

Predictors of Acute Failure Ablation of Intra-atrial Re-entrant Tachycardia in Patients With Congenital Heart Disease: Cardiac Disease, Atypical Flutter, and Previous Atrial Fibrillation

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Background—Intra-atrial re-entrant tachycardia (IART) in patients with congenital heart disease (CHD) increases morbidity and mortality. Radiofrequency catheter ablation has evolved as the first-line treatment. The aim of this study was to analyze the acute success and to identify predictors of failed IART radiofrequency catheter ablation in CHD.

Methods and Results—The observational study included all consecutive patients with CHD who underwent a first ablation procedure for IART at a single center from January 2009 to December 2015 (94 patients, 39.4% female, age: 36.55 ± 14.9 years). In the first procedure, 114 IART were ablated (acute success: 74.6%; 1.21 ± 0.41 IART per patient) with an acute success of 74.5%. Cavotricuspid isthmus—related IART was the only arrhythmia in 51%; non—cavotricuspid isthmus—related IART was the only mechanism in 27.7% and 21.3% of the patients had both types of IART. Predictors of acute radiofrequency catheter ablation failure were as follows: nonrelated cavotricuspid isthmus IART (odds ratio 7.3; confidence interval [CI], 1.9-17.9; P=0.04), previous atrial fibrillation (odds ratio 6.1; CI, 1.3-18.4; P=0.02), transposition of great arteries (odds ratio, 4.9; CI, 1.4-17.2; P=0.01) and systemic ventricle dilation (odds ratio 4.8; CI, 1.1-21.7; P=0.04) with an area under the receiver operating characteristic curve of 0.83 ± 0.056 (CI, 0.74-0.93, P=0.001). After a mean follow-up longer than 3.5 years, 78.3% of the patients were in sinus rhythm (33.1% of the patients required more than 1 radiofrequency catheter ablation procedure).

Conclusions—Although ablation in CHD is a challenging procedure, acute success of 75% can be achieved in moderate—highly complex CHD patients in a referral center. Predictors of failed ablation are IART different from cavotricuspid isthmus, previous atrial fibrillation, and markers of complex CHD (transposition of great arteries, systemic ventricle dilation). (*J Am Heart Assoc.* 2018;7:e008063. DOI: 10.1161/JAHA.117.008063.)

Key Words: ablation • congenital heart disease • flutter

The prognosis of patients with congenital heart disease (CHD) has improved considerably in recent years¹ because of early diagnosis and better surgical results. Intraatrial re-entrant tachycardia (IART) has become a common and potentially lethal complication during the follow-up of

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© 2018 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes. patients with CHD, with a general incidence of $25\%^2$ and even higher (up to 40%–50%) in more complex cardiac diseases.^{3–7} Atrial scars related to previous cardiac surgeries, atrial fibrosis, and cardiac residual lesions leading to hemodynamic atrial overload create slow conduction areas that are the main mechanisms for re-entry.^{2,3,8–16} IART is more related to increased morbidity (heart failure, stroke) and mortality in patients with CHD than other potentially severe complications such as ventricular arrhythmias or heart failure.^{7,17–24} Antiarrhythmic drugs are often unsuccessful to maintain sinus rhythm in these patients, and side effects are frequent.^{25,26} In recent years, radiofrequency catheter ablation (RF) has become the first line treatment for IART in this population.²⁷ Data about predictors of acute success/failure are lacking.

The aim of this study was to assess acute success of IART in a single referral center and to analyze predictors of acute

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Clinical Perspective

What Is New?

- Congenital heart disease complexity (transposition of great arteries and dilation of systemic ventricle) and noncavotricuspid isthmus-related intra-atrial re-entrant tachycardia are factors related to ablation failure.
- · Atrial fibrillation (previous or induced during the ablation procedure) is strongly related to ablation failure.

What Are the Clinical Implications?

• The knowledge of factors related to ablation failure can help in management of patients with congenital heart disease (ablation versus conservative approach, lenient versus strict follow-up).

failure in a large cohort of CHD with a high proportion of moderate to highly complex cardiac defect.

Methods

The data, analytic methods, and study materials will be made available to other researchers for purposes of reproducing the results or replicating the procedure by request to the corresponding author. The ethics review board of our institution approved the study and all patients gave informed consent.

Study Population

This was an ambispective observational single-center study of all consecutive patients who had CHD and who underwent a first ablation procedure for IART in a tertiary referral center. Ablation procedures for recurrences were not included in this study. From January 2009 to December 2015, 94 patients with CHD underwent a first ablation procedure for IART. Clinical data, ECG in sinus rhythm and during IART, and echocardiographic, ablation, and mapping data were recorded. Baseline ECG in sinus rhythm and echocardiogram data were collected from the last tests performed before ablation (<6 months before ablation). Types of cardiac disease and degree of complexity were defined according to CHD patient management guidelines.²⁸ When possible, conventional left ventricular and right ventricular echocardiography measurements following current guidelines were performed. Qualitative assessment was performed in complex anatomies, such as transposition of great arteries (TGA) or univentricular physiology. Quantitative assessment of the right and left atrium area was performed via a 4-chamber apical view. In the absence of a cut-off value in the current guidelines, we considered severe dilatation of right atrium when the area in the 4-chamber apical view was $>40 \text{ cm}^2$.

Electrophysiological Study

duodecapolar catheter around the tricuspid annulus (7F Livewire[™], St Jude Medical) were initially introduced in all patients through the femoral vein, except in those who underwent atrial switch procedures or Fontan patients in whom only a duodecapolar catheter was initially used to record atrial signals. For these exceptions, the catheters were positioned between the inferior and superior vena cava in patients with atrial switch procedures or in the intracardiac tube or esophagus in Fontan patients. A multielectrode noncontact mapping catheter (Array[™], 10F, St Jude Medical) was used in the case of nonmappable IART because of lack of sustainability or poor hemodynamic tolerance. For ablation, cooled-type or conventional ablation catheters (7F Boston[™] EPT Blazer, 7F Therapy[™] Cool Flex[™], St Jude Medical; 7F Tacticath Quartz[™], St Jude Medical; 7F Carto Navistar[™], Biosense Webster; 7F Thermocool[™] Biosense Webster) were used. Atrial stimulation protocol for induction after ablation (or before ablation in patients in sinus rhythm at the beginning of the procedure) was performed. Stimulation protocol was the following: Progressive atrial pacing until loss of atrial capture and atrial programmed pacing with basic pacing cycle of 600 or 500 ms (depending on patient heart rate) and introduction up to 2 extrastimuli with 200 ms as maximum coupling interval. If IART was not induced after baseline stimulation, the protocol was repeated under isoproterenol infusion. Activation mapping with a 3-dimensional navigation system (NavX Ensite, Ensite Velocity or Ensite Precision[™], St Jude Medical or Carto XP or Carto 3[™], Biosense Webster) was performed in all patients. If IART was not present at the onset of the procedure, it was induced using programmed electric stimulation. Activation maps were analyzed before ablation. Critical isthmus of the IART was defined as the point where entrainment (pacing 20-30 ms faster than tachycardia cycle length) produced local concealed fusion²⁹ and the postpacing interval was ± 30 ms tachycardia cycle length. Concealed fusion was determined by no change in activation sequence in the duodecapolar or decapolar catheter during entrainment compared with activation during tachycardia. Entrainment and concealed fusion could be studied in 95.7% of the patients. Areas of scar were delineated from peak-to-peak amplitude of a bipolar electrogram, using a cut-off value of 0.5 mV.³⁰ During ablation, temperature and power were limited to 43°C and 30 to 40 W for irrigated-tip catheter (81% of the procedures) and 60°C to 70°C and 60 to 70 W for no cooled catheter. Ablation success was defined as termination of IART and noninducibility of any kind of IART for all patients. For patients with cavotricuspid isthmus (CTI)-related IART, a line of bidirectional cavotricuspid conduction block was also required for complete success. For non-CTI-related IART, an

Table 1. Baseline Characteristics

Baseline Characteristics			
Age, y	36.55±14.9 (5–83)		
Number of operations	1.7±0.99 (1-4)		
Male sex	60.6 (57)		
Functional class (NYHA classification) III-	V	13 (13.9%)	
Degree of cardiac disease complexity			
I	9 (9.6)		
II	47 (50)		
Ш		38 (40.4)	
Cardiac disease			
Great vessel transposition	27 (28.8)		
Atrial switch procedure (Senning/Mu	istard)	23 (85.2)	
Congenitally corrected		2 (7.4)	
Arterial switch procedure (Jatenne)		2 (7.4)	
Tetralogy of Fallot		21 (22.3)	
Atrial septal defect		15 (16.1)	
Isolated		12 (80)	
Associated with other cardiac lesion	IS	3 (20)	
Single ventricle physiology	10 (10.6)		
Glenn surgery	3 (27.2)		
Systemic-pulmonary fistulas	2 (18.2)		
Fontan surgery	1 (9.1)		
Other	4 (45.5)		
Ventricular septal defect	7 (7.5)		
Atrioventricular septal defect		7 (7.5)	
Ebstein anomaly		5 (5.3)	
Other		2 (2.2)	
Residual cardiac lesion		51 (54.3)	
Previous atrial fibrillation		13 (13.8)	
Previous IART to index episode		47 (50)	
	N	Value	
Basal ECG			
P wave duration	85	85.11±26.1	
PR interval, ms	82	176.1±45.4	
Long PR interval (PR interval >200 ms)	85	26.7 (23)	
QRS duration, ms	86	133.4±32.7	
Ventricular pacing 94		8 (8.5)	
Conduction disturbance 86		70 (81.4)	
Right bundle branch block	Right bundle branch block		
Isolated	Isolated		
Associated with left anterior fascicular block	14 (16.4)		

Continued

Table 1. Continued

	N	Value
Isolated left anterior hemiblock		4 (4.6)
Left bundle branch block		1 (1.8)
Basal echocardiogram		
Moderate-to-severe dilation of systemic ventricle	90	13 (13.8)
LVEDD, mm	82	46.22±9.7 (23–75)
LVESD, mm	77	31.74±9.7 (13–62)
Septum thickness, mm	75	9.8±2.02 (6–16)
Systemic ventricle posterior wall thickness, mm	75	9.7±2.2 (5–15)
Moderate-to-severe dilation of subpulmonary ventricle	90	25 (26.6)
Systemic ventricle systolic dysfunction	91	38 (41.8)
EF (%)	84	57.7±10.3 (10-80)
Subpulmonary ventricle systolic dysfunction	87	38 (46.2)
Moderate-to-severe systemic atrial dilation	62	20 (32.3)
Moderate-to-severe venous atrial dilation	65	31 (48.5)
Moderate-to-severe systemic AV valve regurgitation	80	29 (36.3)
Moderate-to-severe venous AV valve regurgitation	82	27 (32.9)
Moderate-to-severe pulmonary hypertension	51	12 (24)
Intracardiac shunts	94	29 (30.9)

Data are presented as n (%) or mean±SD and range. AV indicates atrioventricular; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; IART, intra-atrial re-entrant tachycardia; LVEDD, left/systemic ventricle end diastolic diameter; LVESD, left/ systemic ventricle end systolic diameter; NYHA, New York Heart Association.

ablation line was continued between scar tissue and another scar or anatomical barrier (ie, inferior or superior vena cava in case of IART around the atriotomy scar in the posterolateral wall of the right atrium). Conduction across this line was not systematically checked in all patients, so conduction block in the ablation line was not mandatory for complete success, but re-mapping of the ablation line to assure voltage <0.1 mV after ablation was performed in all patients. Conscious sedation or general anesthesia (23% of the patients) was performed according to clinical characteristics of the patients.

Statistical Analysis

Continuous variables are expressed as $mean\pm SD$ and range. Categorical variables are represented by frequencies and percentages. A descriptive analysis of clinical, ECG,



Figure 1. Examples of CTI-nonrelated IART. A, Figure-of-eight IART in a patient with severe dilation of right atrium after palliated tricuspid atresia. Activation map (left panel) shows a figure-of-8 pattern and slow conduction area in intermediate tissue (voltage >0.1 and <0.5 mV, red in right panel) between 2 dense scar areas (gray, voltage <0.1 mV, right panel) related to fibrosis and scarring in dilated venous atrium. B, Clockwise IART in lateral wall of venous atrium (left panel). Circuit is related to intermediate tissue (red and yellow, right panel), inferior vena cava, and small posterior scar (right panel) related to atriotomy for cannulation in venous atrium for surgical repair in a patient with ventricular septal defect. CTI indicates cavotricuspid isthmus; IART, intra-atrial re-entrant tachycardia.

echocardiographic, and procedure-related variables was performed. For univariate analysis of acute failure predictors, the χ^2 or Fisher exact test was used for dichotomous categorical variables (with calculation of 95% confidence interval), ANOVA test for nondichotomous categorical variables, and Student *t* test for continuous variables. Two-tailed values of *P*≤0.05 were considered statistically significant. Variables with a *P*≤0.1 in the univariate analysis were considered for a logistic regression multivariate analysis and receiver operating characteristic curve was created with the multivariate model results. Analyses were performed with SPSS software Mac OS version 20.0 (IBM SPSS Statistics, Chicago, IL).

Results

Clinical Characteristics

Ninety-four patients (39.4% female) with CHD were included in the study (mean age: 36.55 ± 14.9 years). Eighty-five (90.4%) patients had moderately to highly complex cardiac defects (grade II or III). Overall, more than half (54.3%) had residual cardiac lesions (cardiac defects related with CHD diagnosis not corrected with the previous cardiac surgery). The main clinical characteristics of the population are detailed in Table 1.

Half of the patients had experienced previous IART before the episode that prompted the ablation procedure and 47.8%

Table 2. Procedure and IART-Related Data

Procedure Data			
Number of IART ablated/patient	1.21±0.41		
IART cycle length, ms	272.3±41.3		
Use of 3D navigation system	100 (94)		
Number of activation map points	287.17±134	.34 (118–421)	
Pathological atrial tissue in right atrium (voltage <0.5 mV)	95.7 (90)		
Procedure time, min	199.6±78.6	(62–405)	
Irrigated-tip catheter*	81.9 (77)		
Radiofrequency time, s 1140.4±716		.8 (73–3464)	
Number of vascular accesses	3.11±0.52 (2	2—6)	
Jugular/subclavian femoral accesses	4.2 (4)		
Transhepatic access	2.1 (2)		
Patients With Non-CTI-IART			
Critical isthmus location, % (n)			
Lateral RA		56.4 (26)	
Posterior/posterolateral RA		24.7 (11)	
Septal RA		6.3 (3)	
Superior vena cava		6.3 (3)	
Anterolateral RA		4.2 (2)	
Systemic atrium		2.1 (1)	
Tissue type in the circuit, % (n)			
Scar (<0.1 mV)		27.8 (13)	
Intermediate (0.1–0.5 mV)		6.5 (3)	
Both		61.1 (28)	
Healthy (>0.5 mV)		4.6 (2)	

CTI indicates cavotricuspid isthmus; 3D, 3-dimensional; IART, intra-atrial re-entrant tachycardia; RA, right atrium.

 * Irrigated-tip catheters were used in 100% of patients with grade II/III of cardiac disease complexity.

patients had received antiarrhythmic drugs before the ablation procedure. In 38 patients (40.4%), a clinically severe event (heart failure, syncope, shock, sudden death, or electromechanical dissociation) occurred in relation to IART, and in 16 patients (17%) symptoms included shock, syncope, sudden death, or electromechanical dissociation. In 21 patients (22.3%), severe symptoms were the first manifestation.

Ablation Procedure

In the 94 patients, 114 IART were ablated (1.21 ± 0.41 IART per patient, cycle length 272.3 ± 41.3 ms). Most of the patients (84, 89.3%) were in IART at the beginning of the procedure. The remaining 10 patients were in sinus rhythm at the time of ablation and in all of them IART was induced. In 5 of those patients the induced arrhythmia was similar to documented clinical IART in



Figure 2. Acute success rate according to CHD diagnosis. CHD indicates congenital heart disease; GVT, great vessels transposition.

terms of F wave cycle length and in F wave morphology. In the other 5 patients, ECG of the clinical IART was not available. Fortyeight patients (51%) had only CTI-related IART, 26 patients (27.7%) had IART unrelated to CTI (scar-related IART), and 20 patients (21.3%) had both types of IART. Examples of non-CTIrelated IART are shown in Figure 1. In patients with IART unrelated to CTI, the critical isthmus was located in the lateral or posterolateral region of the right atrium in 81.1% of the patients. Time from first IART to ablation, procedure duration, and RF delivery time were 37.9±18.1 months, 198.7±78.1 minutes, and 1170.9±735.2 s, respectively. An irrigated-tip catheter was used in 81% of the patients. In patients with TGA with CTI-related IART, a duodecapolar diagnostic catheter was positioned along systemic atria between the superior and inferior vena cava, a tetrapolar catheter was positioned in the subpulmonary ventricle, and when systemic atria needed to be accessed with the ablation catheter it was done retrogradely at first attempt. In 3 patients, a transbaffle puncture was also used in a second attempt. In Fontan patients, a duodecapolar diagnostic catheter was placed in the intracardiac tube for atrial recording and a deflectable tetrapolar catheter was placed retrogradely in a single ventricle.

Details about IART location, procedure, and mapping data are shown in Table 2. Acute success was achieved in 70 patients (74.5%). In 16 patients (17%) IART was stopped during ablation but either IART was inducible at the end of the procedure and/or CTI block was not achieved. In 8 patients (8.5%) IART could not be stopped during RF. The success rate for each subtype of CHD diagnosis is shown in Figure 2.

Ablation Failure Predictors

Several factors were predictors of acute ablation failure in univariate analysis. Main clinical, ECG, echocardiographic, and

Table 3. Univariate Clinical Predictors of RF Failu	ure
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Clinical Factors	N	Success (70)	Failed (24)	OR (95% CI)	P Value
Male sex	94	58.6%	66.7%	1.41 (0.5–3.7)	0.49
НТ	94	2.9%	8.3%	3.09 (0.4–23.3)	0.27
DLP	94	4.2%	4.3%	0.97 (0.1–9.8)	1
DM	94	1.4%	4.2%	3 (0.2–49.9)	0.45
Age, y	94	35.5±14.7	39.4±15.3		0.29
Grade II to III degree of cardiac disease complexity II/III	94	90%	91.7%	1.22 (0.24–6.3)	1
Grade III degree of cardiac disease complexity*	94*	34.3%*	58.3%*	2.68 (11.1–6.9)*	0.04*
TGA*	94*	17.1%*	54.2%*	5.7 (2.1–15.8)*	0.00*
Single ventricle	94	4.9%	12.9%	0.29 (0.03–2.4)	0.44
NYHA III—IV	94	11.4%	16.7%	1.5 (0.42–5.7)	0.49
Age at reparative surgery, y	94	12.9±15.5	13.2±19.9		0.94
Previous palliative surgery	94	24.3%	8.3%	0.28 (0.06–1.3)	0.14
Number of operations	94	1.78±1.04	1.45±0.7		0.17
Wide QRS	86	66.2%	72.2%	1.3 (0.42–4.18)	0.62
QRS duration, ms	86	137.2±33.3	123.1±28.9		0.07
Pacemaker	94	12.9%	12.5%	0.97 (0.24–3.9)	1
P wave duration, ms	86	85.4±24.5	84.1±30.9		0.85
Basal sinus rhythm	94	84.3%	79.2%	0.71 (0.22–2.3)	0.54
Sinus node disease	94	18.8%	33.3%	2.1 (0.76–6.1)	0.14
PR interval, ms	86	173.6±44.7	182.4±47.4		0.43
PR interval >200 ms	86	21.4%	33.3%	1.83 (0.66–5.1)	0.24
Previous atrial fibrillation*	94*	8.6%*	29.2%*	4.4 (1.3–14.8)*	0.02*

Cl indicates confidence interval; DLP, dyslipidemia; DM, diabetes mellitus; HT, hypertension; NYHA, New York Heart Association; OR, odds ratio; RF, radiofrequency catheter ablation; TGA, transposition of great arteries.

*Varaibles with P value < 0.05.

procedure-related factors predictors are shown in Tables 3 through 5 and Figure 3. In multivariate analysis, only scarrelated IART, previous atrial fibrillation (atrial fibrillation documented before the ablation procedure), TGA, and systemic ventricle dilation were the predictors of acute RF failure (Table 6). In Figure 4, the receiver operating characteristic curve of the multivariate model for the prediction of acute failure is shown with an adequate area under the curve: $0.83 {\pm} 0.056$ (0.74 - 0.93).After а follow-up of $44.45{\pm}22.7$ months, 78.3% of the patients were in sinus rhythm (although one third of the patients required more than 1 ablation procedure). Follow-up time was the same in successful or failed ablation patients (46.33±23.3 months versus 42.58±21.8 months, P=0.32).

Discussion

The main findings of this study are the high acute success (74.5%) of IART ablation in patients with moderate or high complex CHD performed in an experienced high-volume

tertiary center, and the identification of some predictors of acute failure such as scar-related IART, previous atrial fibrillation, TGA, and systemic ventricle dilation. Although there was a high proportion of moderate- to high-complex cardiac disease in our population and one third of the patients underwent more than 1 RF procedure, more than 78% of the patients are in sinus rhythm at long-term follow-up.

The acute success rate of 74.5% in our series confirms the data published in the literature, with a success rate ranging from 63% to 90%, $^{14,31-34}$ although definition of success does not always include CTI bidirectional block. $^{35-38}$ Actually, in the largest series where CTI bidirectional block is required to consider ablation as successful, the acute success is lower. 37,39

Very few studies have analyzed the predictors of acute failure. Yap and colleagues³⁴ reported a multicenter series of 130 patients with acute success of 63% and complexity of CHD was related to efficacy of RF. These results were confirmed indirectly by many studies.^{13,40,41} In these studies, most of the patients with failed ablations were patients with



Figure 3. Proportion of RF success in the presence (light grey bars) and absence (black bars) of factors predictors of failure in the univariate analysis. Afib indicates atrial fibrillation; CT, cavotricuspid isthmus; IART, intra-atrial re-entrant tachycardia; RF, radiofrequency catheter ablation; TGA, transposition of the great arteries.

Fontan or atrial switch procedures. In this sense, all patients with failed ablations were patients with high-complex cardiac disease. Another factor reported in the literature is the characteristics of isthmus area, which has lower voltage and lower conduction velocity.⁴² However, these data have not been reported in any other study, so the conclusion of this small study (31 patients) needs to be confirmed.

Procedural or technical aspects of the ablation such as irrigated-tip catheter, 3-dimensional navigation system, and remote ablation have been described as playing a role in the acute success of ablation. Peichl et al in 200343 suggested than 3-dimensional electroanatomical navigation systems could help in these complex patients. More recently, Yap et al³⁴ confirmed that the use of a navigation system was clearly related to ablation success. Irrigated-tip catheter is suggested as a factor related to efficacy,³⁷ although no specific analysis has been made to confirm this and the latest studies use cooled-tip catheter in most of the cases, so no comparative studies between both kinds of catheters are expected to be published. Finally, studies that use remote ablation38,44 report a very high success rate, but the difference from manual ablation is not statistically significant. Cooled-type catheter and 3-dimensional navigation systems were routinely used (>80%) in our series, so that is why they are not related to ablation success in this study.

In our series, 4 factors were related to acute failure in multivariate analysis: patients with IART different than isolated CTI-related IART (odds ratio 7.3), previous atrial

fibrillation (OR 6.07), TGA (OR 4.87), and systemic ventricle dilation (odds ratio 4.8). These last 2 factors confirm the complexity of CHD as predictors of failure suggested by other studies.^{13,34,40,41} In the Yap study, TGA with Mustard procedure patients had the lowest efficacy (43%) of all series. Several reasons explain the low success rate in this population. First, the probability of non-CTI-related IART is higher. In addition, the ablation of CTI-related IART in these patients is technically more difficult because most of the CTI is located in the systemic atrium. In this sense, to ablate the CTI, the systemic atria must be accessed either retrogradely or by a transbaffle puncture. In the first approach, it is very difficult not only to map all the atria but to get good contact with the catheter tip in the isthmus. On the other hand, although good contact in the isthmus can be achieved by a transbaffle approach, this technique is not always easy because of fibrosis and calcification of the baffle.45 The second factor related to CHD complexity that predicts lack of success in our series is dilation of the systemic ventricle, which has not specifically been reported in the literature before. Although dilation of the systemic ventricle is common in patients with TGA, its presence is itself a predictor of acute ablation failure. Furthermore, systemic ventricle dilation is a marker of disease severity and complexity. Cardiac defect complexity has been related to lack of success³⁴ and can partially explain our finding. Additionally, in our series, ventricle dilation has been related to more prevalence of severe atrioventricular valve regurgitation than, in some series,² has been related to lack of

Table 4. Univariate Echocardiographic Predi	ictors of RF Failure
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Factor	N	Success (70)	Failed (24)	OR (95% CI)	P Value
Residual cardiac defect	94	58.6%	41.7%	0.5 (0.19–1.3)	0.16
Intracardiac shunts	86	31.3%	36.4%	1.25 (0.45–3.44)	0.67
Severe systolic systemic ventricle dysfunction	91	16.2%	26.1%	1.83 (0.79–5.67)	0.35
Ejection fraction	84	56.6±10.6	61.1±8.8		0.09
Severe subpulmonary systolic dysfunction	91	19.4%	26.1%	1.46 (0.48-4.45)	0.56
TAPSE	84	16.2±4.17	15.04±4.8		0.29
Systemic ventricle dilation*	90*	25.4%*	52.2%*	3.21 (1.2-8.6)*	0.018*
Moderate-to-severe systemic ventricle dilation*	90*	7.5%*	34.8%*	6.6 (1.9–23.1)*	0.003*
EDD	82	47.54±10.3	42.25±6.5		0.11
ESD	73	33±10.2	27.6±6.7		0.11
Moderate-to-severe subpulmonary ventricle dilation	87	31.3%	17.4%	0.46 (0.14–1.52)	0.19
SA severe dilation	61	34%	22.2%	0.55 (0.1–2.95)	0.65
SA diameter	54	45.26±10.6	44.1±9.4		0.77
SA area, cm ² (4C apical view)	48	26.5±9.6	24.9±9.8		0.65
VA severe dilation	66	46.3%	60%	1.74 (0.44–6.87)	0.51
VA area, cm ² (4C apical view)	48	27.7±10.2	31.3±9.7		0.34
VA or SA severe dilation	69	53.4%	63.6%	1.52 (0.40–5.77)	0.74
Severe systemic AV valve regurgitation	80	30.5%	52.4%	2.51 (0.9–6.9)	0.07
Severe venous AV regurgitation	82	37.1%	20%	0.42 (0.12–1.42)	0.15
Moderate-to-severe venous or systemic AV valve regurgitation	91	52.9%	58.3%	1.25 (0.49–3.19)	0.64
Systolic pulmonary artery pressure, mm Hg	57	40.8±14.01	36.1±5.1		0.10

AV indicates atrioventricular; CI, confidence interval; EDD, systemic ventricle end-diastolic diameter; ESD, systemic ventricle end-systolic diameter; OR, odds ratio; RF, radiofrequency catheter ablation; SA, systemic atria; TAPSE, tricuspid annular plane systolic excursion; VA, venous atria.

ablation success. In fact, the presence of severe atrioventricular valve regurgitation showed a strong tendency in univariate analysis of ablation failure predictors (odds ratio 2.5; confidence interval, 0.9-6.9; *P*=0.07).

The factors more related to failure in our series-non-CTIrelated IART and atrial fibrillation-have not been reported before by any study. In relation to type of IART, only dual-loop IART⁴⁶ has been related to lower success, but in all other studies, CTI and non-CTI-related IART did not have differences in success rate. However, it is well known than Fontan patients who have a higher proportion of non-CTI-related IART have the lowest success rates (53%–75%).^{13,14,34,45,47} Finally, atrial fibrillation is strongly related to ablation failure in our series. This relation, shown only in 1 study,48 could be explained by the possibility that atrial fibrillation could be related to more atrial disease. Furthermore, in our series, patients with atrial fibrillation also had a greater number of induced IART (1.69±0.72 versus 1.23±0.61, P=0.04) and the number of induced IART was related to lack of success in the univariate analysis. This relation between higher number of induced IART and previous atrial fibrillation could confirm the role of atrial fibrillation as a marker of higher atrial electrical remodeling in these patients.

Finally, other treatments are available especially for patients with recurrences after several ablation procedures. Some groups suggest the possibility of "pace and ablate," that is, dual-pacemaker implantation and AV node ablation. However, complications rate because of pacemakers in patients with CHD are higher than in the general population because of more vascular access problems, complex anatomies and, very important, higher incidence of pacinginduced cardiomyopathy.

Limitations

This was an ambispective observational study; thus, in some patients (<13%) data collection was retrospective. Because of technical limitations of the navigation system, the atrial scar area has not been measured in electroanatomical mapping system in many patients, so this factor has not been studied.

of RF Failure				GINAI
Success (70)	Failed (24)	OR (95% CI)	P Value	RE
30.8±48.6	55.3±82.0		0.18	SEA
1.15±0.62*	1.75±0.89*		0.005*	RCH
269.2±44.9	277.8±55.7		0.47	
60%/22.9%/17.1%*	25%/41.7%/33.3%*		0.01*	
17.1%	33.3%	2.47 (0.8–6.9)	0.09	
40%*	75%*	4.5 (1.6–12.7)*	0.004*	
40%	41.7%	0.33 (0.033–3.4)	0.88	
4.3%*	19%*	4.47 (1.01–21.6)*	0.04*	

0.38 (0.08-1.85)

2.37 (0.6-9.3)

1.43 (0.8–1.7)

...

...

Table 5. Univariate Procedure-Related Predictors of RF Failur

Ν

94

94*

88

94*

94

94*

94

94*

48

94

94

94

4

71

67

19%

79.4%

68.6%

86%

25.05±15.7

1070.8±695.3

187.18±75.7

Data are presented as n (%), mean±SD, and range. Afib indicates atrial fibrillation; CI, confidence interval; CTI, cavotricuspid isthmus; IART, intra-atrial re-entrant tachycardia; OR, odds ratio; RF, radiofrequency.

0%

90.9%

37.8±19.5

1389.4±756.2

239.2±76.1

84.2%

100%

*Variables with P value < 0.05.

Factor

Time first IART-ablation, mo

Tachycardia cycle length, ms

IART type: CTI/both/non-CTI (%)*

IART different than isolated CTI*

Clockwise CTI IART vs counterclockwise

Intermediate tissue >0.1 to <0.5 mV

No. IART induced*

Isolated CTI IART

Severity

Afib induction*

Cooled-tip catheter

RF duration time

Procedure duration

Scar tissue < 0.1 mV

Number RF applications

Additionally, in case of non-CTI-related IART, although an ablation line between scars or scars and anatomical barriers has been performed, electrical conduction across this line was not systematically checked. Although both parameters have not been analyzed in any other study, they could be factors related to ablation success. A retrograde approach was used in most TGA patients (21/24). The transbaffle approach could allow more detailed mapping and more tissue contact of the ablation catheter. In this sense, the low success rate in this specific population could be partially related to the ablation approach. Finally, because of the heterogeneity of the

Table 6. Multivariate Analysis of Factors Related to Failed Ablation

Factor*	OR	95% CI	P Value
IART different from isolated CTI-dependent IART	7.3	1.9–27.9	0.004
Previous atrial fibrillation	6.07	1.3–28.4	0.02
TGA cardiac disease type	4.87	1.4–17.2	0.01
Systemic ventricle dilation	4.8	1.1–21.7	0.04

Variables introduced in the multivariate model included TGA, degree II-III of cardiac disease complexity, systemic ventricle dilation, CT-nondependent IART, number of induced IART, previous atrial fibrillation, and induced atrial fibrillation, CI indicates confidence interval; CTI, cavotricuspid isthmus; IART, intra-atrial re-entrant tachycardia; OR, odds ratio; TGA, transposition of the great arteries. *Only factors that were statistically significant are shown.

population with different types of cardiac diseases and the size of the population, the study was statistically underpowered to find statistical differences between some specific diseases as predictive factors of acute RF failure. Moreover, the size of the study does not allow checking for specific acute failure predictors for different cardiac disease groups. Finally, the high proportion of CTI-related IART could be a bias



Figure 4. Receiver operating curve of the multivariate model for the prediction of RF failure. RF indicates radiofrequency catheter ablation.

0.57 0.34

0.002

0.17

0.09

0.19

0.18

for success. In this sense, CTI-dependent flutter could be considered an easy ablation. However, not only in TGA patients is ablation challenging but also in patients with a significantly dilated right atrium (48.5% of non-TGA patients in our series) and in patients with significant venous AV valve regurgitation (32.9% of non-TGA patients).

Conclusions

In our study, with a high proportion of complex CHD, the ablation success rate is 74.5%. Several clinical, electrocardiographic, and echocardiographic factors have been analyzed and only factors related to complexity of cardiac disease (TGA, systemic ventricle dilation) and related to atrial remodeling (non-CTI-related IART and previous atrial fibrillation) have been related to acute failure in multivariate analysis.

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Disclosures

None.

References

- Khairy P, Ionescu-ittu R, Ms C, Mackie AS, Abrahamowicz M, Pilote L, Marelli AJ. Changing mortality in congenital heart disease. J Am Coll Cardiol. 2010;56:1149–1157.
- Koyak Z, Achterbergh RCA, De Groot JR, Berger F, Koolbergen DR, Bouma BJ, Lagrand WK, Hazekamp MG, Blom NA, Mulder BJM. Postoperative arrhythmias in adults with congenital heart disease: incidence and risk factors. *Int J Cardiol.* 2013;169:139–144.
- Kanter RJ, Garson A. Atrial arrhythmias during chronic follow-up of surgery for complex congenital heart disease. *Pacing Clin Electrophysiol*. 1997;20:502– 511.
- Trojnarska O, Grajek S, Kramer L, Gwizdała A. Risk factors of supraventricular arrhythmia in adults with congenital heart disease. *Cardiol J.* 2009;16:218–226.
- Khairy P, Fernandes SM, Mayer JE Jr, Triedman JK, Walsh EP, Lock JE, Landzberg MJ. Long-term survival, modes of death and predictors of mortality in patients with Fontan surgery. *Circulation*. 2008;117:85–92.
- Tripathi A, Black GB, Park YM, Jerrell JM. Factors associated with the occurrence and treatment of supraventricular tachycardia in a pediatric congenital heart disease cohort. *Pediatr Cardiol.* 2014;35:368–373.
- Ghai A, Harris L, Harrison DA, Webb GD, Siu SC. Outcomes of late atrial tachyarrhythmias in adults after the Fontan operation. J Am Coll Cardiol. 2001;37:585–592.
- Delacretaz E. Exploring atrial macroreentrant circuits. J Cardiovasc Electrophysiol. 2005;16:688–689.
- Akca F, Bauernfeind T, De Groot NMS, Shalganov T, Schwagten B, Szili-Torok T. The presence of extensive atrial scars hinders the differential diagnosis of focal or macroreentrant atrial tachycardias in patients with complex congenital heart disease. *Europace*. 2014;16:893–898.
- Triedman JK, Jenkins KJ, Colan SD, Saul JP, Walsh EP. Intra-atrial reentrant tachycardia after palliation of congenital heart disease: characterization of multiple macroreentrant circuits using fluoroscopically based three-dimensional endocardial mapping. J Cardiovasc Electrophysiol. 1997;8:259–270.
- 11. Walsh EP, Cecchin F. Congenital heart disease for the adult cardiologist arrhythmias in adult patients with congenital heart disease. *Circulation*. 2007;115:534–545.

- Ueda A, Adachi I, Mccarthy KP, Li W, Yen S, Uemura H. Substrates of atrial arrhythmias: histological insights from patients with congenital heart disease. *Int J Cardiol.* 2013;168:2481–2486.
- Yap SC, Harris L, Downar E, Nanthakumar K, Silversides CK, Chauhan VS. Evolving electroanatomic substrate and intra-atrial reentrant tachycardia late after Fontan surgery. J Cardiovasc Electrophysiol. 2012;23:339–345.
- Collins KK, Love BA, Walsh EP, Saul JP, Epstein MR, Triedman JK. Location of acutely successful radiofrequency catheter ablation of intraatrial reentrant tachycardia in patients with congenital heart disease. *Am J Cardiol.* 2000;86:969–974.
- Magnin-Poull I, Chillou CDE, Miljoen H, Andronache M, Aliot E. Mechanisms of right atrial tachycardia occurring late after surgical closure of atrial septal defects. J Cardiovasc Electrophysiol. 2005;16:681–687.
- Lukac P, Pedersen AK, Mortensen PT, Jensen HK, Hjortdal V, Hansen PS. Ablation of atrial tachycardia after surgery for congenital and acquired heart disease using an electroanatomic mapping system: which circuits to expect in which substrate? *Heart Rhythm*. 2005;2:64–72.
- Yap S-C, Harris L, Chauhan VS, Oechslin EN, Silversides CK. Identifying high risk in adults with congenital heart disease and atrial arrhythmias. *Am J Cardiol.* 2011;108:723–728. DOI: 10.1016/j.amjcard.2011.04.021.
- Bouchardy J, Therrien J, Pilote L, Ionescu-Ittu R, Martucci G, Bottega N, Marelli AJ. Atrial arrhythmias in adults with congenital heart disease. *Circulation*. 2009;120:1679–1686.
- Dos L, Ferreira IJ, Rodriguez-Larrea J, Miro L, Girona J, Albert DC, Gonçalves A, Murtra M, Casaldaliga J. Late outcome of Senning and Mustard procedures for correction of transposition of the great arteries. *Heart*. 2005;91:652–656.
- Diller G, Giardini A, Dimopoulos K, Derrick G, Giannakoulas G, Gargiulo G, Mu J, Khambadkone S, Lammers AE, Picchio FM, Gatzoulis MA, Hager A. Congenital heart disease predictors of morbidity and mortality in contemporary Fontan patients: results from a multicenter study including cardiopulmonary exercise testing in 321 patients. *Eur Heart J.* 2010;31:3073–3083.
- Kammeraaad J, Van Deursen CJM, Sreeram N, Bink-boelkens MTE, Ottenkamp O, Helbing WA, Lam J, Sobotka-Plojhar M, Daniels O, Balaji S. Predictors of sudden cardiac death after Mustard or Senning repair for transposition of the great arteries. J Am Coll Cardiol. 2004;44:1095–1102.
- Koyak Z, Harris L, De Groot JR, Sivlersides CK, Oechslin EN, Bouma BJ, Budts W, Zwinderman AH, Van Gelder I, Mulder BJM. Sudden cardiac death in adult congenital heart disease. *Circulation*. 2012;126:1944–1954.
- 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;32:245–251.
- Walsh EP. Sudden death in adult congenital heart disease: risk stratification in 2014. *Heart Rhythm*. 2014;11:1735–1742.
- Thorne SA, Barnes I, Cullinan P, Somerville J. Amiodarone-associated thyroid dysfunction: risk factors in adults with congenital heart disease. *Circulation*. 1999;100:149–154.
- Koyak Z, Kroon B, De Groot JR, Wagenaar LJ, Van Dijk AP, Mulder BA, Van Gelder IC, Post MC, Mulder BJM. Efficacy of antiarrhythmic drugs in adults with congenital heart disease and supraventricular tachycardias. *Am J Cardiol.* 2013;112:1461–1467.
- 27. Khairy P, Van Hare GF, Balaji S, Berul C, Cecchin F, Cohen M, Daniels CJ, Deal BJ, Dearani JA, de Groot N, Dubin AM, Harris L, Janousek J, Kanter R, Karpawich P, Perry J, Seslar SP, Shah MJ, Silka MJ, Triedman JK, Walsh EP, Warnes CA. PACES/HRS expert consensus statement on the recognition and management of arrhythmias in adult congenital heart disease: executive summary. *Heart Rhythm.* 2014;11:e81–e101.
- Warnes CA, Williams RG, Bashore TM, Child JS, Conolly MC, Dearani JA, del Nido P, Fasules JW, Graham TP, Hijazi ZM, Hunt SA, King ME, Landzberg MJ, Miner PD, Radford MJ, Walsh EP, Webb GD. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease. J Am Coll Cardiol. 2009;52:e143–e263.
- Morton JB, Sanders P, Deen V, Vohra JK, Kalman JM. Sensitivity and specificity of concealed entrainment for the identification of a critical isthmus in the atrium: relationship to rate, anatomic location and antidromic penetration. J Am Coll Cardiol. 2002;39:896–906.
- Roca-Luque I, Rivas-Gandara N, Dos L, Francisco-Pascual J, Pijuan A, Perez-Rodon J, Subirana MT, Santos-Ortega A, Miranda B, Roses-Noguer F, Ferreira-Gonzalez I, Casaldaliga J, García-Dorado D, Moya-Mitjans A. Intra-atrial reentrant tachycardia in congenital heart disease: types and relation of isthmus to atrial voltage. *Europace*. 2018;20:353–361.
- Mah DY, Alexander ME, Cecchin F, Walsh EP, Triedman JK. The electroanatomic mechanisms of atrial tachycardia in patients with tetralogy of Fallot and double outlet right ventricle. *J Cardiovasc Electrophysiol*. 2011;22:1013–1017.

- De Groot NMS, De Lukac P, Schalij MJ, Makowski K, Szili-torok T, Jordaens L, Nielsen JC, Jensen HK, Gerdes JC, Delacretaz E. Long-term outcome of ablative therapy of post-operative atrial tachyarrhythmias in patients with tetralogy of Fallot: a European multi-centre study. *Europace*. 2012;31:522–527.
- Ueda A, Suman-horduna I, Mantziari L, Gujic M, Marchese P, Ho Y, Babunarayan SV, Ernst S. Contemporary outcomes supraventricular tachycardia ablation in congenital heart disease: a single-center experience in 116 patients. *Circ Arrhythm Electrophysiol.* 2013;6:606–613.
- Yap SC, Harris L, Silversides CK, Downar E, Chauhan VS. Outcome of intraatrial re-entrant tachycardia catheter ablation in adults with congenital heart disease: negative impact of age and complex atrial surgery. J Am Coll Cardiol. 2010;56:1589–1596.
- Chan DP, Van Hare GF, Mackall JA, Carlson MD, Waldo AL. Importance of atrial flutter isthmus in postoperative intra-atrial reentrant tachycardia. *Circulation*. 2000;102:1283–1289.
- Kannankeril PJ, Anderson ME, Rottman JN, Wathen MS, Fish FA. Frequency of late recurrence of intra-atrial reentry tachycardia after radiofrequency catheter ablation in patients with congenital heart disease. *Am J Cardiol.* 2003;92:879– 881.
- Tanner H, Lukac P, Schwick N, Fuhrer J, Pedersen AK, Hansen PS, Delacretaz E. Irrigated-tip catheter ablation of intraatrial reentrant tachycardia in patients late after surgery of congenital heart disease. *Heart Rhythm*. 2004;1:268–275.
- Wu J, Deisenhofer I, Ammar S, Fichtner S, Reents T, Zhu P, Jilek C, Kolb C, Hess J, Hessling G. Acute and long-term outcome after catheter ablation of supraventricular tachycardia in patients after the Mustard or Senning operation for Dtransposition of the great arteries. *Europace*. 2013;15:886–891.
- De Groot NMS, Atary JZ, Blom NA, Schalij MJ. Long-term outcome after ablative therapy of postoperative atrial tachyarrhythmia in patients with congenital heart disease and characteristics of atrial tachyarrhythmia recurrences. *Circ Arrhythm Electrophysiol.* 2010;3:148–154.
- 40. Kalman JM, Vanhare GF, Olgin JE, Saxon LA, Stark SI, Lesh MD. Ablation of "incisional" reentrant atrial tachycardia complicating surgery for congenital

heart disease. Use of entrainment to define a critical isthmus of conduction. *Circulation*. 1996;93:502–512.

- Akar JG, Kok LC, Haines DE, DiMarco JP, Mounsey JP. Coexistence of type I atrial flutter and intra-atrial re-entrant tachycardia in patients with surgically corrected congenital heart disease. J Am Coll Cardiol. 2001;38:377–384.
- Drago F, Russo MS, Marazzi R, Salerno-Uriarte JA, Silvetti MS, De Ponti R. Atrial tachycardias in patients with congenital heart disease: a minimally invasive simplified approach in the use of three-dimensional electroanatomic mapping. *Europace*. 2011;13:689–695.
- Peichl P, Kautzner J, Cihák R, Vancura V, Bytesník J. Clinical application of electroanatomical mapping in the characterization of "incisional" atrial tachycardias. *Pacing Clin Electrophysiol*. 2003;26:420–425.
- 44. Akca F, Bauernfeind T, Witsenburg M, Dabiri Abkenari L, Cuypers JA, Roos-Hesselink JW, de Groot NMS, Jordaens L, Szili-Torok T. Acute and long-term outcomes of catheter ablation using remote magnetic navigation in patients with congenital heart disease. Am J Cardiol. 2012;110:409–414.
- 45. Correa R, Walsh EP, Alexander ME, Mah DY, Cecchin F, Dominic J, Triedman JK. Transbaffle mapping and ablation for atrial tachycardias after Mustard, Senning, or Fontan operations. J Am Heart Assoc. 2013;2:e000325. DOI: 10. 1161/JAHA.113.000325.
- Seiler J, Schmid DK, Irtel TA, Tanner H, Rotter M, Schwick N, Delacrétaz E. Dual-loop circuits in postoperative atrial macro re-entrant tachycardias. *Heart*. 2007;93:325–330.
- Correa R, Sherwin ED, Kovach J, Mah DY, Alexander ME, Cecchin F, Walsh EP, Triedman JK, Abrams DJ. Mechanism and ablation of arrhythmia following total cavopulmonary connection. *Circ Arrhythm Electrophysiol.* 2015;8:318– 325.
- 48. Triedman JK, Alexander ME, Love BA, Collins KK, Berul CI, Bevilacqua LM, Walsh EP. Influence of patient factors and ablative technologies on outcomes of radiofrequency ablation of intra-atrial re-entrant tachycardia in patients with congenital heart disease. J Am Coll Cardiol. 2002;39:1827– 1835.