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CLINICAL RESEARCH

Ten-year outcomes of monomorphic ventricular tachycardia catheter ablation in repaired tetralogy of Fallot

Résultats à 10 ans de l'ablation par cathéter des tachycardies ventriculaires monomorphes dans la tétralogie de Fallot réparée

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KEYWORDS
Tetralogy of Fallot;
Sudden cardiac death;
Ventricular tachycardia;
Catheter ablation;

Summary
Background. — Monomorphic ventricular tachycardia (MVT) is common in adults with repaired tetralogy of Fallot (TOF), and is associated with sudden cardiac death. Management of MVT is not defined, and results of catheter ablation (CA) are limited.
Aims. — To evaluate long-term outcomes of MVT CA in repaired TOF.
Methods. — Thirty-four patients (mean age 32 ± 10.3 years; 59% male) with repaired TOF underwent CA for symptomatic MVT between 1990 and 2012 in our centre; direct-current ablation (DCA) was used in 6%, radiofrequency followed by DCA in 29% and radiofrequency alone in 65%.
Results. — Right ventricular (RV) dysfunction was present in 35% and left ventricular (LV) dysfunction in 21%. Mean numbers of clinical and induced MVTs were 1 and 2, respectively. Mean VT

Abbreviations: CA, catheter ablation; CHD, congenital heart disease; DCA, direct-current ablation; ICD, implantable cardioverter-defibrillator; LV, left ventricle/ventricular; LVEF, left ventricular ejection fraction; MVT, monomorphic ventricular tachycardia; RV, right ventricle/ventricular; RVOT, right ventricular outflow tract; TOF, tetralogy of Fallot; VT, ventricular tachycardia.

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Implantable cardioverter-defibrillator

rate was 225 ± 95 bpm. Ablation targeted a single site (range 1–2), which was RV outflow tract in 85%. Primary success, defined as ventricular tachycardia (VT) termination during CA and final non-inducibility, was obtained in 82%. Seven patients (21%) required redo ablation in the first 3 months (before 2004; DCA). No death related to CA occurred. Mean follow-up time was 9.5 ± 5.2 years. Antiarrhythmic therapy was discontinued in 71%. There were two cases of sudden cardiac death and four VT recurrences. Freedom from death and arrhythmia recurrence was 94% at 5 years, 81% at 10 years and 70% at 20 years. Global survival was 91% at 20 years. Baseline LV ejection fraction < 60% was significantly associated with ventricular arrhythmia recurrence (hazard ratio 16.4, 95% confidence interval 1.8–147; $P = 0.01$).

Conclusions. — CA can safely address macroreentrant MVT in repaired TOF patients with an acceptable long-term rate of recurrence in this high-risk population. Anatomical classification of isthmuses with electroanatomical mapping provides reproducible endpoints for CA. Attention should be given to LV systolic function in risk assessment and selection of candidates for implantable cardioverter-defibrillator.

MOTS CLÉS
Tétralogie de Fallot ;
Mort subite cardiaque ;
Tachycardie ventriculaire ;
Ablation par cathéter ;
Défibrillateur automatique implantable

Résumé

Contexte. — Les tachycardies ventriculaires monomorphes (TVM) sont fréquentes chez les adultes ayant une tétralogie de Fallot réparée (TDFr) et sont associées à la survenue d'une mort subite (MS). Le traitement des TVMs n'est pas défini et les résultats de l'ablation par cathéter (AC) sont limités.

Objectifs. — Evaluer les résultats à long-terme de l'AC des TVM dans la TDFr.

Méthodes. — Trente-quatre patients (32 ± 10,3 ans ; 59 % hommes) ayant une TDFr ont eu une AC de TVM symptomatique entre 1990 et 2002. La fulguration seule a été utilisée chez 6 % des patients, la radiofréquence suivie de fulguration chez 29 % et la radiofréquence seule chez 65 %.

Résultats. — Il existait une dysfonction ventriculaire droite (VD) chez 35 % et une dysfonction ventriculaire gauche (VG) au moins mineure chez 21 %. Le nombre moyen de TVMs cliniques et déclenchées était de 1 et 2 respectivement. La fréquence moyenne était de 225 ± 95 bpm. Il y a eu en moyenne un seul site d'ablation (de 1 à 2), qui était la voie d'éjection VD dans 85 %. Un succès primaire, défini par un arrêt de la TVM pendant le tir et une non-inductibilité finale a été obtenue dans 82 % des cas. Sept patients ont eu une ré-ablation dans les 3 premiers mois (avant 2004 et par fulguration). Aucun décès en rapport avec l'AC n'est survenu. La durée moyenne de suivi était de 9,5 ± 5,2 ans. Les traitements anti-arythmiques ont été arrêtés chez 71% des patients. Il y eut 2 MS et 4 récidives d'arythmies. La survie sans MS, récidive de TV et choc approprié était de 94 %, 81 % et 70 % à 5, 10 et 20 ans, respectivement. La survie totale était de 91 % à 20 ans. Une fraction d'éjection VG (FEVG) < 60 % était significativement associée aux récidives d'arythmie ventriculaire (HR 16,4, IC 95 % 1,8–147 ; $p = 0,01$).

Conclusions. — L'AC est une technique fiable pour traiter les TVM par macro-réentrée dans la TDFr, avec une sécurité et un taux de récidive d'arythmies à long terme acceptables dans cette population à haut risque. L'identification des isthmes des TVM par cartographie électro-anatomique fournit une cible reproductible pour l'AC. Une attention particulière devrait être accordée à la fonction systolique du VG dans l'évaluation du risque rythmique et la sélection des candidats au défibrillateur automatique implantable.

Background

The population of adults with repaired congenital heart disease (CHD) is increasing [1]. Tetralogy of Fallot (TOF) is the most common cyanotic CHD. Late ventricular arrhythmias are the leading cause of sudden cardiac death in adults with repaired TOF [2]. Monomorphic ventricular tachycardia (MVT) is the most frequent form of ventricular arrhythmia, accounting for more than 80% of ventricular arrhythmias in patients with repaired TOF carrying an implantable cardioverter-defibrillator (ICD) [3,4]. Several risk factors for sudden cardiac death in adults with repaired TOF have been identified, and are useful for selection of ICD candidates in a primary prevention setting [4], but lack predictive value, and might not be as relevant in the current era of early surgical repair. In the past decade, with the spread

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of electroanatomical mapping, important efforts have been made to characterize the anatomical basis of repaired TOF MVTs that seem to rely on the presence of scar tissue areas within the right ventricle (RV), corresponding to ventriculotomy or right ventricular outflow tract (RVOT) patch or ventricular septal defect patch. These scar areas create substrate for macroreentry, and MVT occurrence depends on their anatomical and electrophysiological properties, a finding that creates a path for individualized arrhythmic risk prediction in repaired CHD [5–8]. However, less is known about the management of monomorphic ventricular tachycardias (VTs). Antiarrhythmic therapies and antitachycardia pacing lack efficacy [9], whereas ICDs do not prevent VT recurrence, and are associated with frequent complications and inappropriate therapies in this young population [9–11]. Several small case series have suggested favourable outcomes after MVT catheter ablation (CA) in repaired CHD, with a VT-free long-term survival rate of 75–100% [12–14]. To date, the largest series included 34 patients (eight with non-TOF CHD; seven with non-documented VT), and provided a limited follow-up of 46 months, hampering the evaluation of CA long-term efficacy [5]. Here, we present the results of VT CA at 10 years in 34 patients with repaired TOF referred for symptomatic monomorphic VT.

Methods

Patients

We included 34 consecutive patients with surgical repair of TOF who underwent VT CA in our arrhythmia department between 1990 and 2012. Patients referred for preoperative electrophysiological study or who had other CHDs, such as pulmonary valvular stenosis or ventricular septal defect, were excluded. All patients had symptomatic VT, either sustained or non-sustained, but incessant on Holter electrocardiogram monitoring. Surgical repair of TOF was performed during an extended period ranging from 1962 to 1987, at a variable age, with or without previous palliative anastomosis, reflecting the evolution in surgical management of TOF. All ventricular septal defects were closed using a transventricular approach.

Electrophysiological study and endocardial mapping

Programmed ventricular stimulation was performed with three extrastimuli, at two drive cycle lengths of 600 and 400 ms, using a 6-Fr bipolar catheter placed at the right ventricular (RV) apex and the RVOT, until induction of sustained VT. When no VT could be induced, the same protocol was repeated under isoproterenol infusion. The induced VT was considered clinical when the 12-lead electrocardiogram morphology was identical to the documented VT with the same rate ± 20 bpm.

Endocardial mapping was performed during VT with a quadripolar ablation catheter under fluoroscopic guidance. The region of interest was identified by the presence of negative unipolar potentials (filter 0.05–500 Hz) and early bipolar potentials (presystolic or diastolic) to the surface electrocardiogram QRS complex. As described by Stevenson et al. [15], entrainment pacing identified slow-conduction zones corresponding to VT critical isthmus. When VT was not inducible ($n = 1$), pacemapping was performed near the RVOT scar (<0.2 mV), and in the presence of late potentials during sinus rhythm. After 1999, electroanatomical mapping was used for 13 patients (CARTO®, Biosense Webster Inc., Diamond Bar, CA, USA; and NavX™, St Jude Medical Inc., St. Paul, MN, USA). These systems allowed identification of scar areas corresponding to ventriculotomy, RVOT patch or ventricular septal defect, defined by a bipolar voltage < 0.5 mV. Dense scar was defined by a bipolar voltage < 0.1 mV with no capture by pacing. Activation mapping identified, as described [16], the earliest activation site and the VT mechanism (focal or macroreentry). Activation mapping also determined the isthmus type according to the anatomical classification of macroreentrant VT isthmuses in repaired TOF by Zeppenfeld et al. [8]: isthmus 1 between the anterior tricuspid annulus and ventriculotomy or RVOT patch; isthmus 2 between the anterior pulmonary valve and ventriculotomy or RVOT patch; isthmus 3 between the posterior pulmonary valve and ventricular septal defect patch; and isthmus 4 between the ventricular septal defect patch and posterior tricuspid annulus.

CA

Direct-current ablation (DCA) alone ($n = 2$) was performed between November 1990 and January 1992, using quadripolar USCI catheters (BARD, Murray Hill, NJ, USA) with 3 J/kg anodic shocks. From 1992 to 1996, ablation was achieved with 4 mm-tip catheters and 50 W radiofrequency generators ($n = 5$). From 1997 to 2006, 8 mm-tip and/or 4 mm irrigated catheters and 150 W radiofrequency generators were used ($n = 16$). From 2006 to 2012, all ablations were performed with 4 mm irrigated catheters ($n = 12$), except for one procedure in 2010 with an 8 mm-tip ablation catheter. From 1993 to 2003, when radiofrequency alone failed to terminate VT, modified DCA (consisting of a double 160 J cathodic shock delivered by the ablation catheter) was performed under deep general anaesthesia and curarization ($n = 13$). Final programmed ventricular stimulation was carried out after CA. Primary success was defined as VT termination during CA and inability of final programmed ventricular stimulation to induce any sustained VT without and with isoproterenol infusion. An indeterminate result was defined as the ability to induce a non-clinical sustained VT by programmed ventricular stimulation after CA, or when no VT was inducible at the beginning and end of the session. Failure was defined as the absence of VT termination by CA or by clinical VT inducibility at the end of the procedure.

Following the CA, patients were monitored in the cardiac intensive care unit for 48 hours, after which they were discharged from hospital if no complication had occurred.

Follow-up

Patients were referred to their primary cardiologist for follow-up. Control programmed ventricular stimulation was performed 7–30 days after CA in 19 patients. Control programmed ventricular stimulation was considered positive when any sustained VT was induced.

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Need for redo CA in the first 3 months after CA for early clinical VT recurrence was not considered as VT recurrence during follow-up, and the beginning of the follow-up period was set as the date of the last ablation.

Long-term outcome was assessed retrospectively by inpatient visits, and was completed by telephone calls. VT recurrence was defined as recurrence of symptomatic VT, either sustained or unsustained, documented by Holter electrocardiogram monitoring, or the need for antitachycardia pacing therapy or the need for redo CA 3 months after the initial procedure.

Statistical analysis

The alpha risk value was set at 0.05. All statistical analyses were performed with IBM SPSS Statistics, version 23 (IBM Corp., Armonk, NY, USA). The log-rank test was used to compare survival of multiple groups. Univariate analyses were performed with the Cox proportional hazards model. The study was approved by our institutional review board.

Results

Patients

Thirty-four patients with repaired TOF underwent VT CA in our centre between 1990 and 2012. Patient characteristics are summarized in Table 1. A transventricular approach was performed in every patient, and a RVOT patch was used in 94%. An abnormal coronary distribution was present in 18%. Among the 14 patients (41%) who underwent reintervention before CA, four had pulmonary valve replacement, two had pacemaker implantation and one had ICD implantation for VT secondary prevention. Two patients had undergone previous CA of atrial tachyarrhythmia. Fifteen patients (44%) were in New York Heart Association class II or more (mean 1.4 ± 0.6). The mean QRS complex duration was 169 ± 37 ms. Echocardiography showed RV dilatation in 47%, and RV systolic dysfunction in 35%. Accurate evaluation of RV systolic function was not available. Moderate-to-severe pulmonary regurgitation was present in 29%, and moderate-to-severe tricuspid regurgitation in 12%. RVOT aneurysm was observed in 8%. Mean left ventricular ejection fraction (LVEF) was 59 ± 8.6%. Among patients with LVEF < 60%, three had moderate aortic regurgitation, one had a residual ventricular septal defect, one had moderate mitral regurgitation and two had severe left ventricular (LV) systolic dysfunction (LVEF < 35%), in both cases related to myocardial infarction consecutive to surgical injury of an anomalous left anterior descending artery crossing the RVOT.

VT

The mean delay from surgical correction to first symptomatic VT was 21 ± 9.9 years (Table 1). Overall, 59% of patients experienced more than one symptomatic VT episode. VT was sustained in every case except one, which was non-sustained but incessant on Holter electrocardiogram monitoring. The mean number of tried antiarrhythmic medications was 2.1 ± 1.5. Antiarrhythmic therapy is detailed in Table 1. Syncope was present in 32%, haemodynamic instability in 9% and congestive heart failure in 6%; 56% of patients had a single documented VT morphology and 38% had two documented morphologies, while two patients had three and five documented morphologies, respectively; 74% of the clinical VTs had left bundle branch block QRS morphology (Fig. 1), and 71% had an inferior axis of 90° to 120°.

Table 1 Population and arrhythmia characteristics ($n = 34$).

Variable	
Patients	
Age at surgical correction	5.4 years (3 months to 22.7 years)
Male sex	20 (59)
Irregular TOF	9 (24)
Transannular patch	22 (65)
Previous palliative shunt	12 (35)
Reoperation following surgical correction	14 (41)
Previous ICD	1 (3)
Antiarrhythmic therapy	31 (91)
Amiodarone	20 (59)
Beta-blocker	17 (50)
Class I drug	8 (24)
Sotalol	4 (9)
QRS complex duration ≥180 ms	10 (29)
RV systolic dysfunction	12 (35)
Moderate to severe PR	10 (29)
LVEF < 60%	7 (21)
VT	
Age at first documented VT (years)	27 ± 11.3
>1 documented VT morphology	16 (46)
VT rate (bpm)	225 ± 95
Poor clinical tolerance[a]	20 (59)

Data are expressed as median (range), number (%) or mean ± standard deviation. ICD: implantable cardioverter-defibrillator; LVEF: left ventricular ejection fraction; PR: pulmonary regurgitation. RV: right ventricular; TOF: tetralogy of Fallot; VT: ventricular tachycardia.

[a] Poor clinical tolerance is defined by symptoms such as dizziness, syncope, haemodynamic instability or heart failure caused by VT.

Electrophysiological study and CA

Mean age at VT CA was 31.2 ± 10.3 years, with a mean delay from first symptomatic VT to VT CA of 4.7 ± 6.6 years. For the 12 procedures after 2009, this delay was reduced to 9.2 ± 8.7 months. The electroanatomical mapping system was used systematically from 2005 (35% of patients). Programmed ventricular stimulation induced a sustained and clinical VT in all but one patient, for whom substrate-based ablation was performed in the peritricuspid region where late potentials were recorded in sinus rhythm. A single sustained VT was induced in 38% of patients, two in 38% and

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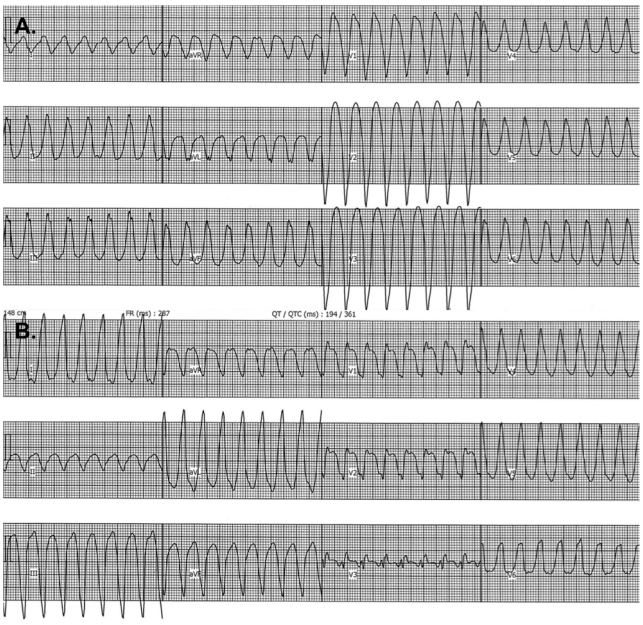

Figure 1. Two examples of clinical monomorphic ventricular tachycardias (VTs) in repaired tetralogy of Fallot. A: inferior-axis left bundle branch block-morphology VT (255 bpm) in a 27-year-old patient referred for syncopal episodes; this morphology was the most common VT morphology in our population. B: left-axis left bundle branch block-morphology VT (260 bpm) in a 47-year-old patient, responsible for haemodynamic instability.

more than two in six patients (26%), with a maximum of five different morphologies (Table 2). The mean rate of induced VTs was 204 ± 32.7 bpm. A slow-conduction zone was present in all inducible patients. Over a total of 42 ablation sites, 79% were located at the RVOT (67% anterior; 12% septal), and the remaining 21% were located at the mid anterior wall of the RV. For 13 patients, electroanatomical mapping systems allowed identification of scar regions in repaired TOF RVs (Fig. 2) and precise reentry circuit characterization (Fig. 3). Isthmus 1 was the most frequent target. Despite 62% of patients having more than one inducible VT, 76% of patients had a single ablated site, with a maximum of two ablated sites. The median number of radiofrequency applications was 10 (range 1—27); median radiofrequency time was 325 s (range 54—1690 s), with a mean procedural time of 185 ± 69 min and a mean fluoroscopic time of 37 ± 35 min.

Table 2 Electrophysiological study and catheter ablation ($n = 34$).

Variable	
Age at procedure (years)	32 ± 10.3
Electrophysiological study	
Number of induced VT morphologies	2 (1—5)
>1 induced morphology	21 (62)
Ablation energy	
DCA alone	2 (6)
Radiofrequency followed by DCA	10 (29)
Radiofrequency alone	22 (65)
Ablation sites	
Number of ablated sites	1 (1—2)
Two ablated sites	8 (24)
RVOT targeted	21 (85)
RV targeted	5 (15)
Electroanatomical mapping-assisted procedures	13 (59)
Isthmus 1 targeted	7 (58)
Isthmus 2 targeted	3 (25)
Isthmus 3 targeted	3 (25)
Isthmus 4 targeted	1 (3)
Early results	
Success	28 (82)
Indeterminate	5 (15)
Failure	1 (3)
Control programmed ventricular stimulation[a]	19 (56)
Negative	16 (84)
Positive[b]	3 (16)
Early redo CA[c]	7 (21)

Data are expressed as mean ± standard deviation, number (%) or median (range). CA: catheter ablation; DCA: direct-current ablation; RV: right ventricle; RVOT: right ventricular outflow tract; VT: ventricular tachycardia.
[a] In the first month following CA.
[b] Inducibility of any sustained VT.
[c] In the first 3 months following CA, for early clinical VT recurrence.

Early results

In the only procedure that resulted in primary failure, electromechanical dissociation occurred after VT induction, requiring the interruption of the procedure and cardiopulmonary resuscitation, which was successful; this was the only major complication in the study population. Two early minor complications occurred: one femoral pseudoaneurysm and one pneumothorax. For the seven patients who had early clinical VT recurrence after the first ablation, the median delay between the initial and redo procedures was 0.9 months (range 0.4—2.43 months). Three patients who had an RVOT aneurysm required three procedures during this period. Primary success was obtained after the last ablation in every patient requiring early redo CA. There were 42 procedures in total. Since 2004, no early redo procedure was performed.

Long-term results

Kaplan—Meier representations of event-free survival and survival are shown in Fig. 4. Mean follow-up time was 9.5 ± 5.2 years. Freedom from death, VT recurrence and ICD appropriate shock was 94% at 5 years, 81% at 10 years and 70% at 20 years (Fig. 4A). Survival was 100% at 5 years and 91% at 20 years (Fig. 4B). Baseline LVEF < 60% was significantly associated with arrhythmia recurrence following VT CA (hazard ratio 16.4, 95% confidence interval 1.8—147; $P = 0.01$) (Fig. 4C). Other variables, such as age at procedure, baseline QRS complex duration, RV dysfunction and VT CA immediate result, were not statistically associated with long-term outcome following VT CA (Table 3). There

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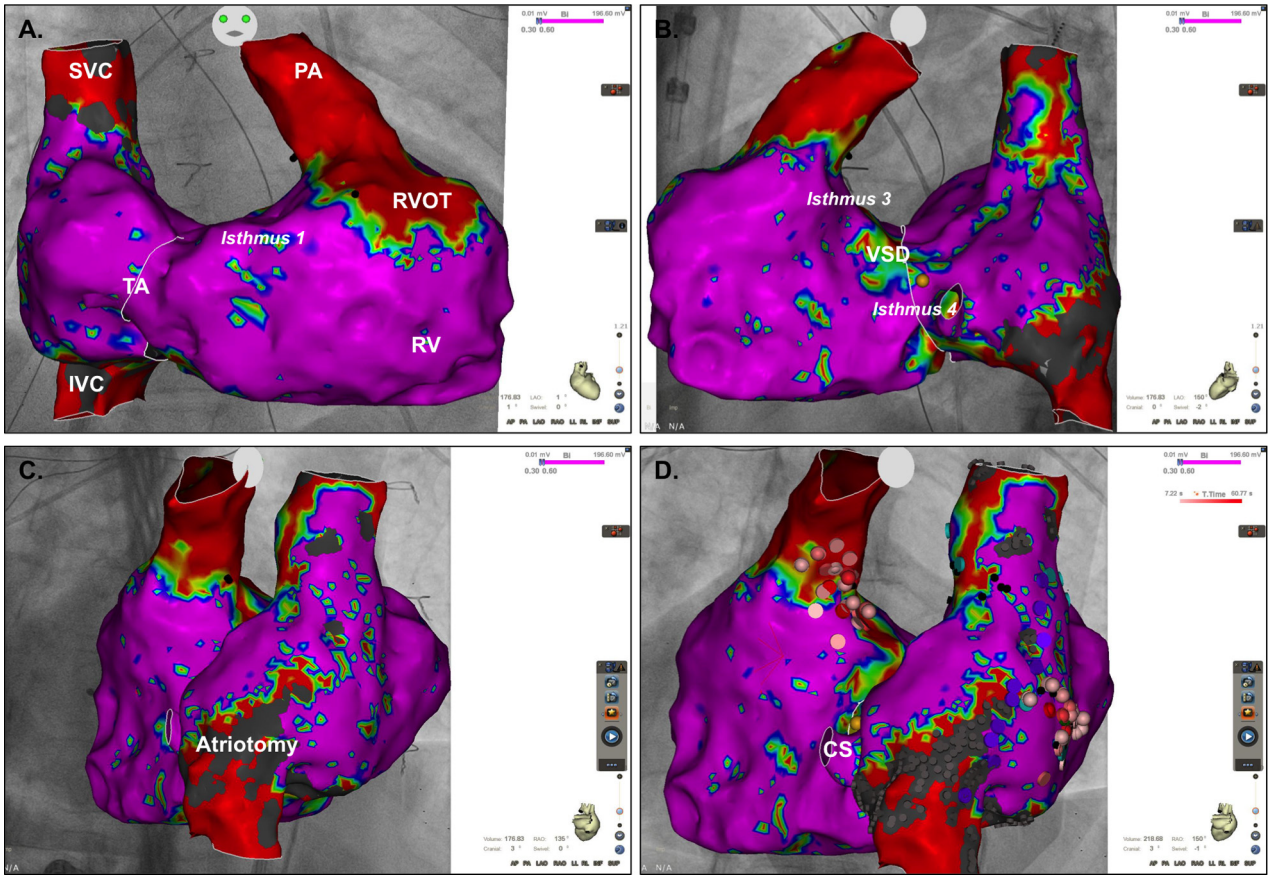

Figure 2. Bipolar voltage map in sinus rhythm showing right ventricle (RV) scar areas and anatomical isthmuses in a repaired tetralogy of Fallot patient undergoing ventricular tachycardia catheter ablation. A: right anterior oblique view of the three-dimensional bipolar voltage map of the right cavities merged to conventional fluoroscopy (CARTO® 3 UniVu™ electroanatomical mapping system; Biosense Webster Inc., Diamond Bar, CA, USA). Regions in red have low-amplitude local electrograms (0.01—0.30 mV) corresponding to scar areas unresponsive to pacing. Regions in purple correspond to normal myocardium. Regions in grey in the right atrium correspond to dense surgical scar consecutive to atriotomy or cannulation. Black dots indicate fragmented and late potentials in sinus rhythm. A large scar area in continuity with the pulmonary annulus (PA) is seen in the anterosuperior portion of the RV, corresponding to a transannular right ventricular outflow tract (RVOT) patch. Isthmus 1 is located between the RVOT patch and the lateral tricuspid annulus (TA). B: septal view. The scar area corresponding to the ventricular septal defect patch is identified in its usual superior position, anterior to and above the His bundle (yellow ball). Isthmus 3 is located between the pulmonary annulus and the ventricular septal defect patch, and isthmus 4 is between the ventricular septal defect patch and the TA. C: posterior view. A large scar area in the posterior right atrium is identified and corresponds to the atriotomy. Fragmented potentials are seen in the isthmus 3 region. D: posteroseptal view. Radiofrequency applications are delivered in the isthmus 3 region (light pink to red balls). CS: coronary sinus; IVC: inferior vena cava; SVC: superior vena cava.

was no statistical interaction between LVEF and RV dysfunction ($P = 0.2$). No adverse event occurred in the follow-up period of patients who underwent VT CA during or after 2009, although statistical significance could not be demonstrated (Fig. 4D) because of the absence of event in this subgroup. There were two deaths during follow-up and four VT recurrences, which included two ICD appropriate shocks.

One patient died in 2005 (aged 35 years) of ventricular fibrillation, 7.3 years after VT CA; he had severe RV dilatation and systolic dysfunction related to severe pulmonary and tricuspid regurgitation. Before VT CA, he underwent pacemaker implantation following His bundle CA for uncontrolled atrial tachyarrhythmia, for which he underwent radiofrequency CA later during follow-up. He also had severe LV systolic dysfunction (LVEF 26%) related to myocardial infarction during surgical correction and moderate aortic regurgitation. He had a single successful VT CA procedure. Necropsic study showed areas of fibrofatty remodelling in the RVOT, but also in the left ventricle (LV) (Fig. 5A).

Another patient died at the age of 39 years of ventricular fibrillation, 7.4 years after VT CA; he underwent pulmonary valve replacement at the age of 20 associated with LV-to-right atrium fistula closure and tricuspid annuloplasty. He was left with severe RV dysfunction, right-sided congestive heart failure, moderate mitral regurgitation and mild LV systolic impairment (LVEF 54%). A 12-lead electrocardiogram showed a 200 ms QRS complex and QRS complex enlargement over time (3.8 mm/year), with the appearance of parietal block in right precordial leads (Fig. 5B). The patient underwent a single successful VT CA procedure and left atrial radiofrequency CA during follow-up.

Among the four patients who experienced VT recurrence during follow-up, one had end-stage RV failure leading to heart transplantation, one had LV systolic dysfunction (LVEF

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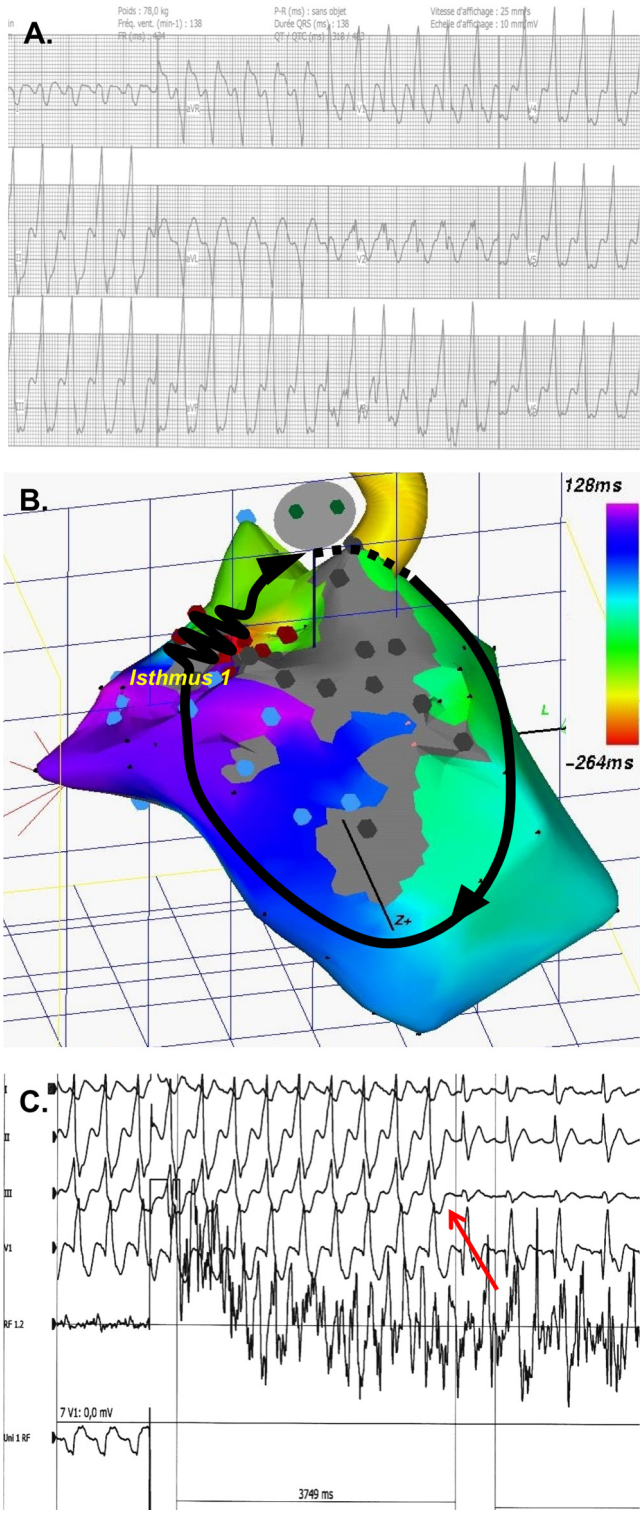

Figure 3. Catheter ablation of macroreentrant ventricular tachycardia (VT) in a repaired tetralogy of Fallot recipient. A: unusual right bundle branch block-morphology VT with positive concordance in the precordial leads. B: three-dimensional VT activation map using the CARTO® system. Colour scale indicates local activation times from the earliest (red) to the latest (purple). All colours are seen within the right ventricle (RV), indicating macroreentry. The slow-conduction zone (sinusoidal black line) is located at the anterolateral wall of the RV, between the transannular right ventricular outflow tract patch and the tricuspid annulus, defining isthmus. 1 — radiofrequency applications are delivered on the slow-conduction zone (red dots). The right bundle branch block morphology with positive concordance is explained by the initial superior and basal septal activation related to a posterior VT exit beneath the pulmonary annulus C: VT termination (red arrow) after 3.7 s of successful radiofrequency application in the slow-conduction zone.

35%), related to myocardial infarction during surgical correction, and one had mild LV systolic dysfunction (LVEF 52%) related to moderate aortic regurgitation. RV systolic dysfunction was present in two out of four of these patients. These four patients had a single successful procedure, but two of the four had a positive control programmed ventricular stimulation during follow-up.

Antiarrhythmic therapy was discontinued in 71% of patients. Nineteen patients (56%) underwent programmed ventricular stimulation later during follow-up, which was positive in three patients. Two patients required heart transplantation for end-stage RV failure. Surgical reintervention was necessary for seven patients (21%), with six pulmonary valve replacements and one Bentall surgery. Five patients (15%) underwent atrial tachyarrhythmia CA.

ICD implantation

Eight (24%) patients underwent ICD implantation during follow-up. Two were implanted epicardially during surgical reintervention. Two were implanted for documented infrahisian block. Three patients with end-stage RV failure were implanted (bridge-to-heart transplantation in two). Two patients received an ICD for VT recurrence during follow-up. Three patients had ICD complications: two inappropriate shocks for SVT in two; and lead fracture in one.

Discussion

We report the long-term results of a large series of MVT CA in adults with repaired TOF over a 26-year period, reflecting the evolution of CA techniques from a focal approach during VT to substrate-based mapping and ablation. Despite a high rate, MVTs were inducible in all but one patient, and mappable, with good haemodynamic conditions. As described in previous studies [12,13], electrophysiological studies showed the presence of a slow-conduction zone in all patients, a finding that confirms that MVTs in repaired TOF are related to macroreentry around RV surgical scars, mainly within the RVOT. Based on the anatomical classification proposed by Zeppenfeld et al. [8], we observed a predominance of isthmus 1 (ventriculotomy or RVOT patch to lateral tricuspid annulus) as the MVT's critical isthmus. This finding underlines the superiority of the transatrial over the transventricular approach for ventricular septal defect closure in TOF, and supports recent results stating that empirical cryosurgery of isthmus 1 during reintervention, such as pulmonary valvular replacement, might be beneficial [17]. Despite an average number of two clinical and inducible VT morphologies per patient, CA was successfully achieved by targeting a single site for most patients, suggesting that several different VTs can share the same circuit, circling around RV scars in opposite directions. A small but

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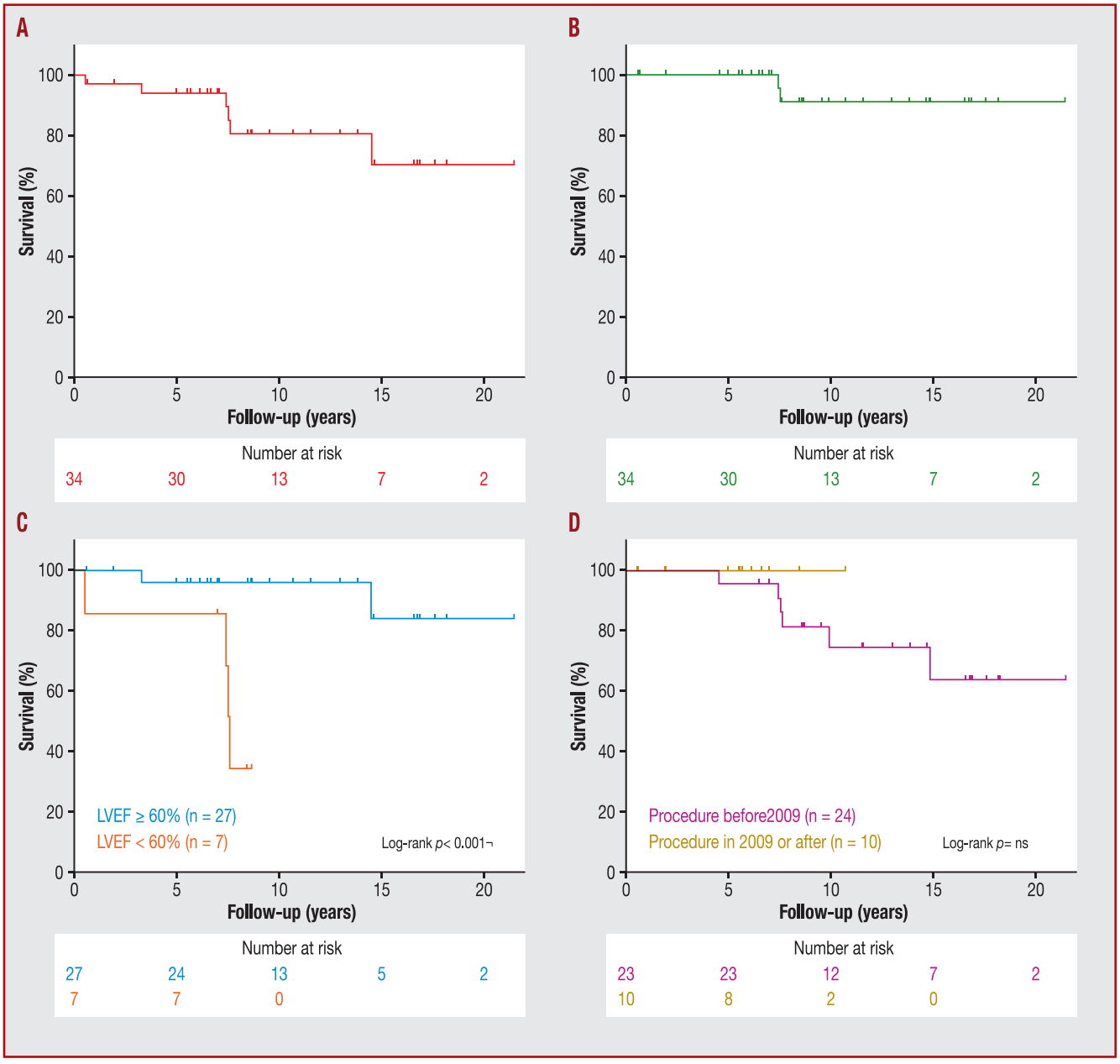

Figure 4. Long-term results. A, C and D: Kaplan–Meier estimates of freedom from death, ventricular tachycardia (VT) recurrence and implantable cardioverter-defibrillator (ICD) appropriate shock. B: Kaplan–Meier estimate of survival. LVEF: left ventricular ejection fraction.

significant proportion of VTs had right bundle branch block QRS complex morphology. This should not mislead electrophysiologists into performing an LV approach, given that all patients presenting right bundle branch block morphology had satisfactory criteria for RV macroreentry. However, some authors suggest that some VT CA failures might be explained by the presence of septal isthmuses requiring left-sided CA [18], a situation that we did not encounter. An important consideration is the presence of RVOT aneurysm, which reduced CA efficacy considerably in our experience.

Seven patients required early redo CA. In these cases, which took place before 2004, the first procedure used DCA alone or radiofrequency with a 4 mm-tip catheter combined with DCA, and was not guided by electroanatomical mapping. For these reasons, we considered that early redo CA did not qualify as arrhythmia recurrence during follow-up. With a 70% rate of 20-year survival free of VT recurrence, we report encouraging results of monomorphic VT CA in a cohort of 34 patients with sustained VT and repaired TOF. VT CA allowed antiarrhythmic therapy discontinuation in 71% of the patients, which is of importance in a young population exposed to long-term drug side-effects, which are particularly frequent with amiodarone, which was prescribed in 59% of the patients before ablation. To our knowledge, this is the largest published series of CA of symptomatic VT in adults with repaired TOF, and has the longest follow-up – an important feature, given that adverse events in repaired TOF occur mostly after the 20th year following surgical correction [19]. Thus, in our study, long-term arrhythmia-free survival also reflects the evolution of

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Table 3 Univariate predictors of death, ventricular tachycardia recurrence and implantable cardioverter-defibrillator appropriate shocks.

Variable	Hazard ratio (95% CI)	*P*
Age at surgical repair	1 (0.83—1.21)	0.9
Age at procedure	1 (0.93—1.10)	0.8
Time between first VT and VT CA	1 (0.94—1.16)	0.5
QRS complex duration	1 (0.99—1.04)	0.23
QRS complex duration ≥180 ms	0.42 (0.08—2.29)	0.3
RV systolic dysfunction	0.19 (0.03—1.04)	0.056
Moderate to severe PR	1.7 (0.2—14.65)	0.6
LVEF ≤ 60%	16.35 (1.82—147)	0.013
>1 induced VT morphology	3.43 (0.4—29.4)	0.26

CA: catheter ablation; CI: confidence interval; LVEF: left ventricular ejection fraction; PR: pulmonary regurgitation RV: right ventricular; VT: ventricular tachycardia.

structural heart disease, which is entangled with arrhythmogenesis. With two ventricular fibrillations occurring during follow-up, we report a small risk of sudden cardiac death among our population; these two patients had a reduced LVEF. Although results from Cox regression should be interpreted with caution in our small population with a low event rate, we identified LV systolic dysfunction as a predictor of unfavourable outcome following VT CA. LV dysfunction has been previously identified as a risk factor for sudden cardiac death in repaired TOF patients, especially when combined with classical criteria, such as QRS complex enlargement [20,21]. Elevated LV filling pressure predicted appropriate shocks in 121 patients with repaired TOF and ICD implanted for primary or secondary prevention [11]; and in a large cohort of 413 patients with repaired TOF, Diller et al. identified LV longitudinal dysfunction as a strong predictor of life-threatening arrhythmias [22]. One possible mechanism of LV dysfunction in repaired TOF is RV-LV interaction [20]. Our RV function evaluation was qualitative, and we did not have enough patients to perform robust interaction analysis. However, LV systolic impairment seemed rather to be related to ischaemic cardiomyopathy or left valvular diseases. With histological proof of extensive LV fibrosis, one patient had a clear substrate for LV arrhythmia. We hypothesize that arrhythmic events observed in our population might be related, in part, to LV dysfunction, and it is possible that the two sudden cardiac deaths were related to malignant arrhythmias with an LV origin.

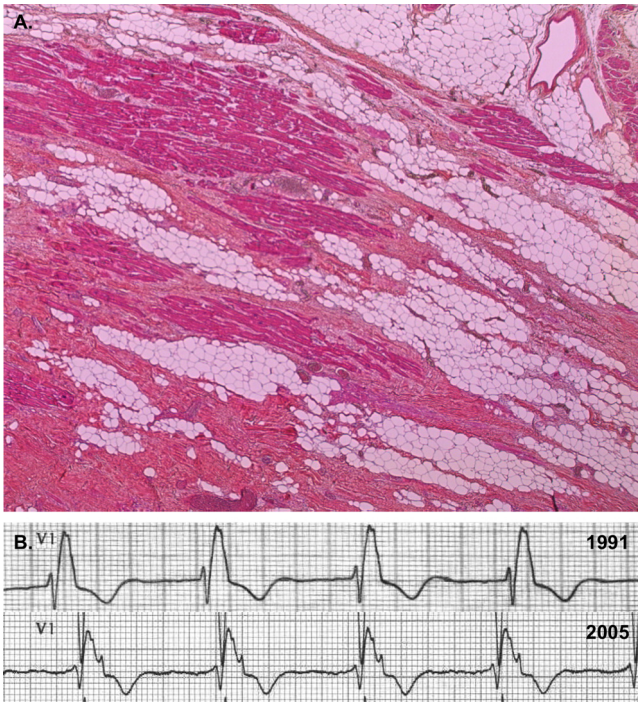

Figure 5. Two cases of sudden cardiac death. A: patient 1: necropsic study showing left ventricular fibrofatty remodelling consecutive to myocardial infarction (2.5× magnification; haematoxylin—eosin staining). B: patient 2: QRS complex evolution in a subject who presented ventricular fibrillation-related sudden cardiac death in 2005; there is a marked QRS complex enlargement over time and the apparition of a pseudoepsilon wave in V1, corresponding to right ventricular parietal block.

In our study, conventional sudden cardiac death risk factors, such as RV function and QRS complex duration, were not associated with adverse prognosis following VT CA. In their more powered study, Kapel et al. did not show any statistical association between VT inducibility and RV function [6]. One explanation could be that while RV dysfunction plays an important role in arrhythmogenesis, it does not impair successful CA of MVTs.

The two patients who died of sudden cardiac death were not followed by a multidisciplinary team, and did not have ICD implantation, despite an associated ischaemic cardiomyopathy, with LVEF < 35% in one and severe RV failure in the other. Nevertheless, our results suggest that most of our population would not have required an ICD, which have many caveats in grown-up CHD. In primary prevention settings, appropriate ICD intervention rates are low compared with ischaemic cardiomyopathy, another paradigm of macroreentrant VT [23], and device-related complications and inappropriate therapies occur in 30—50% [20]. In accordance with current guidelines [4,24], we believe that some repaired TOF patients with symptomatic MVTs and preserved biventricular function might be cured by CA, with no need for an ICD, although great attention should be given to patients with LV systolic dysfunction, even if mild.

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Study limitations

The main limitation to our study was the heterogeneity of CA techniques, with a significant proportion of CA procedures using DCA, reflecting more than 20 years of evolution of CA. This complicates the interpretation of short-term outcomes and the need for early redo CA. In addition, given the great improvements in the surgical and haemodynamic management of patients with repaired TOF over the years, the arrhythmia-free survival rates of our patients might differ significantly from patients undergoing VT CA in the contemporary era. Another limitation is the low proportion of electroanatomical mapping-guided procedures, which limits insights gained by our study into the electrophysiological comprehension of TOF ventricular arrhythmias. Finally, retrospective echocardiographic assessment of RV function was also limited.

Conclusions

CA can safely address macroreentrant MVT in patients with repaired TOF, with an acceptable long-term rate of recurrence in this high-risk population. Anatomical classification of isthmuses with electroanatomical mapping provides reproducible endpoints for CA. Attention should be given to LV systolic function in risk assessment and selection of candidates for ICD.

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Disclosure of interest

The authors declare that they have no competing interest.

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