

Arrhythmia Susceptibility and Management in Adult Patients with Repaired Tetralogy of Fallot

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Abstract

Tetralogy of Fallot is the most common cyanotic congenital valvular heart lesion. Successful neonatal repair has led to improved survival into and through adulthood. Severe pulmonary regurgitation occurs as a consequence of surgical repair, resulting in right ventricular volume overload, tricuspid regurgitation, and atrial and ventricular scarring and fibrosis. Repair also involves atriotomy and ventriculotomy, as well as the placement of patch material. These interventions contribute to an increased arrhythmia burden in these patients. Management strategies are variably successful and include pharmacotherapy, catheter ablation, device implantation, and pulmonary valve replacement.

Introduction

Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart defect, occurring in approximately 10% of all congenital heart disease. Repair is typically performed in infancy, with an increasing trend toward early neonatal repair. Adult patients who have undergone repair in infancy or childhood are at risk for developing atrial and ventricular arrhythmias, and consequently, sudden death. This review will highlight the propensity of arrhythmia development in these patients, current therapy, and the role of pulmonary valve replacement in potentially reducing arrhythmia burden.

Anatomy

Tetralogy of Fallot represents a group of findings with a broad spectrum of clinical severity. The fundamental abnormality is a large malaligned ventricular septal defect (VSD) caused by anterior and cephalad deviation of the outlet septum, which results in override of the aorta over the VSD, right ventricular outflow tract (RVOT) obstruction, and right ventricular hypertrophy. Fetal development of cardiac structures is postulated to be flow-dependent, such that obstruction of flow into the right ventricular outflow tract results in pulmonary valve stenosis, as well as hypoplasia of the pulmonary artery vasculature [1]. The pulmonary valve in the majority of patients with TOF is abnormal, and may be bicuspid or unicuspid [2].

The degree of RVOT obstruction is variable, resulting in a diverse range of clinical severity. Patients may present with modest RVOT obstruction and thus mild or even absent cyanosis. At the other extreme, newborns may have critical RVOT obstruction and ductal-dependent pulmonary circulation.

Surgical correction

The goal of surgery is to close the VSD and relieve obstruction throughout the RVOT and pulmonary arteries. The VSD may be closed either through a transatrial or ventricular approach. Resection of the RVOT obstruction can be accomplished through either transatrial, ventricular, or transpulmonary approaches. Atrial and pulmonary approach has gained acceptance as the importance of scar-dependent reentry circuits has been increasingly appreciated as an important cause of sudden death [3]. The infundibular incision may be extended across the pulmonary valve annulus if there is valve hypoplasia, and transannular patching of the annulus may be required if the annulus is severely hypoplastic [4]. If this step is undertaken, there will be effectively no pulmonary valve function. A monocusp valve may be placed at the time of repair to preserve some degree of pulmonary valve function,

though long-term data do not indicate a lower risk of reoperation or reintervention in these patients [5]. Pulmonary insufficiency is initially well tolerated, but has been demonstrated to eventually result in progressive right ventricular dilatation with attendant RV dysfunction and reduced exercise tolerance [6]. Pulmonary valve replacement may be indicated in these patients. A variety of bioprosthetic valves, as well as the recently introduced Melody transcatheter valve [7] are available. Bioprosthetic valves may, in turn, fail for a variety of reasons, and may require redo pulmonary valve replacement [8].

Arrhythmia substrate

Adult patients with a history of surgically repaired TOF have a high arrhythmia burden. In one large study of 556 patients with a mean age of 36.8 ± 12 years, 43.3% had documented atrial or ventricular tachyarrhythmias [9]. Of these, the most prevalent was ventricular tachycardia (14.2%), followed by intra-atrial reentrant tachycardia (IART), including typical atrial flutter (11.5%). Other studies have also reported a high rate of ventricular tachycardia (VT), including a high rate of sudden cardiac death (8.3%) [10].

Arrhythmias in these patients occur for a variety of reasons. Chronic RV volume overload as a result of pulmonary regurgitation results in progressive right ventricular enlargement and QRS prolongation. QRS duration of 180 milliseconds or longer has been identified as a highly sensitive (100%) and specific (96%) predictor of life-threatening VT [11,12].

VT also occurs as a sequela of initial surgical repair. Right ventriculotomy results in the formation of scar, around which reentrant circuits can develop [14]. These circuits typically require an isthmus of slow conduction that is most often bordered by the electrically

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unexcitable scar tissue that is pathognomonic of a ventriculotomy scar or patch material. Thus scar-related reentry is most often identified in the RVOT and in the vicinity of the VSD patch [15].

Intra-atrial reentrant tachycardia is the most frequently occurring atrial arrhythmia seen in adults late after TOF repair. The occurrence of atrial tachycardia is significantly associated with a higher rate of clinical events, including death, heart failure, reoperation and stroke ($p < 0.001$). The mechanism for development of atrial tachycardia appears to be hemodynamic in nature. In animal models that reproduced different physiologic states following TOF repair, those animals with chronic RV volume overload resulting from pulmonary valvotomy were significantly more likely to develop sustained atrial arrhythmias ($p = 0.01$) [16]. Patients with atrial tachycardia have been reported to have significantly larger mean right atrial dimensions and volume compared to age-matched patients without arrhythmias [17]. Tissue Doppler imaging assessment of RV diastolic function has suggested reduced early RV diastolic velocity is significantly reduced in TOF patients that develop atrial arrhythmias [18]. Despite the frequent presence of an atriotomy scar, the most frequently observed atrial tachycardia is still isthmus-dependent atrial flutter, and the cavotricuspid isthmus has been identified as the critical area for ablation in the majority of patients (53%) in tetralogy of Fallot and a related lesion, double outlet right ventricle [19].

In the cited study, 13/127 atrial arrhythmias were identified as focal atrial tachycardia. Right atrial dilation from chronic volume overload, as well as an atriotomy incision, can create scarring and fibrosis of the atrium and result in micro-reentrant focal tachycardia. These areas are commonly found adjacent to suture points and spread radially.

Arrhythmia management

Options available for management of arrhythmias include antiarrhythmic pharmacotherapy, catheter ablation, and device implantation. Focal atrial tachycardia and intra-atrial reentrant tachycardia are highly amenable to ablation, but recurrence rates as high as 27% [19] have been reported. Recurrence is often due to the presence of multiple reentrant circuits or mechanisms (e.g. a focal tachycardia and a macroreentrant atrial tachycardia). The initial step in atrial anatomy is assessment of involvement of the cavotricuspid isthmus by evaluating the response to entrainment. If the response to entrainment indicates that the isthmus is a critical part of the circuit, a line of ablation lesions is placed across the isthmus. Tachycardia may terminate during this step, but frequently converts to a second tachycardia with a different isthmus, often in the lateral right atrial wall, necessitating entrainment maneuvers at that site [20].

Mapping of focal atrial tachycardia is usually performed first by creating a 3-dimensional anatomy, followed by activation mapping, in which activation of a point in the atrial myocardium is measured relative to a stable reference catheter. Ablation is then performed at the site of earliest activation.

Ventricular tachycardia may be polymorphic and result in hemodynamic instability, making mapping and ablation challenging. When tachycardia is monomorphic, it most often displays ECG morphology suggestive of RVOT origin, with left bundle branch block morphology and an inferior frontal plane axis. Stable monomorphic tachycardia can be mapped using point-by-point activation mapping, aided by a 3-dimensional mapping system. For unstable polymorphic tachycardia, voltage mapping may be performed, in which areas of low voltage are identified, corresponding to unexcitable scar tissue.

An anatomic isthmus is then identified by pace mapping, which is the ablation target. In one series utilizing voltage mapping, all VT's were successfully ablated, and 91% of patients were free of VT in 30 ± 29 months follow-up [15]. Another series reported an overall success rate of 80%, with a recurrence rate of 25% in long-term follow-up [21]. In this series, all patients received an implantable cardioverter-defibrillator (ICD).

ICD implantation is indicated for both primary and secondary prevention of ventricular tachycardia. Primary prevention indications include unexplained presyncope/syncope, palpitations, $QRS \geq 180$ msec, non-sustained VT, decreased ventricular function, and inducible VT. The incidence of both appropriate and inappropriate ICD discharge is high in this population. In one large, prospective, multicenter study, 30.6% of ICD recipients received an appropriate shock and 24.6% received an inappropriate shock [22]. A smaller, single-center, retrospective review reported overall lower rates of appropriate vs. inappropriate discharge (19% vs. 15%), but a similar proportion [23].

Role of pulmonary valve replacement

Pulmonary valve replacement is indicated in patients with severe pulmonary regurgitation and RV dilation [24], and has been shown to restore normal RV dimensions and improve functional status [25].

The impact of PVR on arrhythmia risk is less well defined. Significant reduction in QRS width has been demonstrated in medium-term follow-up after PVR, and appears to correlate with reduction in RV end-diastolic volume [26]. Other studies with longer follow-up have demonstrated stabilization of QRS width, but not overt reduction [27]. These findings suggest that QRS reduction may be a transient phenomenon.

In patients who have developed atrial or ventricular arrhythmias prior to PVR, surgery is frequently performed with intraoperative cryoablation. In the study by Therrien et al., use of concomitant cryoablation significantly reduced the recurrence of atrial and ventricular arrhythmias. Another large study found that PVR did not result in any improvement in survival or decreased incidence of VT [28]. This was a single-center study in which intraoperative cryoablation was not routinely performed.

Conclusion

Tetralogy of Fallot is the most common cyanotic congenital valvular lesion. In the modern era, children born with this defect often survive well into adulthood. The management of adults with repaired tetralogy of Fallot requires the multidisciplinary efforts of congenital cardiologists, electrophysiologists, and surgeons. The potential for these patients to develop arrhythmias needs to be anticipated and regular assessment of QRS width as well as ectopic burden should be performed. Pulmonary valve replacement, in conjunction with intraoperative cryoablation of the critical isthmus of slow conduction, may be helpful in alleviating the arrhythmia risk.

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