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ORIGINAL ARTICLE
Rare arrhythmias

Arrhythmias in adult patients after total correction of tetralogy of Fallot (RCD code: V-2B.0)

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Abstract

Improvement of the long-term survival of patients with Tetralogy of Fallot has been observed in the last few years. Among the late complication arrhythmias are detected most frequently. The aim of this study was to estimate the frequency of atrial and ventricular arrhythmias in the group of 53 adult tetralogy patients.

Mean age was 29 years, 21 patients (39,6%) were women. In 4 cases (7,5%) palliative pulmonary-systemic shunt was performed. Average age of total surgical correction was 6,55 years. Significant ventricular arrhythmias were present in 15 patients (28,3%). 9 (17%) had relevant atrial arrhythmias. Patients with atrial arrhythmia were older (35,4 vs 27,7 years). Older were also patients with ventricular arrhythmias (34,7 vs 26,4 years). Group with atrial arrhythmia used more digoxin (p=0,002) and diuretics (p = 0,021). 3 patients on oral anticoagulants had atrial flutter. Similar data was collected in group with ventricular arrhythmias (diuretics p = 0,0053). There was a high incidence of coexisting ventricular and atrial arrhythmias (p=0,0057). Left ventricular enlargement was present in patients with atrial (p = 0,002) and ventricular (p = 0,027) arrhythmias. Right atrium area and left atrium diameter were greater in group with supraventricular arrhythmias (31,6 vs 21,6 cm^2 and 40,4 vs 34,3 mm; respectively). Ventricular arrhythmias were associated with greater right (27,8 vs 21,0 cm^2) and left atrium areas (18,5 vs 15,1 cm^2).

Younger age at the time of corrective surgery is associated with lower frequency of arrhythmias in adults. Arrhythmias however remain one of the most significant problems in this group of patients. Close observation in centers specialized in Grown-Up Congenital Heart Defects and management of symptoms seems to be the best option in long-term follow-up. JRCD 2013; 1 (4): 144–149

Key words: Grown-Up Congenital Heart Defects, supraventricular arrhythmia, ventricular arrhythmia

Background

In the times before management and interventional catheterization, only one fifth of children with congenital heart disease achieve adulthood [1]. Progress in surgical correction and interventional cardiology causes the improvement in long-term survival. Most of the patients reach adulthood and face late complications, among which arrhythmias are the most common [2-4]. Symptomatic atrial tachycardias develop in one third of patients with corrected Tetralogy of Fallot, almost 10% have high risk ventricular arrhythmias, about 5% need peacemaker implantation due to sinus node dysfunction [4]. The percentage of ventricular and supraventricular arrhythmias is significantly higher than in healthy population, moreover morbidity and mortality is strongly connected with their presence [3,5].

While the role of ventricular arrhythmias in sudden cardiac death (SCD) is stressed in many studies, the supraventricular arrhythmias are underestimated [5,6]. They are connected mainly with frequent hospital admission, presence of symptoms and worse quality of life [2]. Patients with congenital heart disease and sustained atrial fibrillation (AF) have over 50% higher risk of stroke and two to three times higher risk of congestive heart failure [3]. Supraventricular arrhythmias develop years after surgical manipulations, the most important risk factors are hemodynamic disturbances, dilatation, hypertrophy and tissue fibrosis of atrium, which are responsible for non-homogenic electric impulses conduction. Abnormalities of conduction system and postoperative scars provide background for

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atrial arrhythmias [2]. Other risk factors noticed in previous studies are ageing, compound congenital heart disease, lack of surgical correction, heart failure [5-7].

Ventricular arrhythmias are triggered around tissue scars after ventriculotomy or VSD patches in mechanism of "incisional" re-entry [3,4,8]. Hypoxemia and pressure overload of right ventricle lead to degeneration of cardiomyocytes and tissue fibrosis. Those are responsible for progression of heart dysfunction and appearance of ventricular arrhythmias, which are associated with the risk of SCD. This risk in patients with Tetralogy of Fallot is well known and estimated at the level of 2% per decade. The main contributor is sustained VT [3]. While indications for implantable cardioverter defibrillator (ICD) implantation in primary prophylaxis of SCD are not yet certain and recognized around the world, many studies concentrate on prognostic factors for SCD in tetralogy patients [4,6,8,9]. Numerous were explored: QRS duration over 180 msec, severe pulmonary insufficiency, older age at the first surgery, left and right ventricle dysfunction, ventricular fibrosis, previous palliative operations, ageing, high-grade ventricular ectopy in ECG Holter monitoring. The value of this risk factors is still not certain and needs further investigation [8-11].

The aim of this study is to estimate the prevalence of ventricular and supraventricular arrhythmias among adult population of tetralogy patients and define dependences between arrhythmias and clinical, electrocardiological and echocardiographical features.

Methods

This is a descriptive study of 53 adult patients after total correction of the Tetralogy of Fallot, who remain in the follow-up of the Department of Cardiac and Vascular Diseases of the John Paul II Hospital in Krakow, Poland. Mean age was 29 years. 21 patients (39,6%) were women. Previous medical history of the patients was examined (the incidence of previous pulmonary-systemic shunt, concomitant heart defects), as well as ECG Holter monitoring (heart rate, episodes of arrhythmias, QRS complex width), NYHA (New Your Heart Association) functional class and cardiac ultrasound results.

As relevant supraventricular arrhythmias were classified:

- supraventricular tachycardia (SVT) 5 QRS complexes >100 bpm,
- atrial flutter (AFl) and atrial fibrillation (AF) [5].

Ventricular arrhythmias were classified as significant according to ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death [12]. The group of potentially dangerous ventricular arrhythmias consists of:

- sustained ventricular tachycardia (sVT) ≥30 sec.
- non-sustained ventricular tachycardia (nsVT) ≥3 QRS, <30 sec.
- premature ventricular contractions (PVCs) ≥ 10 per hour

QRS complex widening was defined as width over 120 msec.

Echocardiographic measurements were acquired in parasternal long axis and apical window. Dimensions of the heart chambers (LVEDD – left ventricle end diastolic diameter, RVOT PROX – right ventricle outflow track in parasternal long-axis view, RAA – right atrium area, LAA – left atrium area) left ventricle ejection fraction (LVEF), tricuspid annulus diameter, TAPSE – Tricuspid Annular Plane Systolic Excursion, aortic annulus diameter, ascending aorta diameter, pulmonary trunk diameter, presence of any aortic regurgitation and presence of significant pulmonary regurgitation (jet width occupies >65% of right ventricle outflow tract width) were noted. Abnormalities of the measurements were classified due to recognized criteria [13-16].

Statistic analysis

Continuous variables are presented by mean and standard deviation. Categorical variables are presented as percentages. The probability distribution was determined by the Kolmogorov-Smirnov test. Comparisons between subgroups were performed by the Mann-Whitney U test. Association between variables was determined by logistic regression. For all analyses, value of $p< 0,05$ was used as criterion of statistical significance.

All statistical analyses were performed with the use of Statistica Software (version 10, license number: JLVP110D131518AR-V).

All authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Table 1. Characteristics of the patients included in the study

	Mean/percentage	Standard deviation
Age	28.86 years	9.53
Female	39.62% (21 patients)	5.35
Age of Ist operation	5.05 years	7.87
Age of total correction	6.55 years	
Palliative pulmonary – systemic shunt	7.5% (4 patients)	
>1 heart defect	18.9% (10 patients)	
Symptoms:		
NYHA functional class ≥2	41.5% (22 patients)	
Dizziness	3.8% (2 patients)	
Cyanosis	0	
Medications:		
Beta blockers	20.7% (11 patients)	
Digoxin	3.8% (2 patients)	
Sotalol/propafenon	3.8% (2 patients)	
Diuretics	5.7% (3 patients)	
Oral anticoagulants	5.7% (3 patients)	
≥2 medications	28.3% (15 patients)	

NYHA – New York Heart Association.

Results

Study group characteristic is shown in table 1. Mean age of the first surgical procedure was 5.05 years; majority of patients undergone the first surgery at early childhood – <2 years old – 14 patients (26.4%), between 2 and 5 years – 23 (43.4%), 6–11 years – 10 (18.9%), late operations – after the age of 12 years – 6 patients (11.3%). Mean age of definitive surgical correction was 6.55 years. In 4 cases (7.5%) palliative pulmonary-systemic shunt was done before the total correction (Blalock-Taussig procedure). 2 patients (3.8%) underwent pacemaker implantation due to sick sinus syndrome.

One patient died during study period. The death occurred in postoperative period after homograft implantation in pulmonary valve position due to right ventricle failure.

On a review of Holter recording, sinus rhythm was present in 46 patients (86.8%), persistent atrial flutter in 3 (5.7%), 2 patients (3.8%) were pacemaker dependent.

Mean heart rate was 70 bpm (±8 bpm). QRS complex widening diagnosed as width over 120 msec was present in 20 patients (37.7%). There was no patient with QRS complex width over 180 msec.

Significant ventricular arrhythmias were present in 15 patients (28.3%). PVCs >10 per hour were observed in 12 patients (22.6%), nsVT in 6 patients (11.3%), sVT wasn't noticed. In 9 patients (17%) significant supraventricular arrhythmias were registered, 3 (5.7%) had atrial flutter, other 6 (11.3%) supraventricular tachycardia.

Echocardiographic data are presented in table 2.

Subgroup analysis was performed due to comparison of patients with and without arrhythmias. Echocardiographic findings, demographic data and clinical symptoms were investigated.

Comparison of patients with atrial and ventricular arrhythmias is shown in table 3.

As shown in table 3, both significant atrial and ventricular arrhythmias were more common among men than women. Mean age in groups with arrhythmia was higher than mean age of the whole group. Also age of the Ist operation and total correction were both higher in arrhythmias subgroups. One third of the patients with one of the arrhythmia reported symptoms' presence.

While comparing arrhythmia subgroup with arrhythmia-free group, statistically significant correlations were found. Summation for atrial arrhythmias' group in presented in table 4.

As mentioned before, patients with supraventricular arrhythmias were older. Also both subgroups were older: SVT – mean age 36 years, AFl 33.5 years. There was a relevant difference in medications intake between patients with and without atrial arrhythmia: digoxin (p=0.002) and diuretics (p=0.021). There were 3 patients on oral anticoagulants (p<0.00011), all of them had atrial flutter. Ventricular arrhythmias were significantly more likely to occur in patients with atrial arrhythmias (p=0.0057). Considering echocardiographic findings, measurements of left ventricle (LV), right atrium (RA) and left atrium (LA) were greater in group with arrhythmia. Other investigated variables showed no statistical significance.

The same comparison was done for ventricular arrhythmias – table 5.

Table 2. Echocardiographic characteristics of studied patients

	Mean/ percentage	Standard deviation
LVEDD	44.8 mm	7.36 mm
LV enlargement (>53 mm ♀; >59 mm ♂)	3.8% (2 patients)	
LVEF <55%	18.9% (10 patients)	
RVOT PROX	30.5 mm	5.91 mm
RV enlargement (RVOT PROX >33 mm)	30.2% (16 patients)	
Tricuspid annulus	36.0 mm	7.28 mm
Tricuspid annulus widening (>35 mm)	34% (18 patients)	
Pulmonary trunk diameter	22.02 mm	5.97 mm
Severe pulmonary regurgitation	37.7% (20 patients)	
TAPSE	22.02 mm	4.85 mm
Aortic regurgitation (mild and moderate)	45.3% (24 patients)	
Ascending aorta	34.0 mm	6.04 mm
Aortic annulus	27.9 mm	6.03 mm
RAA	22.79 cm^2	7.86 cm^2
RA enlargement (RAA>18 cm^2)	51% (27 patients)	
LAA	15.97 cm^2	3.49 cm^2
LA enlargement(LAA>20 cm^2)	22.6% (12 patients)	

* LVEDD – left ventricle end diastolic diameter, LV – left ventricle, LVEF – left ventricle ejection fraction, RVOT PROX – right ventricle outflow track in parasternal long-axis view, RV – right ventricle, TAPSE – Tricuspid Annular Plane Systolic Excursion, RAA – right atrium area, RA – right atrium, LAA – left atrium area, LA – left atrium

Table 3. Comparison of patients with atrial and ventricular arrhythmias

	Atrial arrhythmias (total n = 9)	Ventricular arrhythmias (total n = 15)
Age	35.38 ±3.07 years	34.67 ±12.04
Women	3 patients (33.3%)	5 patients (33.3%)
Men	6 patients (66.7%)	10 patients (66.7%)
Age of Ist procedure	6.56 ±6.69 years	5.87 ±7.8 years
Age of total correction	7.25 ±6.8 years	10.0 ±13.32 years
Shunt operation	0	1 (6.7%)
Symptoms presence	3 patients (33.3%)	5 patients (33.3%)

Table 4. Comparison of patients without and with atrial arrhythmias

	No atrial arrhythmias (total n = 44)	Atrial arrhythmias (total n = 9)	p
Age	27.65±9.85 years	35.38±3.07	**0.0047**
Symptoms	19 patients (43.2%)	3 patients (33.3%)	0.77
NYHA functional class > II	19 patients (43.2%)	3 patients (33.3%)	0.77
Digoxin	0	2 patients (22.2%)	**0.002**
Diuretics	1 patients (2.3%)	2 patients (22.2%)	**0.021**
Oral anticoagulants	0	3 patients (33.3%)	**0.00 011**
Ventricular arrhythmias	9 patients (20.5%)	6 patients (66.7%)	**0.0057**
LVEDD	43.63 ±7.31 mm	50.22±4.97 mm	**0.0051**
LV enlargement	0	2 patients (22.2%)	**0.002**
LVEF	65.2% ± 9.24%	68.9% ± 12.1%	0.53
TAPSE	22.02 ± 4.44 mm	22.0 ± 7.79 mm	0.59
Severe pulmonary regurgitation	18 patients (40.9%)	2 patients (22.2%)	0.89
RAA	21.6±7.55 cm^2	31.6±3.05 cm^2	**0.0069**
RA diameter	45.3±9.1 mm	54.4±11.83 mm	**0.038**
LA diameter	34.3±6.29 mm	40.4±6.94 mm	**0.039**

Older age was connected with occurrence of the ventricular arrhythmias (34.67±12.04 years; p=0.016), in case of PVC>10/h mean age was 34.3 years, nsVT – 41.5 years. Considering medications consumption, correlation was found in digoxin and diuretics intake, however 2 patients that took digoxin had atrial arrhythmia as well as ventricular one. Greater measurements of both atria and LV enlargement were connected with presence of ventricular arrhythmias. Other variables' statistics weren't significant.

Discussion

Previous studies of the arrhythmias burden in adult patients after total correction of Tetralogy of Fallot emphasized high prevalence of both ventricular and supraventricular arrhythmias. According to the sources, occurrence of ventricular arrhythmias differed from 16,3% to 94% [5,17]. In our study it was 28,3%. SVT and atrial flutter were observed in 17%, which was consistent with other results: 11%, 19%, 24% [5,18,19; respectively]. Presence of any arrhythmia: atrial or ventricular, wasn't connected with higher frequency of all reported symptoms or NYHA functional class. Mean age in both arrhythmia groups was higher than in general group, arrhythmias frequency increased with patients age. This result was consistent with other studies in both adult and children populations – constant increase in atrial and ventricular arrhythmias was observed with ageing [2,4].

In our study, atrial arrhythmias were less common than ventricular. Other studies results were opposite to our observation [2,20], nevertheless arrhythmias frequencies depended strongly on methodology used in the study – methods of arrhythmia recording or definition of its significance [2,5,20]. In our study population was relatively young, mean age of the patient with atrial arrhythmia was 35 years and was approximately 8 years greater than without arrhythmia. Mean age of patient with atrial flutter was 33,5 years, which was much earlier than in general population [21,22]. Correlation between ageing and presence of supraventricular arrhythmias is well described, connected with electrophysiological changes such as decreased capability to adapt to heart rate and increased variability of repolarization in heart chamber [4]. Therefore, the assuming prevalence of atrial arrhythmias will probably increase with population ageing [2–11].

Our study showed a significant positive correlation between occurrence of the ventricular arrhythmia and age. Patients with rhythm disorders were older (34,7 vs 26,4 years). This correlation was also present in patients with nsVT (41,5 years). Ventricular arrhythmias, especially nsVT, usually occurs in macroreentrant circuits in regions of surgical scars and natural conduction barriers, especially in case of hemodynamic overload with ventricle dysfunction [4]. No correlation was found between the presence of ventricular arrhythmia and diameter of right ventricle (RV) or its function (measured as TAPSE). Also no association was found between LV dysfunction (measured as LVEF) and presence of ventricular arrhythmias. This results might be a merit of relatively young age of this population. Most of the patients were operated on in early childhood, before pathophysiological changes occurred. Moreover those changes intensifies in time, most patients are arrhythmia-free during their early adulthood [2,4].

Table 5. Comparison of patients without and with ventricular arrhythmias

	No ventricular arrhythmias (total n = 38)	Ventricular arrhythmias (total n = 15)	p
Age	26.4±7.17 years	34.67±12.04 years	**0.016**
Symptoms	16 patients (42.1%)	6 patients (40%)	0.88
NYHA functional class > II	16 patients (42.1%)	6 patients (40%)	0.88
Digoxin	0	2 patients (13.3%)	**0.025**
Diuretics	0	3 patients (20%)	**0.0053**
Atrial arrhythmias	3 patients (7.9%)	6 patients (40%)	**0.057**
LVEDD	44.46 ± 5.73 mm	45.53 ± 10.6 mm	0.12
LV enlargement	0	2 (13.3%)	**0.027**
LVEF	65.97% ±9.14%	65.53% ± 11.49%	0.88
TAPSE	21.6 ±4.07 mm	22.9 ± 6.39 mm	0.94
Severe pulmonary regurgitation	15 patients (39.5%)	5 patients (33.3%)	0.9
RAA	21.0 ±7.51 cm^2	27.82±6.79 cm^2	**0.01**
RA diameter	44.9 ±9.34 mm	53.4±10.71 mm	**0.048**
LAA	15.1 ±3.07 cm^2	18.5±3.6 cm^2	**0.014**

* NYHA – New York Heart Association, LVEDD – left ventricle end diastolic diameter, LV – left ventricle, LVEF – left ventricle ejection fraction, TAPSE – Tricuspid Annular Plane Systolic Excursion, RAA – right atrium area, RA – right atrium, LAA – left atrium area.

Atrial and ventricular arrhythmias were associated with greater LA and RA measurements. The correlation between RA and LA larger diameter and presence of atrial arrhythmias was reported previously [2,5]. Perhaps, relation between larger atria and ventricular arrhythmias might be explained by coincidence of both arrhythmias. Greater measurements of atria in echocardiography seemed a strong predictor of development of arrhythmias. Both types of arrhythmia were related to LV enlargement. There was a correlation between larger LVEDD and atrial arrhythmias. Probably more observation is necessary to establish the value of this information.

Relation of ventricular arrhythmias and sudden cardiac death remains a topic of intense research [9,10,20]. Studies report many "risk factors" in tetralogy patients, including older age at total correction, previous palliative shunts, QRS complex width over 180 msec, presence of symptoms, worse RV hemodynamics, significant ventricular ectopy, severe pulmonary insufficiency [4,20,23]. So far, no approved risk stratification scale has been established. In analyzed population sudden cardiac deaths didn't occur, although tetralogy patients are particularly prone to this complication and need close observation.

Conclusion

Analyzed data seems to confirm high frequency of arrhythmias in tetralogy patients, as they affect nearly one third of them. Younger age at the time of corrective surgery is related with lower frequency of arrhythmias in adults, however they remain one of the most significant problems. While patients with Tetralogy of Fallot are particularly prone to SCD, any symptoms intensification or new symptom manifestation needs careful evaluation. Active searching for "risk factors" and their valuation seems the best direction in long-term monitoring of patients with Tetralogy of Fallot. Tetralogy patients need close follow-up, thus they should be observed in centers specializing in GUCH (Grown Ups with Congenital Heart defects).

Limitations

Our study is restricted to population of adult patients after total correction of Tetralogy of Fallot, who are monitored in our Hospital. The group is small, inhomogeneous. All data collection was retrospective, based on medical history and examination results. The study was designed to assess the frequency of arrhythmias and their relations with selected clinical data.

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Ethical standards

All the study have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Patients gave their informed consent prior to inclusion in the study.