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ORIGINAL RESEARCH

Arrhythmias and Clinical Outcomes in a Swiss Multicenter Cohort of Patients With Dextro-Transposition of the Great Arteries and Atrial Switch

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BACKGROUND: Data on the incidence of arrhythmias, associated cardiac interventions, and outcome in patients with dextro-transposition of the great arteries and atrial switch are scarce.

METHODS AND RESULTS: In this multicenter analysis, we included adult patients with dextro-transposition of the great arteries and atrial switch regularly followed up at 3 Swiss tertiary care hospitals. The primary outcome was a composite of left ventricular assist device, heart transplantation, and death. The secondary outcome was occurrence of ventricular tachycardia, ventricular fibrillation, or sudden cardiac death. We identified 207 patients (34% women; median age at last follow-up, 35 years) with dextro-transposition of the great arteries and atrial switch. Arrhythmias occurred in 97 patients (47%) at a median age of 22 years. A pacemaker or an implantable cardioverter-defibrillator was implanted in 39 (19%) and 13 (6%) patients, respectively, and 33 (16%) patients underwent a total of 51 ablation procedures to target 60 intra-atrial re-entry tachycardias, 4 atrioventricular nodal re-entry tachycardias, and 1 atrial fibrillation. The primary outcome occurred in 21 patients (10%), and the secondary outcome occurred in 18 patients (9%); both were more common in patients with concomitant ventricular septum defect than in those without (hazard ratio [HR], 3.06 [95% CI, 1.29–7.27], *P*=0.011; and HR, 3.62 [95% CI, 1.43–9.18], *P*=0.007, respectively).

CONCLUSIONS: In patients with dextro-transposition of the great arteries and atrial switch reaching adulthood, arrhythmias occur in almost half of patients, and associated rhythm interventions are frequent. One-tenth of those patients do not survive until the age of 35 years free from left ventricular assist device or heart transplantation, and the outcome is worse in patients with concomitant ventricular septum defect.

Key Words: atrial switch procedure ■ cardiac arrhythmia ■ implantable cardioverter-defibrillator ■ intra-atrial re-entry tachycardia ■ pacemaker ■ sudden cardiac death ■ transposition of the great arteries

Approximately 700 children with congenital heart disease (CHD) are born in Switzerland every year.[1] Dextro-transposition of the great arteries (d-TGA) accounts for 6% to 7% of all patients with CHD.[2] Over 90% of children who undergo a surgical repair of d-TGA will reach adulthood.[3] Until the late 1980s, d-TGA patients underwent an atrial switch operation according to Senning or Mustard. These patients have now reached

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CLINICAL PERSPECTIVE

What Is New?

- Half of adult patients with dextro-transposition of the great arteries and atrial switch experience a clinically relevant, sustained arrhythmia.
- Rhythm interventions are frequent and include device therapy in a quarter and ablation procedures in a sixth of patients.
- Ablation procedures in adult patients with dextro-transposition of the great arteries and atrial switch most commonly target cavotricuspid isthmus–dependent intra-atrial re-entry tachycardia.

What Are the Clinical Implications?

- Transbaffle access is critical for ablation success and requires a dedicated team experienced with the specific challenges of this patient population.
- Vigilant interdisciplinary follow-up of adult patients with dextro-transposition of the great arteries and atrial switch is indicated, because one-tenth do not survive free from left ventricular assist device and heart transplantation until the age of 35 years.

Nonstandard Abbreviations and Acronyms

AVNRT	atrioventricular-nodal re-entry tachycardia
CTI	cavotricuspid isthmus
d-TGA	dextro-transposition of the great arteries
EPS	electrophysiological study
IART	intra-atrial re-entry tachycardia
PVA	pulmonary-venous atrium
SCD	sudden cardiac death

adulthood and are experiencing the long-term arrhythmic sequelae of atrial switch surgery. Arrhythmias in these patients include atrial and ventricular tachyarrhythmias, as well as sinus node dysfunction and atrioventricular node disease, and are associated with increased morbidity and mortality, and impaired quality of life.[4–8]

Within 20 years after the atrial switch procedure, tachyarrhythmias, most commonly intra-atrial reentrant tachycardia (IART), have been reported in up to 24% of d-TGA patients, and bradyarrhythmias requiring a pacemaker implantation have been reported in 11% of patients.[6] Many of these patients also need long-term antiarrhythmic drug therapy for rhythm control, but data on the long-term treatment of tachyarrhythmias in large populations of d-TGA patients are scarce.[2,4] Furthermore, ablation procedures and implantations of pacemakers or implantable cardioverters-defibrillators (ICDs) in patients with d-TGA are challenging after an atrial switch procedure because of the particular anatomic features.

As with other types of CHD, only a few studies of larger sample size have been published, which report on outcome of patients with d-TGA and atrial switch operation. The objective of this study was to analyze the full spectrum of clinically relevant arrhythmias in patients with d-TGA, the treatment of tachyarrhythmias and bradyarrhythmias, and clinical outcomes.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Population

In this multicenter, retrospective cohort study, adult patients with d-TGA and atrial switch according to Mustard or Senning who were followed up at the University Hospitals of Bern, Lausanne, and Zurich up to 2020 were included. Follow-up at all 3 institutions was usually performed on an annual basis and included assessment of functional status and detailed history taking, including occurrence of palpitations or arrhythmias. Patients with congenitally corrected transposition of the great arteries, those who underwent an arterial switch procedure, and those with a written objection to the use of health records for research purposes were excluded from the study. The study protocol was approved by the regional ethics committees and complies with the Declaration of Helsinki. General consent that allows for the further use of health-related data for research was available from all patients.

Clinical, Procedural, and Follow-Up Data

All baseline clinical, procedural, and follow-up data were retrospectively obtained from electronic health records. Congenital malformations and corrective procedures are coded as described in these records. Antiarrhythmic drug therapy included treatment with β-blockers, nondihydropyridine calcium channel blockers, amiodarone, sotalol, dronedarone, ibutilide, and class I antiarrhythmic drugs at any time.

Mode of death was classified according to accepted definitions.[9] Specifically, sudden cardiac death (SCD) was defined as death occurring within 1 hour of symptom onset in witnessed cases, or within 24 hours after the patient was last seen alive in unwitnessed cases. The primary outcome was survival free from left ventricular assist device implantation, heart transplantation, and death. The secondary outcome was survival free from occurrence of ventricular tachycardia (VT), ventricular fibrillation (VF), and SCD.

Classification of Arrhythmias

Only data on clinically relevant bradyarrhythmias and tachyarrhythmias were collected for the current study. Arrhythmias were considered as clinically relevant when: (1) pharmacological, device, and/or interventional therapy was required; and/or (2) tachyarrhythmias were sustained for ≥30 seconds and documented by an ECG or on a rhythm strip.

For further description and analysis, arrhythmias were classified as follows: (1) sick sinus syndrome; (2) advanced atrioventricular block defined as 2° atrioventricular block type Mobitz II, 2:1 atrioventricular block, or complete atrioventricular block; (3) IART; (4) atrioventricular-nodal re-entry tachycardia (AVNRT); (5) atrial fibrillation; and (6) VT/VF. Arrhythmias classified as IART included those described as focal atrial tachycardia as well as atrial microreentrant and macroreentrant tachycardia (cavotricuspid isthmus [CTI]-dependent and -independent).

Interventions

Implantations of pacemakers and ICDs and subsequent reinterventions, electrophysiological studies (EPSs), and catheter ablations were performed at the discretion of treating electrophysiologists at the 3 institutions. ICD was considered implanted for primary prevention when implanted in patients without documented prior sustained ventricular arrhythmia, and for secondary prevention when implanted after aborted SCD, spontaneously occurring sustained VT, or inducible VT during an EPS in patients with previous palpitations or syncope. The treating electrophysiologist decided on the EPS protocol, which usually included burst pacing and programmed electrical stimulation from the right ventricular apex at drive trains of 600 or 500 ms and 400 ms and up to 3 extrastimuli with repetition of the EPS protocol during isoproterenol infusion. ICD interventions included shock therapy and antitachycardia pacing and were classified as appropriate when delivered for a ventricular tachyarrhythmia, and otherwise as inappropriate.

Data on ablation procedures and EPS were extracted from reports, and, if available, from 3-dimensional electroanatomical maps generated during the procedures. Evaluation of bidirectional block across the CTI line was assessed according to standard criteria, if possible. Complete procedural success of ablation procedures was defined as the inability to induce any arrhythmia at the end of the procedure, and/or confirmed bidirectional block across the CTI if ablation of the CTI was a target of the procedure. Partial procedural success was defined as the inability to induce at least one of the clinical arrhythmias at the end of the procedure, and/or confirmed bidirectional block across the CTI, with persistence of at least one other arrhythmia. Isuprel infusion for tachycardia induction was used at the discretion of the treating electrophysiologist.

Table 1. Patient Characteristics

Characteristic	Total (n=207)	No VSD (n=170)	VSD (n=37)	*P* value
Female sex	70 (34)	63 (37)	7 (19)	0.035
Additional malformations				
VSD	30 (15)	…	30 (81)	…
VSD and valve stenosis	7 (4)	…	7 (19)	…
Valve stenosis/LVOT obstruction	11 (5)	11 (7)	…	…
PFO	1 (<1)	1 (<1)	…	0.821
PDA	26 (13)	23 (14)	3 (8)	0.275
ASD type II	9 (4)	7 (4)	2 (5)	0.501
Coronary anomaly	3 (1)	3 (2)	…	0.552
Corrective procedures				
Initial palliative procedure				
None	4 (2)	4 (2)	…	0.434
Blalock-Hanlon procedure	66 (32)	57 (34)	9 (24)	0.197
Rashkind procedure	141 (68)	116 (68)	25 (68)	0.587
Pulmonary banding	9 (4)	3 (2)	6 (16)	0.002
Banding of SVC	4 (2)	4 (2)	…	0.434
Immediate atrial switch	4 (2)	2 (1)	2 (5)	0.159
Unknown	9 (4)	9 (5)	…	0.163
Type of atrial switch				
Mustard	68 (33)	57 (34)	11 (30)	0.656
Senning	139 (67)	113 (67)	26 (70)	
Age at atrial switch, mo	11 (7–21)	12 (7–19)	11 (6–61)	0.652
Last follow-up				
Age at last follow-up, y	35 (31–42)	35 (31–42)	35 (31–44)	0.524
Status				
Alive	189 (91)	159 (93)	30 (81)	0.024
Deceased	18 (9)	11 (7)	7 (19)	
SCD	13 (72)	7 (4)	6 (16)	0.316
HF	3 (17)	3 (2)	…	
Other	2 (11)	1 (<1)	1 (3)	
Advanced HF therapy	6 (3)			0.001
LVAD	3 (1)	…	3 (8)	
Heart transplant	3 (1)	2 (1)	1 (3)	

Data are shown as median (interquartile range) or number (percentage). ASD indicates atrial septum defect; HF, heart failure; LVAD, left ventricular assist device; LVOT, left ventricular outflow tract; PDA, persistent ductus arteriosus; PFO, patent foramen ovale; SCD; sudden cardiac death; SVC, superior caval vein; and VSD, ventricular septum defect.

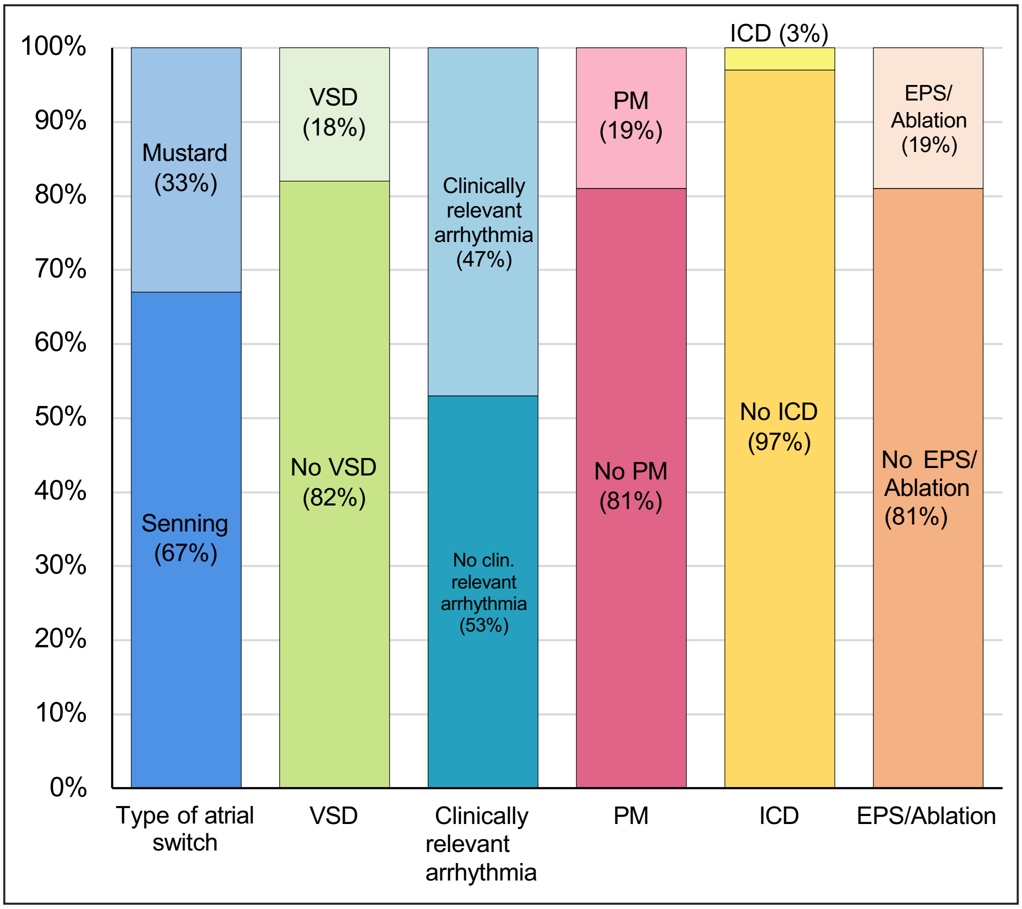

Figure 1. Key findings on type of atrial switch, presence of ventricular septum defect (VSD), arrhythmia burden, and rhythm interventions in patients with dextro-transposition of the great arteries and atrial switch.
EPS indicates electrophysiological study; ICD, implantable cardioverter-defibrillator; and PM, pacemaker.

Statistical Analysis

Categorical variables are expressed as numbers with percentages, and continuous variables are expressed as medians with interquartile range (IQR). Comparisons between groups were made using χ^2 method for categorical variables and Mann-Whitney *U* test for continuous variables. Univariate analyses for prediction of primary and secondary outcomes were performed using Cox regression. Kaplan-Meier curves of primary and secondary outcomes were drawn, and presence versus absence of a ventricular septum defect (VSD) was compared with the log-rank test. The proportionality hazards assumption was tested by generating time-dependent covariates, creating interactions of the predictors and a function of survival time, which was included in the models. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM, Armonk, NY). All tests were performed at a 2-sided 5% significance level with 2-sided 95% CIs.

RESULTS

Patient Characteristics

A total of 207 adult patients (34% women; median age at last patient contact, 35 years) with d-TGA and atrial switch were followed up regularly at the participating institutions. The baseline patient characteristics, including type of CHD, corrective surgical procedures, and status at last follow-up, are summarized in Table 1. In total, 97 patients (47%) had at least one clinically relevant arrhythmia at a median age of 22 years (IQR, 14–32 years). An overview of arrhythmias and treatment is shown in Figure 1, Table 2, and Tables S1–S3.

Device Therapy and SCD

A total of 52 patients (25%) received a pacemaker or an ICD at a median age of 22 years (IQR, 11–34 years). A total of 93 device reinterventions were performed in 36 patients. Initial device indications, reasons for reintervention, device types, and implantation sites are

Table 2. Prevalence and Treatment of Arrhythmias

Variable	Total (n=207)	No VSD (n=170)	VSD (n=37)	*P* value
History of arrhythmia	97 (47)	76 (45)	21 (57)	0.183
Age at first arrhythmia, y	22 (14–32)	23 (14–31)	18 (11–35)	0.739
Type of arrhythmia				
SSS	33 (16)	26 (15)	7 (19)	0.585
Atrioventricular block	12 (6)	7 (4)	5 (14)	0.043
IART	79 (38)	65 (38)	14 (38)	0.964
AF	5 (2)	3 (2)	2 (5)	0.218
VT/VF	9 (4)	4 (2)	5 (14)	0.01
Arrhythmia treatment				
Antiarrhythmic drug therapy	61 (30)	48 (28)	13 (35)	0.404
Electrical cardioversion	51 (25)	40 (24)	11 (30)	0.428
EPS/ablation	40 (19)	31 (18)	9 (24)	0.395
Device implantation	52 (25)	37 (22)	15 (41)	0.017
Pacemaker	39 (19)	28 (17)	11 (30)	0.062
ICD	13 (6)	9 (5)	4 (11)	0.184

Data are shown as median (interquartile range) or number (percentage). AF indicates atrial fibrillation; EPS, electrophysiological study; IART, intra-atrial re-entry tachycardia; ICD, implantable cardioverter-defibrillator; SSS, sick sinus syndrome; VF, ventricular fibrillation; VSD, ventricular septum defect; and VT, ventricular tachycardia.

summarized in Table 3. Among 13 patients with an ICD implantation, 7 (54%) were implanted for primary prevention and 6 (46%) were implanted for secondary prevention. During a median follow-up of 52 months (IQR, 17–77 months) after ICD implantation, 5 patients (39%) received ICD interventions. Two patients (15%) had inappropriate ICD interventions attributable to IART with 1:1 atrioventricular conduction, and 3 patients (23%) had appropriate ICD interventions. Thirteen patients (6%) experienced SCD during follow-up. Two of these were ICD recipients with lethal VF episodes despite appropriate, but unsuccessful, ICD interventions.

EPSs and Ablation Procedures

A total of 51 ablation procedures were performed in 33 patients, which are described in detail in Table 4 and Tables S2 and S3. All ablation procedures were performed with radiofrequency energy. Two patients had agenesis of the inferior vena cava requiring a superior or retrograde approach to access the heart. Access to the pulmonary venous atrium (PVA) was obtained in 33 of 51 ablation procedures (65%), via baffle leak or baffle puncture in 22 (67%) procedures, and via retrograde aortic access in 11 (33%) procedures. A total of 60 IARTs were targeted during 49 ablation procedures, of which 40 (67%) were CTI-dependent, 5 (8%) were CTI-independent macroreentries, and 15 (25%) were microreentries. Bidirectional block across the CTI was assessed using standard criteria in 14 (35%) of the procedures targeting the CTI, with block across the line confirmed in all 14 patients (100%) at the end of the procedures. Of 29 patients with CTI ablation, 20 had one ablation (with PVA access in 17 patients [85%]), and 9 had repeated ablations (with PVA access during the first ablation in 2 patients [22%]). All microreentries were successfully terminated with a focal ablation except one, which was not ablated because of proximity to the sinus node region and risk of subsequent pacemaker dependency. Of the 4 patients with an AVNRT, detailed information was available in 3. AVNRT was typical in one, atypical in another, and both typical and atypical in the third. The slow pathway was identified in the systemic-venous atrium in 1 patient and in the PVA in 2 patients, the His bundle in the systemic-venous atrium in 2 patients, and in the PVA in 1 patient. In the 2 patients with the slow pathway in the PVA, access was achieved via baffle puncture in 1 patient. In the other patient, a first ablation attempt identified agenesis of the inferior vena cava, and a second ablation attempt with superior access through the right jugular vein failed because of inability to puncture the superior baffle because of calcification. A third ablation was successful with retrograde access via the aorta by means of remote magnetic navigation.

Data on procedural success were available in 49 of 51 (96%) ablation procedures. Arrhythmia inducibility was tested at the end of the procedure in 36 cases (74%), and no arrhythmia was inducible in 32 cases (89%). Complete procedural success was achieved in 35 cases (71%), partial success was achieved in 7 cases (14%), and ablation failed in 7 cases (14%). Most failed or only partially successful ablations were performed before May 2013 (n=10 [71%]). The main causes for partial success or failure were the following: (1) no access or only retrograde access to the PVA for

Table 3. Pacemakers and ICDs

Variable	Value
Patients with a pacemaker or an ICD	52 (25)
Age at first implantation, y	22 (11–34)
Age at first pacemaker implantation, y	18 (9–30)
Age at first ICD implantation, y	37 (33–40)
Time since first implantation, y	15 (5–28)
Indications	
ICD	13 (25)
Primary prevention	7 (54)
Secondary prevention	6 (46)
Spontaneous VF	4 (67)
Positive EPS	2 (33)
Pacemaker	45 (87)
SSS	33 (73)
Atrioventricular block	10 (22)
Iatrogenic atrioventricular block after ablation	2 (4)
Device type at first implant	
AAI	6 (12)
VVI	17 (33)
DDD	22 (42)
VVI-ICD	2 (4)
DDD-ICD	1 (2)
CRT-D	2 (4)
S-ICD	2 (4)
Initial implantation site	
Epicardial	28 (54)
Transvenous	22 (42)
Epicardial and transvenous	2 (4)
Device reinterventions	
Patients with ≥1 device reintervention	36 (69)
Total no. of device reinterventions	93
No. of reinterventions per patient	2 (1–4)
Indication for reintervention	
Battery depletion	38 (41)
Lead failure	28 (30)
Lead fracture	3 (11)
Lead dislocation	6 (21)
Sensing/pacing abnormality	6 (21)
Unspecified type of lead failure	13 (46)
Device upgrade	15 (16)
Upgrade to ICD	3 (20)
Upgrade to dual-chamber device	8 (53)
Upgrade to CRT-D	2 (13)
Upgrade to CRT-P	2 (13)
Device infection	3 (3)
Pocket revision attributable to bleeding/pain	4 (4)
Exchange of epicardial lead for transvenous lead	3 (3)
Exchange of transvenous lead for epicardial lead	1 (1)
Reimplantation 10 y after explantation for lead failure	1 (1)

Data are shown as median (interquartile range) or number (percentage). CRT indicates cardiac resynchronization therapy; EPS, electrophysiological study; ICD, implantable cardioverter-defibrillator; S-ICD, subcutaneous ICD; SSS, sick sinus syndrome; and VF, ventricular fibrillation.

ablation of the CTI or arrhythmias localized in the PVA (n=8 [57%]), (2) arrhythmia origin located close to the sinus node or atrioventricular node (n=3 [21%]), and (3) undetermined arrhythmia mechanism (n=3 [21%]).

Complications of ablation procedures included uncomplicated groin hematoma without need for further intervention in 4 patients (6%) and urethral bleeding after urinary catheter insertion in 1 patient (2%). Two patients received a pacemaker because of complete atrioventricular block induced by ablation (Table S2). One was implanted in a patient after ablation of a CTI-dependent IART and pulmonary vein isolation for atrial fibrillation. The other was implanted in a patient with 3 previous ablations of multiple IARTs and after ablation of a microreentry located at the base of the remaining interatrial septum during a fourth procedure.

Clinical Outcomes

The primary outcome occurred in 21 patients (10%): 15 patients (7%) died, 3 (2%) received a left ventricular assist device, and 3 (2%) underwent heart transplantation (Table 1). The secondary outcome occurred in 18 patients (9%): 9 (4%) experienced SCD, and 9 (4%) had nonfatal VT or VF. Primary and secondary outcomes were more common in patients with concomitant VSD than in patients without VSD (hazard ratio [HR], 3.06 [95% CI, 1.29–7.27], *P*=0.011; and HR, 3.62 [95% CI, 1.43–9.18], *P*=0.007, respectively; Figure 2 and Table 5). In the test of proportionality, the time-dependent covariate was not significant; thus, VSD as a predictor was proportional over time (the time-dependent covariate was 0.765 for the composite outcome of left ventricular assist device, heart transplantation, or death and 0.531 for the composite outcome of VT, VF, and SCD). There were no differences in the primary or secondary outcomes for sex, presence of IART, type of atrial switch, and age at which atrial switch was performed (Table 5).

DISCUSSION

Our study shows that in patients with d-TGA and atrial switch reaching adulthood:

1. Half of patients experience a clinically relevant sustained arrhythmia.
2. Rhythm interventions are frequent and include device therapy in a quarter and ablation procedures in one-sixth of patients.
3. CTI-dependent IART is the most common arrhythmia, and ablation success improves with transbaffle access.
4. One-tenth of those patients do not survive free from left ventricular assist device and heart transplantation until the age of 35 years.
5. Clinical outcome is worse in patients with concomitant VSD.

In a recent, systematic review of 29 studies including >5000 patients with d-TGA and atrial switch with a median follow-up time of 10 to 35 years, arrhythmia-free survival 20 years after atrial switch was observed in 40%, similar to our cohort.[10] Pacemakers were required in 10% of patients (IQR, 6%–17%), and sick sinus syndrome was the most common indication. In comparison, 22% of the patients in our cohort received a pacemaker at a median age of 35 years, and sick sinus syndrome was the most common indication also in our study. For ICDs, mean implantation age range was 26 to 35 years in the systematic review, and 79% were implanted for primary prevention of SCD; however, the rate of ICD implantation was not reported.[10] We found a low ICD implantation rate of 6% in our cohort with a median implantation age of 37 years. Only half of ICDs were implanted for primary prevention of SCD. Such a rather conservative strategy of ICD implantation may be appropriate in view of the high rate of inappropriate ICD discharges of 92% reported in the systematic review, mainly because of IART. Notably, 2 patients in our cohort experienced SCD because of VF despite appropriate ICD interventions. This highlights the fact that general concepts of ICD therapy may need to be adopted with caution in populations with CHD, as other mechanism may be responsible for SCD, such as ischemia triggered by high ventricular rate during supraventricular tachycardia.[11]

Device reinterventions were frequent in our population, and lead failure was a common indication. Our findings are consistent with the high rates of lead-related complications previously reported in patients with d-TGA and other CHDs.[12–14] Indeed, up to a third of patients with d-TGA and an ICD have been observed to experience short-term and/or late lead-related complications, with at least half of those being attributable to lead failure.[15,16] Lead failure is another common reason for inappropriate shocks besides IART in patients with CHD. In a study by Khairy et al, inappropriate shocks occurred in 24% of patients, and 62% of these were attributable to lead failure.[15] Device upgrades as well as replacement of epicardial leads with

Table 4. EPSs and Ablation Procedures

Variable	Value
Patients with an EPS or an ablation procedure	40 (19)
Patients with an EPS only	7 (18)
Patients with an ablation procedure	33 (83)
Age at first EPS or ablation procedure, y	36 (26–43)
Total EPS and ablation procedures performed	64
EPS only	13 (20)
No. of EPSs only per patient	1 (1–1)
Ablation procedures	51 (80)
No. of ablation procedures per patient	1 (1–2)
Type of access for ablation procedures	51
Access only to the systemic venous baffle	18 (35)
Access to both the systemic and pulmonary venous baffle	33 (65)
Retrograde access to the pulmonary venous baffle	11 (33)
Access to the pulmonary venous baffle via baffle leak	6 (18)
Baffle puncture for access to the pulmonary venous baffle	14 (42)
Baffle puncture or baffle leak and retrograde	2 (6)
Types of arrhythmias targeted during the 51 ablation procedures	
≥1 IART	49 (96)
AVNRT	4 (8)
Atrial fibrillation	1 (2)
Details on IARTs targeted during the 49 ablation procedures with IART ablation	
No. of IARTs ablated	60
CTI	40 (67)
Not CTI-dependent	5 (8)
Microreentry	15 (25)
Cycle length, ms	290 (190–610)
Ablation details of the 40 procedures with CTI ablation	
Ablation of CTI in systemic venous baffle only	13 (33)
Ablation of CTI in pulmonary venous baffle only	19 (48)
Ablation of CTI in both the systemic and the pulmonary venous baffle	8 (20)
No. of patients with CTI ablation	29
1 CTI ablation	20 (69)
2 CTI ablations	8 (28)
4 CTI ablations	1 (3)
Evaluation of CTI block	14
Standard evaluation	8 (57)
Alternative evaluation	6 (43)
Bidirectional block achieved and confirmed	14 (100)
Conduction time (ms) across CTI block	200 (190–230)

Data are shown as number (percentage) or median (interquartile range). AVNRT indicates atrioventricular-nodal re-entry tachycardia; CTI, cavotricuspid isthmus; EPS, electrophysiological study; and IART, intra-atrial re-entry tachycardia.

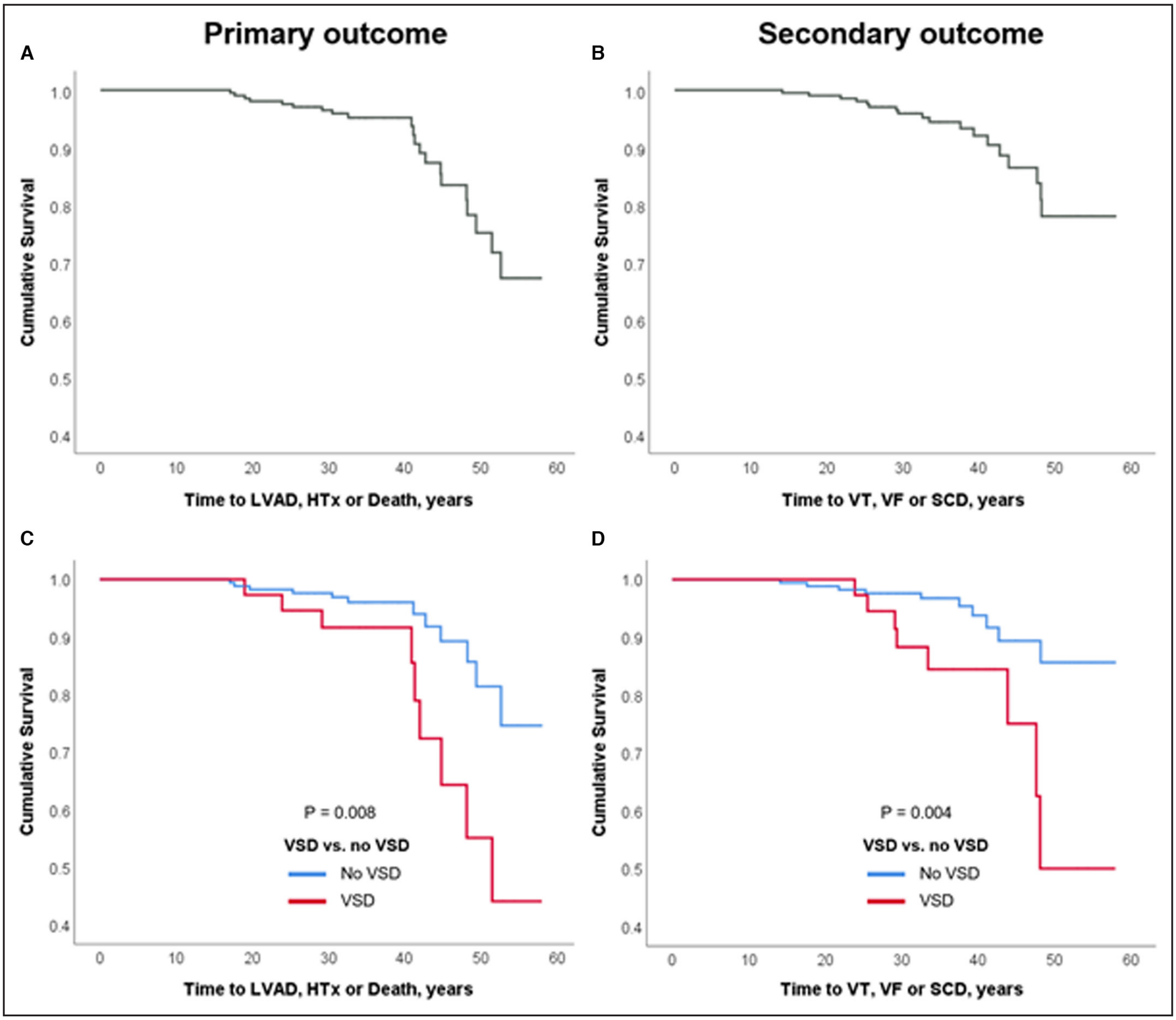

Figure 2. Primary and secondary outcome in patients with dextro-transposition of the great arteries and atrial switch.
Kaplan-Meier curves showing primary outcome (survival free from left ventricular assist device [LVAD], heart transplantation [HTx], and death) (**A**) and secondary outcome (survival free from ventricular tachycardia [VT], ventricular fibrillation [VF], and sudden cardiac death [SCD]) (**B**), stratified according to the presence of ventricular septum defect (VSD) (**C** and **D**).

endocardial leads or vice versa, often attributable to lead failure, add to the device reintervention burden in this patient population.

With 51 ablation procedures in 33 patients, our cohort forms the largest description of ablation procedures in patients with d-TGA and atrial switch to date. In line with previous reports, most tachycardias were IART, and two-thirds of them were CTI-dependent. In addition, a few AVNRTs and one atrial fibrillation were treated. Correa et al reported IART to be the tachycardia mechanism in >80% of 29 ablation procedures in patients with d-TGA and atrial switch.[17] Gallotti et al described 38 ablation procedures in 28 patients with the main arrhythmia mechanism again being IART in 21 patients, which was CTI-dependent in 76%.[18] They additionally targeted AVNRTs in 3 patients and focal, atrial tachycardia in 6 patients. In the experience of a German group with 34 ablation procedures in 26 patients with d-TGA and atrial switch, IARTs were present in 88% of cases, and AVNRTs were present in 12% of cases.[19] Reported ablation success rates in patients with d-TGA and atrial switch depend on the type of access to the PVA. Correa et al obtained transbaffle access in 83% of the procedures and achieved a success rate of 92% in case of transbaffle access, which decreased to 60% in cases without transbaffle access.[17] Gallotti et al obtained transbaffle access in 75% of initial procedures and reported a success rate of 96%.[18] In their cohort, tachycardia recurred in 32% of patients, but the mechanism was different from those

Table 5. Predictors of Outcome in Patients With d-TGA and Atrial Switch

Univariate analysis	HR (95% CI)	*P* value
LVAD, HTx, or death		
Type of atrial switch, Mustard	0.67 (0.27–1.63)	0.373
Age at atrial switch, <12 mo	0.44 (0.15–1.31)	0.141
Ventricular septum defect	3.06 (1.29–7.27)	0.011
Male sex	2.52 (0.84–7.5)	0.098
IART	1.38 (0.55–3.45)	0.492
VT, VF, or SCD		
Type of atrial switch, Mustard	0.66 (0.25–1.75)	0.404
Age at atrial switch, <12 mo	0.37 (0.12–1.11)	0.077
Ventricular septum defect	3.62 (1.43–9.18)	0.007
Male sex	2.79 (0.81–9.63)	0.106
IART	1.56 (0.59–4.15)	0.375

d-TGA indicates dextro-transposition of the great arteries; HR, hazard ratio; HTx, heart transplantation; IART, intra-atrial re-entry tachycardia; LVAD, left ventricular assist device; SCD, sudden cardiac death; VF, ventricular fibrillation; and VT, ventricular tachycardia.

encountered at the index procedure in 77% of cases. In contrast, Roca-Luque et al used mainly a retrograde aortic access to the PVA in 23 patients with d-TGA and atrial switch and achieved a success rate of 52%.[20] When including patients with other forms of CHD, the presence of d-TGA was a predictor of ablation failure in their study. Wu et al also used only a retrograde access to the PVA in 34 ablation procedures, but in 9 procedures remote magnetic navigation was used.[19] All IARTs targeted with remote magnetic navigation were successfully ablated, compared with a success rate of only 77% with a retrograde aortic approach. In earlier cases of our cohort, access to the PVA was not obtained, or only by a retrograde aortic approach. Lack of transbaffle access was frequent in our failed cases, and most of these cases were performed before 2013. Since then, we obtain transbaffle access in most ablation procedures, resulting in a high success rate. It is of utmost importance to be familiar with and prepared for transbaffle access for ablation procedures in patients with d-TGA and atrial switch. Methods on how to obtain transbaffle access have been described in detail in the literature.[21,22] If available, retrograde access with remote magnetic navigation may be used as an alternative.[19] The coronary sinus ostium may drain into the PVA or the systemic-venous atrium, depending on the surgical technique.[23] Accordingly, if an AVNRT is encountered, the slow pathway may also have to be ablated from the PVA, ideally via transbaffle puncture.[24]

In the systematic review mentioned above, survival rate was 76% at the age of 30 years and 65% at the age of 40 years.[10] Similar to our study, survival was worse in patients with VSD, defined as complex d-TGA, but additionally, survival was also worse in patients with Mustard procedure and a history of supraventricular tachycardia. SCD was the most common cause of late mortality, which decreased in recent populations.[10] As mentioned by previous publications, the worse survival of patients with d-TGA and atrial switch with a history of VSD may be attributable to a combination of increased arrhythmogenesis caused by postoperative scars and the hemodynamic consequences of volume overload and ventricular remodeling.[25] The fact that patients with a history of VSD in our population more frequently received advanced heart failure therapy and atrioventricular block was more prevalent support this hypothesis. A large study, including >1100 patients with d-TGA, recently reported independent predictors of survival to be prior ventricular arrhythmia, heart failure admission, complex anatomical features, QRS duration >120 ms, and severe right ventricle dysfunction.[26] Another study also found right ventricular dysfunction and permanent pacing to be associated with adverse events.[27] We found no association of IART with outcome, nor was outcome different according to the type of atrial switch. However, it has to be mentioned that IART with 1:1 atrioventricular conduction may also lead to SCD, as does electromechanical dissociation. Thus, not all instances of SCD may have been attributable to ventricular arrhythmias.

Our study is limited by its retrospective design. Documentation of arrhythmias, ablation, and device procedures was limited in some of the earlier cases.

In conclusion, arrhythmia burden is high in patients with d-TGA and atrial switch, and associated rhythm interventions are common in those reaching adulthood. Mortality is substantial up to a median age of 35 years, and a concomitant VSD is associated with a worse outcome.

ARTICLE INFORMATION

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Supplemental Material

Tables S1–S3

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Supplemental Material

Table S1. Oral anticoagulation and antiarrhythmic drugs.

	Total (n=207)
Patients with oral anticoagulation	71 (34%)
Acenocoumarol/phenprocoumon	25 (35%)
NOAC	31 (44%)
Type of oral anticoagulation unclear	15 (21%)
Indications for oral anticoagulation	
IART/atrial Fibrillation	42 (59%)
Baffle leak	4 (6%)
Baffle leak and IART	2 (3%)
Baffle stenosis	2 (3%)
Ischemic stroke/transient ischemic attack	7 (10%)
IART and LVAD	2 (3%)
Pulmonary Embolism	1 (1%)
Unknown	11 (16%)
Patients on antiarrhythmic drugs	61 (30%)
Betablocker	25 (41%)
Amiodarone	31 (51%)
Sotalol	8 (13%)
Verapamil	3 (5%)
Flecainide, ibutilide, propafenone and/or dronedarone	6 (10%)

Shown are numbers with percentages in parentheses. IART: intra-atrial reentry tachycardia;

LVAD: left ventricular assist device; NOAC: novel oral anticoagulant.

Table S2. Electrophysiological studies and ablation procedures continued.

Electrophysiological studies and ablation procedures	
Number of patients/procedures	40/64
One procedure	25 (63%)
Two procedures	9 (23%)
Three procedures	4 (10%)
Four procedures	1 (3%)
Five procedures	1 (3%)
Procedural characteristics	
Use of 3D mapping system	48 (96%)
Irrigated ablation	42 (82%)
Force-sensing catheter	31 (62%)
Procedure duration, minutes	240 (180; 272)
Fluoroscopy time, minutes	16 (7; 25)
Complications	
Groin hematoma without intervention	4 (6%)
Complete AV block with pacemaker implantation	2 (3%)
Urethral bleeding after urinary catheter insertion	1 (2%)

Shown are numbers with percentages in parentheses or median with interquartile range.

Percentages are total of those with available data. 3D: three-dimensional; AV: atrioventricular.

Table S3. Detailed description of electrophysiological studies and ablation procedures.

Patient ID	Procedure #	Year	Description of ablation targets and complications	Access	Success
TGA-012	1	2018	CTI-dependent IART, ablation of CTI performed. Typical and atypical AVNRT, ablation performed. Complication: groin hematoma without need for further intervention.	PV-p	Complete
TGA-021	1	2015	CTI-dependent IART and micro-reentry located in region of CTI, ablation of CTI and micro-reentry performed.	PV-l	Complete
TGA-026	1	2018	CTI-dependent IART, ablation of CTI performed.	PV-p	Complete
TGA-031	1	2003	AVNRT (not specified whether typical/atypical), ablation performed.	SV	Unknown
TGA-036	1	2019	CTI-dependent IART, ablation of CTI performed.	PV-p	Complete
TGA-046	1	2009	CTI-dependent IART, ablation of CTI performed.	PV-r	Complete
	2	2017	Micro-reentry located on the roof of the right atrium just behind the tricuspid valve annulus, ablation performed. Complication: groin hematoma without need for further intervention.	SV&PV-p	Complete
TGA-048	1	2002	CTI-dependent IART, ablation of CTI performed.	SV	Partial
	2	2004	CTI-dependent IART, ablation of CTI performed. Scar-related IART, ablation line from the scar to the tricuspid annulus performed.	PV-r	Complete
	3	2005	CTI-dependent IART, ablation of CTI performed.	PV-r	Complete
	4	2006	Atypical AVNRT, ablation performed.	SV&PV-r	Complete
	5	2018	CTI-dependent IART, ablation of CTI performed. Scar-related IART located in the lateral right atrium, ablation of scar region performed.	SV&PV-p	Complete
TGA-051	1	2018	CTI-dependent IART, ablation of CTI performed.	PV-l	Partial
TGA-052	1	2019	CTI-dependent IART, ablation of CTI performed. Scar-related IART located in the lateral right atrium, ablation line to the inferior vena cava performed. Micro-reentry located at the remaining atrial septum, focal ablation performed. Complication: urethral bleeding after urinary catheter insertion	PV-p	Complete
TGA-055	1	2015	CTI-dependent IART, ablation of CTI performed.	PV-l	Complete
TGA-060	1	2012	CTI-dependent IART, ablation of CTI performed.	SV&PV-r	Failure
	2	2012	Micro-reentry located in the right lateral region of the right atrium next to the tricuspid valve, focal ablation performed.	PV-p	Complete
	3	2012	EPS performed, no arrhythmia inducible.	SV	NA
TGA-063	1	2018	CTI-dependent IART, ablation of CTI performed. Micro-reentry located at the superior SV baffle at the junction to a stent and near to the sinus node. No ablation performed because of proximity to the sinus node with risk of subsequent pacemaker dependency. Complication: groin hematoma without need for further intervention.	PV-p	Failure
TGA-065	1	2011	CTI-dependent IART, ablation of CTI performed.	PV-l&PV-r	Complete
TGA-067	1	2013	CTI-dependent IART, ablation of CTI performed.	PV-p	Complete

TGA-068	1	2018	CTI-dependent IART, ablation of CTI performed. Micro-reentry located at the anterior superior segment of the SV baffle at the lateral suture line, ablation performed. Micro-reentry located at the remaining atrial septum, not ablated because clinically not relevant.	SV&PV-p	Partial
TGA-069	1	2019	CTI-dependent IART, ablation of CTI performed.	PV-p	Complete
TGA-070	1	2019	Procedure aborted because of agenesis of vena cava inferior.	NA	NA
	2	2019	Access via jugular veins, failure of superior baffle puncture due to extensive calcification.	NA	NA
	3	2019	CTI-dependent IART, ablation of CTI performed. Typical AVNRT, ablation performed.	PV-r	Complete
TGA-077	1	2013	CTI-dependent IART, ablation of CTI performed.	PV-p	Complete
	2	2020	EPS, no inducible arrhythmia.	PV-p	NA
TGA-082	1	2019	EPS for VT negative (non-sustained VT detected on implantable cardiac monitor)	NA	NA
TGA-085	1	2001	CTI-dependent IART, ablation of CTI performed.	SV	Complete
TGA-095	1	2002	CTI-dependent IART, ablation of CTI performed.	SV	Failure
	2	2012	CTI-dependent IART, ablation of CTI performed.	PV-r&PV-p	Complete
TGA-103	1	2006	EPS for unclear syncope negative.	NA	NA
TGA-105	1	2001	EPS for VT (documentation of VT on pacemaker). VF inducible. ICD subsequently implanted.	NA	NA
TGA-113	1	2012	CTI-dependent IART, ablation of CTI performed.	SV	Failure
	2	2016	CTI-dependent IART, ablation of CTI performed.	PV-r	Complete
TGA-118	1	2002	EPS for palpitations and syncope. IART inducible. Amiodarone therapy initiated.	NA	NA
TGA-125	1	2013	CTI-dependent IART, ablation of CTI performed. Complication: groin hematoma without need for further intervention.	SV	Partial
	2	2013	CTI-dependent IART, ablation of CTI performed.	PV-r	Complete
TGA-127	1	2018	CTI dependent IART, ablation of CTI performed. Pulmonary vein isolation for atrial fibrillation. Complication: complete AV block with subsequent pacemaker implantation.	SV&PV-p	Complete
TGA-129	1	2016	CTI dependent IART, ablation of CTI performed. Non-CTI-dependent IART located in the inferior right atrium, linear ablation in SV baffle performed with extension to an inter-caval line.	SV&PV-r	Partial
	2	2017	Micro-reentry located at the posterior junction of the superior vena cava with the right atrium, focal ablation performed.	SV	Complete
	3	2017	CTI-dependent IART, ablation of CTI performed. Focal re-ablation of the previously described arrhythmia.	SV	Complete
	4	2019	Micro-reentry located at the base of the remaining inter-atrial septum, ablation performed. Complication: complete AV block with subsequent pacemaker implantation.	PV-p	Complete
TGA-135	1	2003	EPS, no data available.	NA	NA
	2	2003	CTI-dependent IART, ablation of CTI performed.	SV	Unknown
	3	2003	CTI-dependent IART, ablation of CTI performed.	SV	Complete
TGA-138	1	2005	EPS, no inducible arrhythmia.	NA	NA
	2	2016	Micro-reentry located in the left atrium in the region of the right upper pulmonary vein, focal ablation performed. Mitral isthmus-dependent tachycardia, ablation line from the inferior mitral annulus to the inferior vena cava.	SV&PV	Complete

TGA-141	1	2013	Micro-reentry located at the junction of the superior vena cava with the right atrium and distal to the sinus node, ablation performed.	SV	Failure
	2	2016	CTI-dependent IART, ablation of CTI performed.	SV&PV-l	Complete
	3	2019	CTI-dependent IART, ablation of CTI performed.	SV&PV-l	Complete
TGA-142	1	2006	CTI-dependent IART, ablation of CTI performed.	SV	Complete
	2	2015	CTI-dependent IART, ablation of CTI performed.	SV&PV-r	Complete
TGA-145	1	2012	EPS, no inducible arrhythmia.	NA	NA
TGA-155	1	2010	EPS, no inducible arrhythmia.	NA	NA
TGA-168	1	2016	Microreentry , no data available.	SV	Complete
TGA-174	1	2002	CTI-dependent IART, ablation of CTI performed.	SV	Partial
	2	2002	CTI-dependent IART, ablation of CTI performed.	SV	Failure
TGA-175	1	2008	CTI-dependent IART, ablation of CTI performed.	SV	Failure
TGA-176	1	1998	EPS, VF induced.	NA	NA
TGA-181	1	2004	CTI-dependent IART, ablation of CTI performed. Micro-reentry located in the posterior right atrium, ablation performed.	SV	Partial
TGA-190	1	2018	Micro-reentry located in the region of a baffle leak at the tricuspid valve annulus, ablation performed.	PV-l	Complete
	2	2018	Micro-reentry located in the region of the SV baffle, ablation performed.	PV-l	Complete

AVNRT: atrioventricular nodal reentry tachycardia; CTI: cavotricuspid isthmus; EPS: electrophysiological study; IART: intra-atrial reentry tachycardia; NA: not applicable; PV-l, PV-p and PV-r: pulmonary venous baffle accessed via leak (-l), via baffle puncture (-p), or retrograde via aorta (-r), respectively; SV: systemic venous baffle; VF: ventricular fibrillation; VT: ventricular tachycardia