H = head.

volume and RV end-systolic volume, as well as an increase in corrected RV ejection fraction, subsequently improving patient symptoms, which can be objectified using the New York Heart Association functional classification (1–3). Studies have shown that the rates of PVR in adults with TOF have doubled over the past decade (7). This trend likely reflects evidence on the consequences of PR and strategies to optimize timing of PVR (7). Improvements in surgical technique and the availability of percutaneous valves have led to a growing group of adults with TOF. We as physicians must provide post-operative care to these patients and must learn to recognize the deleterious effects associated with this condition.

FOLLOW-UP

The patient had undergone placement of a Melody transcatheter pulmonary valve that appeared to be normal with unobstructed movement, with a peak gradient across the valve of 15 mm Hg and mild pulmonary insufficiency indicating excellent results (**Figure 6**).

FIGURE 5 Initial Pressures and Saturations Obtained as Detailed on the Diagram



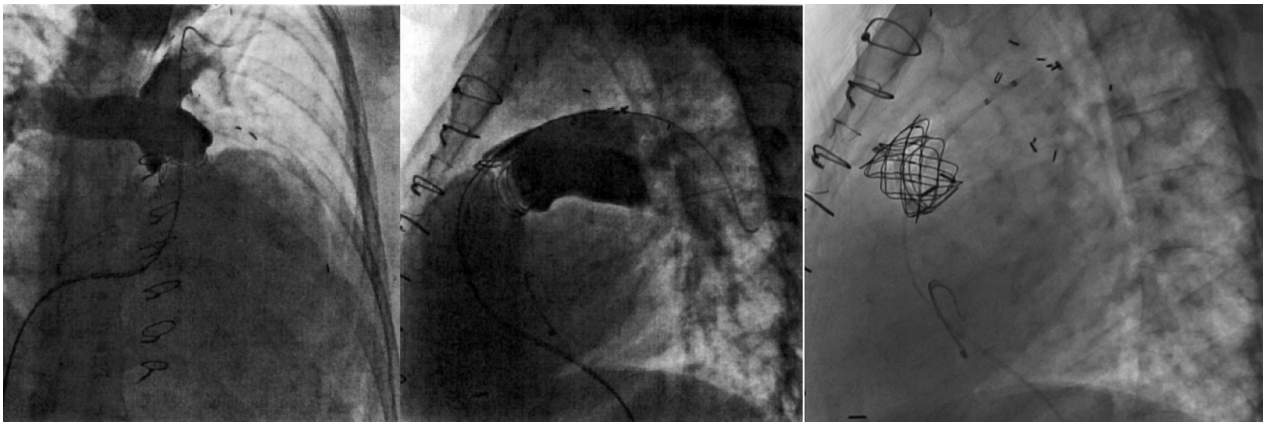
Arrows indicate catheter course.

TABLE 2 Management of TOF: A Timeline of Key Events

Birth	TOF Diagnosed
Neonatal period	Blalock-Taussig shunt undertaken
Age 3 yrs	Complete TOF repair
Age 26 yrs	Delivered of a healthy child without complications
Age 26–43 yrs	No subsequent cardiac complications or procedures
Age 43 yrs	Initial hospital admission: Presented with shortness of breath and found to have bilateral PE and DVT • Experienced 30-lb weight loss over 6 months • Hypercoagulable work-up initiated, including endoscopy and colonoscopy → found to have cecal mass • Managed with oral anticoagulation (rivaroxaban) • Residual cardiac findings: ○ TTE showed severe RV enlargement with mildly reduced RV function. ○ Moderate tricuspid regurgitation, severe pulmonary valve regurgitation seen on TTE and confirmed by CMR (RF 46%, RVEDV 218 ml/m^2, RVESV 131 ml/m^2). Also seen in CMR is a severely enlarged RV outflow tract and main pulmonary artery. 4 months later: • Underwent PVR with Magna-Ease 27-mm bioprosthetic valve (Edwards Lifesciences, Irvine, California) and TV repair with an Edwards No. 32 annuloplasty ring • Post-operative TTE at 2 months and 6 months showed improvement with a moderately enlarged RV cavity and mild tricuspid and pulmonary valve regurgitation
Age 44 yrs	10 months after PVR and TV repair • Patient presented to the emergency department for right-sided back pain • TTE during admission demonstrated moderate TV regurgitation and mild to moderate pulmonary valve regurgitation; evidence of thickening of the bioprosthetic valve leaflets is noted, dilated IVC of 21–22 mm 1 yr after PVR and TV repair • Follow-up CMR showed severe pulmonary valve regurgitation (RF 45%, RVEDV 161 ml/m^2, RVESV 91 ml/m^2) with an RVEDV index of 161 • Patient experiencing extreme fatigue, fluid retention, and dyspnea with minimal exertion indicating early failure of surgical bioprosthetic pulmonary valve with severe pulmonary insufficiency • Underwent successful placement of 22-mm Melody (Medtronic, Minneapolis, Minnesota) transcatheter pulmonary valve

CMR = cardiac magnetic resonance; DVT = deep vein thrombosis; IVC = inferior vena cava; PE = pulmonary embolism; PVR = pulmonary valve replacement; RF = regurgitation fraction; RV = right ventricular; RVEDV = right ventricular end-diastolic volume; RVESV = right ventricular end-systolic volume; TOF = tetralogy of Fallot; TTE = transthoracic echocardiogram; TV = tricuspid valve.

FIGURE 6 Cardiac Catheterization During Transcatheter Pulmonary Valve Replacement With Melody 22-mm Valve (Medtronic, Minneapolis, Minnesota)



CONCLUSIONS

Advances in diagnosis, medical management, and surgical repair of TOF have markedly improved prognosis and resulted in long-term survival. This success, however, presents unique challenges as functional capacity considerably improves and duration of follow-up increases. It is crucial that these patients be monitored closely by an adult congenital cardiac specialist or by a trained general cardiologist who is able to identify residual abnormalities and development of comorbidities.

ADDRESS FOR CORRESPONDENCE: Dr. Alexandra M. Sanchez, Internal Medicine Residency, University of Miami at Holy Cross Hospital, 4725 North Federal Highway, Fort Lauderdale, Florida 33308. E-mail: Alexandra.sanchez@ochsner.org. Twitter: AlySanchezMD.

REFERENCES

1. Atik FA, Atik E, da Cunha CR, et al. Long-term results of correction of tetralogy of Fallot in adulthood. Eur J Cardiothorac Surg 2004;25:250–5.

2. Henkens IR, van Straten A, Schalij MJ, et al. Predicting outcome of pulmonary valve replacement in adult tetralogy of Fallot patients. Ann Thoracic Surg 2007;3:907–11.

3. Horer J, Friebe J, Schreiber C, et al. Correction of tetralogy of Fallot and of pulmonary atresia with ventricular septal defect in adults. Ann Thorac Surg 2005;80:2285–92.

4. Ammash NM, Dearani JA, Burkhart HM, Connolly HM. Pulmonary regurgitation after tetralogy of Fallot repair: clinical features, sequelae, and timing of pulmonary valve replacement. Congenit Heart Dis 2007;2:386–403.

5. de Ruijter FT, Weenink I, Hitchcock FJ, et al. Right ventricular dysfunction and pulmonary valve replacement after correction of tetralogy of Fallot. Ann Thorac Surg 2002;73:1794–800; discussion 1800.

6. Stout KK, Daniels CJ, Aboulhosn JA, et al. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2019;73:1494–563.

7. Schmidt AS, Yeh DD, Tabtabai S, et al. National trends in hospitalizations of adults with tetralogy of Fallot. J Am Coll Cardiol 2016;118:906–11.

KEY WORDS adult congenital heart disease, complications, follow-up, pulmonary valve replacement, tetralogy of Fallot