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REVIEW

Ventricular arrhythmias and sudden death in tetralogy of Fallot

Arythmies ventriculaires et mort subite dans la tétralogie de Fallot

Philippe Maury[a,b,*], Frederic Sacher[c], Anne Rollin[a], Pierre Mondoly[a], Alexandre Duparc[a], Katja Zeppenfeld[d], Sebastien Hascoet[e,f], on behalf of the Réseau francophone de rythmologie pédiatrique et congénitale

[a] *University Hospital Rangueil, 31059 Toulouse cedex 09, France*
[b] *Unité Inserm U1048, Toulouse, France*
[c] *Inserm 1045, LIRYC Institute, Bordeaux University Hospital, Bordeaux, France*
[d] *Department of Cardiology, C5-P, Leiden University Medical Centre, Leiden, The Netherlands*
[e] *University Children Hospital, Toulouse, France*
[f] *Marie-Lannelongue Hospital, Department of Congenital Heart Diseases, Le Plessis-Robinson, France*

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Summary Malignant ventricular arrhythmias and sudden cardiac death may late happen in repaired tetralogy of Fallot, although probably less frequently than previously thought, especially with the advent of new surgical techniques/management. Ventricular tachycardias are caused by reentry around the surgical scars/patches and valves. Many predictive factors have been proposed, which suffer from poor accuracy. There is currently no recommended indication for prophylactic implantable cardioverter defibrillator implantation—except maybe in the case of multiple risk factors—while radiofrequncy ablation may be proposed in secondary prevention with or even without a back-up implantable cardioverter defibrillator in selected cases.

Abbreviations: ACHD, adult congenital heart disease; GUCH, grown-up congenital heart disease; ICD, implantable cardioverter defibrillator; RVOT, right ventricular outflow tract; SCD, sudden cardiac death; TOF, tetralogy of Fallot; VT, ventricular tachycardia.

* Corresponding author. Department of Cardiology, University Hospital Rangueil, 31059 Toulouse cedex 09, France.
E-mail address: mauryjphil@hotmail.com (P. Maury).

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Repeated cardiological investigations and monitoring should be proposed for every operated patient.

MOTS CLÉS
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Cardiopathie congénitale de l'adulte ;
Ablation

Résumé Des arythmies ventriculaires malignes ou une mort subite peuvent survenir tardivement après correction chirurgicale de tétralogie de Fallot, quoique probablement moins fréquemment que précédemment supposé, surtout avec l'avènement de nouvelles techniques chirurgicales ou de prise en charge. Les tachycardies ventriculaires sont dues à des réentrées autour/entre les cicatrices de ventriculotomie ou patchs et les anneaux valvulaires. Un certain nombre de facteurs favorisants ont été proposés qui souffrent cependant de valeurs prédictives insuffisantes pour être utilisés seuls en pratique clinique. Il n'y a actuellement pas de recommandation pour l'implantation prophylactique de défibrillateur en prévention primaire — sauf peut-être en cas d'association de facteurs prédictifs multiples — alors que l'ablation percutanée par radiofréquence peut être proposée en prévention secondaire avec ou même sans défibrillateur dans certains cas sélectionnés. Des investigations cardiaques répétées et une surveillance au long cours doivent être effectués chez chaque patient opéré.

Background

Congenital heart disease is present in 0.9% of living births; currently, 90% of those affected will reach adulthood because of recent progress made in paediatrics, cardiology, surgery and resuscitation [1,2]. Among what are commonly called ''grown-up congenital heart diseases'' (GUCHs) or, more recently, ''adult congenital heart diseases'' (ACHDs), tetralogy of Fallot (TOF) has a preponderant place, because of its relatively high prevalence (7—10% of all congenital heart diseases; 1/3500 to 1/4300 in the adult population) [3,4], and because it is possible to have corrective surgery, leading to almost normal anatomy and physiology in adulthood. Indeed, very long-term follow-up has demonstrated that health status is excellent, with a mortality rate that is considered to be low (14% mortality for hospital survivors at 40-year follow-up, after surgery performed in the 1970s), even if it is still higher than in the general population, mainly because of heart failure and ventricular arrhythmias [5]. Thus, the third reason for making TOF one of the main GUCHs of concern is the late risk of malignant ventricular arrhythmias and sudden cardiac death (SCD).

The aim of this review is to highlight the mechanisms of ventricular arrhythmias in TOF, and to present current knowledge of secondary and primary prevention of SCD in this setting.

SCD in GUCH patients

The occurrence of SCD in patients with previous surgical repair of congenital heart defects is a tragic event, as many are usually considered to be ''cured'' of their congenital heart disease (even if this terminology may be a bit too optimistic), with rather low mortality rates and usually excellent quality of survival. Some of these SCDs are probably linked to paroxysmal high-degree atrioventricular block (e.g. in repaired TOF with relevant intraventricular conduction disturbances, but also in ventricular septal defect, cushion defect or congenitally corrected transposition of the great arteries). Some other SCDs are caused by ventricular fibrillation induced by fast ventricular rates during supraventricular tachycardia (e.g. atrial tachycardia with 1/1 atrioventricular conduction after atrial switch for transposition of the great arteries, or after Fontan procedures for single ventricle). Other causes probably include haemodynamic compromise, embolism, myocardial infarction or aneurism rupture, but it is now clear that most SCDs (a proportion estimated at around 75% [6]) are secondary to arrhythmias, and among these, malignant ventricular arrhythmias have been documented in 85% of cases at the time of the cardiac arrest [6].

Even if the culprit GUCH for SCD has changed in recent decades, TOF remains one of the main GUCHs carrying the risk of late SCD. In 1974, congenital aortic stenosis, Eisenmenger's syndrome, TOF and hypertrophic obstructive cardiomyopathy were responsible for more than half of SCDs in children (non-operated defects in most) [2]; whereas TOF, systemic to pulmonary anastomosis, pulmonary hypertension caused by left to right shunt and dilated cardiomyopathy were present in half of the SCDs in a report published 10 years later (postoperative in a significant number of cases) [7]. In 1998, Silka et al. found that in 3600 patients with GUCH, most late SCDs were linked to aortic stenosis, aortic coarctation, transposition of the great arteries and TOF, leading to a yearly SCD rate of 0.22% (50 to 200 times higher than in the general population); most were suspected to have an arrhythmic cause [6]. Similar causes of SCD have been found in more recent studies [8]. However, even if it is always a clinically relevant issue, SCD is not the major cause

of death in GUCH, representing only one-quarter of all-cause mortalities in adults with GUCH in many series [6,9,10], or even fewer, according to more recent data [11], while it is known to account for half of cardiac deaths among those with acquired heart disease.

Prospective trials regarding SCD in GUCH are lacking for many reasons:

- first, these are very heterogeneous defects;
- second, the number of cases needed to reach statistical power makes any trial almost unachievable (e.g. TOF would require 1700 patients to be followed for 10 years) [12];
- third, earlier conclusions may not be relevant to newer generations of patients with GUCH (complete repairs during the neonatal period, improved physiological outcomes, extended survival of patients with more complex forms) [13].

SCD and ventricular arrhythmias in TOF

The modern management of TOF began before the 1960s, after the first surgical complete repair performed by Dr D. C. Lillehei in 1954. As early as 1975 — around 15 to 20 years later — the first cases of unexpected cardiac arrest in repaired TOF were noticed, and were already suspected to be caused by malignant ventricular arrhythmias [14—16].

Since then, SCD has been identified repeatedly as the major cause of mortality in repaired TOF, representing, however, only one-third to half of all-cause mortalities in different series [14,17—19]. Over the past 30 years, many studies have evaluated the risk of SCD in TOF to be between 0 and 0.8% yearly [6,14,16—23]. In a meta-analysis including 39 studies and 4583 patients, the late rate of SCD in TOF was evaluated to be 1.8% over more than 8 years of follow-up, i.e. an annual SCD rate of only 0.15% [21], which is, of course, higher than in the general population, but does not constitute an objectively ''high'' risk sufficient to warrant systematic prevention. For comparison, a yearly risk of SCD of up to 0.8% in hypertrophic cardiomyopathy does not constitute an indication for an implantable cardioverter defibrillator (ICD) [24]. Interestingly, the risk of late SCD in TOF is not linear but increases over time, especially 20—25 years after the surgery [6,19]. However, it is still unclear if this increase is simply caused by ageing or is dependent on ongoing progress in surgical techniques.

For the occurrence of sustained ventricular tachycardia (VT), the risk has been evaluated as 4% at 21-year follow-up (i.e. 0.2% yearly) [17], and as 14% in 556 adults operated on for TOF after a follow-up of around 30 years [25]. The risk also changes with age, with an increase at around 40 years of age [25]. Thus, it is tempting and logical to mainly link SCD in TOF to the occurrence of sustained VT.

Mechanisms of VT and SCD in TOF

Data on unrepaired TOF are scarce, as these usually have a very poor prognosis [26]; what we know comes from ancient studies, where ventricular arrhythmias were commonly found in older TOF patients before repair [27,28].

For repaired TOF, conduction disturbances are probably not a common cause of SCD because long-term evolution from right bundle branch block to bi-/tri-fascicular block is uncommon [22], and because postoperative bi-fascicular block (without transient high-degree atrioventricular block) has never been shown to lead to late SCD [18,22,29,30]. Only transient complete heart block that persisted beyond the third postoperative day has been correlated with the risk of late SCD [31]. Even if prolonged QRS duration has been correlated with SCD [17,32], QRS prolongation relates rather to right ventricular size, and predicts malignant ventricular arrhythmias [32]. Moreover, autopsies in patients with TOF who died from SCD revealed that the conduction tissues were undamaged, but found extensive fibrosis of the right ventricular myocardium at both the ventriculotomy site and the septum [33]. Ventricular arrhythmias such as premature beats [22,30] and documented ventricular fibrillation [30] were soon suspected to be involved in SCD mechanisms and, finally, repeated documentation of sustained VT during aborted SCD in repaired TOF patients [32] sealed the causal relationship between ventricular arrhythmias and SCD.

After the first cases of surgical or intracardiac mapping and ablation, reentry circuits around the surgical ventriculotomy scars, using fibrotic areas of slow conduction, have been shown to be the cause of sustained VT in repaired TOF [34—37]. It is not known, however, if ventricular fibrillation is always caused by degenerating monomorphic sustained VT.

Factors associated with SCD in TOF

Many factors have been proposed to try to better define the risk of SCD in repaired TOF (Table 1). These factors are based on history, clinical features, surface electrocardiogram or signal-averaged electrocardiogram, and the presence of spontaneous or inducible arrhythmias or surgical characteristics, but also on echocardiographic or haemodynamic variables thought to be associated with a poorer prognosis. A review of all these variables can be found elsewhere [12]. However, if the holy grail of TOF risk stratification lies in any of these variables, it would surely have been found already. Apart from the combination of QRS prolongation and increased JT dispersion, which has been associated with good positive and negative predictive values [38], none of these factors has sufficient accuracy, at least individually, to allow their use alone for risk stratification in primary prevention. Moreover, most of these variables are probably not independent of each other [12] and would be better used in combination (see later).

When trying to explore risk stratification further, it seemed to make sense to first consider the presence of complex asymptomatic ventricular arrhythmias as one of the major variables linked to SCD; these were found in 13% of patients when looking at routine electrocardiograms, and in around half of patients when looking at ambulatory recordings [15,20]. The dramatically lower rate of premature beats on routine electrocardiograms in uneventful compared with sudden-death patients, together with the lower SCD rate in patients with frequent ventricular premature beats successfully versus unsuccessfully/not treated with antiarrhythmic drugs [15], supported this hypothesis. However,

Table 1 Factors proposed to be related to the risk of sudden cardiac death in repaired tetralogy of Fallot (modified from [12]).

Atrioventricular conduction block
Right bundle branch block with left axis deviation
Atrial arrhythmias
Sustained ventricular tachycardia
Non-sustained ventricular arrhythmias on 24-hour ambulatory monitoring
Ventricular arrhythmias on exercise testing
Right ventricular hypertension
Residual ventricular septal defect
Right ventricular dilation
Residual right ventricular outflow tract obstruction
Ventricular hypertrophy
Size of ventriculotomy scar
Diminished right ventricular myocardial blood flow reserve
Restrictive right ventricular physiology
Size of ventriculotomy scar
Diminished right ventricular myocardial blood flow reserve
Left ventricular end-diastolic pressure
Left ventricular involvement
Abnormal signal-averaged electrocardiogram
Complex or multiple operations
Transventricular as opposed to transatrial approach to repair
QRS duration on electrocardiogram
Older age at operation
Early surgical era
Coronary artery disease

conflicting data exist on that point [17], while symptomatic non-sustained VT has been associated with a poorer outcome [39].

The logical next step was to consider the role of inducible ventricular arrhythmias in selecting patients prone to SCD, despite the fact that inducible patients may have excellent outcome [20] and that SCD may occur in non-inducible patients with TOF [40]. Khairy et al. reported the prognostic value of programmed ventricular stimulation after TOF repair, as determined in a multicentre cohort study including 252 patients investigated from 1985 to 2002 (mean age 16 ± 12 years) [41]. Of note, two-thirds of these patients had already presented with syncope, palpitations, sustained VT or even cardiac arrest. Sustained monomorphic VT was inducible during standard programmed ventricular stimulation in 30% of cases, and polymorphic VT in 5% of cases (under isoproterenol in a quarter of cases). After multivariable analysis, inducible patients were older, and presented with palpitations, high-grade ventricular premature beats, previous palliative surgery and a large cardiothoracic ratio. A quarter of inducible patients were implanted with an ICD (and only a very few non-inducible patients). Overall, 17% of patients experienced SCD or sustained VT during the 6-year follow-up. Inducibility of any VT was significantly linked to arrhythmia-free survival in a multivariable analysis [41]. Analyses performed in patients without ICDs or in asymptomatic patients yielded similar results; however, even if negative and positive predictive values of inducibility of any VT were considered interesting (98% and 25% respectively), with a relative risk of 10.4 in asymptomatic patients, the 95% confidence intervals were very large, and the statistical analysis could be considered to be of borderline significance ($P = 0.0425$). Moreover, a subsequent publication by the same group did not confirm these results in patients with ICD [42] (see later).

According to the 2014 guidelines for management of arrhythmias in GUCH [1] and the 2015 European guidelines for SCD [24], programmed ventricular stimulation can be useful in risk stratification in adults with repaired TOF who have more than one risk factor for SCD (including left ventricular systolic or diastolic dysfunction, non-sustained VT, QRS duration > 180 ms or extensive right ventricular scarring; class IIa indication). According to the same guidelines, an ICD may be proposed for primary prevention in selected patients with TOF in case of multiple risk factors (i.e. those mentioned above, inducible sustained VT; class IIa indication). In our opinion and experience, however, prophylactic ICD implantation is rare, and should be reserved mainly for left ventricular alteration and/or very broad QRS and impaired right ventricular function.

Medications for ventricular arrhythmias in TOF

There has been no dedicated study of antiarrhythmic drugs in TOF or, more generally, in GUCH. Drug management in GUCH is adapted from what has been largely demonstrated in acquired heart disease. Beta-blockers are probably useful, while sotalol and amiodarone should be avoided — at least as first-intention treatment — because of the risk of proarrhythmia and relevant non-cardiological side effects during long-term therapy [1]. Class I antiarrhythmic drugs may be harmful in case of diseased ventricle [1], as is present in TOF.

ICDs in TOF

GUCH and children represent fewer than 1% of all ICD implantations. Series are few, and are usually limited to tens of patients, and, of course, there have been no randomized trials. ICDs in GUCH are hampered by an important rate of inappropriate therapy, late technical or psychological issues or complications with residual significant mortality rates and even relevant SCD rates [43].

Patients with TOF form by far the largest subgroup of ICD recipients with congenital heart disease [44—46]. In secondary prevention, an older report on 25 operated patients with TOF revealed 45% oversensing, 20% appropriate antitachycardia pacing, 5% appropriate ICD shock, 20% inappropriate antitachycardia pacing, 20% inappropriate ICD shock and 5% mortality over 2 years [47].

In 2008, Khairy et al. reported their experience of ICDs in 121 implanted patients with TOF, half of whom were implanted for primary prevention (although a large number had symptoms compatible with ventricular arrhythmia) [42]. Thirty per cent of patients experienced appropriate therapy over 3.5 years (81% VT, 19% ventricular fibrillation). The only

independent predictor was previous ventriculotomy incision. One-quarter of patients presented with inappropriate therapy — either in primary or secondary prevention — and ICD-related complications occurred in 30%. Interestingly, the all-cause mortality rate was high (2% yearly, rather higher than for unselected TOF), and half of the deaths were sudden, despite the ICD [42]. In the subgroup of patients implanted for primary prevention, appropriate shocks happened in 23%, and independent predictors were elevated left ventricular end-diastolic pressure and the presence of non-sustained VT. Interestingly, inducibility was not significantly linked to the occurrence of appropriate shock. The authors built a risk score for predicting appropriate ICD shock in primary prevention, but other authors failed to validate it in a subsequent series of 36 patients with TOF also implanted for primary prevention [39]. In this work, only symptomatic non-sustained VT was associated with future appropriate therapy in a univariate analysis (which, in fact, challenges the notion that these were really ''primary prevention'' TOF patients). In this report, there was 19% appropriate therapy, 42% inappropriate therapy and 5% mortality over the 5-year follow-up [39]. However, it is not clear if fast VT prompting ICD therapy was non-sustained when different ICD settings were programmed.

In a recent French retrospective registry of 62 implanted patients with TOF (18% in primary prevention), 9% received appropriate therapy in primary prevention compared with 50% in secondary prevention, while 34% experienced major ICD-related complications, and 10% died over a follow-up of 3.5 years (Bouzeman, unpublished data). Thus, inappropriate therapies equal or exceed appropriate therapies in patients with TOF implanted in primary prevention.

No relevant data are available today on the use of subcutaneous ICDs in GUCH and hence in TOF. What is known from very limited early experience is a high rate of inappropriate shocks (issues in tachycardia discrimination because of intraventricular conduction disturbances or T-wave abnormalities) and the drawback of the impossibility of anti-brady/tachy pacing, which may be relevant in TOF [48,49]. An increased risk of device exteriorization and the use of right parasternal screening have also been evoked in GUCH or children implanted with a subcutaneous ICD [48,50].

Finally, recent new modalities of surgical epicardial ICD implantation in congenital heart disease have been proposed, but with limited experience to date [51].

VT ablation in TOF

Successful catheter ablation using conventional mapping techniques, with or without drugs, has been reported in short series of patients with TOF [52,53], although only limited success rates have been reported in other series [54] because of complex anatomy, hypertrophied myocardium, dense fibrosis, broad isthmuses, haemodynamic instability or non-inducibility.

Zeppenfeld et al. were the first to investigate in depth the details of various VT reentry circuits in repaired TOF using three-dimensional mapping [55]. Four potential slow-conducting VT isthmuses were present in most patients with TOF referred for sustained VT, and were also found in autopsied hearts from patients with TOF who died shortly after surgery: two isthmuses were bordered by the anterior/lateral right ventricular outflow tract (RVOT) scar/patch and the tricuspid (the main one) or pulmonary annulus (absent if transannular patch); while the other two were delineated by the ventricular septal defect scar/patch and the tricuspid (absent after closure of perimembranous septal defect) or pulmonary annulus (Fig. 1) [55]. Transecting anatomic isthmuses by linear radiofrequency lesions during sinus rhythm (Fig. 2) abolished all inducible VT, and led to a lack of VT recurrence in 90% of cases at 30-month follow-up [55]. Of note, only half of the patients were finally implanted with an ICD during follow-up.

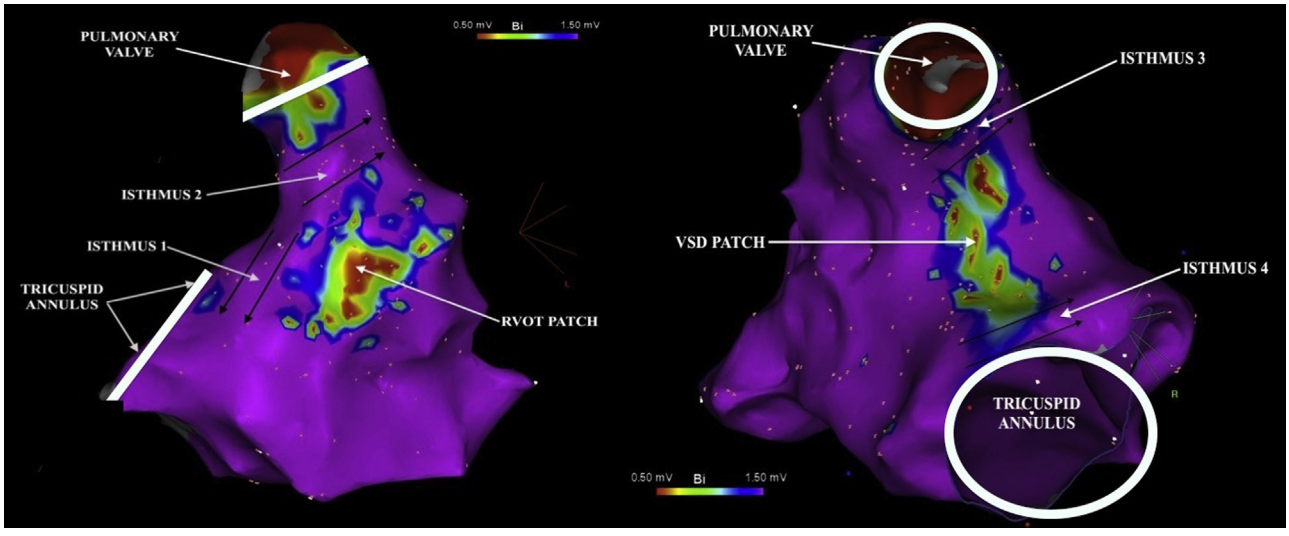

Figure 1. Anterior (left) and posterior (right) views of repaired tetralogy of Fallot right ventricular voltage map, showing scars at the sites of the ventriculotomy/patch at the outflow tract (left) and the ventricular septal defect (VSD) patch (right), together with the four potential isthmuses described by Zeppenfeld et al. [55] (see text). RVOT: right ventricular outflow tract.

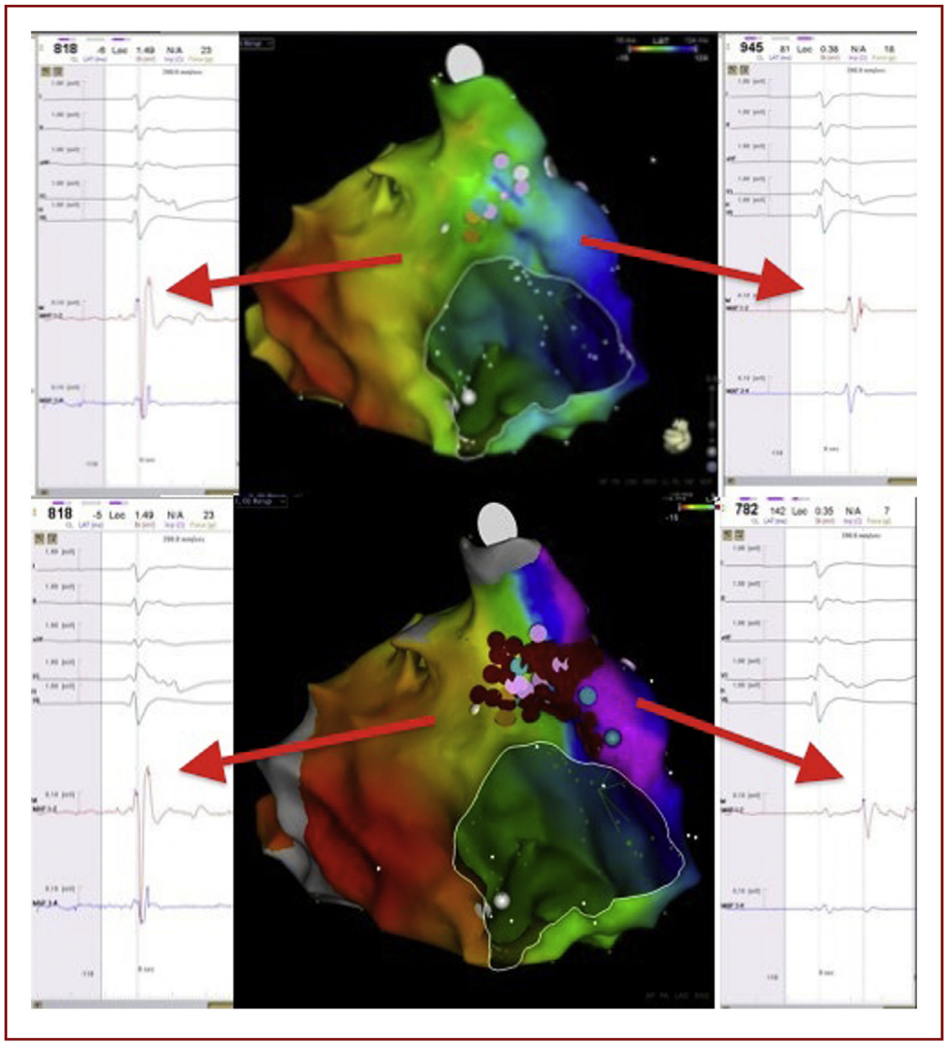

Figure 2. Activation during sinus rhythm before (above) and after (below) radiofrequency-induced block of the isthmus located between tricuspid and pulmonary annulus, with the respective electrograms from both sides of the isthmus. Activation is coded by rainbow colours (from red to purple), showing progressive activation from left to right through the isthmus (above) and inversion of the activation once the block is achieved (below).

All operated patients with TOF have at least one potential anatomical VT isthmus, but isthmuses were narrower, longer and had slower conduction in patients with inducible VT, according to recent work from the same group [56]. Patients without a slow-conducting isthmus did not present with VT during follow-up [56]. This factor may be proposed in the future for stratifying the risk of late SCD. The same group also demonstrated that right-sided ablation may fail because of septal hypertrophy, overlying pulmonary homograft or overlying ventricular septal defect patch. In these cases, representing 15% of the patients, VT had to be ablated from the left ventricle (septum or aortic root) [57].

Current guidelines recommend a role for ablation only as an alternative to ICD therapy in carefully selected patients with TOF (class I indication) [1]. Otherwise, ablation is indicated as adjunctive therapy to ICD in adults with TOF and recurrent monomorphic VT, with or without failed drug therapy [1].

Towards better prevention of ventricular arrhythmia

Some surgical procedures may decrease late VT occurrence. For example, better cardioprotection during extracorporeal circulation, shorter transannular incisions or lack of transection of the annulus, less aggressive muscle resection and less generous RVOT patching [58,59] should be preferred when possible. Earlier correction is probably worthwhile because of less prolonged cyanosis, less pressure overload of the right ventricle, and avoidance of aortopulmonary bypass and subsequent less left ventricular volume overload [17]. Earlier correction of pulmonary valve stenosis or regurgitation by surgical or even percutaneous intervention [60] is probably also beneficial, even if still unproved. Subpulmonary resection and ventricular septal defect closure can be accomplished transatrially, while pulmonary valve/artery surgery can be achieved through a pulmonary arteriotomy (''RV infundibulum sparing repair'') [61,62],

which will probably carry a reduced arrhythmia risk in the long term [63], despite experience still being lacking.

Finally, surgical ablation guided by electrophysiological mapping performed during or before surgery may be considered in TOF with inducible sustained monomorphic VT with an identified critical isthmus (class IIb indication) [24]. Studies are still pending, however, for the evaluation of the clinical role of this dual strategy in decreasing late SCD occurrence.

Conclusions

Malignant ventricular arrhythmias and SCD probably occur less frequently than previously thought in repaired TOF, and will possibly become even less common with the advent of new surgical techniques/management. There are currently no recommended indications for prophylactic ICDs (except perhaps in very selected cases based on multiple risk factors), while radiofrequency ablation may be proposed in secondary prevention, with or even without a back-up ICD in selected cases. Repeated cardiological investigations and monitoring should be proposed for every operated patient.

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Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Khairy P, Van Hare GF, Balaji S, et al. PACES/HRS Expert Consensus Statement on the Recognition and Management of Arrhythmias in Adult Congenital Heart Disease: developed in partnership between the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Endorsed by the governing bodies of PACES, HRS, the American College of Cardiology (ACC), the American Heart Association (AHA), the European Heart Rhythm Association (EHRA), the Canadian Heart Rhythm Society (CHRS), and the International Society for Adult Congenital Heart Disease (ISACHD). Heart Rhythm 2014;11:e102—65.

[2] Lambert EC, Menon VA, Wagner HR, Vlad P. Sudden unexpected death from cardiovascular disease in children. A cooperative international study. Am J Cardiol 1974;34:89—96.

[3] Marelli AJ, Ionescu-Ittu R, Mackie AS, Guo L, Dendukuri N, Kaouache M. Lifetime prevalence of congenital heart disease in the general population from 2000 to 2010. Circulation 2014;130:749—56.

[4] Villafane J, Feinstein JA, Jenkins KJ, et al. Hot topics in tetralogy of Fallot. J Am Coll Cardiol 2013;62:2155—66.

[5] Cuypers JA, Menting ME, Konings EE, et al. Unnatural history of tetralogy of Fallot: prospective follow-up of 40 years after surgical correction. Circulation 2014;130:1944—53.

[6] Silka MJ, Hardy BG, Menashe VD, Morris CD. A population-based prospective evaluation of risk of sudden cardiac death after operation for common congenital heart defects. J Am Coll Cardiol 1998;32:245—51.

[7] Garson Jr A, McNamara DG. Sudden death in a pediatric cardiology population, 1958 to 1983: relation to prior arrhythmias. J Am Coll Cardiol 1985;5:134B—7B.

[8] Koyak Z, Harris L, de Groot JR, et al. Sudden cardiac death in adult congenital heart disease. Circulation 2012;126:1944—54.

[9] Harrison DA, Connelly M, Harris L, Luk C, Webb GD, McLaughlin PR. Sudden cardiac death in the adult with congenital heart disease. Can J Cardiol 1996;12:1161—3.

[10] Oechslin EN, Harrison DA, Connelly MS, Webb GD, Siu SC. Mode of death in adults with congenital heart disease. Am J Cardiol 2000;86:1111—6.

[11] Diller GP, Kempny A, Alonso-Gonzalez R, et al. Survival prospects and circumstances of death in contemporary adult congenital heart disease patients under follow-up at a large tertiary centre. Circulation 2015;132:2118—25.

[12] Bricker JT. Sudden death and tetralogy of Fallot. Risks, markers, and causes. Circulation 1995;92:158—9.

[13] Silka MJ, Bar-Cohen Y. A contemporary assessment of the risk for sudden cardiac death in patients with congenital heart disease. Pediatr Cardiol 2012;33:452—60.

[14] Garson Jr A, Nihill MR, McNamara DG, Cooley DA. Status of the adult and adolescent after repair of tetralogy of Fallot. Circulation 1979;59:1232—40.

[15] Garson Jr A, Randall DC, Gillette PC, et al. Prevention of sudden death after repair of tetralogy of Fallot: treatment of ventricular arrhythmias. J Am Coll Cardiol 1985;6:221—7.

[16] James FW, Kaplan S, Chou TC. Unexpected cardiac arrest in patients after surgical correction of tetralogy of Fallot. Circulation 1975;52:691—5.

[17] Gatzoulis MA, Balaji S, Webber SA, et al. Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot: a multicentre study. Lancet 2000;356:975—81.

[18] Murphy JG, Gersh BJ, Mair DD, et al. Long-term outcome in patients undergoing surgical repair of tetralogy of Fallot. N Engl J Med 1993;329:593—9.

[19] Nollert G, Fischlein T, Bouterwek S, Bohmer C, Klinner W, Reichart B. Long-term survival in patients with repair of tetralogy of Fallot: 36-year follow-up of 490 survivors of the first year after surgical repair. J Am Coll Cardiol 1997;30:1374—83.

[20] Chandar JS, Wolff GS, Garson Jr A, et al. Ventricular arrhythmias in postoperative tetralogy of Fallot. Am J Cardiol 1990;65:655—61.

[21] Garson Jr A. Ventricular arrhythmias after repair of congenital heart disease: who needs treatment? Cardiol Young 1991;1:177—81.

[22] Quattlebaum TG, Varghese J, Neill CA, Donahoo JS. Sudden death among postoperative patients with tetralogy of Fallot: a follow-up study of 243 patients for an average of twelve years. Circulation 1976;54:289—93.

[23] Waien SA, Liu PP, Ross BL, Williams WG, Webb GD, McLaughlin PR. Serial follow-up of adults with repaired tetralogy of Fallot. J Am Coll Cardiol 1992;20:295—300.

[24] Priori SG, Blomstrom-Lundqvist C, Mazzanti A, et al. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). Eur Heart J 2015;36:2793—867.

[25] Khairy P, Aboulhosn J, Gurvitz MZ, et al. Arrhythmia burden in adults with surgically repaired tetralogy of Fallot: a multi-institutional study. Circulation 2010;122:868—75.

[26] Bertranou EG, Blackstone EH, Hazelrig JB, Turner ME, Kirklin JW. Life expectancy without surgery in tetralogy of Fallot. Am J Cardiol 1978;42:458—66.

[27] Deanfield JE, McKenna WJ, Presbitero P, England D, Graham GR, Hallidie-Smith K. Ventricular arrhythmia in unrepaired and repaired tetralogy of Fallot. Relation to age, timing of repair, and haemodynamic status. Br Heart J 1984;52:77—81.
[28] Sullivan ID, Presbitero P, Gooch VM, Aruta E, Deanfield JE. Is ventricular arrhythmia in repaired tetralogy of Fallot an effect of operation or a consequence of the course of the disease? A prospective study. Br Heart J 1987;58:40—4.
[29] Cairns JA, Dobell AR, Gibbons JE, Tessler I. Prognosis of right bundle branch block and left anterior hemiblock after intracardiac repair of tetralogy of Fallot. Am Heart J 1975;90:549—54.
[30] Gillette PC, Yeoman MA, Mullins CE, McNamara DG. Sudden death after repair of tetralogy of Fallot. Electrocardiographic and electrophysiologic abnormalities. Circulation 1977;56:566—71.
[31] Hokanson JS, Moller JH. Significance of early transient complete heart block as a predictor of sudden death late after operative correction of tetralogy of Fallot. Am J Cardiol 2001;87:1271—7.
[32] Gatzoulis MA, Till JA, Somerville J, Redington AN. Mechanoelectrical interaction in tetralogy of Fallot. QRS prolongation relates to right ventricular size and predicts malignant ventricular arrhythmias and sudden death. Circulation 1995;92:231—7.
[33] Deanfield JE, Ho SY, Anderson RH, McKenna WJ, Allwork SP, Hallidie-Smith KA. Late sudden death after repair of tetralogy of Fallot: a clinicopathologic study. Circulation 1983;67:626—31.
[34] Chinushi M, Aizawa Y, Kitazawa H, Kusano Y, Washizuka T, Shibata A. Successful radiofrequency catheter ablation for macroreentrant ventricular tachycardias in a patient with tetralogy of Fallot after corrective surgery. Pacing Clin Electrophysiol 1995;18:1713—6.
[35] Horton RP, Canby RC, Kessler DJ, et al. Ablation of ventricular tachycardia associated with tetralogy of Fallot: demonstration of bidirectional block. J Cardiovasc Electrophysiol 1997;8:432—5.
[36] Misaki T, Tsubota M, Watanabe G, et al. Surgical treatment of ventricular tachycardia after surgical repair of tetralogy of Fallot. Relation between intraoperative mapping and histological findings. Circulation 1994;90:264—71.
[37] Stevenson WG, Delacretaz E, Friedman PL, Ellison KE. Identification and ablation of macroreentrant ventricular tachycardia with the CARTO electroanatomical mapping system. Pacing Clin Electrophysiol 1998;21:1448—56.
[38] Berul CI, Hill SL, Geggel RL, et al. Electrocardiographic markers of late sudden death risk in postoperative tetralogy of Fallot children. J Cardiovasc Electrophysiol 1997;8:1349—56.
[39] Koyak Z, de Groot JR, Bouma BJ, et al. Symptomatic but not asymptomatic non-sustained ventricular tachycardia is associated with appropriate implantable cardioverter therapy in tetralogy of Fallot. Int J Cardiol 2013;167:1532—5.
[40] Alexander ME, Walsh EP, Saul JP, Epstein MR, Triedman JK. Value of programmed ventricular stimulation in patients with congenital heart disease. J Cardiovasc Electrophysiol 1999;10:1033—44.
[41] Khairy P, Landzberg MJ, Gatzoulis MA, et al. Value of programmed ventricular stimulation after tetralogy of fallot repair: a multicenter study. Circulation 2004;109:1994—2000.
[42] Khairy P, Harris L, Landzberg MJ, et al. Implantable cardioverter-defibrillators in tetralogy of Fallot. Circulation 2008;117:363—70.
[43] Berul CI, Van Hare GF, Kertesz NJ, et al. Results of a multicenter retrospective implantable cardioverter-defibrillator registry of pediatric and congenital heart disease patients. J Am Coll Cardiol 2008;51:1685—91.
[44] Jordan CP, Freedenberg V, Wang Y, Curtis JP, Gleva MJ, Berul CI. Implant and clinical characteristics for pediatric and congenital heart patients in the national cardiovascular data registry implantable cardioverter defibrillator registry. Circ Arrhythm Electrophysiol 2014;7:1092—100.
[45] Koyak Z, de Groot JR, Van Gelder IC, et al. Implantable cardioverter defibrillator therapy in adults with congenital heart disease: who is at risk of shocks? Circ Arrhythm Electrophysiol 2012;5:101—10.
[46] Vehmeijer JT, Brouwer TF, Limpens J, et al. Implantable cardioverter-defibrillators in adults with congenital heart disease: a systematic review and meta-analysis. Eur Heart J 2016;37:1439—48.
[47] Witte KK, Pepper CB, Cowan JC, Thomson JD, English KM, Blackburn ME. Implantable cardioverter-defibrillator therapy in adult patients with tetralogy of Fallot. Europace 2008;10:926—30.
[48] Bordachar P, Marquie C, Pospiech T, et al. Subcutaneous implantable cardioverter defibrillators in children, young adults and patients with congenital heart disease. Int J Cardiol 2016;203:251—8.
[49] Jarman JW, Lascelles K, Wong T, Markides V, Clague JR, Till J. Clinical experience of entirely subcutaneous implantable cardioverter-defibrillators in children and adults: cause for caution. Eur Heart J 2012;33:1351—9.
[50] Okamura H, McLeod CJ, DeSimone CV, et al. Right parasternal lead placement increases eligibility for subcutaneous implantable cardioverter defibrillator therapy in adults with congenital heart disease. Circ J 2016;80:1328—35.
[51] Pospiech T, Roubertie F, Jalal Z, Bordachar P, Thambo JB. New technique for surgical epicardial implantation of a cardioverter-defibrillator in children and adults with congenital heart disease. Ann Thorac Surg 2016;102:615—9.
[52] Furushima H, Chinushi M, Sugiura H, et al. Ventricular tachycardia late after repair of congenital heart disease: efficacy of combination therapy with radiofrequency catheter ablation and class III antiarrhythmic agents and long-term outcome. J Electrocardiol 2006;39:219—24.
[53] Gonska BD, Cao K, Raab J, Eigster G, Kreuzer H. Radiofrequency catheter ablation of right ventricular tachycardia late after repair of congenital heart defects. Circulation 1996;94:1902—8.
[54] Morwood JG, Triedman JK, Berul CI, et al. Radiofrequency catheter ablation of ventricular tachycardia in children and young adults with congenital heart disease. Heart Rhythm 2004;1:301—8.
[55] Zeppenfeld K, Schalij MJ, Bartelings MM, et al. Catheter ablation of ventricular tachycardia after repair of congenital heart disease: electroanatomic identification of the critical right ventricular isthmus. Circulation 2007;116:2241—52.
[56] Kapel GF, Sacher F, Dekkers OM, et al. Arrhythmogenic anatomical isthmuses identified by electroanatomical mapping are the substrate for ventricular tachycardia in repaired tetralogy of Fallot. Eur Heart J 2016 [In press].
[57] Kapel GF, Reichlin T, Wijnmaalen AP, et al. Left-sided ablation of ventricular tachycardia in adults with repaired tetralogy of Fallot: a case series. Circ Arrhythm Electrophysiol 2014;7:889—97.
[58] Atallah-Yunes NH, Kavey RE, Bove EL, et al. Postoperative assessment of a modified surgical approach to repair of tetralogy of Fallot. Long-term follow-up. Circulation 1996;94: II22—6.
[59] Dietl CA, Cazzaniga ME, Dubner SJ, Perez-Balino NA, Torres AR, Favaloro RG. Life-threatening arrhythmias and RV dysfunction after surgical repair of tetralogy of Fallot. Comparison between transventricular and transatrial approaches. Circulation 1994;90:II7—12.
[60] Hascoet S, Acar P, Boudjemline Y. Transcatheter pulmonary valvulation: current indications and available devices. Arch Cardiovasc Dis 2014;107:625—34.

[61] Giannopoulos NM, Chatzis AK, Karros P, et al. Early results after transatrial/transpulmonary repair of tetralogy of Fallot. Eur J Cardiothorac Surg 2002;22:582—6.
[62] Morales DL, Zafar F, Fraser Jr CD. Tetralogy of Fallot repair: the right ventricle infundibulum sparing (RVIS) strategy. Semin Thorac Cardiovasc Surg 2009:54—8.
[63] Sfyridis PG, Kirvassilis GV, Papagiannis JK, et al. Preservation of right ventricular structure and function following transatrial-transpulmonary repair of tetralogy of Fallot. Eur J Cardiothorac Surg 2013;43:336—42.