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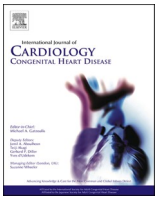

Atrial arrhythmia predicts late events and mortality in patients with D-transposition of the great arteries and atrial switch repair

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ABSTRACT

Aims: Patients with D-transposition of the great arteries (D-TGA) and atrial switch experience late morbidity and mortality related to atrial arrhythmias and systemic right ventricular (SRV) failure. We sought to analyze the influence of atrial arrhythmias on long-term outcomes in this group.

Methods: A retrospective review of all patients with D-TGA and atrial switch followed at a tertiary care center was performed.

Results: 148 patients (63.5 % male; age 30.4 ± 10.6 years) were followed for 12 ± 9.8 years. Death or cardiac transplantation occurred in 22(15 %) patients and heart failure hospitalization occurred in 30(20 %) patients. Atrial arrhythmias were documented in 82(55.4 %) patients. Atrial fibrillation at the first visit (Kaplan-Meier estimate, $p = 0.003$) and atrial fibrillation as a time-dependent variable (HR 3.50, $p = 0.006$) predicted increased risk of death or cardiac transplantation. A triad of atrial fibrillation, prolonged QRS duration/RBBB, and severe SRV dysfunction (SRV EF < 35 %) emerged as a unique signature of a higher-risk population.

Atrial tachycardia and flutter, while not associated with mortality, increased the risk of heart failure hospitalization (HR 3.5, $p = 0.001$). Moreover, 2/6 cases of resuscitated sudden cardiac arrest were caused by atrial flutter, and more patients received inappropriate shocks for atrial arrhythmias(16 %) than appropriate shocks (2.3 %).

Conclusion: In D-TGA patients with atrial switch, there is a complex interplay between atrial arrhythmias and the SRV. Key ECG parameters, arrhythmia events and sequelae create a unique patient-specific fingerprint strongly associated with future events and mortality. This higher-risk cohort will need further characterization to delineate who may benefit from preemptive arrhythmia intervention.

1. Introduction

Prior to arterial switch operations, older patients with Dextro-Transposition of the Great Arteries (D-TGA) were palliated with atrial switch repairs, utilizing atrial redirection baffles (Mustard or Senning). These patients now face the many downstream effects of the transposed circulation with its altered hemodynamic demands and post-surgical scars with potential arrhythmic consequences [1–6].

The extensive atrial reconstruction and abnormal atrial substrate provide an ideal nidus for reentrant arrhythmias [7], as well as impact sinus node and AV node function. The hemodynamic profile also predisposes some patients to progressive volume and pressure overload of the systemic right ventricle (SRV); consequent maladaptive ventricular remodelling places certain patients at risk for ventricular arrhythmias and sudden cardiac death [8].

In this D-TGA retrospective single center multisite cohort study, we sought to characterize atrial arrhythmias and understand their influence over late events (heart failure hospitalization, death, or cardiac transplantation). This approach may help the clinician recognize the higher-risk patient and prioritize early targeted intervention. Furthermore, we describe the approaches and impact of atrial arrhythmia interventions at a tertiary referral ACHD center.

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Abbreviations

D-TGA – Dextro-Transposition of the Great Arteries
ECG - Electrocardiogram
SRV – Systemic Right Ventricle (Ventricular)
SRV EF – Systemic Right Ventricular Ejection Fraction
LV EF – Subpulmonary Left Ventricular Ejection Fraction
RBBB – Right Bundle Branch Block on the ECG
Atrial MAZE – Surgical procedure to treat atrial fibrillation
ICD – Implantable Cardioverter Defibrillator
CTI – Cavo-tricuspid Isthmus
IART – Intra-atrial Reentrant Tachycardia (non-CTI dependent atrial flutter for the purposes of this study)
FAT – Focal Atrial Tachycardia (may be caused by abnormal automaticity, triggered activity, or microreentry)

2. Methods

2.1. Patient population

Patients with D-TGA, atrial switch, two-ventricle physiology, and SRV followed at one of the three Mayo Clinic sites in Rochester, Minnesota, Jacksonville, Florida, or Scottsdale, Arizona were considered for enrollment. Exclusion criteria included single ventricle and eventual anatomic repair with arterial switch. The study protocol was approved by the Mayo Clinic Institutional Review Board and individual consent was waived due to the retrospective and deidentified nature of the data.

2.2. Data collection

A comprehensive review of the electronic medical record (EMR) was performed, including all relevant notes, 12-lead ECGs, ambulatory recordings, echocardiograms, cardiac CTs and MRIs, as well as the original operative reports, electrophysiology study reports, device implantation reports, and follow-up device interrogation data. Data was collected using REDCap (Research Electronic Data Capture), a secure web platform within the internal Mayo Clinic network.

To avoid comparing pediatric ECGs with adult ECGs, we established the baseline for the survival analysis using ECGs and echocardiograms as the time of the first adult ECG performed closest to the age of 18. The baseline echocardiogram was also the first echocardiogram closest to the age of 18 for each patient.

Clinical events, including atrial and ventricular arrhythmia, sinus node or AV node dysfunction, indication and timing of any arrhythmia interventions or cardiac implantable devices, presence of syncope, coronary artery disease, thromboembolic complications, stroke, pregnancy, heart failure symptoms, and timing of the first heart failure hospitalization, were all documented. The dates and circumstances of key events were recorded.

2.2.1. The D-TGA cohort

Patients underwent atrial switch with either Mustard (82.4 %) or Senning (15.6 %) operations. Additionally, 104(70 %) had a balloon atrial septostomy or septectomy, and 2(1.4 %) patients had Blalock-Taussig shunts prior to atrial switch. Mean age at the time of atrial switch was 1.9 ± 2.9 years. While most patients underwent atrial switch during infancy or childhood, 3 patients underwent atrial switch later in life (at ages 14, 16, and 20), for palliative purposes.

Additional details on cardiac anatomy, procedural, and surgical history are summarized in Table 1.

Table 1
Baseline Characteristics of the D-TGA cohort.

	Overall (N = 148)
Male	94 (63.5 %)
Age at first cardiology visit (years)	30.4 ± 10.6
Mean ± SD	31 (23, 37)
Median (Q1, Q3)	31.6 ± 8.7
Age at first adult ECG[a] (years)	31 (24, 38)
Mean ± SD	12 ± 9.8
Median (Q1, Q3)	10.9 (3.9, 16.9)
Duration of follow-up after the first visit	11 ± 8
Mean ± SD	10.4 (4, 16)
Median (Q1, Q3)	42 ± 9.4
Duration of follow-up after the first ECG	41 (36, 49)
Mean ± SD	
Median (Q1, Q3)	
Age at last ECG (years)	
Mean ± SD	
Median (Q1, Q3)	
Associated congenital defects	
N	148 (100 %)
VSD	21 (14.2 %)
ASD	6 (4.1 %)
PDA	9 (6.1 %)
Coarctation of the aorta	2 (1.4 %)
Subpulmonary outflow tract obstruction	18 (12.2 %)
Systemic outflow tract obstruction	1 (0.7 %)
Dextrocardia	1 (0.7 %)
Heterotaxy syndrome	1 (0.7 %)
Coronary artery anomalies	11 (7.4 %)
Atrial switch operations	148 (100 %)
N	122 (82.4 %)
Mustard	26 (15.6 %)
Senning	104 (70 %)
Balloon septectomy/atrial septostomy prior to atrial switch	2 (1.4 %)
Palliative Blalock-Taussig shunt prior to atrial switch	1.9 ± 2.9
Age at atrial switch[b] (years)	1 (0.5, 2)
Mean ± SD	1978 (1973, 1982)
Median (Q1, Q3)	1955–1999
Year of first atrial switch operation	148 (100 %)
Median (Q1, Q3)	51 (34.5 %)
Range	31 (21 %)
Baffle complications and revision	5 (3.4 %)
N	29 (19.6 %)
Baffle obstruction	23 (15.5 %)
Baffle leak	5 (3.4 %)
Thrombus	148 (100 %)
Baffle revision/stenting	4 (2.7 %)
Surgical baffle revision	7 (4.7 %)
Percutaneous closure of baffle leak or iatrogenic ASD	3 (2 %)
Additional cardiac surgeries	4 (2.7 %)
N	14 (9.5 %)
Right sided cryo MAZE and cryoablation of the cavotricuspid isthmus	7 (4.7 %)
Systemic AV valve surgery	7 (4.7 %)
Mechanical valve replacement	5 (3.4 %)
Valve repair with annuloplasty ring	2 (1.4 %)
VSD closure	1 (0.7 %)
Palliative pulmonary artery banding (before closing large shunts)	2 (1.4 %)
Subpulmonary outflow tract obstruction relief	7 (4.7 %)
Subpulmonary resection/pulmonary valvotomy	2 (1.4 %)
LV to PA conduit and VSD repair	16 (10.8 %)
Pulmonary valve replacement	11 (7.4 %)
Aortic valve replacement	10 (6.8 %)
PDA ligation	2 (1.4 %)
Coarctation of the aorta repair	
Epicardial pacing leads	
Atrial pacing (Sinus node dysfunction)	
Ventricular pacing (AV block)	
Epicardial defibrillator leads (ICD)	

VSD - Ventricular septal defect; ASD - Atrial septal defect; PDA - Patent ductus arteriosus; PA – Pulmonary artery; AV valve – Atrioventricular valve (left, right); Cryo MAZE – Surgical operation for atrial fibrillation; LV- Left ventricle; ICD-Implantable cardioverter defibrillator.

[a] **Age at first adult evaluation** was the age at the first Mayo Clinic ECG closest to the age of 18; this was considered the baseline for the survival analysis.
[b] While most patients underwent atrial switch operations during infancy or childhood, 3 patients with large VSDs underwent atrial switch operations later in life (at ages 14, 16, and 20), for palliative purposes.

2.3. Baffle-related complications

Baffle obstruction was documented in 51(34.5 %) patients, baffle leak in 31(21 %) patients, and baffle revision or stenting occurred in 29 (19.6 %) patients. Surgical baffle revision was performed in 23(15.5 %) cases. Percutaneous closure of a baffle leak or iatrogenic ASD was performed in 5(3.4 %) cases. Cardiac thrombus was recorded in 5(3.4 %) patients.

2.4. Other cardiac surgical interventions

Systemic AV valve surgery was performed in 7(4.7 %) patients; 3(2 %) underwent mechanical valve replacement, and 4(2.7 %) underwent valve repair. A right atrial cryo-MAZE, including cryoablation of the cavotricuspid isthmus (CTI), was performed in 4(2.7 %) patients.

Surgical VSD closure was performed in 14(9 %) patients; 7(4.7 %) required palliative pulmonary artery banding before closing large shunts. Surgery to relieve a hemodynamically significant subpulmonary outflow tract obstruction was performed in 7(4.7 %) patients; a left ventricular to pulmonary artery conduit and VSD repair was employed in 2(1.4 %) patients.

Additional cardiac surgeries are summarized in Table 1.

3. Final outcomes and establishing the cause of death

All patients were followed until the end of study (last documented clinic visit as of December 30, 2021), death, or cardiac transplantation. A cause of death (either sudden death, cardiac death, or non-cardiac death) was established based on the physician documentation in the EMR, autopsy reports and death certificates, when available. Sudden cardiac death (SCD) was defined as sudden unexpected death within 24 h of the patient being well. Cardiac death was directly related to end-stage heart failure, cardiogenic shock, or arrhythmia. A non-cardiac death was assigned if none of the above etiologies were present (e.g, an accident, infection, malignancy, liver cirrhosis, or another complication was the direct cause of death).

For patients with unknown causes of death based on the Mayo Clinic record, a search was performed within the United States National Death Index (NDI) database and the cause of death was also categorized as sudden death, cardiac death, or non-cardiac death following the above predefined criteria. This helped reclassify the cause of death from unknown to either cardiac or non-cardiac in 7 patients. Even patients without a direct cardiac cause of death had advanced cardiomyopathy (Details about the cause of death and autopsy reports are found in Supplemental Table 1). The final analysis was performed using all-cause mortality.

4. 12-Lead electrocardiography (ECG)

The first adult ECG and the last ECG performed at Mayo Clinic were recorded. The rhythm was documented as either sinus rhythm, ectopic atrial rhythm, atrial fibrillation, atrial tachycardia or flutter, supraventricular tachycardia, junctional rhythm or atrial pacing. Presence of ventricular pacing, native QRS interval duration, QTc interval duration (using the Bazett formula), presence of QRS fragmentation, right or left bundle branch blocks (considering cardiac situs), and voltage criteria for right or left ventricular hypertrophy were recorded. QRS fragmentation was defined for the non-paced QRS as the presence of extra positive notches (R') or extra notches on the nadir of the R wave or of the S wave, in 2 continuous leads. For patients with prolonged QRS duration >120msec or right bundle branch block pattern, QRS fragmentation was adjudicated in the presence of >2 notches (as bundle branch block already has 2 notches), as previously defined [9].

2D Transthoracic Echocardiography.

The first and last adult Mayo Clinic echocardiograms were reviewed, including ventricular chamber size, systolic function, AV valve function, outflow tract obstruction, the presence of pulmonary hypertension (in the absence of any significant pulmonary outflow tract gradient), and any evidence of intracardiac thrombus, baffle stenosis, baffle leak, or shunt.

4.1. Cardiac CTs and MRIs

SRV measurements (end-diastolic volume index, SRV EDVI, and ejection fraction, SRV EF) were recorded. Additional information on atrial anatomy, baffle stenosis, leak, shunt, or thrombus, and the presence of scar/late gadolinium enhancement on MRI were also recorded.

4.1.1. ICD therapies

All available device interrogations and all the electrophysiology consultation notes were reviewed, and defibrillator shocks were classified as either appropriate (for ventricular arrhythmia), inappropriate (for supraventricular tachycardia/atrial arrhythmia or for lead/device malfunction), and of unknown appropriateness (no recording was available and there was no consensus regarding the shock appropriateness in the EMR).

4.2. Statistical analysis

Continuous variables were summarized with mean and standard deviation (mean ± STDEV), as well as median with first and third quartiles (median (Q1, Q3). Categorical variables were summarized with number and percentage of patients. Time-to-event outcomes were estimated using the Kaplan-Meier method. Univariate Cox proportional hazards models were used to assess the associations of patient demographics, background anatomy, surgical history and clinical variables with each of the endpoints. Significantly associated variables of interest (two-sided p-values <0.05) were obtained. A series of multivariate Cox proportional hazards models were completed, including different combinations of 2 or 3 statistically significant univariate predictors of interest at a time. The low number of events ($N = 22$) precluded using more variables to build the multivariate model. The statistical analysis was performed using the BlueSky Statistics software version 10.3.1 (Chicago, IL) available on the Mayo Clinic network, and also confirmed with SAS version 9.4(Cary, NC).

5. Results

5.1. Patient population and outcomes

A cohort of 148 patients with D-TGA and atrial switch (94 (63.5 %) male, mean age 30.4 ± 10.6 years) were followed for 12 ± 9.8 years (median 10.9 (3.9, 16.9) years). The primary outcome, death or cardiac transplantation, occurred in 22(15 %) patients; 19 patients died and 3 underwent cardiac transplantation. Sudden cardiac arrest (SCA), defined as cardiovascular collapse requiring resuscitation, was documented in 9(6.1 %) patients; of these, 6(4 %) were initially resuscitated and the other 3 were included in the SCD outcome. However, onepatient with SCA due to poorly tolerated atrial flutter, initially successfully resuscitated, eventually succumbed to recurrent SCA/SCD, with no rhythm recordings available at the time.

Of the 4 patients with SCD, 1 patient had a spontaneous coronary artery dissection (SCAD), 2 patients had SCD in the setting of severe SRV dysfunction (PEA arrest and ventricular fibrillation respectively), and a 4th patient had an out-of-hospital cardiac arrest with no rhythm recordings available at the time (prior SCA secondary to atrial

arrhythmia).

Of the 7 patients with cardiac death, 1 patient developed irreversible hypotension during induction of anesthesia in the setting of severe pulmonary hypertension, and 6 patients succumbed to severe SRV dysfunction.

The final decompensation and death were also a consequence of their underlying cardiac condition in 4/8 patients classified as "non-cardiac death", who suffered infectious complications secondary to permanent pacing or ventricular assist devices - all related to their primary cardiac diagnosis.

The etiology of SCA was a rapidly conducted atrial flutter in 2 patients with severe SRV dysfunction, presumed ventricular tachycardia in 2 patients (with documented VT in 1 case), and undocumented etiologies, presumed arrhythmic, in 2 patients.

5.2. Clinical characteristics of the D-TGA population

Syncope was documented in 37(25 %) patients (Table 2). Coronary artery disease (more than mild) was documented in 4(2.7 %) patients; of these, 2(1.4 %) patients underwent percutaneous coronary intervention.

Stroke occurred in 22(15 %) patients, with events arising more frequently during infancy or childhood and peri-operatively circa cardiac surgeries or percutaneous cardiac interventions. Two patients sustained stroke in the context of transvenous pacemaker leads and baffle leaks. One patient was treated with lead extraction, baffle stenting, and an epicardial device; the other patient was treated with anticoagulation. One patient sustained a stroke in the context of a non-restrictive VSD; another patient developed a cerebral abscess in the context of a baffle leak; and one patient suffered a transient neurologic event in the setting of staphylococcus endocarditis.

Deep vein thrombosis and pulmonary embolism were documented in 7(4.7 %) and 5(3.4 %) patients respectively.

Clinical heart failure symptoms (NYHA class ≥ II) were documented in 62(42 %) patients, and heart failure hospitalization occurred in 30(20 %).

Twenty-two patients had documented pregnancies, and live births occurred in 19/22(86.4 %). Pregnancy was associated with decompensated heart failure in 5/22(23 %) patients, new onset atrial arrhythmias in 6/22(27.3 %) patients, and preeclampsia in 1(4.5 %) patient.

5.2.1. Medical therapy

Heart failure/ventricular dysfunction was managed with beta-blockers in 90(61 %) patients, ACE-inhibitors/angiotensin receptor blockers in 106(72 %) patients, loop diuretics in 59(40 %) patients, and aldosterone receptor blockers in 40(27 %) patients. Advanced pulmonary hypertension therapies were prescribed in 9 patients (6 %). Antiarrhythmic management is reviewed separately. Oral anticoagulation was used in 68(46 %) patients (vitamin K antagonists were used at one point in 49(33 %), and direct oral anticoagulants in 22(15 %)).

5.2.2. Atrial arrhythmia

At the time of the first visit, a history of atrial arrhythmia (defined as atrial tachycardia, flutter or fibrillation) was already present in 45(30.4 %) patients (Table 2). Atrial tachycardia or flutter were diagnosed in 41 (28 %) patients, and atrial fibrillation in 17(11 %) patients.

By the end of the study, atrial arrhythmias were diagnosed in a total 82(55.4 %) patients; of these, atrial tachycardia or flutter were diagnosed in 73(49.3 %) patients, and atrial fibrillation in 33(22.3 %).

Using the time of the first known atrial arrhythmia episode, a visual representation of the atrial arrhythmia prevalence by decade of age was constructed for this cohort (Fig. 1). Atrial arrhythmia was already diagnosed in 7 % of patients by age 20, in 18 % of patients by age 30, in 45 % of patients by age 40, and in 53 % of patients by age 50.

Table 2
Clinical characteristics and outcomes of the D-TGA cohort.

	Overall (N = 148)
	22 (15 %)
Primary outcome: death or cardiac transplantation	19 (13 %)
All-cause mortality	3 (2 %)
Cardiac transplantation	9 (6.1 %)
Sudden cardiac arrest (SCA)	4 (2.7 %)
Sudden cardiac death (SCD)	6 (4 %)
Resuscitated SCA*	37 (25 %)
Syncope (any type)	4 (2.7 %)
Coronary artery disease	2 (1.4 %)
Myocardial infarction	2 (1.4 %)
Percutaneous coronary intervention	22 (15 %)
Cerebrovascular accident (stroke)	7 (4.7 %)
Deep vein thrombosis	5 (3.4 %)
Pulmonary embolism	62 (42 %)
Clinical heart failure symptoms (NYHA class ≥ II)	**30 (20 %)**
Heart failure hospitalization	**82 (55.4 %)**
Atrial fibrillation, atrial tachycardia, or atrial flutter	33 (22.3 %)
Atrial fibrillation	73 (49.3 %)
Atrial tachycardia or flutter	7 (4.7 %)
AV nodal reentrant tachycardia (AVNRT)	13 (8.8 %)
SVT unknown**	50 (33.8 %)
No supraventricular arrhythmia	31 (21 %)
Junctional rhythm or junctional tachycardia	6 (4 %)
	47 (31.7 %)
Ventricular arrhythmia	8 (5.4 %)
Frequent PVCs (>5000/24 h)	73 (49.3 %)
Nonsustained ventricular tachycardia (NSVT <30sec.)	13 (8.8 %)
Ventricular tachycardia (VT > 30 s or treated due to hemodynamic instability)	N = 60/148 (40.5 %)
Documented sinus node dysfunction	24.4 ± 13
High-grade or complete AV block	23 (14, 33)
Received a pacemaker	0.9–60
Age at first pacemaker (years)	44 (30 %)
Median age (Q1, Q3)	13 (8.8 %)
Range (years)	5 (3.4 %)
Reason for pacemaker	N = 5/148 (3.4 %)
Sinus node dysfunction only	4/5
High-grade or complete AV block	1/5
Both sinus node and AV node dysfunction	Total N = 60
Cardiac resynchronization therapy	44/60 (73.3 %)
Epicardial lead on the systemic RV	11/60 (18.3 %)
Endocardial Bi–V pacing	5/60 (8.3 %)
Type of pacing leads	N = 43/148 (29 %)
Transvenous leads	36.5 ± 9.4 %
Epicardial leads	36 (30, 43)
Both transvenous and epicardial leads are present	17–55
Received a defibrillator (ICD)	Total N = 43
Age at first defibrillator implant (years)	32/43 (74.3 %)
Median age (Q1, Q3)	2/43 (4.7 %)
Range (years)	9/43 (21 %)
Type of defibrillator	10/43 patients
Transvenous ICD lead	1/43 (2.3 %)
Epicardial ICD lead	7/43 (16 %)
Subcutaneous defibrillator (S-ICD)	2/43 (4.7 %)
ICD shocks	33/43 (77 %)
Appropriate shocks for ventricular arrhythmia	
Inappropriate shocks for supraventricular tachycardia/atrial arrhythmia	
Shocks of unknown appropriateness	
No shocks	

Resuscitated SCA* was defined as cardiovascular collapse requiring resuscitation. This was secondary to a supraventricular tachycardia in 2/6 (33.3 %) patients. In 4/6 patients, a malignant ventricular arrhythmia was either known or suspected, and secondary prevention ICDs were implanted (however, no shocks were reported on subsequent follow-up).

SVT unknown** was defined as either non-sustained runs of supraventricular tachycardia on ambulatory monitoring or mention of supraventricular arrhythmia in clinical notes, with no ECG documentation and no electrophysiology study available.

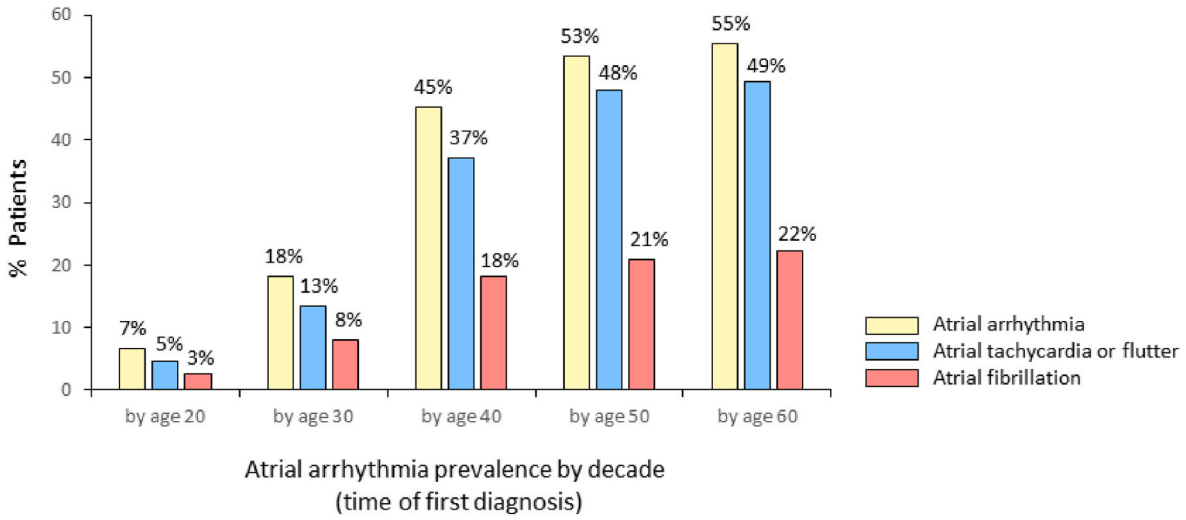

Fig. 1. Atrial Arrhythmia Prevalence in the D-TGA cohort. Atrial arrhythmia was defined as documented atrial tachycardia, atrial flutter, or atrial fibrillation. AVNRT was excluded.

5.2.3. Ventricular arrhythmia

Frequent premature ventricular complexes (PVCs, >5000 per hour) were documented in 6(4 %) patients. Non-sustained ventricular tachycardia (NSVT, <30 s) was noted on ambulatory monitoring in 47 (31.7 %) patients. Ventricular tachycardia (VT, >30sec or requiring intervention for hemodynamic instability) was documented in 8 (5.4 %) patients (Table 2).

5.2.3.1. Sinus node dysfunction, AV block, and pacing devices. The most common complication of baffle surgery was damage to the sinus node area, creating the need for atrial pacing. Injury to the AV node area was a consequence of baffle surgery, VSD repair, or tricuspid valve surgery in 12(8 %) patients, while 1(0.7 %) patient developed iatrogenic complete heart block during a ventricular tachycardia ablation procedure.

Sinus node dysfunction was documented in a total of 73(49.3 %) patients, and high-grade AV block or complete heart block in 13(8.8 %). A pacemaker was placed in 60(40.5 %) patients, with a mean age at pacemaker implant of 24.4 ± 13 years (range 0.9–60 years). The main reason for pacemaker implantation was the need for atrial pacing (44/60, 73.3 % patients with pacemakers); yet ventricular pacing was also necessary in the 13(8.8 %) patients (Table 2).

At the time of the last clinic visit, pacing was being accomplished via transvenous leads in 44/60 (73.3 %) patients, via epicardial leads in 11/60 (18.3 %) patients, and via a combination of transvenous and epicardial leads in 5/60 (8.3 %) patients.

5.2.4. Implantable cardioverter defibrillators (ICDs) and inappropriate shocks

Implantable cardiac defibrillators, present in 43/148 (29 %) patients, with a mean age at implant of 36.4 ± 9.4 years (range 17–55 years), utilized transvenous leads in 32/43(74.4 %) and epicardial leads in 2/43(4.6 %) patients. Subcutaneous ICDs were also utilized in 9/43 (21 %) patients. Of these, 10 out of the 43 patients with ICDs experienced at least one device shock.

While 1(2.3 %) patient received an appropriate shock for documented ventricular tachycardia and 2(4.7 %) patients received shocks of unknown appropriateness, 7(16 %) patients received inappropriate shocks for supraventricular or atrial tachycardia.

5.2.5. Atrial fibrillation is associated with a higher-risk phenotype in D-TGA

Kaplan-Meier estimates were obtained to assess the association between baseline atrial arrhythmia and the primary outcome (Supplemental Fig. 1). Only atrial fibrillation emerged as a significant predictor of this outcome (Fig. 2).

Furthermore, atrial fibrillation as a time-dependent variable also emerged as a significant predictor of death or cardiac transplantation (HR 3.50 (1.45, 8.47), p = 0.006). Atrial tachycardia or flutter were not significantly associated with mortality in this study (p = 0.17).

5.3. Atrial tachycardia or flutter are associated with increased risk of heart failure hospitalization

Hospitalization for decompensated heart failure occurred in 30(20 %) patients. Atrial arrhythmias were encountered in 28(93 %) of these patients. Kaplan-Meier estimates were obtained to assess the effect of baseline atrial arrhythmia on future heart failure hospitalization. Baseline atrial arrhythmia (p = 0.026) and baseline atrial tachycardia or flutter (p < 0.001) were associated with increased risk of heart failure hospitalization (Fig. 3).

5.4. Atrial fibrillation is an independent predictor of death or cardiac transplantation

We sought to devise a practical risk prediction model using only arrhythmia history, a snapshot ECG, and a snapshot echocardiogram - tests routinely obtained in clinical practice.

Kaplan-Meier analyses were performed and revealed a significant change in the risk of death or cardiac transplantation for a QRS duration >140msec and a systemic right ventricular ejection fraction (SRV EF) < 35 % (Supplemental Figure II).

I. Risk Prediction Based on the ECG

Atrial arrhythmia present on the first ECG was associated with a greater than 3-fold increase in the risk of death or cardiac transplantation (HR 3.74, p = 0.003). Furthermore, it was atrial fibrillation that emerged as a distinctive marker (HR 5, p = 0.01), while atrial tachycardia or flutter did not reach statistical significance (p = 0.06) (Fig. 4).

Prolonged QRS duration was associated with the primary outcome (p = 0.002), and a QRS >140msec was associated with a 6-fold increased risk (HR 6.33, p = 0.005). Similarly, right bundle branch block (RBBB) on the first ECG conferred a greater than 6-fold increased risk (HR 6.44, p = 0.001) (Fig. 4).

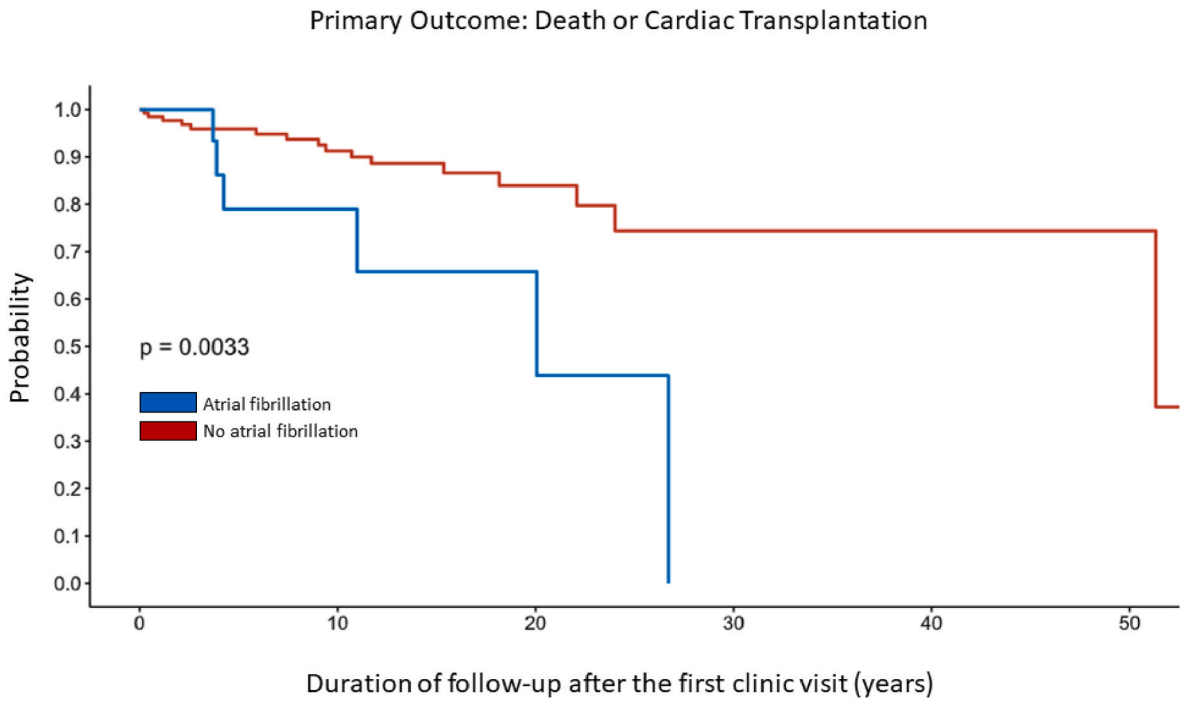

Fig. 2. Kaplan-Meier estimates reveal atrial fibrillation as a marker of increased risk of death or cardiac transplantation.

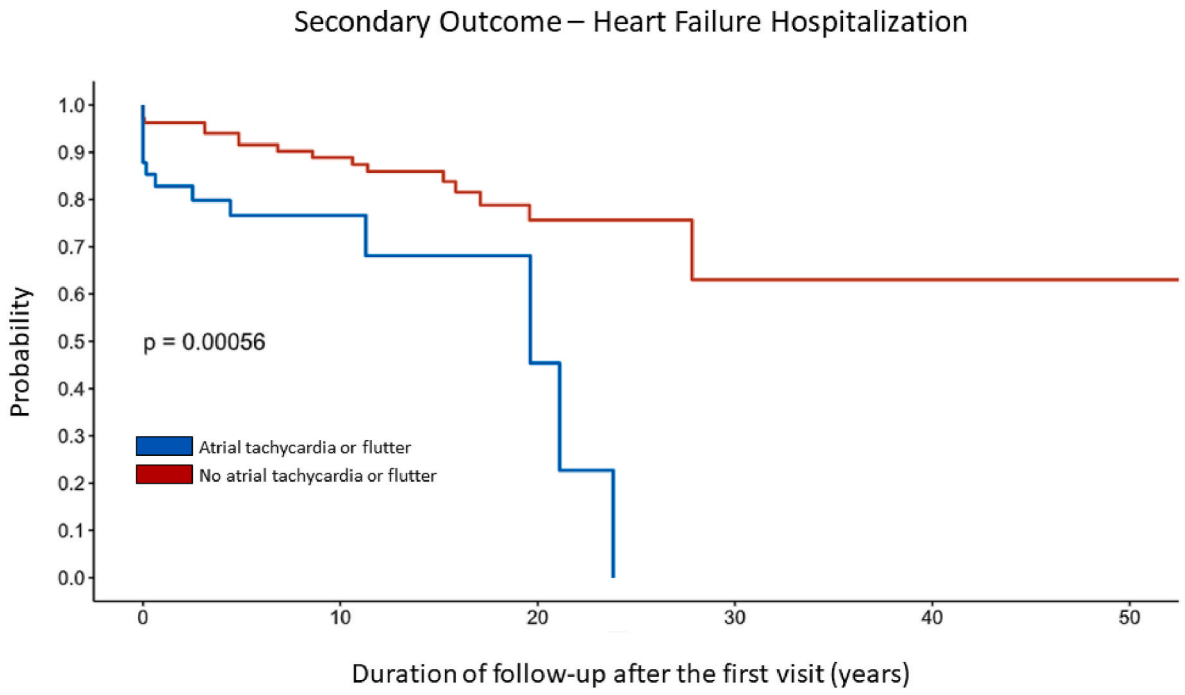

Fig. 3. Kaplan-Meier estimates reveal atrial tachycardia or flutter as a marker of increased risk of heart failure hospitalization.
While not associated with mortality, a history of atrial tachycardia or flutter was associated with increased risk of heart failure hospitalization.

II. Risk Prediction Based on the Echocardiogram

All echocardiograms were reviewed by a congenital echocardiographer in real-time. Original echocardiogram reports contained a visual estimate of the SRV size (i.e., severely enlarged, moderately enlarged, mildly enlarged or normal) and SRV EF (i.e., severely reduced, moderately reduced, mildly reduced or normal). An SRV EF numerical value or visual estimate was also provided in 119/148 (80 %) patients. If there was a range, for example 30–35 %, we used 32.5 % for the statistical analysis. Severe SRV systolic dysfunction was present in 27(18 %) patients (mean RVEF 20 ± 6.6 %), moderate dysfunction in 55(36 %) patients, and mild dysfunction in 49(33 %) patients. The mean RVEF for the entire cohort was 36.5 ± 12 %.

Severe SRV enlargement (HR 2.88, $p = 0.026$), severe SRV systolic dysfunction (HR 6, $p < 0.001$), and severe systemic AV valve regurgitation (HR 8.12, $p < 0.001$) were associated with increased risk of death or cardiac transplantation. For SRV EF <35 %, there was a 5-fold increased risk (HR 5.26, $p < 0.001$) (Fig. 5).

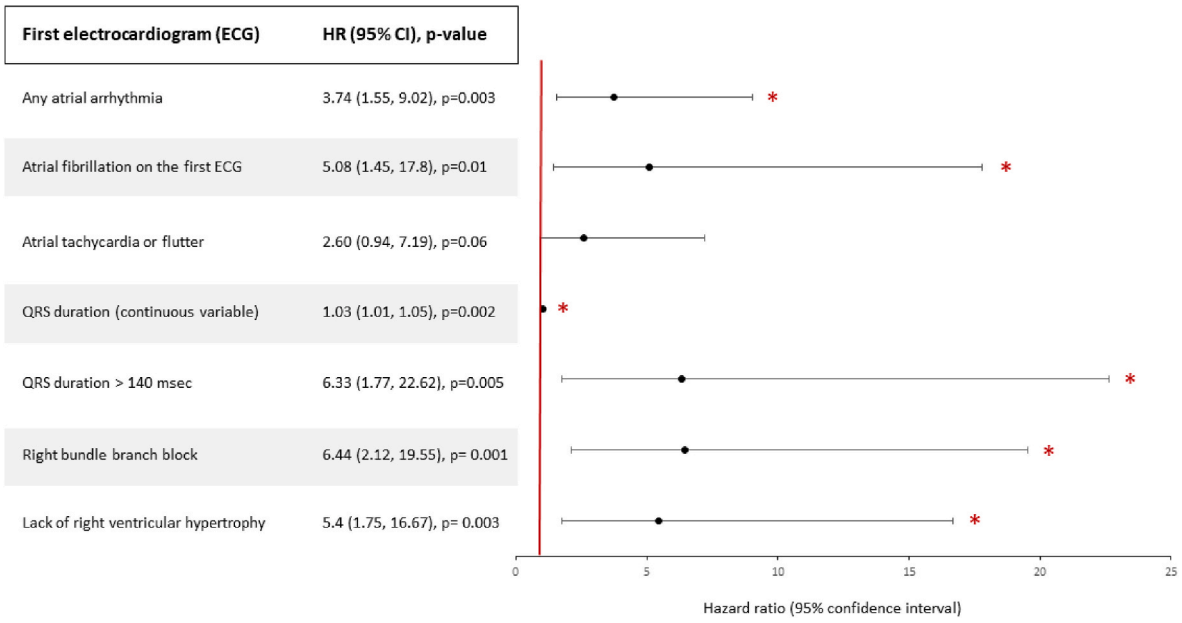

Fig. 4. Univariate predictors of death or cardiac transplantation on the first ECG

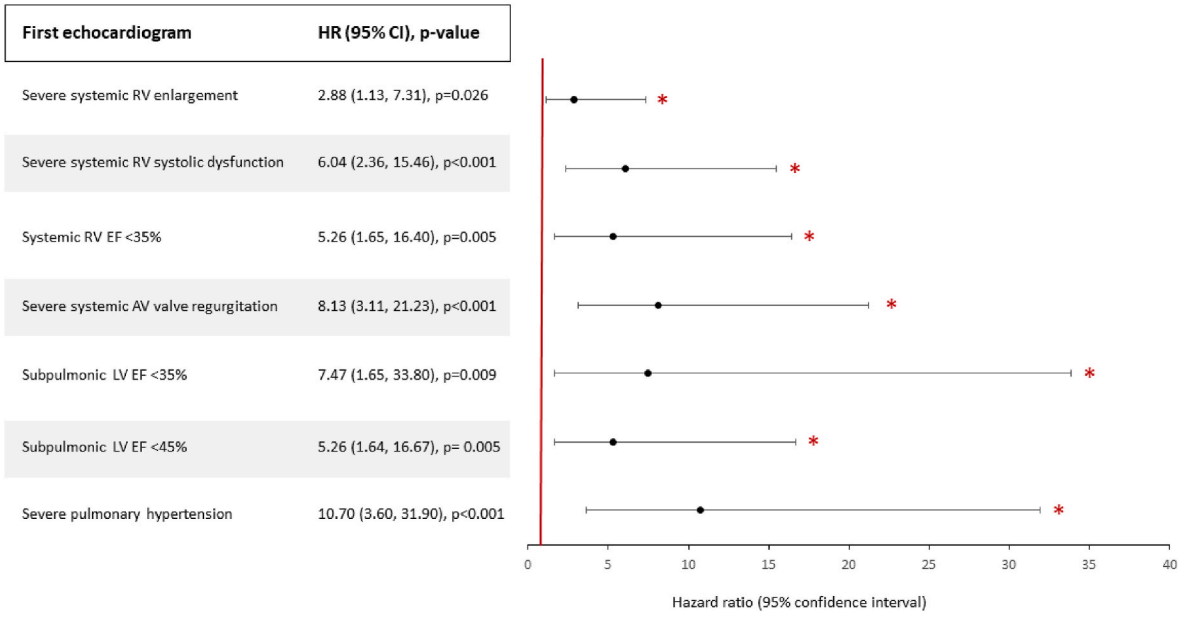

Fig. 5. Univariate predictors of mortality or cardiac transplantation on the first echocardiogram.

Subpulmonary left ventricular dysfunction was also associated with the primary outcome (LVEF <35 %, HR 7.47, p = 0.009). Severe pulmonary hypertension conferred a greater than 10-fold increased risk of death (HR 10.7, p < 0.001).

5.4.1. Risk Prediction Based on clinical, time-dependent variables

Atrial fibrillation as a time-dependent variable (HR 3.5, p = 0.006), but not atrial tachycardia or flutter, again emerged as a significant predictor of the primary outcome (Fig. 6).

Patients who required implantable cardiac electronic devices carried an inherently higher risk compared to their counterparts who did not require these devices. Having a pacemaker (HR 2.93, p = 0.002) or defibrillator (HR 4.7, p = 0.0007) was associated with worse outcomes.

Syncope (of any etiology) was associated with the primary outcome (HR 5.32, p = 0.0005).

Heart failure hospitalization predicted a markedly increased risk of death or cardiac transplantation (HR 7.5, p < 0.0001). Finally, patients who experienced transient heart failure decompensation during pregnancy (HR 4.44, p = 0.02) had an increased long-term risk of death or cardiac transplantation.

IV. A Clinical Signature for Increased Risk of Death or Cardiac Transplantation

The primary outcome, death or cardiac transplantation, occurred in a small number of patients (N = 22), thus precluding inclusion of more than 2–3 variables in the multivariate analysis at a time. A series of multivariate analyses were performed using combinations of 2 significant univariate predictors including atrial fibrillation, prolonged QRS duration or RBBB on the ECG, and SRV EF <35 % on the

Time-dependent variables	HR (95% CI), p-value
Atrial fibrillation (time)	3.50 (1.45, 8.47), p=0.006
Atrial tachycardia or flutter (time)	1.85 (0.77, 4.43), p=0.17
Pacemaker	2.98 (1.23, 7.26), p=0.02
Defibrillator	4.6 (1.89, 10.97), p=0.0007
Syncope	5.32 (2.07, 13.64), p=0.0005
Heart failure during pregnancy	4.44 (1.22, 16.18), p= 0.02
Heart failure hospitalization	7.51 (3.17, 17.81), p<0.0001

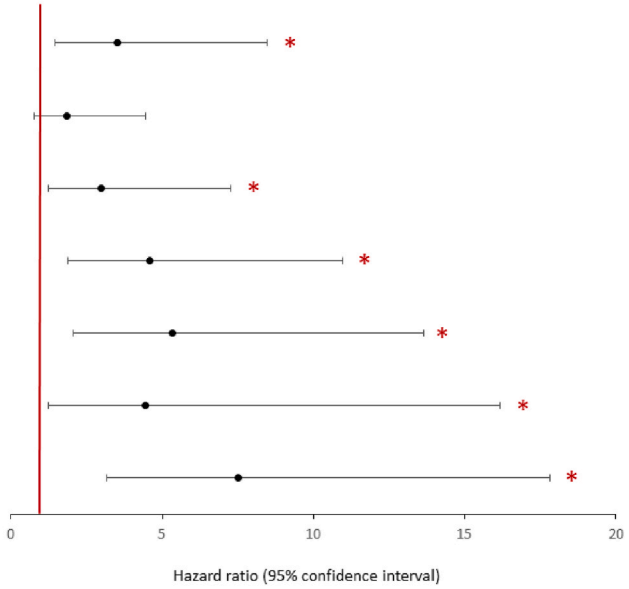

Fig. 6. Time-dependent variables associated with death or cardiac transplantation.

echocardiogram. All these paired combinations were significant in the multivariate analysis (Fig. 7).

Furthermore, a triad of atrial fibrillation, prolonged QRS duration or RBBB on the ECG, and reduced SRV EF <35 % on the echocardiogram emerged as a powerful signature of a higher-risk sub-population (Fig. 8 – Graphical Abstract).

5.5. A Clinical Signature that predicts heart failure hospitalization

A history of atrial tachycardia or flutter (HR 2.9 (1.44, 6.65), p = 0.0036) and SRV EF < 35 % (HR 3.4 (1.76, 8.1), p = 0.0006) were significant independent predictors of heart failure hospitalization.

5.5.1. Poor prediction of sudden cardiac arrest (SCA) or sudden cardiac death (SCD)

There were no significant predictors of SCA or SCD in this cohort, possibly due to the small number of events (9 and 4 patients respectively) – there were no particular congenital defect associations (e.g., VSD repair, outflow tract reconstruction, complex D-TGA), and no significant predictors on the baseline ECG or echocardiogram. Furthermore, there was no association between atrial arrhythmias, ventricular arrhythmias, bundle branch block, ventricular hypertrophy, QRS duration, QRS fragmentation, ventricular pacing, QTc duration, or reduced SRV EF or LVEF and SCA/SCD events.

While cardiac MRI was not systematically performed, it was available in 50(33.8 %) patients and uncovered myocardial scar/late gadolinium enhancement in 3 patients. There was no association between SCA, SCD or all-cause mortality and the presence of ventricular scar.

5.6. Are there anatomic or surgical predictors of atrial arrhythmia?

The different clinical characteristics of the atrial arrhythmia cohort are outlined in Table 3.

In the univariate analysis, the atrial arrhythmia cohort (N = 82) was

Multivariate analysis	HR (95% CI), p-value
Atrial fibrillation (time)	3.27 (1.16, 9.27), p=0.025
QRS duration on the first ECG	1.03 (1.01, 1.05), p=0.005
Atrial fibrillation (time)	3.70 (1.43, 9.76), p=0.007
Right bundle branch block on the first ECG	4.90 (1.56, 15.40), p=0.006
Atrial fibrillation (time)	3.00 (1.00, 8.90), p=0.05
SRV EF <35% on the first echocardiogram	4.24 (1.33, 13.48), p=0.01
SRV EF <35% on the first echocardiogram	5.75 (1.45, 22.80), p=0.01
QRS duration on the first ECG	1.02 (1.00, 1.04), p=0.02
SRV EF <35% on the first echocardiogram	5.20 (1.34, 20.30), p=0.017
Right bundle branch block on the first ECG	5.40 (1.60, 18.10), p=0.006

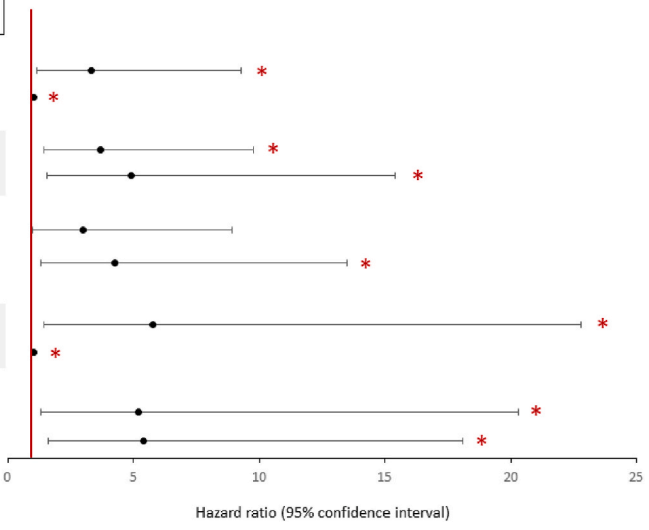

Fig. 7. Multivariate predictors of death or cardiac transplantation.

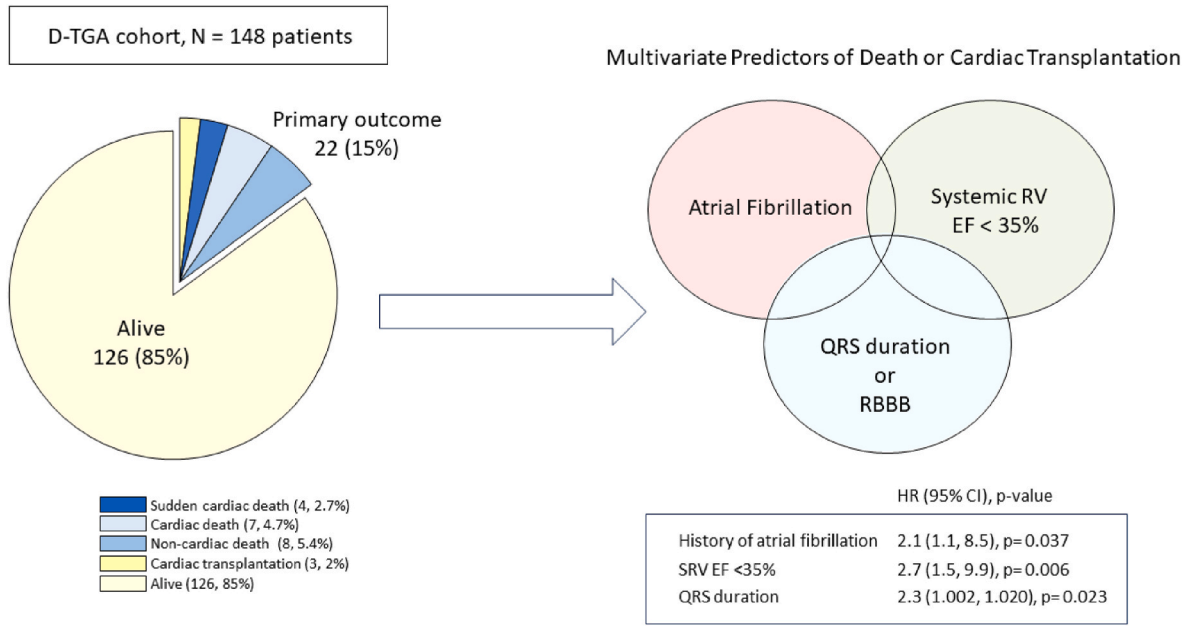

Fig. 8. Graphical Abstract - A Clinical Fingerprint of Increased Risk of Death or Cardiac transplantation in D-TGA with Atrial Switch.
A triad of atrial fibrillation, prolonged QRS duration/RBBB on the ECG, and severely reduced SRV systolic function (SRV EF< 35 %) on the echocardiogram, constitute a practical and quick assessment tool, easy to implement in clinical practice. In this multivariate analysis, "history of atrial fibrillation" was adjudicated if atrial fibrillation was already diagnosed at the time of the first adult ECG. Similarly, the presence of RBBB, the QRS duration in milliseconds, and the presence of severe SRV dysfunction (SRV EF <35 %) were also adjudicated at the time of the first ECG and echocardiogram.
RBBB, right bundle branch block. SRV EF, systemic right ventricular ejection fraction.

Table 3
Comparison of Atrial Arrhythmia and Arrhythmia-Free Groups
Red highlights significant differences between groups.

Clinical characteristics (N, % of each group)	Atrial arrhythmia	No atrial arrhythmia
Number of patients	N = 82	N = 66
Male	58 (70.7 %)	36 (54.5 %)
Age at first contact (years)	32.7 ± 11	27.6 ± 9.4
Age at last contact (years)	44 ± 8	38 ± 9.5
ASD	3 (3.7 %)	3 (4.5 %)
VSD	12 (14.6 %)	9 (13.6 %)
VSD closure	9 (11 %)	5 (7.6 %)
Subpulmonary outflow tract surgery	6 (7.3 %)	1 (1.5 %)
Balloon septostomy or atrial septectomy	55 (66 %)	50 (75.8 %)
Mustard versus Senning operation	73 (89 %)	49 (74 %)
Age at atrial switch operation (years)	2.1 ± 2.8	1.7 ± 3
Surgical baffle revision	15 (18.3 %)	8 (12 %)
Right atrial MAZE	4 (5 %)	0 (0 %)
Systemic AV valve surgery	3 (3.7 %)	4 (6 %)
3 or more cardiac surgeries	38 (46 %)	28 (42.4 %)
Cardiac thrombi	5 (6.4 %)	0 (0 %)
Baffle obstruction	31 (38 %)	20 (30 %)
Baffle leak	20 (24 %)	11 (16.7 %)
Baffle stent	15 (18 %)	14 (21 %)

most likely to have Mustard baffles (HR 2.3 (1.12, 4.5), p = 0.02) and more complex cardiac anatomy, with subpulmonary outflow tract obstruction requiring surgical intervention (HR 2.3 (1.01, 5.4), p = 0.04). There was also an association between atrial arrhythmias and MAZE (HR 3.3 (1.2, 9.2), p = 0.02), however, MAZE was only performed in the setting of known atrial arrhythmias. There was a strong association between atrial arrhythmias and baffle thrombi (HR 5 (2, 12.8), p < 0.001).

There was a positive association between an earlier surgical era at the time of baffle intervention and risk of subsequent atrial arrhythmia (p = 0.017). However, patient age at the time of baffle surgery, presence of baffle complications (obstruction, leak), the need for percutaneous or surgical baffle revision, the presence of an ASD, systemic AV valve surgery, or the total number of cardiac surgical interventions were not associated with subsequent arrhythmia risk.

A multivariate analysis including the above significant univariate predictors of interest revealed that complex cardiac anatomy, atrial MAZE, and baffle thrombi remained significantly and independently associated with atrial arrhythmias. Therefore, when correcting for complex anatomy and surgical era, there was no longer any significant difference in atrial arrhythmia risk between Mustard and Senning operations.

5.7. Atrial arrhythmia: clinical presentation and therapeutic approach

Symptomatic atrial arrhythmia was adjudicated in the presence of palpitations, shortness of breath, dizziness, lightheadedness, or fluid overload/heart failure exacerbation. In this cohort of atrial arrhythmia patients (N = 82), the arrhythmia was symptomatic in 75(91.5 %) patients, and incidentally discovered in 7(8.5 %).

Arrhythmia was rate-controlled with beta-blockade in 40/82(48.8 %) patients and calcium channel blockade in 8/82(9.8 %) patients. Digoxin was used in 34(41.5 %) patients. Antiarrhythmic therapy consisted mainly of Vaughan Williams Class III agents (amiodarone in 22 (26.8 %) cases, sotalol in 21(25.6 %) cases, dofetilide in 13(15.8 %) and dronedarone in 3(3.7 %) cases). Class I, sodium channel blockers, were also utilized in 7(8.5 %) patients.

Cardioversions were performed in 38/82(46 %) patients, and electrophysiology studies in 42/82(51 %) patients. Ablations were documented in a total of 40/82 (48.8 %) patients. Of these, 32 patients had available electrophysiology study reports (26 patients underwent a total of 31 ablation procedures at our institution, while 6 patients had only outside procedures). Details of the arrhythmia mechanism and ablation techniques employed in this cohort were separately reported [10].

The majority of ablations were performed for macroreentrant atrial arrhythmias or flutters. Only 2 patients underwent documented pulmonary vein isolation, and one patient required further isolation of the pulmonary veins, in addition to atrial flutter ablation at a redo procedure. Focal atrial tachycardia was documented less frequently, only at

redo procedures and in the setting of more advanced atrial myopathy and scar [10].

Overall, atrial arrhythmia was addressed with a combination of antiarrhythmic therapy, cardioversion or ablation - at least at one point during their follow-up - in 74/82 (90 %) of patients in this D-TGA cohort. Of the atrial tachycardia or flutter group, 58/73 (80 %) patients were treated with an intended rhythm control strategy. A primary rate control strategy was employed in 20 % of patients.

6. Discussion

In patients with DTGA and atrial switch, a history of atrial fibrillation - coupled with a prolonged QRS duration or right bundle branch block on the ECG and severe systemic right ventricular dysfunction on the echocardiogram – signal a higher risk population. These findings highlight that atrial fibrillation is a fundamental arrhythmia marker of increased risk. Atrial tachycardia or flutter, while not directly associated with mortality, were associated with increased risk of heart failure hospitalization.

Atrial arrhythmias - related to atrial reconstruction and surgical scars - were common in this D-TGA cohort (55.4 %), with 45 % of patients being diagnosed by age 40 and 53 % by age 50 (Fig. 1). There seems to be an anatomic risk for atrial arrhythmias, as patients with more complex congenital defects (e.g., those with subpulmonary outflow tract reconstruction in addition to atrial switch) carried a higher risk of developing subsequent atrial arrhythmias.

In a multivariate analysis taking into account the type of baffle (Mustard versus Senning), surgical era, and complexity of cardiac anatomy, only the latter remained a significant independent predictor of future atrial arrhythmia. While prior studies showed conflicting results, with either Mustard [3] or Senning [5] repairs suggested to carry the highest risk of adverse long-term events, the present study did not demonstrate any significant difference between Mustard or Senning baffles in terms of atrial arrhythmia, all-cause mortality, or SCD risk.

In this study, all cases of baffle thrombi were diagnosed in patients with known atrial arrhythmias. This finding may be biased, as not all patients underwent systematic screening for thrombus; yet it underscores the importance of imaging prior to elective cardioversion or ablation, even in the presence of systemic anticoagulation, as thrombus may be present.

To understand the difference in primary outcome between patients with atrial fibrillation compared to the more organized atrial arrhythmias, atrial tachycardia or futter, we performed further analysis. Atrial tachycardia and flutter were analyzed together, with most of these arrhythmias confirmed to be macroreentrant flutters at the time of the electrophysiology study. Conceptually, atrial fibrillation is more likely to be associated with a failing heart and more advanced atrial myopathy, with more extensive scar. Left atrial size and hemodynamics are distinctly altered after atrial switch, and prior work has demonstrated that non-pulmonary vein sources, focal atrial tachycardia, and atypical flutters are important triggers for atrial fibrillation in the congenital population, different from the atrial fibrillation in a normal heart [11,12].

From a management standpoint, atrial tachycardia or flutter were more likely to be treated with ablation, while pulmonary vein isolation was infrequently performed, in only 2(1.4 %) patients. The arrhythmia substrate at the time of ablation was previously described and included cavotricuspid isthmus flutter (CTI-flutter) in 75 % of patients at the first ablation, scar-related intra-atrial reentrant tachycardia (IART) in 53 % of patients, and focal atrial tachycardia (FAT) in 6 % of patients [10]. In this cohort, ablation was associated with clinical improvement, with less frequent and less symptomatic arrhythmia episodes after ablation. Despite potential recurrence, patients were noted to be more amenable to previously failed antiarrhythmic therapy or require only infrequent cardioversion [10]. Yet, atrial fibrillation ablation was rarely performed. This practice is reflected in a recent multicenter study in which only 7/240 (2.9 %) patients with congenital heart disease who underwent catheter ablation for atrial fibrillation had D-TGA [13].

Our cohort demonstrated increased mortality with atrial fibrillation and increased risk of heart failure hospitalization with any atrial arrhythmias. In a metaanalysis of over 5000 patients with D-TGA from 29 heterogeneous observational studies, the presence of supraventricular tachycardia (83 % were atrial flutters) predicted increased mortality [3]. Yet, no further risk stratification based on the type of atrial arrhythmia was performed. The present study furthers our understanding and suggests that atrial fibrillation is primarily driving the increased mortality, as opposed to the other more organized atrial arrhythmias.

In addition to atrial fibrillation, this data also identifies two central pathological features for patients with D-TGA: prolonged QRS duration or RBBB on the ECG and severely reduced systemic right ventricular function (SRV EF <35 %) on the echocardiogram.

Prolonged QRS duration and RBBB may be driven by prior VSD repair or outflow tract surgery, or by progressive ventricular fibrosis in the context of SRV dilation and stretch. Kaplan-Meier estimates revealed a crisp demarcation in outcomes for a QRS duration greater than 140msec and SRV EF less than 35 %.

Presence of a pacemaker or defibrillator, both associated with a higher risk of death or cardiac transplantation in this cohort, even in the absence of a high burden of ventricular pacing, appear to highlight a more advanced disease phenotype with more scar, more advanced conduction system disease, more atrial arrhythmias requiring AV-nodal blocking agents, or worse cardiomyopathy.

In addition to the above highlighted risk factors, other complications in the D-TGA cohort, strongly associated with increased risk of death or cardiac transplantation, included subpulmonary left ventricular dysfunction (LVEF <35 %, HR 7.47, $p = 0.009$) and severe pulmonary hypertension (HR 10.7, $p < 0.001$). All patients with LVEF <35 % and 75 % of patients with severe pulmonary hypertension also had atrial arrhythmias.

Finally, a history of syncope of any cause was associated with the primary outcome (HR 5.32, $p = 0.0005$), and a history of resuscitated SCA, documented in 6(4 %) patients, was strongly associated with future mortality/cardiac transplantation (HR 13.2, $p < 0.0001$). Yet, the etiology of SCA was a rapidly conducted atrial flutter in 2 patients who also had severe SRV dysfunction, presumed ventricular tachycardia in 2 patients (with documented VT in 1 case), and undocumented etiologies - presumed arrhythmic - in 2 patients. Furthermore, 1 of the 4 patients with SCD experienced a prior SCA event attributed to rapid atrial arrhythmia, prior to the fatal event. This observation further highlights the potential significant hemodynamic impact of rapid atrial arrhythmias in the setting of the failing SRV; atrial arrhythmias may lead to cardiovascular collapse, precipitate ischemia, ventricular tachycardia, or SCD [8,14].

Furthermore, there were more inappropriate shocks for atrial arrhythmias (16 % patients) than appropriate shocks (2.3 % patients) for ventricular tachycardia and this cohort. Given the high risk of both atrial arrhythmias and inappropriate shocks, refining the optimal risk stratification strategy is very important prior to placing a primary prevention defibrillator. This is compounded by the very real long-term consequences of transvenous leads placed through baffles (baffle obstruction, thrombosis, infection) [4]. A recent multicenter study, including a large number of patients with D-TGA and atrial switch, developed a novel risk prediction calculator for ventricular arrhythmias and SCD to help identify those patients with SRV who are most likely to benefit from primary prevention ICD implantation. Critical variables for this ventricular arrhythmia/sudden death risk prediction model, validated in a large number of patients, included a weighted combination of age, syncope, heart failure, severe SRV dysfunction, prolonged QRS duration, and increased gradient across the pulmonary outflow tract - these individual factors were also identified as important predictors of mortality in our study. In addition, our study underscores the critical importance of atrial arrhythmias, with their potential to cause significant

hemodynamic decompensation and mortality in the setting of the failing SRV [15].

6.1. Study limitations

This study was performed at a large tertiary care institution and referral bias was inevitable, however, this reflects the contemporary practice of treating complex congenital arrhythmia patients at designated centers. Furthermore, the immortal time bias is relevant here, as patients may be more likely to present to the tertiary care center when they start to decompensate or when they fail conservative arrhythmia treatment. This study assessed atrial arrhythmia prevalence and the effects of arrhythmia exposure, rather than a true arrhythmia burden. Moreover, not all patients had their complete follow-up at Mayo Clinic and some follow-up events may have been missed.

7. Conclusions

In this well-characterized D-TGA cohort, atrial fibrillation emerges as a major contributor to poor outcomes – distinct from atrial tachycardia or flutter – and especially in patients with prolonged QRS/RBBB and severe SRV dysfunction. This combination appears most pathological and is most predictive of mortality and cardiac transplantation. Patients presenting with these clinical features represent a higher risk cohort, and should be considered for more vigilant ambulatory follow-up, and possibly earlier arrhythmia intervention – before degenerating into atrial fibrillation. This last conclusion requires further multi-center study.

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CRediT authorship contribution statement

Anca Chiriac: Conceptualization, Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Davide Giardi:** Conceptualization, Data curation, Writing - original draft. **Kamal P. Cheema:** Conceptualization, Data curation, Writing - original draft. **Samantha Espinosa:** Conceptualization, Data curation, Writing - original draft. **Goyal Umadat:** Data curation, Writing - original draft. **David O. Hodge:** Conceptualization, Data curation, Formal analysis, Methodology, Resources, Software, Writing - original draft. **Malini Madhavan:** Conceptualization, Investigation, Methodology, Writing - original draft. **Samuel Asirvatham:** Conceptualization, Writing - original draft. **Sabrina D. Phillips:** Conceptualization, Methodology, Writing - original draft. **Christopher J. McLeod:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Supervision, Writing - original draft, Writing - review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcchd.2023.100491.

References

[1] Warnes CA. Transposition of the great arteries. Circulation 2006;114:2699–709. https://doi.org/10.1161/CIRCULATIONAHA.105.592352.
[2] Brida M, Diller GP, Gatzoulis MA. Systemic right ventricle in adults with congenital heart disease: anatomic and phenotypic spectrum and current approach to management. Circulation 2018;137:508–18. https://doi.org/10.1161/CIRCULATIONAHA.117.031544.
[3] Venkatesh P, Evans AT, Maw AM, et al. Predictors of late mortality in D-transposition of the great arteries after atrial switch repair: systematic review and meta-analysis. J Am Heart Assoc 2019;8:e012932. https://doi.org/10.1161/JAHA.119.012932.
[4] Gaur L, Cedars A, Diller GP, Kutty S, Orwat S. Management considerations in the adult with surgically modified d-transposition of the great arteries. Heart 2021;107:1613–9. https://doi.org/10.1136/heartjnl-2020-318833.
[5] Khairy P, Landzberg MJ, Lambert J, O'Donnell CP. Long-term outcomes after the atrial switch for surgical correction of transposition: a meta-analysis comparing the Mustard and Senning procedures. Cardiol Young 2004;14:284–92. https://doi.org/10.1017/S1047951104003063.
[6] Vejlstrup N, Sorensen K, Mattsson E, et al. Long-term outcome of mustard/senning correction for transposition of the great arteries in Sweden and Denmark. Circulation 2015;132:633–8. https://doi.org/10.1161/CIRCULATIONAHA.114.010770.
[7] Khairy P, Van Hare GF. Catheter ablation in transposition of the great arteries with Mustard or Senning baffles. Heart Rhythm 2009;6:283–9. https://doi.org/10.1016/j.hrthm.2008.11.022.
[8] Khairy P. Sudden cardiac death in transposition of the great arteries with a Mustard or Senning baffle: the myocardial ischemia hypothesis. Curr Opin Cardiol 2017;32:101–7. https://doi.org/10.1097/HCO.0000000000000353.
[9] Das MK, Zipes DP. Fragmented QRS: a predictor of mortality and sudden cardiac death. Heart Rhythm 2009;6:S8–14. https://doi.org/10.1016/j.hrthm.2008.10.019.
[10] Chiriac A, Cheema KP, Giardi D, et al. Atrial arrhythmia ablation in patients with D-transposition of the great arteries and atrial switch. Circ Arrhythm Electrophysiol 2022;15:e010546. https://doi.org/10.1161/CIRCEP.121.010546.
[11] Waldmann V, Laredo M, Abadir S, Mondesert B, Khairy P. Atrial fibrillation in adults with congenital heart disease. Int J Cardiol 2019;287:148–54. https://doi.org/10.1016/j.ijcard.2019.01.079.
[12] Waldmann V, Khairy P. Pathophysiology, risk factors, and management of atrial fibrillation in adult congenital heart disease. Card Electrophysiol Clin 2021;13:191–9. https://doi.org/10.1016/j.ccep.2020.10.007.
[13] Griffiths JR, Nussinovitch U, Liang JJ, et al. Catheter ablation for atrial fibrillation in adult congenital heart disease: an international multicenter registry study. Circ Arrhythm Electrophysiol 2022;15:e010954. https://doi.org/10.1161/CIRCEP.122.010954.
[14] Khairy P, Fernandes SM, Mayer Jr JE, et al. Long-term survival, modes of death, and predictors of mortality in patients with Fontan surgery. Circulation 2008;117:85–92. https://doi.org/10.1161/CIRCULATIONAHA.107.738559.
[15] Ladouceur M, Van De Bruaene A, Kauling R, et al. A new score for life-threatening ventricular arrhythmias and sudden cardiac death in adults with transposition of the great arteries and a systemic right ventricle. Eur Heart J 2022;43:2685–94. https://doi.org/10.1093/eurheartj/ehac288.