Misra *et al*. *Vessel Plus* 2022;6:32
DOI: 10.20517/2574-1209.2021.104

Vessel Plus

Review

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Multimodality imaging for repaired tetralogy of Fallot

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How to cite this article: Misra A, Gupta P, Aggarwal S, Singh G. Multimodality imaging for repaired tetralogy of Fallot. *Vessel Plus* 2022;6:32. https://dx.doi.org/10.20517/2574-1209.2021.104

Received: 15 Jul 2021 **First Decision:** 15 Dec 2021 **Revised:** 27 Jan 2022 **Accepted:** 24 Feb 2022 **Published:** 17 May 2022

Academic Editors: P Syamasundar Rao, Yajing Wang **Copy Editor:** Jia-Xin Zhang **Production Editor:** Jia-Xin Zhang

Abstract

Despite complete repair at an optimal time in the current era, almost all patients with tetralogy of Fallot will have residual anatomic and hemodynamic sequelae, which make ongoing surveillance of paramount importance. Echocardiography suffices surveillance matrix in most pre-operative cases unless there is a specific question about coronary artery anomaly or branch pulmonary arteries when cardiac catheterization or computed tomography scan can be extremely helpful. For long-term follow-up of repaired tetralogy of Fallot patients, several diagnostic/imaging monitoring modalities are available; however, no single modality is perfect in terms of obtaining all the necessary information. A multimodality approach is suggested for long-term surveillance where a diagnostic test is selected based on the clinical circumstances/questions raised and institutional preference/expertise.

Keywords: Tetralogy of Fallot, echocardiography, magnetic resonance imaging

INTRODUCTION

Tetralogy of Fallot (TOF) is one of the most common cyanotic heart defects that was first described in 1888 by Arthur Fallot[1]. Survival in un-operated patients is related to the degree of right ventricular outflow tract obstruction. In one of the series of 566 necropsy cases in unoperated patients, only 3% were alive at 40 years[2,3]. In the current era, with the advances in diagnoses and management, survival of patients with repaired TOF exceeds 98% in the first year, and 30-year survival approaches 90%[4,5]. This has led to an interesting phenomenon where the adult survivors of this condition outnumber the incidence of children with this condition[6]. Today, TOF is one of the most common diagnoses seen in an adult congenital clinic. Under optimal conditions, complete repair of TOF is performed during infancy, while some of the patients may require a palliative procedure such as a systemic to pulmonary shunt, most likely a modified Blalock-Taussig shunt prior to complete repair. Despite a complete repair at an optimal time, almost all patients with TOF will have residual anatomic and hemodynamic sequelae that will require follow-up and or intervention at a later time[7,8]. This makes lifelong surveillance imperative for this group of patients.

Several imaging modalities are available for the purposes of surveillance[9,10,11,12]. The commonly used diagnostic tools include echocardiography, cardiac computed tomography (CT), cardiac magnetic resonance imaging (CMR), cardiac catheterization, and nuclear scan. None of the diagnostic tools mentioned here stands perfect in isolation in terms of obtaining all the necessary information. A tailored multimodality approach is needed to identify anatomic and functional abnormalities, assess the degree of severity, and associated abnormalities to help the clinical decision making.

In this review, we will discuss the role of each of the imaging modalities mentioned above, along with its advantages and limitations. We will also focus on repaired TOF patients.

ECHOCARDIOGRAPHIC IMAGING FOR EVALUATION OF REPAIRED TOF

Diagnostic role

Echocardiography is the mainstay of imaging of the patient with TOF. An experienced operator can obtain valuable information regarding the physiology of a patient with repaired TOF, which can be used to guide clinical management[13]. The echocardiogram provides valuable qualitative information regarding right ventricular (RV) size and function as well as pulmonary regurgitation.

Clinical information

Evaluation of a new patient with a history of Tetralogy of Fallot typically starts with an echocardiogram[12]. Based on the clinical status of the patient, a routine transthoracic echocardiogram should be obtained at least every 1-2 years[12]. Transesophageal echocardiogram is utilized for peri- and post-operative evaluation of the right ventricular outflow tract (RVOT) and pulmonary valve in patients undergoing surgical revision of their cardiac lesion.

Repair of Tetralogy of Fallot typically consists of patch closure of the ventricular septal defect (VSD), resection of muscle bundles that are obstructing the RVOT, and transannular patch repair, in which the RVOT is augmented in order to provide adequate forward pulmonary blood flow. A sequela of this procedure is that patients can develop significant pulmonary regurgitation over time, leading to RV volume overload [Figure 1] and free pulmonary insufficiency [Figure 2, Video 1].

The key elements of the echocardiographic evaluation of the patient with repaired TOF include evaluation of the RV size and function, measurement of the severity of obstruction and/or regurgitation of the pulmonary valve, as well as the measurement of right ventricular systolic pressure[13]. Fractional area change (FAC) and tricuspid annulus plane systolic excursion (TAPSE) have been shown to correlate with Magnetic Resonance Imaging (MRI) measurements of ejection fraction, with one study suggesting a FAC < 40% or a TAPSE < 17 mm correlated with RV ejection fraction < 47% on MRI[14]. For PR, there is some evidence that the ratio of the pulmonary regurgitation jet width to the valve annulus can correlate with MRI

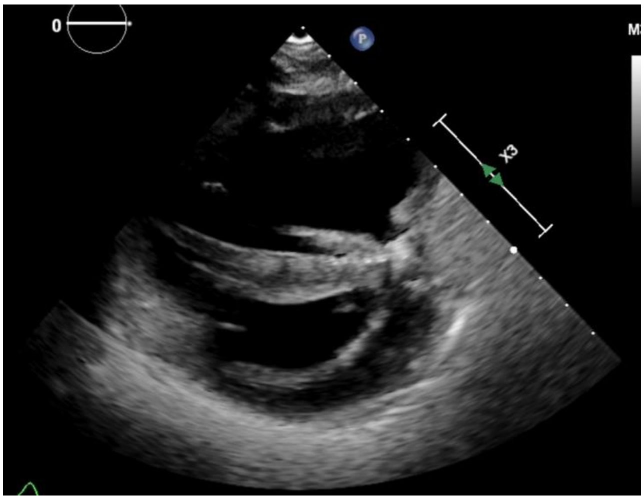

Figure 1. Parasternal short-axis view showing a dilated right ventricle with septal bowing.

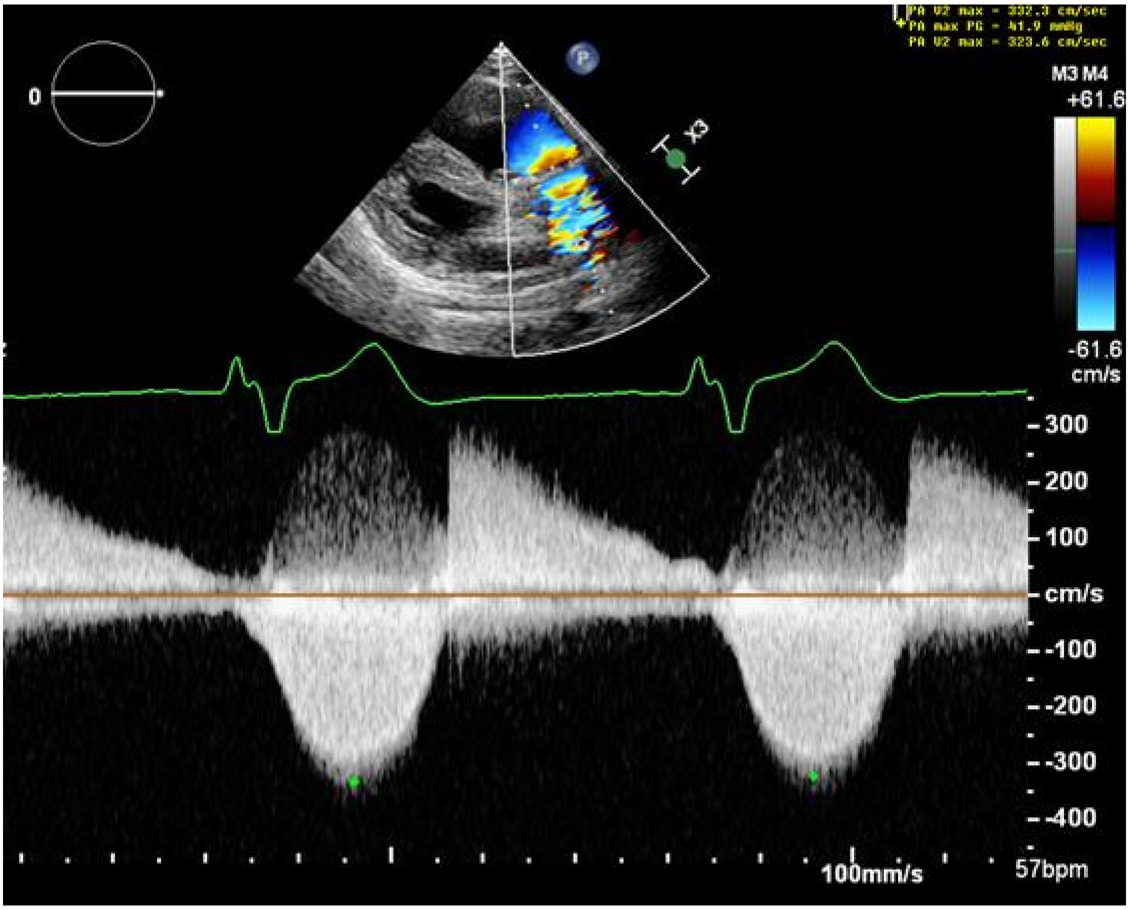

Figure 2. Doppler through trans-annular patch, demonstrating free pulmonary insufficiency

measurements of PR, with a ratio of 0.5 or greater correlated with a regurgitation fraction (RF) of 20% and a ratio of 0.7 correlating with an RF of 40%[15].

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In patients with adequate echocardiographic windows, the branch pulmonary arteries dimensions and RV outflow tract size should be measured as this information can be useful in future surgical or catheter-based intervention planning[16].

Recently, RV strain has been a topic of interest in evaluating RV function in patients with repaired TOF; 2D RV global longitudinal strain less than -17% has been associated with reduced RV ejection fraction on cardiac MRI[17]. Three-dimensional speckle-tracking has also been utilized in order to evaluate dysynchrony between the right and left ventricles in a patient with TOF[18].

Advantages

Transthoracic echocardiography is noninvasive and provides excellent information in pediatric patients, especially those who have optimal acoustic windows for imaging. It is considered the first-line modality in the diagnostic toolbox for evaluating patients with TOF[13]. It has higher axial and lateral resolution than CT and MR imaging[13]. Besides, it provides excellent morphological definitions of heart valves and, in some cases, coronary arteries. It can also provide usable hemodynamic data, including RV systolic pressure and pressure gradients across RVOT[12]. The left ventricle (LV) anatomy, dimensional measurements, and function can reliably be obtained by 2D and 3D echocardiography.

Limitations

In some patients, especially adults with congenital heart disease, the right ventricular outflow tract and pulmonary valve annulus may be difficult to see, especially in patients who have multiple previous operations. Additionally, the RVOT is an anterior structure and is difficult to visualize for patients who have had extensive revisions. For surgical planning purposes, measurements of the right ventricular outflow tract and pulmonary valve dimensions are not entirely accurate, and it is preferred to have CT and/or MRI imaging[12]. The echocardiography is limited in defining RV dimensions and systolic function. It may not reliably define branch pulmonary artery anatomy[13].

CARDIAC MAGNETIC RESONANCE IMAGING FOR EVALUATION OF REPAIRED TOF

Diagnostic role

Advances in MRI have made this modality an important tool for the evaluation of congenital heart disease. Faster scanning techniques, high spatial resolution, limitless windows, lack of ionizing radiation, lack of dependence on contrast material, and capability for functional imaging have made it a noninvasive diagnostic tool of great potential in patients with repaired TOF.

Advantages

Cardiac MR is the single noninvasive modality that provides all the information needed (see below) in patients with repaired TOF, which no other single modality has the capability to provide. It is a particularly effective tool in patients with limited acoustic windows. It has a wide field of view covering and is capable of imaging extra-cardiac blood vessels[19]. It can provide all hemodynamic data needed for decision making. For all these reasons, CMR has become the preferred method of noninvasive imaging in adult patients with repaired TOF[19,20,21].

Limitations

CMR, particularly in children, is not available in all centers. It is a time-intensive procedure and also an expensive tool. In infants and children, there is a requirement for sedation/anesthesia to perform CMR, limiting its wide applicability. CMR usually cannot be performed in patients with pacemaker and ferromagnetic devices[13].

Clinical information

- Cardiac MR (CMR) can provide the following information for the management of most of the patients with repaired tetralogy of Fallot:

- RV volumetric and function to assess the volume/pressure overload and functional status due to the type of repair of TOF

- VSD patch and atrial septal defect (ASD) patency to assess the residual intracardiac shunt

- Tricuspid valve regurgitation status and right atrial size

- Evaluation of the RVOT, including prosthetic pulmonary valve for obstruction and/or aneurysm

- Pulmonary regurgitant fraction

- Main and branch pulmonary anatomy to assess obstruction or aneurysm and flow distribution

- LV volumetric and function

- Aortic dimensions to assess aortic ectasia

- Aortic regurgitant fraction

- Coronary artery anatomy

- Myocardial tissue characterization to assess myocardial viability

Technique and clinical information of CMR

CMR is widely considered the gold standard for the quantification of RV size, RV function, PR, and myocardial tissue characterization in patients with repaired TOF[10]. One of the criteria for pulmonary valve placement based on recent guidelines includes mild or moderate RV or LV systolic dysfunction and enlarged RV dimensions, which are defined as RV end-diastolic volume index greater than or equal to 160 mL/m^2 or RV end-systolic volume index > 80 mL/m^2[12].

Cardiac anatomy and dimensions

After localization, the first images obtained are usually black blood sequences. These include HASTE (half acquisition single-shot turbo spin-echo), double or triple IR FSE/TSE (inversion-recovery fast spin-echo)[22], or TSE/FSE T1-weighted sequences. However, bright blood cine sequences such as sequential FLASH (fast low-angle shot), FASTCARD, trueFISP (fast imaging with steady-state precession), or FIESTA (fast imaging employing steady-state precession) are essential for demonstrating functional pathology, and for visualizing some intracardiac shunts[23,24]. Cine sequences (GRE, gradient-echo) [Figure 1] are done (i.e., static bright blood sequences) to assess the great vessels (i.e., sidedness of the arch, etc.). Cine sequences are then performed in the long and short axes of the heart, ventricular volumetric, LV outflow tract, and RVOT [Figure 3], and then through the aortic and pulmonic valve planes to assess for patency and stenoses. Turbo spin-echo (TSE) imaging [Figure 4] provides a good definition of soft tissue, and has decreased sensitivity to metallic artifacts compared with gradient-echo sequences.

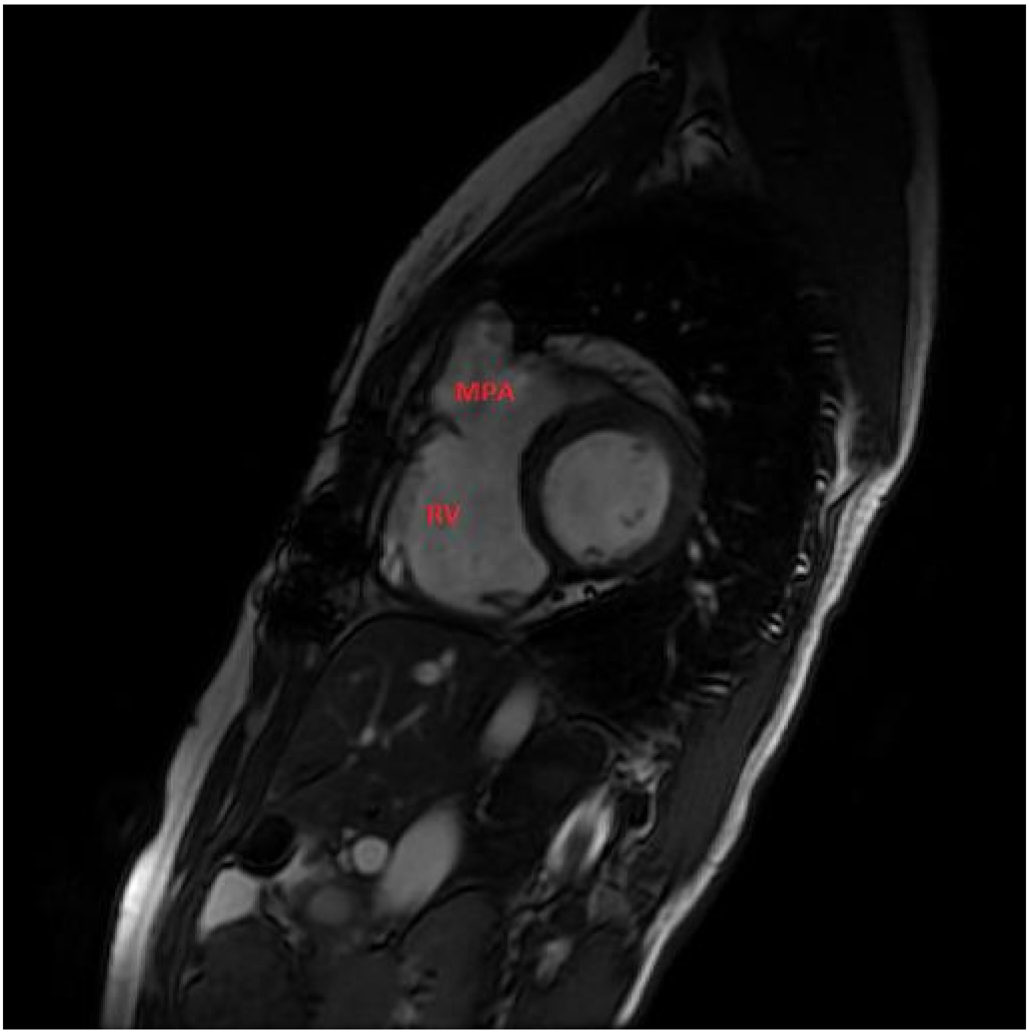

Figure 3. Cine bright blood sequences in short axis view showing right ventricular outflow tract (RVOT) patch aneurysm in a patient with tetralogy of Fallot repaired with trans-annular patch with dilated RV. MPA: main pulmonary artery; RV: right ventricle.

Cardiac and extra-cardiac blood vessels assessment by MR angiography

Contrast-enhanced magnetic resonance angiography provides excellent anatomy of the extra-cardiac blood vessel and uses a maximum intensity projection reconstruction technique. Both pre- and post-contrast images are acquired, with the pre-contrast image serving as a mask for image subtraction. After image acquisition, post-processed 3D maximum intensity projection (MIP) images can be created. These MIP images should always be evaluated together with source images in order to avoid misdiagnoses secondary to MIP-induced artifacts.

Blood flow measurement

Velocity encoded cine (VENC) MRI sequences, also known as phase-contrast sequences (PC), measure peak velocities through the area of interest and provide quantification of blood flow to calculate stroke volume and cardiac output, in great arteries and veins and differential pulmonary artery flow. Thus, regurgitant volumes (e.g., pulmonary regurgitation, aortic regurgitation) and regurgitant fraction in aortic and pulmonary valve insufficiency can be determined by assessing the ratio of regurgitant to forward flow across the valve.

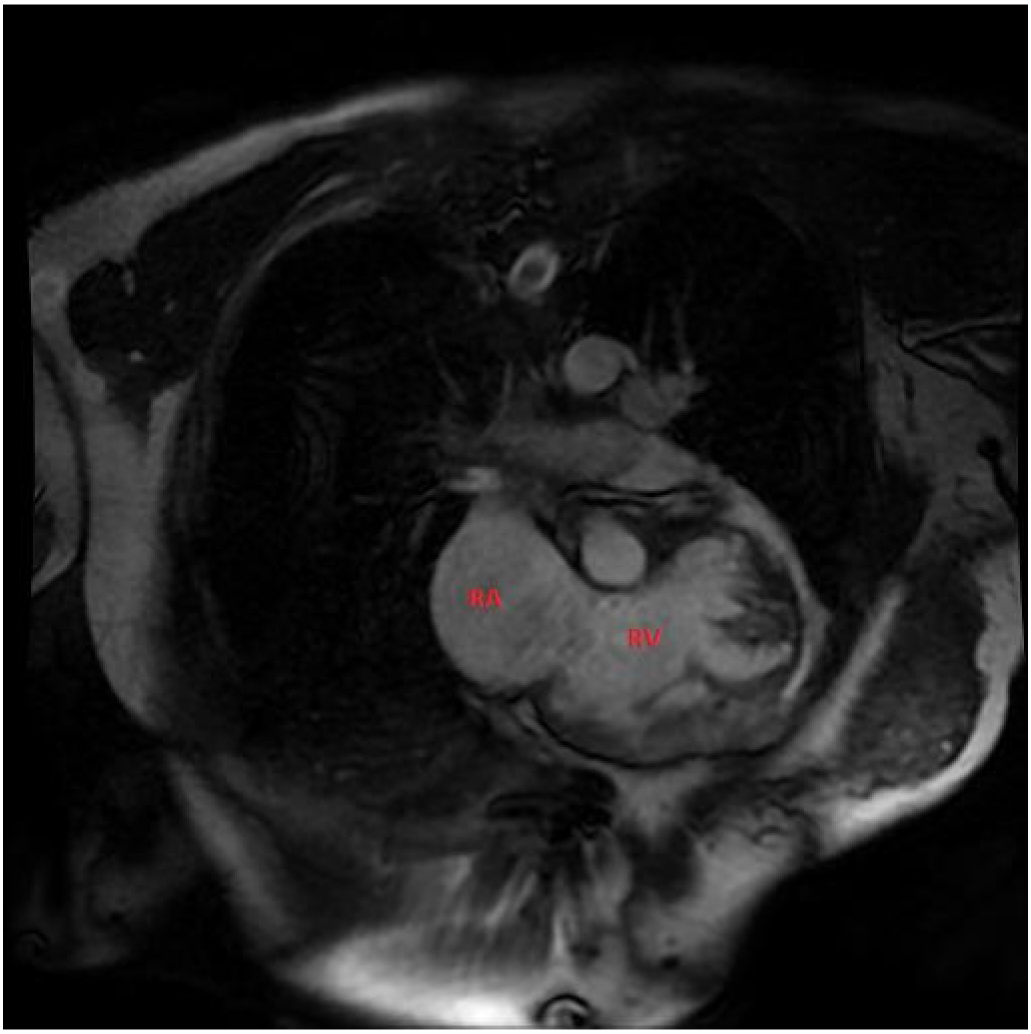

Figure 4. Turbo spin-echo (TSE) image of prosthetic pulmonary valve in RVOT, dilated right atrium (RA) and right ventricle (RV).

Myocardial tissue characterization

MR techniques can provide myocardial tissue characterization, including for myocardial perfusion, ischemia, and scar tissue. The most commonly used technique for the assessment of gross myocardial fibrosis in patients with repaired TOF is the late gadolinium enhancement (LGE) sequence [Figure 5]. This technique has been shown to be helpful in this group of patients for identifying those at risk for ventricular tachyarrhythmias and exercise intolerance[25,26]. Additionally, LGE of the LV has been posited as a risk factor for sudden cardiac death; a recent article has included the presence of LV LGE as a part of its scoring system to identify repaired TOF patients at higher risk for sudden cardiac death[27].

Shunt physiology

In assessing for a small or residual VSD, ASD, or patent foramen, ovale cine sequences are vital to visualize the jet caused by turbulent flow. With MR, shunt (Qp/Qs) ratios can be calculated by prescribing a VENC or phase-contrast sequence. These sequences provide information regarding both the velocity and direction of flowing blood. Using this data, right and left ventricular stroke volumes and shunt can be calculated and compared, and a ratio calculated. A shunt ratio of 2:1 or greater is considered clinically significant[28,29].

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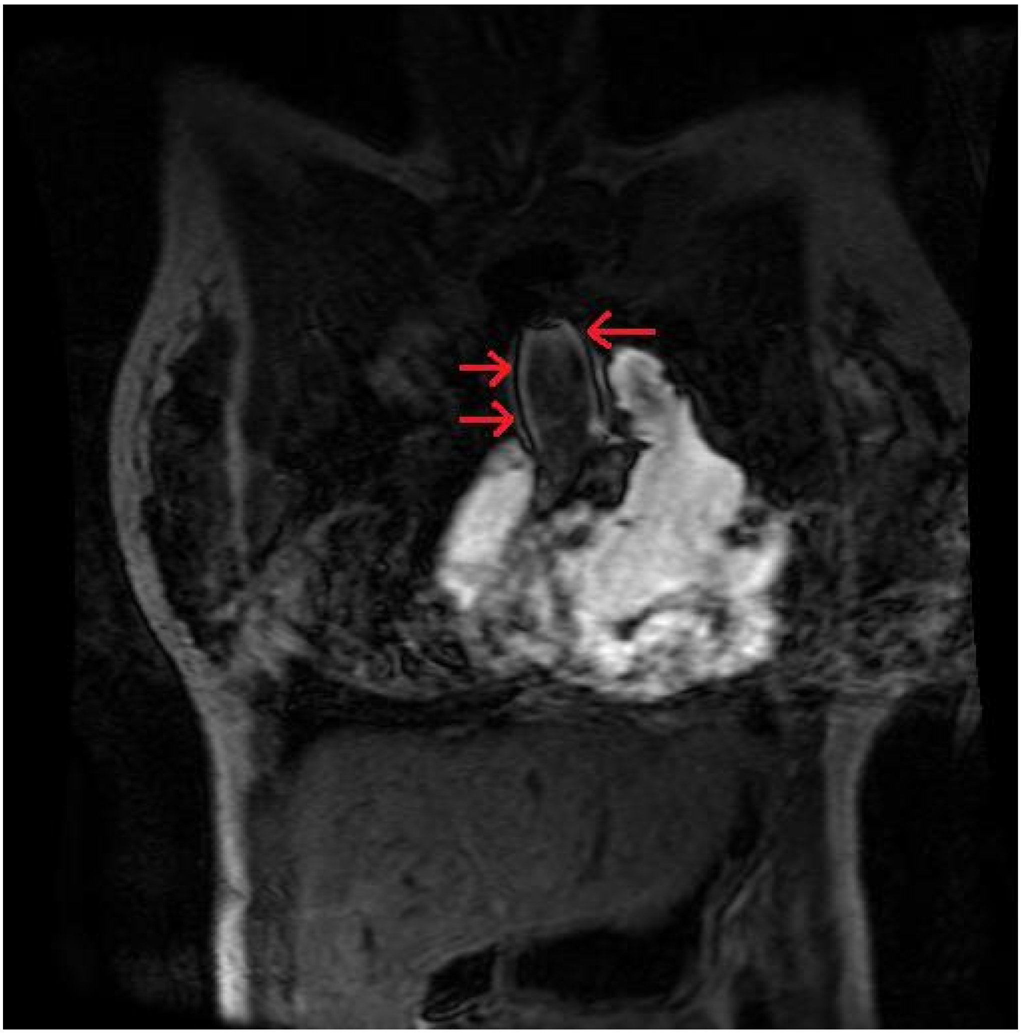

Figure 5. Late gadolinium enhancement (LGE) sequence image showing dilated right ventricle, and late enhancement in right ventricular outflow tract (red arrowheads).

CT SCAN IMAGING FOR EVALUATION OF REPAIRED TOF

Diagnostic role

Improvement in technology and significant advancement in the area of multi-detector computed tomography (MDCT) has revolutionized imaging in the congenital heart disease world. TOF is one of the most common cyanotic heart diseases, and MDCT plays a very important role in answering specific questions in the management of repaired patients with this condition. Foremost indication would include patients with pacemakers and defibrillators where CMR is contraindicated. The next most relevant indication would be for anatomical assessment, 3D reconstruction and/or printing. With some advanced MDCT, volumetric data can be acquired using a single breath-hold examination[30,31,32].

Clinical information

Pulmonary arterial anatomy:

Information obtained from this modality would include anatomic detail about right ventricular outflow tract/conduit/branch pulmonary arteries in terms of its origin, course, narrowing, obstruction, stenosis, and or aneurysmal dilatation [Figure 6]. It may provide an excellent opportunity to assess pulmonary arterial

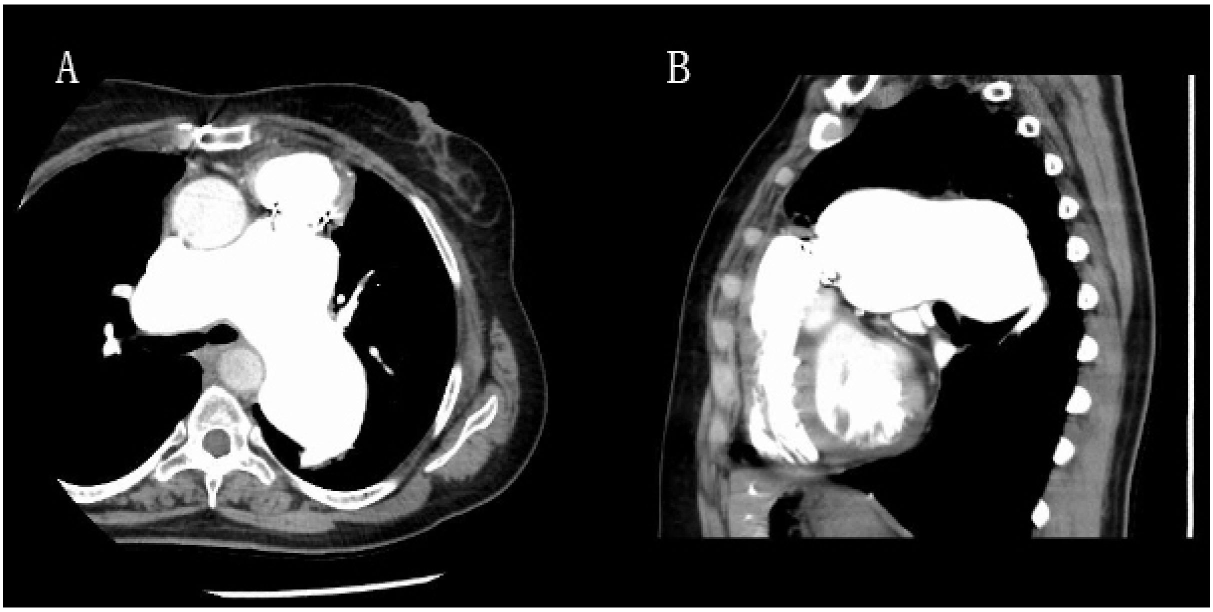

Figure 6. Axial (A) and sagittal (B) slice of cardiac CT imaging of a 54-year-old woman with repaired TOF with absent pulmonary valve who had a transcatheter pulmonary valve placement. Dilated main and branch pulmonary arteries are typically seen in this phenotype of TOF.

anatomy in the presence of stents or other metallic items. Presence of new intimal proliferation, stent fracture, aneurysm/pseudoaneurysm can be easily detected.

Aorto-pulmonary collaterals:

Due to high spatial resolution with this technique, it heals itself to the accurate assessment of aorto-pulmonary collaterals.

Airway and lungs:

Airway anatomy in relation to the heart/great vessels can also be assessed. Needless to say that other organs in the chest, including lung parenchyma, pleural space, and other mediastinal structures, can also be assessed.

Coronaries:

Delineation of coronary arteries origin and course in relation to right ventricular outflow tract would be crucial in the context of percutaneous valve placement or surgical intervention and can be accurately done. Assessment of coronary arteries for stenosis is gaining more significance as patients with repaired TOF are getting older and reaching the age range for acquired coronary artery disease.

Volumetric assessment:

ECG gated multiphase data set can be acquired using advanced MDCT, which will allow measurement of end-diastolic and end-systolic volumes of right and left ventricles and their respective stroke volume, cardiac output, and ejection fraction. These measurements cannot be reliably obtained with a close correlation with CMR but remain the gold standard for this purpose.

Aortic root dilation:
Aortic root dilation that has been well-established and reported in patients with repaired TOF can be accurately assessed. Inadequate presentation suspicious for dissection CT scan may be an imaging modality of choice due to the rapidity with which it can be obtained and the spatial resolution it provides.

Advantages
Widely available, very quickly performed, noninvasive, excellent spatial resolution such that anatomical abnormalities/smaller structures such as coronary arteries can be easily resolved (high contrast-to-noise ratio), can be performed in patients with contraindications for CMR such as pacemakers and defibrillators, and allows successful imaging in those patients with significant metallic artifacts on CMR[33]. Shorter scan duration makes it attractive for those with claustrophobia, anxiety and in less co-operative patients such as children. RV volumetric and functional data can be obtained with offline processing.

Limitations
CT scan Involves ionizing radiation that increases the risk for carcinogenesis, particularly with the need for recurrent scanning and electrocardiographically gated scans[34]. For this reason, pregnancy would be a relative contraindication. Temporal resolution is somewhat lower than CMR and echocardiography. There is a need for a robust kidney function for the use of contrast, and risks/complications related to contrast can be of importance, particularly in those with compromised renal function. To improve image quality, minimize cardiac motion, and prolong the diastolic window in order to image coronary arteries accurately, beta-blockade (oral or intravenous) can be used. Another limitation may be the unavailability of advanced scanner/scanning capabilities in many institutions. Finally, the inability to obtain hemodynamic information such as velocity of flow/rate may make this less attractive of an option in general except for those situations when there is a contraindication for CMR.

Images

NUCLEAR SCAN IMAGING FOR EVALUATION OF REPAIRED TOF

Diagnostic role
There is a clear role for nuclear scintigraphy in those situations when a CMR cannot be performed, and there is a need for quantification of differential pulmonary artery blood flow[35]. The quantification of differential flow to each lung assumes an important role in patients with branch pulmonary artery stenosis, particularly before and after intervention in the form of angioplasty/stent placement. Inherent to the technique, a quantitative assessment of ventilation-perfusion ratio can be obtained. Other occasional instances where nuclear imaging can be utilized include ventricular function evaluation, myocardial perfusion evaluation, and assessment of viability[36].

Advantages
Nuclear scintigraphy is a reliable technique to measure differential blood flow, ventricular function, and viability. It can be performed in those with contraindications for CMR, such as incompatible metallic implants/pacemakers/ICD.

Limitations
Nuclear scanning leads to exposure to ionizing radiation, which increases with the repeated examination. It is not a perfect technique for the assessment of RV function/viability.

CARDIAC CATHETERIZATION IMAGING FOR EVALUATION OF REPAIRED TOF

Diagnostic role

Cardiac catheterization has redefined its role since the advent and advancement of other imaging modalities of noninvasive nature such as echocardiography, CMR, CT scan. Cardiac catheterization is no longer the primary diagnostic modality though it assumes an important role when along with diagnostic components, therapeutic intervention is desired[37,38,39]. This could include dilation of pulmonary artery/conduit, stent placement, percutaneous pulmonary valve placement, coiling of aorto-pulmonary collaterals, and closure of residual septal shunts and or coronary artery intervention. With the increase in the number of adult patients with repaired TOF and they are advancing age, coronary artery assessment/interventions may assume a disproportionately increased role. Inherently, hemodynamic data at various levels in the heart/great vessel/conduit allows assessment of narrowing in the vascular structures, residual shunt by oximetry, diastolic function by pressure measurement, and cardiac index by oximetry/thermo-dilution method. As a result, pulmonary vascular resistance and systemic vascular resistance can be calculated. Angiography allows the assessment of degree of valvular narrowing or regurgitation in addition to aorto-pulmonary collateral and great vessel anatomy such as pulmonary artery stenosis, aortic root dilation, aneurysm formation, pseudo-aneurysm formation or dissection. Angiography also allows visual assessment of ventricular function and residual shunt.

Advantages

Cardiac catheterization is the gold standard modality of imaging in patients with repaired TOF when it comes to measurement of hemodynamics such as pressures inside the heart and great vessels (aorta and pulmonary arteries/conduit), course of coronary arteries in relation to right ventricular outflow tract and the impact on the coronary lumen from percutaneous valve implantation. It is definitely a modality of choice for intervention for branch pulmonary arteries, if needed coronary arteries and if percutaneous valves are feasible. This is the only imaging modality that can be therapeutic in nature.

Limitations

Need for venous/arterial access with floating of intra-cardiac catheters, devices, stents, coils makes it invasive in nature with the potential for complications related to invasive nature. High cost, need for sedation/anesthesia/intubation, exposure to ionizing radiation, increasing the risk of carcinogenesis, and need for training and expertise in the field are some of the other limitations.

CONCLUSIONS

Long-term prognosis of patients with repaired TOF fulcrums on optimal outpatient surveillance due to high incidence of residual anatomic and hemodynamic sequelae and need for re-intervention. We have reviewed the commonly used and available imaging modality in terms of the role it plays, questions it can answer, and limitations. It is clear that the various available diagnostic tools are not exclusive of each other but complementary. A diagnostic tool can be selected depending on the age of the patient, clinical circumstances, questions to be answered, and institutional preferences/expertise[9]. Hence a multimodality approach is recommended. Younger patients who are less than 10 years of age may not be able to cooperate for a CMR, while echocardiography may provide excellent images and all the required information. A CMR may be more appropriate for older patients who may require a quantitative assessment of the right ventricle/pulmonary insufficiency[19]. Those with contraindications for CMR may utilize CT scan as an option keeping in mind the increased risk of cancer due to exposure to ionizing radiation. Nuclear scan can be beneficial to calculate the differential flow to the lungs when CMR fails to provide that information. This could be related to artifacts from previously placed coils/metal. Once again, we have to be cognizant of the radiation exposure and risks involved. Cardiac catheterization may not only be used as a diagnostic tool but will have the advantage of performing therapeutic interventions at the same time and can prove extremely beneficial in many cases. Advent of percutaneous valves is changing the paradigm of re-interventions in repaired TOF patients. A multimodality approach where diagnostic tools are utilized based on the age of the patients, clinical scenario, and institutional practices/expertise forms the cornerstone of ongoing care and surveillance for repaired TOF patients.

DECLARATIONS

Acknowledgments

We thank our colleagues at Children's Hospital of Michigan for their collaborative care in taking care of our patients. We thank our patients for allowing us the opportunity to be partners in their care.

Authors' contributions

All authors contributed to the manuscript.

Aggarwal S, Singh G served as senior authors and edited and reviewed the final drafts of the manuscript.

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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