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ORIGINAL ARTICLE

Routine Detection of Atrial Fibrillation/Flutter Predicts a Worse Outcome in a Cohort of Tetralogy of Fallot Patients During 23 Years of Follow-Up

Gabriela Machado de Castilhos[1] · Antonio Lessa Gaudie Ley[1] · Nestor Santos Daudt[1] · Estela Suzana Kleiman Horowitz[1] · Tiago Luiz Luz Leiria[1]

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Abstract
Atrial flutter/fibrillation (AFL/AF) is a late complication in adults with repaired tetralogy of Fallot (TOF). Its effects on long-term prognosis are not fully understood. We evaluate the impact of AFL/AF in adults with repaired TOF on global mortality and unplanned hospitalizations during follow-up, and the predictors for AFL/AF occurrence. The presence of AFL/FA was analysed in all exams performed during the last 10 years of outpatients follow up in a unicentric cohort of repaired TOF between 1980 and 2003. Two-hundred and six patients were included; at a mean follow-up of 21 ± 8.2 years, there were 5 deaths (19.2%) in the AFL/AF group and 2 (1.1%) in those without arrhythmia ($p < 0.001$). Patients with AFL/AF where older at the time of the surgical repair ($p < 0.001$) and had a higher rate of reinterventions ($p = 0.003$). No differences were observed between the groups regarding the use of a transannular patch, ventriculotomy and previous palliative shunt. QRS duration was longer in patients with AFL/AF (174 ± 33.4) when compared to those without arrhythmia (147 ± 39.6; $p < 0.0001$). Age at surgery, QRS duration, and tricuspid regurgitation ≥ moderate were independent risk predictors for AFL/AF. In the multivariate analysis, atrial flutter/fibrillation and QRS duration were predictors of death and hospitalization. AFL/AF is associated with an increased risk of death and hospitalization during the follow-up of patients with repaired TOF. Early detection of AFL/AF and their predictors is an essential step in the evaluation of such population.

Keywords Atrial flutter/fibrillation · Tetralogy of Fallot · Atrial tachyarrhythmias

Introduction

The number of adults with tetralogy of Fallot, as well as other congenital heart diseases, has been increasing substantially in the last decades [1]; the reason for this can be attributed to the advances in intervention techniques and the improvement of specialized medical care. Currently, approximately 85% of patients undergoing repair surgery reach adulthood [2, 3].

Patients with repaired TOF often require repeated surgical or catheter based reinterventions to minimize the long-term effects of volume and pressure overloads in the cardiac chambers [4], which may contribute to an increase in the risk of supraventricular and ventricular tachyarrhythmias and even death [5-8].

Several studies have shown an increase in the incidence of atrial flutter/fibrillation (AFL/AF) in the population with repaired TOF [9-13], increasing progressively after repairing surgery and being the main cause of late morbidity [14-16]. These tachyarrhythmias may reduce ventricular refractoriness and increase the risk of ventricular tachycardia or fibrillation in this setting [17].

The main objective of this study was to evaluate whether AFL/AF detection in patients with repaired TOF is associated with an increase in mortality during a routine clinical follow-up. In addition, we analysed possible predictors of risk for AFL/AF occurrence and their relationships with worse outcomes.

✉ Tiago Luiz Luz Leiria
drleiria@gmail.com

[1] Institute of Cardiology of Rio Grande Do Sul / University Foundation of Cardiology, Av. Princesa Isabel, 395, Santana, Porto Alegre, RS CEP 90620-000, Brazil

Methods

This is a historical cohort study on detection of atrial flutter/fibrillation in adults with repaired tetralogy of Fallot and its possible relationship with increased morbidity and mortality. The ethics committee of our Institution approved the study.

Patients

We initially identified all patients with tetralogy of Fallot who underwent repaired surgery from 1980 to 2003 at our hospital. From this initial screening of 350 patients, we included individuals aged ≥ 18 years at the last outpatient visit and who were followed up at our service, analysing the records available in the last 10 years (2008–2018), making up a total of 206 patients included in the study. The last follow-up date was March 2018.

Our centre is specialized in the care of patients (children and adults) with the most diverse congenital heart diseases, being a reference for performing reparative TOF surgeries in the southern region of Brazil. Thus, many patients referred to our centre come from different regions of the country, often making it impossible to continue the follow-up after the surgical repair. This justifies, to a great extent, the initial loss of 41% of the individuals in the period under analysis (Fig. 1).

We excluded patients who were lost to regular clinical follow-up, as well as cases of tetralogy of Fallot with pulmonary atresia, usually defined as an extreme variant of TOF [18]. We divided the patients into two groups, with AFL/AF and no AFL/AF.

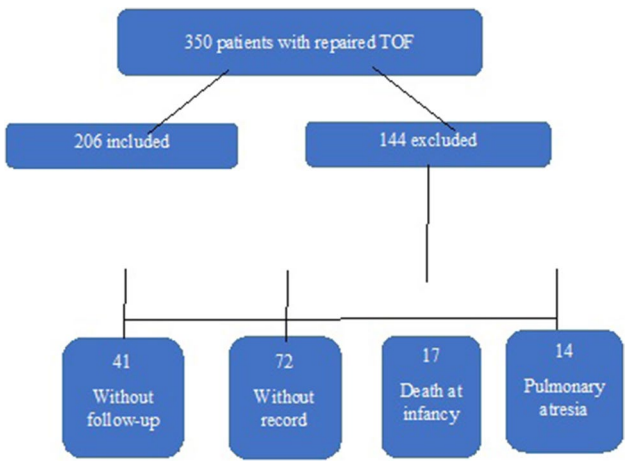

Fig. 1 Study flowchart. Three-hundred and fifty patients who underwent reconstructive surgery of ToF from 1980 to 2003 were identified; 206 were included in the study according to the pre-established criteria. One-hundred and forty four were excluded; 41 with incomplete follow-up (at least one visit in the last 10 years), 72 without medical records (only surgery reports—they had undergone surgical repair as a child and were not followed in our centre), 17 due to death during the reconstructive surgery or due to immediate surgical complications, and 14 due to severe T4F with pulmonary atresia

Data Collection

Surgical data, including the type of initial surgical procedure, associated cardiac abnormalities, and the need for previous palliative shunts, were verified in properly archived surgical reports. The surgical technique used was carefully analysed to evaluate the use of ventriculotomy, transannular patch for enlargement of the right ventricular outflow tract (RVOT), and the age of the patient at the time of surgery. Data from routine cardiac examinations, such as electrocardiogram (ECG), 24-h Holter, echocardiogram and stress testing, and those requested in specific situations, such as magnetic resonance imaging (MRI), cardiac catheterization, and electrophysiological study (EPS), were collected from physical and electronic records. None of the imaging data were re-measured for this study.

All identified exams were reviewed for atrial flutter and/or fibrillation documentation. The diagnose of the arrhythmias under study was defined according to the current guidelines [19]. Atrial flutter was not differentiated into typical or atypical, and atrial fibrillation into paroxysmal, permanent, or persistent since such differentiations cannot always be based only on punctual analyses. The presence of AFL/AF in the immediate postoperative period of cardiac reinterventions (the first 48 h) was not considered. The follow-up period was defined as the interval (in years) between the time of complete surgical repair and the date of the last outpatient follow-up visit.

Outcomes

The primary outcome was defined as death from all causes (sudden death, death from heart failure, other cardiac or noncardiac causes). The secondary outcome (combined outcome) was the association of death and hospital admissions in the last 3 years in our centre—we included only hospitalizations that occurred after emergency care due to cardiac causes such as arrhythmias and heart failure.

Statistical Analysis

The collected data were analysed using the SPSS programme, version 22.0 (Armonk, NY, US: IBM corp.). Continuous variables were described as the means ± standard deviations or the medians and interquartile ranges, depending on the normality of the distribution. Differences in the means and medians were calculated using Student *t* test or Wilcoxon rank-sum test. For categorical variables, frequencies and percentages were used, and the comparison between

the groups was performed using Fisher's exact test or Chi-square test. We estimated the probability of event-free survival in the follow-up period using the Kaplan–Meyer method. The comparisons of the survival curves and the mortality rates between the two groups of patients were performed by the long-rank test. The possible predictors of atrial flutter/fibrillation and of the combined outcome, verified in binary univariate logistic regression, were analysed by multivariate logistic regression using the stepwise backward selection model. The combination of these factors was based on clinical relevance, odds ratios, and high univariate significance ($p < 0.05$). The possible predictors of death were evaluated using the Cox regression method.

Results

Patients studied

Of the 350 patients initially allocated, 206 met the inclusion criteria and formed the study cohort, of which, 118 were males (57.2%) (Table 1). The primary outcome occurred in 7 patients (3.39%), 5 in the AFL/AF group ($p < 0.0001$). The mean follow-up time after surgery repair was 21 ± 8.2 years, and the subjects underwent surgery at a mean age of 3 years old (2–4 years old). Fifty-two patients (25.2%) received an aortopulmonary shunt; the intracardiac approach was performed via the right ventricle in 191 procedures (92.7%), and the transpulmonary or transatrial route was used in the remaining cases. Transannular patch was used in 65 patients (31.5%), and 78 patients (37.8%) had other associated cardiac abnormalities. The electrocardiogram was performed in all the patients in the study, most of whom had right bundle branch block ($n = 192$ (93.2%)) (Table 2), and the mean duration of QRS was 150.7 ± 31.3 ms.

Arrhythmia

Atrial flutter/fibrillation was detected in 26 patients (12.6%) through analysis of the data of cardiac exams. As shown in Table 1, patients with arrhythmias were older at the time of surgical repair [4 years old (2.75–11); $p < 0.001$]. No differences were identified between the groups regarding ventriculotomy, transannular patch, and previous palliative shunt.

The need for surgical reintervention throughout life was higher in the individuals with AFL/AF ($n = 21$ (80.8%); $p = 0.003$). Among these patients, we observed greater numbers of pulmonary valve replacement ($n = 12$ (46.1%); $p < 0.001$), implantable cardioverter defibrillator (ICD) ($n = 5$ (19.2%); $p = 0.001$), pacemaker

Table 1 Demographic, surgical, and clinical characteristics

Variable	All patients (*n*: 206)	AFL/AF (*n*: 26)	Without AFL/AF (*n*: 180)	*p*
Male gender [*n* (%)]	118 (57.2%)	20 (76.9%)	98 (54.4%)	0.05
White race [*n* (%)]	192 (93.2%)	24 (92.3%)	168 (93.3%)	0.23
Follow-up time (year)	21 ± 8.2	25.8 ± 11.2	20.8 ± 7.1	0.01
Age at surgical repair (year*)	3 (2.0–4.0)	4 (2.75–11)	3 (2.0–4.0)	< 0.001
Age at the last visit (year)	26 ± 9	24.1 ± 8.8	26.2 ± 9	0.26
Age at death (year)	26.2 ± 13.7	2 27 ± 15.9	24.5 ± 10.6	0.8
Previous palliative shunt [*n* (%)]	52 (25.2%)	8 (30.7%)	44 (24.4%)	0.6
Ventriculotomy [*n* (%)]	191 (92.7%)	24 (92.3%)	167 (92.7%)	1.0
Transannular patch [*n* (%)]	65 (31.5%)	11 (42.3%)	54 (30%)	0.2
Reinterventions [*n* (%)]	108 (52.4%)	21 (80.8%)	87 (48.3%)	0.003
PV replacement [*n* (%)]	39 (18.9%)	12 (46.1%)	27 (15%)	< 0.001
ICD [*n* (%)]	9 (4.3%)	5 (19.2%)	4 (2.2%)	0.001
Pacemaker [*n* (%)]	9 (54.3%)	4 (15.3%)	5 (2.7%)	0.01
Residual VSD correction [*n* (%)]	27 (13.1%)	9 (34.6%)	18 (10%)	0.02
TV repair [*n* (%)]	11 (5.3%)	6 (23%)	5 (2.7%)	< 0.001
Other cardiac abnormalities [*n* (%)]	78 (37.8%)	8 (30.7%)	70 (38.8%)	0.56
Clinical manifestations [*n* (%)]	68 (33%)	12 (46.1%)	56 (31.1%)	0.19
Syncope [*n* (%)]	3 (4.4%)	0	3 (5.3%)	1.0
Signs/symptoms of HF [*n* (%)]	53 (77.9%)	5 (41.6%)	48 (85.7%)	0.56
Palpitations [*n* (%)]	17 (25%)	8 (66.6%)	9 (16%)	< 0.001

AFL/AF atrial flutter/fibrillation, *PV* pulmonary valve, *ICD* implantable cardioverter defibrillator, *VSD* ventricular septal defect, *TV* tricuspid valve, *HF* heart failure

*Continuous variables that were not normally distributed were analysed by the medians and interquartile ranges (25th and 75th percentiles)

Table 2 Cardiological examinations analysed

Variable	All patients (*n* 206)	AFL/AF (*n* 26)	Without AFL/AF (*n*: 180)	*p*
Electrocardiogram [*n* (%)]	206 (100%)	26 (100%)	180 (100%)	
CRBB [*n* (%)]	192 (93.2%)	26 (100%)	166 (92.2%)	0.29
QRS duration (ms)	150.7 ± 31.3	174.2 ± 33.4	147.3 ± 39.6	< 0.001
Echocardiogram [*n* (%)]	192 (93.2%)	24 (92.3%)	168 (93.3%)	
Residual lesions [*n* (%)]	156 (81.2%)	20 (83.3%)	136 (80.9%)	1.0
LVEF (%)	65.3 (56.1–73.3)	62.9 (53.7–71.3)	66.1 (56.6–73.8)	0.18
RV/RA (mmHg)	31 (26–43.2)	57 (39.2–71)	30.5 (26–59.1)	0.004
LA (mm)	33.1 ± 6.8	39.1 ± 6.9	32.4 ± 6.4	< 0.001
RV (mm)	28.5 (23–37)	33 (28–40)	28 (22–36)	0.003
PR ≥ moderate [*n* (%)]	89 (46.3%)	7 (29.1%)	82 (48.8%)	0.13
TR ≥ moderate [*n* (%)]	30 (15.6%)	9 (37.5%)	21 (12.5%)	0.005
Cardiac catheterization [*n* (%)]	76 (36.8%)	13 (50%)	63 (35%)	
PASP (mmHg)	20 (15.5–29.5)	30 (19–39.5)	20 (15–26.7)	0.02
RVSP (mmHg)	35 (25.7–45)	40 (32.5–82.5)	35 (25–45)	0.05
RASP (mmHg)	8 (6–11)	13 (11.2–16.5)	8 (5.5–14.6)	0.02
MR [*n* (%)]	19 (9.2%)	3 (11.5%)	16 (8.8%)	
RVEDV index (mL/m^2)	131.5 (102.3–171.7)	137 (108.4–177)	120 (102–145)	0.82
EPS [*n* (%)]	33 (16%)	14 (53.8%)	19 (10.5%)	
Ablation [*n* (%)]	9 (27.2%)	8 (57.1)	1 (5.2%)	0.005
VT [*n* (%)]	15 (7.2%)	5 (19.2%)	10 (5.5%)	0.035

AFL/AF atrial flutter/fibrillation, *CRBB* complete right bundle branch block, *LVEF* left ventricular ejection fraction, *RV/RA* pressure gradient right ventricle/right atrium, *LA* left atrium, *RV* right ventricle, *PR* pulmonary regurgitation, *TR* tricuspid regurgitation, *PASP* pulmonary artery systolic pressure, *RVSP* right ventricular systolic pressure, *RASP* right atrium systolic pressure, *MR* magnetic resonance, *RVEDV* right ventricular end-diastolic volume, *EPS* electrophysiological study, *VT* ventricular tachycardia

insertion ($n = 4$ (15.3%); $p = 0.01$), residual VSD correction ($n = 9$ (34.6%); $p = 0.02$), and tricuspid valve repair ($n = 6$ (23%); $p < 0.001$) in the comparison between the groups. Patients with atrial flutter/fibrillation on routine exams had more palpitation symptoms at outpatient visits ($p < 0.001$). The QRS duration was significantly higher (174.2 ± 33.4; $p < 0.001$) in the arrhythmia group (Fig. 2).

In the analysis of echocardiographic data, no difference was found between groups in relation to left ventricular ejection fraction. However, the RV/RA gradient [57 mmHg (39.2–71) vs. 30.5 mmHg (36–59.1); $p = 0.004$], left atrial (39.1 ± 6.9 mm vs. 32.4 ± 6.4 mm; $p < 0.001$) and right ventricle size [33 mm (28–40) vs. 0.28 mm (22–36); $p = 0.003$], were higher in the AFL/AF group. The presence of tricuspid regurgitation ≥ moderate was more often observed in the group with arrhythmia ($p = 0.005$), but no difference was found regarding the presence of pulmonary regurgitation ($p = 0.13$). Patients with AFL/AF had more episodes of ventricular tachycardia (OR 4.04; 95% CI 1.26–12.98; $p = 0.035$).

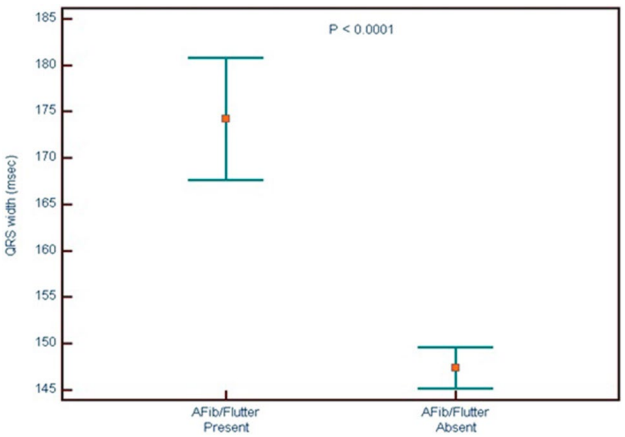

Fig. 2 QRS duration comparison between the group with atrial fibrillation/flutter and the group without atrial fibrillation/flutter

Predictors of Atrial Flutter/Fibrillation

Demographic, clinical, electrocardiographic and echocardiographic variables were associated with atrial flutter/fibrillation. The possible predictors of AFL/AF in the univariate analysis included age at surgical repair (OR 1.08, $p = 0.01$),

QRS duration (OR 1.03, $p < 0.001$), follow-up time from repair (OR 1.07, $p = 0.004$), tricuspid regurgitation ≥ moderate (OR 15.5, $p < 0.001$), left atrial size (OR 1.14, $p < 0.001$) and the number of reinterventions (OR 1.84, $p = 0.002$) (Table 3). The use of transannular patch, aortopulmonary palliative shunt and ventriculotomy for the intracardiac approach appeared to be less important for the occurrence of atrial flutter/fibrillation.

In the multivariate analysis (Table 4), we identified QRS duration (OR 1.02; 95% CI 1008–1046; $p = 0.004$) and age at surgical repair (OR 1.08; 95% CI 1.017–1.167; $p = 0.015$) as independent predictors of AFL/AF. The presence of tricuspid regurgitation ≥ moderate was strongly associated with the atrial tachyarrhythmias under study, with an OR of 18.02 (95% CI 4.4–73.8; $p < 0.001$).

Survival After AFL/AF Detection

In our patient population, the median time from AFL/AF detection to death was 112 days (percentile 25th–75th: 92–115). Of the 26 cases identified as having the arrhythmia, 19% died during the follow-up.

Overall Survival

A total of seven patients (3.39%) died during the follow-up. The main cause of death in our cohort was the final stage of heart failure, which occurred in 4 subjects (57.1%; age 18–54 years). The other causes were sudden death in 1 individual (14.2%, age 18 years) and postoperative cardiogenic shock in 2 patients (28.5%, ages 18 and 32 years).

Table 3 Univariate analyses of atrial flutter/fibrillation predictors

	AFL/AF		
	OR	95% CI	*p*
Univariate analysis			
Age at surgical repair (year)	1.08	1.015–1.155	0.01
QRS duration (ms)	1.03	1.015–1.048	< 0.001
Previous palliative shunt (%)	0.72	0.296–1.790	0.48
Ventriculotomy (%)	1.07	0.227–5.038	0.93
Transannular patch (%)	0.58	0.252–1.355	0.21
Follow-up time (year)	1.07	1.022–1.124	0.004
Tricuspid regurgitation ≥ moderate (%)	15.55	4.601–52.591	< 0.001
RV/RA gradient (mmHg)	1.04	1.018–1.072	0.001
Left atrium (mm)	1.14	1.067–1.234	< 0.001
Number of reinterventions (%)	1.84	1.263–2.694	0.002

AFL/AF atrial flutter/fibrillation, *RV/RA* gradient pressure gradient right ventricle/right atrium

Table 4 Multivariate analyses of atrial flutter/fibrillation predictors

	AFL/AF		
	OR	95% CI	*p*
Multivariate analysis			
QRS duration (ms)	1.02	1.008–1.046	0.004
Age at surgical repair (year)	1.08	1.017–1.167	0.015
Follow-up time (year)	1.03	0.987–1.093	0.14
Tricuspid regurgitation ≥ moderate (%)	18.02	4.403–73.809	< 0.001
Number of reinterventions (%)	1.47	0.912–2.399	0.11

AFL/AF atrial flutter/fibrillation

Predictors of the Primary and Secondary Outcomes

The presence of atrial flutter/fibrillation was negatively associated with survival rates during the follow-up by multivariate analysis (OR 11.27; 95% CI 1.991–63.885; $p = 0.006$) (Table 8) (Fig. 3). The other variables in the univariate analysis did not show a relationship with increased mortality in our cohort.

In the univariate analysis (Table 5), QRS duration (OR 1.04; $p < 0.001$), previous palliative shunt (OR 2.09, $p = 0.04$), transannular patch (OR 2.49; = 0.008), follow-up time after surgical repair (OR 1.08, $p < 0.001$), atrial flutter/fibrillation (OR 13.75; $p < 0.001$) and the number of reinterventions (OR 2.15; $p < 0.001$) were identified as the possible predictors of the combined outcome (death + hospitalization). QRS duration (OR 1.02; 95% CI 1.026–1.046; $p = 0.04$) and the presence of AFL/AF (OR 16.97; 95% CI 2.18–131.9; $p = 0.007$) were independent risk predictors for the combined outcome of death and hospital admissions (Table 6).

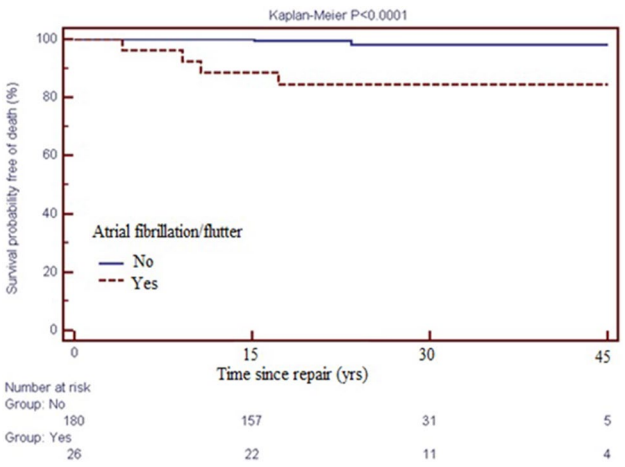

Fig. 3 Comparison of death-free survival between the group with atrial fibrillation/flutter (dotted line) and the group without atrial fibrillation/flutter (continuous line)

Table 5 Univariate analyses of predictors of the combined outcome (death + hospitalization)

	Death + H		
	OR	95% CI	*p*
Univariate analysis			
QRS duration (ms)	1.04	1.025–1.056	< 0.001
Previous palliative shunt (%)	2.09	1.033–4.243	0.04
Ventriculotomy (%)	0.86	0.232–3.189	0.82
Transannular patch (%)	2.49	1.269–4.903	0.008
Follow-up time (year)	1.08	1.042–1.136	< 0.001
Tricuspid regurgitation ≥ moderate (%)	1.04	0.276–3.973	0.94
RV/RA gradient (mmHg)	1.00	0.985–1.026	0.63
Left atrium (mm)	1.04	0.992–1.100	0.10
Number of reinterventions (%)	2.15	1.530–3.034	< 0.001
AFL/AF (%)	13.75	2.749–73.543	< 0.001
LVEF (%)	0.98	0.960–1.017	0.40
Age at surgical repair (year)	1.02	0.965–1.078	0.48

H hospitalizations, *RV/RA gradient* pressure gradient right ventricle/right atrium, *AFL/AF* atrial flutter/fibrillation, *LVEF* left ventricular ejection fraction

Table 6 Multivariate analyses of predictors of the combined outcome (death + hospitalization)

	Death + H		
	OR	95% CI	p
Multivariate analysis			
QRS duration (ms)	1.02	1.026–1.046	0.04
Previous palliative shunt (%)	2.81	0.985–5.242	0.24
AFL/AF (%)	16.97	2.183–131.931	0.007
Number of reinterventions (%)	0.60	0.268–1.362	0.23

AFL/AF atrial flutter/fibrillation

Discussion

Our study has important clinical implications for the management of patients with tetralogy of Fallot. Possible predictors of the electrophysiological and haemodynamic substrate of the development of atrial tachyarrhythmias, together with the late age of surgical repair in the group with atrial flutter/fibrillation, are the main contributions of this study. The primary outcome occurred in 3.39% of patients during the follow-up period. Previous studies have shown similar mortality at the same follow-up time in patients with corrected TOF [16]. The prevalence of atrial flutter/fibrillation was 12.6% in our cohort, correlating with the prevalence of atrial tachyarrhythmias described in the literature in this study population [15, 20] (Tables 7 and 8).

Table 7 Univariate analyses of death predictors

	Death		
	OR	95% CI	*p*
Univariate analysis			
QRS duration (ms)	1.02	0.997–1.044	0.08
Previous palliative shunt (%)	2.87	0.580–14.256	0.19
Ventriculotomy (%)	0.39	0.046–3.356	0.39
Tricuspid regurgitation ≥ moderate (%)	3.48	0.557–21.846	0.18
RV/RA gradient (mmHg)	1.01	0.962–1.067	0.61
Left atrium (mm)	1.09	0.940–1.284	0.23
Number of reinterventions (%)	1.13	0.560–2.297	0.72
AFL/AF (%)	13.75	2.571–73.543	0.02
LVEF (%)	0.97	0.881–1.076	0.60
Age at surgical repair (year)	1.07	1.007–1.149	0.03

RV/RA pressure gradient right ventricle/right atrium, *AFL/AF* atrial flutter/fibrillation, *LVEF* left ventricular ejection fraction

Table 8 Multivariate analyses of death predictors

	Death		
	OR	95% CI	*p*
Multivariate analysis			
Age at surgical repair (year)	1.05	0.947–1.165	0.35
AFL/AF (%)	11.27	1.991–63.885	0.006

AFL/AF atrial flutter/fibrillation

The occurrence of atrial flutter/fibrillation has a substantial impact on clinical events and appears to identify patients at an increased risk of death. The survival time was significantly reduced in the AFL/AF group compared to that in the group without arrhythmias, with an increase in the prevalence of arrhythmias with the increasing age. These results are consistent with those of previous studies demonstrating a relatively quiescent period of 10 to 15 years after surgical repair, followed by a decline in atrial flutter/fibrillation-free survival [11, 16]. The association between advanced age and atrial fibrillation is also established in patients without tetralogy of Fallot due to electrophysiological changes in cells, including a reduced duration of action potentials, a decreased capacity of the action potential to adapt to heart rate, and increased spatial variability of repolarization [21].

In this study cohort, we selected all-cause mortality as the primary outcome and the combination of death and hospital admissions as the secondary outcome due to the extreme clinical importance of such events and the impact that they have on patients with tetralogy of Fallot.

We observed that the age at surgical repair was higher in patients with atrial flutter/fibrillation, which may reflect a group that underwent surgery in an earlier era when

myocardial repair and preservation techniques had not been optimized, since progressive myocardial fibrosis with the increasing repair age is an impetus for atrial tachyarrhythmias [22]. These findings are consistent with those of previous studies by Khairy et al. and Gatzoulis et al. [12, 23]. A previous palliative shunt and ventricular incision for the intracardiac approach were not predictors of AFL/AF according to the analysis of our data.

No evidence of a higher probability of atrial flutter/fibrillation was found in patients in whom surgical reconstruction of the RVOT was performed with a transannular patch compared to that in the group that did not require intervention involving the pulmonary valve ring, which was also demonstrated by Gatzoulis et al. [14] in a multicentre study with 793 patients. Therefore, the characteristics of surgical repair appear to be less relevant to the onset of atrial flutter/fibrillation, although ventriculotomy, transannular patch and palliative shunt have previously been demonstrated to be predictors of the risks for sustained ventricular tachycardia and sudden cardiac death [12]. In contrast to previous studies [9, 15], left ventricular dysfunction did not influence the incidence of AFL/AF in our cohort, which may be explained by the gap in the retrospective data from echocardiograms for this specific analysis.

The need for surgical reintervention over the years was significantly higher in patients with atrial flutter/fibrillation. Among the main reinterventions needs, we observed a higher prevalence of pulmonary valve replacement, ICD and pacemaker implantation, residual VSD correction, and tricuspid valve repair, suggesting that patients who develop atrial flutter/fibrillation of these older cohorts, where the surgical techniques are not the same as those currently used, may have presented a palliative and repairing surgical result below that considered ideal.

Tricuspid regurgitation was the predominant haemodynamic lesion among the individuals exhibiting the arrhythmias under study, which was presumably caused by dilation of the right atrium and the tricuspid ring, thus creating the substrate for atrial arrhythmogenesis [24]. Pulmonary regurgitation was not associated with atrial flutter/fibrillation in our study; however, it is the primary residual lesion in patients with episodes of ventricular tachycardia.

A longer QRS duration was also a predictor of the risk for arrhythmic events as previously reported. This prolonged QRS is the result of the combined effects of surgical injury to the myocardium, as in the case of a right bundle branch block, and a later effect related to ventricular dilatation, thus providing an ideal environment for the onset of tachyarrhythmias. Patients who develop atrial flutter/fibrillation present an immediate increase in the QRS duration postoperatively, followed by a slow increase over the years in contrast to the faster increase in patients who progress to ventricular tachycardia and sudden death [25].

The patients with AFL/AF presented more frequent progression to ventricular tachycardia than the arrhythmia-free group during the study period. Since the tricuspid regurgitation usually observed in these patients, has a potential to increase the volume of the right ventricle (RV), and this can lead to progressive dilatation of the RV when combined with pulmonary regurgitation, being the ideal place to cause ventricular arrhythmias [23, 26].

Limitations of the Study

Because our study is retrospective in nature, patients who did not undergo an outpatient follow-up in the last 10 years, especially because they lived in distant cities, were eventually excluded, leading to a significant loss to follow-up. Study limitations also include the fact that routine cardiac exams were not performed in all patients or the data in physical and digital records were incomplete. Limitations regarding echocardiographic data of RV function were present, which is currently assessed using more precise imaging modalities such as magnetic resonance imaging and three-dimensional echocardiography; however, because this population receives health care predominantly through the public sector, major financial limitations often deter requests for these exams. Extensive data reflect the outcomes of surgeries that were performed at an earlier time, and the surgical strategies used today may lead to different outcomes.

Conclusion

We determine in this study that atrial flutter/fibrillation are predictors of death in adults with repaired tetralogy of Fallot. We verified that the different surgical techniques employed to correct TOF do not directly influence the development of AFL/AF, whereas they are determinants for the onset of VT and the increased risk of sudden death, as already observed in previous studies. The preservation of tricuspid valve function, as well as factors that increase right ventricular pressure, appear to be important factors in reducing the risk of atrial flutter/ fibrillation and its consequent increase in mortality. Routine cardiological exams, especially those of low cost and easy accessibility, such as electrocardiogram, echocardiogram and 24-hours Holter, are essential tools in the control of patients at risk.

Thus, continuous monitoring throughout the life of individuals with tetralogy of Fallot, with specialized medical follow-up and tests of easy access to the population, has shown to be primordial for early detection of elements indicative of worse outcomes. Therefore, we can employ preventive measures to reduce arrhythmias and consequent mortality.

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Compliance with Ethical Standards

Conflict of interest The authors declare no conflicts of interest in this study.

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