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Early Post-Operative Arrhythmias and Their Risk Factors after Total Repair of Tetralogy of Fallot in Pediatric Patients

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ABSTRACT

Background: Conduction disturbances can occur early after total correction of Tetralogy of Fallot (TOF). Some of these arrhythmias and alterations like complete right bundle branch block are permanent, while some others like Junctional Ectopic Tachycardia (JET) are transient.

Objective: This study aimed to evaluate the early post-operative arrhythmias and their risk factors among pediatric patients with TOF after surgical total correction.

Methods: This retrospective study was conducted on pediatric patients aged six months to 15 years old (52.5% male and 47.5% female) with TOF who had consecutively underwent surgical total correction during 2015 - 2017. Patients with additional concomitant cardiac operations, previous arrhythmias before the surgery, or any co-existing cardiac anomalies as well as those with severe post-operative complications were excluded. All pertinent data and Electrocardiographic (ECG) documents were recorded several times right after the operation to detect arrhythmias and ECG changes and to find any association between the related risk factors and the occurrence of arrhythmias.

Results: Out of the 118 TOF patients who underwent total correction, 27% were under the age of one year and 73% were above one year old. Among the patients, 78.5% developed permanent ECG changes, mostly complete right bundle branch block and left anterior or posterior hemiblock. Out of these patients, 8.5% had JET together with other permanent arrhythmias and 8.5% had transient JET solely. Therefore 17% of all patients developed JET and 21.5% had no permanent noticeable ECG changes. The most permanent arrhythmia was right bundle branch block followed by left anterior hemiblock and left posterior hemiblock. These arrhythmias mainly manifesed amongst the patients with lower age and those with severe subvalvar pulmonary stenosis. The results showed a significant relationship between the incidence of JET and use of milrinon after the operation. There was no myocardial ischemia or infarction from injury to aberrant coronary arteries passing over the right ventricular outflow tract.

Conclusion: Early post-operative permanent arrhythmias after total TOF repair was probably more common amongst the patients who were below one year old with more severe subvalvar pulmonary stenosis. Nonetheless, the occurrence of transient JET was mostly observed in the patients who were given milrinone as a post-operative inotrope medicine.

1. Background

Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart disease with reduced pulmonary blood flow (1-3). Surgical correction of TOF includes resection of obstructive muscle bundles in the subvalvar pulmonary region and closure of the Ventricular Septal Defect (VSD). If the pulmonary valve annulus or subvalvar region are very small and stenotic, patch augmentation of the pulmonary valve and subvalvar area might be performed (4-7). In patients who undergo corrective surgery, short-term complications, such as right ventricular failure, cardiac arrhythmia, residual VSD shunting, and myocardial

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infarction from an aberrant coronary artery injury, might occur (8-15). In addition, the atrioventricular node, His bundle and its branches, and hemi-branches might be damaged during surgery due to their location, which is near the VSD. Therefore, complete or incomplete Right Bundle Branch Block (RBBB) with or without Left Anterior Hemiblock (LAHB) can be detected early after repair (16-21). Jet is an important arrhythmia, which might happen early on after operation. It is a self-limiting arrhythmia that might be life-threatening by making the patient hemodynamically unstable (22, 23). The exact mechanism of JET is still unknown, but the hypothesis is that mechanical trauma, such as suturing or indirect stretch injury, can result in JET. In addition, resultant edema to the proximal conductive tissue during resection of muscle bundles or correction of VSDs might lead to JET. Moreover, cardiopulmonary bypass, ischemia-reperfusion, cellular biochemical effects, medical treatments, electrolyte imbalances, and catecholamine administration might affect the cellular membrane, resulting in the instability of the myocardium and automaticity (24).

Some studies have claimed that younger age, longer cardiopulmonary bypass time, and more frequent usage of some inotropes were associated with higher rates of post-operative JET occurrence (25-31). On the contrary, some researchers revealed that older age might predispose patients to develop arrhythmia. Indeed, the duration of cardiopulmonary bypass time and aortic cross-clamping time were not associated with the development of post-operative arrhythmias (32). Hence, there are some controversies regarding early post-operative arrhythmia and the associated causes in patients.

2. Objectives

This study aims to evaluate the changes in electrocardiograms and the factors affecting these abnormalities in pediatric patients.

3. Patients and Methods

After obtaining approval from the local Ethics Committee of Shiraz University of Medical Sciences, this retrospective study was conducted in 2015- 2017 under the ethical code 95-01-01-12167. Consecutive pediatric patients aged six months to 15 years with TOF who underwent surgical total correction in Faghihi hospital, Shiraz, Iran were recruited. The medical records of the patients who were operated on with pulmonary valve and subvalvar patch augmentation technique were obtained. Patients who had other cardiac operations, previous arrhythmias before surgery, or any co-existing cardiac anomalies as well as those with severe post-operative complications were excluded. The patients' laboratory data, including BUN, creatinine, sodium, potassium, calcium, and magnesium, were also recorded. The patients with abnormal laboratory data before operation were excluded from the study, as well. The following data were also gathered: age, gender, type of pulmonary stenosis that could be either valvar, sub-valvar, and supra-valvar, confluency of the pulmonary artery branches, any previous intervention, such as shunt insertion or patent ductus arteriosus stenting, duration of anesthesia (more or less than four hours), cardiopulmonary bypass time (above or below 90 minutes), aorta cross clamping time (above or below 60 minutes), and hypothermia [mild (30 - 35° centigrade), moderate (22 - 30° centigrade), and deep (17 - 22° centigrade)].

All patients had been treated with some types of inotropic agents either solely or in combination after the surgery. Hence, consumption of medications, such as dopamine, dobutamine, epinephrine, noreinephrine, and milrinone, was recorded. Additionally, all patients had electrocardiography (ECG) before and every day after the operation. Thus, the electrocardiograms taken before and up to five days after the surgery were reviewed to distinguish the patterns of older arrhythmias from any new arrhythmia after the operation. In this regard, minor alterations, such as sinus tachycardia, sinus bradycardia, incomplete RBBB, and right axis deviation, were not considered to be important. However, three types of permanent arrhythmias, including cRBBB, LAHB, and Left Posterior Hemiblock (LPHB), and transient JET were considered to be important heart rhythm abnormalities.

3.1. Statistical Analysis

All data analyses were done using IBM SPSS Statistical for Windows, version 25.0. Armonk, NY: IBM Corp. Descriptive statistics were used for qualitative data. Frequency and percentage were reported, as well. Besides, univariate analysis was applied by Chi-square and Fisher's exact test for qualitative data. Frequency, percentage, and P-value were reported, as well. Moreover, logistic regression model was used for multivariate analysis. In this regard, all the variables with P-values < 0.3 were entered in to the model where backward elimination was applied. Odds ratios and 95% confidence intervals were reported, as well. P-values less than 0.05 were considered to be statistically significant.

4. Result

This study was conducted on 118 consecutive patients aged six months to 15 years, with the mean age of 2.38 ± 2.37 years. The demographic data, some important criteria, and different risk factors for arrhythmia amongst the patients have been presented in Table 1.

After the operation, 93 out of the 118 cases (78.5%) developed one type of important permanent arrhythmias, which did not exist before the surgery. Furthermore, 83 cases (70%) solely had one type of three permanent arrhythmias solely (cRBBB, LAHB and LPHB), 10 (8.5%) had JET together with three other arrhythmias, and 10 (8.5%) only had transient JET. Thus 17% of the patients developed JET and 21.2% had no permanent noticeable ECG changes (Table 2).

The most permanent arrhythmia was RBBB followed by LAHB and LPHB (Table 3). These arrhythmias could develop solely or in combination. The frequency of occurrence of arrhythmias separately or in combination has been depicted in Figure 1.

The results of comparison of the patients with and without arrhythmias regarding the relationships between the variables have been presented in Table 4.

Table 1. The Frequency and Percentage of the Variables

Variables		Frequency (n = 118)	Percentage (%)
Gender	Male	62	52.5
	Female	56	47.5
Age	Under 1 year (mean 7.5 months)	31	26.3
	Above 1 year (mean 30 months)	87	73.7
Anesthesia time	Below 4 hours (mean 3.56)	35	29.7
	Above 4 hours (mean 4.72)	83	70.3
Cardiopulmonary bypass time	Below 90 min (mean 67.7)	62	52.5
	Above 90 min (mean 107.8)	56	47.5
Aortic cross-clamping time	Below 60 min (mean 41.6)	66	55.9
	Above 60 min (mean 76.9)	52	44.1
Pulmonary artery branches	Mild (mean 31.3° centigrade)	108	91.5
	Moderate (mean 28.7° centigrade)	10	8.5
	Deep	0	0
	Confluent	110	93.2
	Non-confluent	8	6.8
Previous shunt	Yes	10	8.5
	No	108	91.5
Valvar	Yes	109	92.4
	No	9	7.6
Sub-valvar	Yes	103	87.3
	No	15	12.7
Supra-valvar	Yes	38	32.2
	No	80	67.8
Dopamine	Yes	41	34.7
	No	77	65.3
Dobutamine	Yes	2	1.7
	No	116	98.3
Epinephrine	Yes	102	86.4
	No	16	13.6
Norepnephrine	Yes	3	2.5
	No	115	97.5
Milrinone	Yes	30	25.4
	No	88	74.6

Table 2. The Frequency of Arrhythmias

Type of Arrhythmias		Frequency (n = 118)	Percentage (%)
Complete RBBB	Yes	83	70.3
	No	35	29.7
LAHB	Yes	28	23.7
	No	90	76.3
LPHB	Yes	8	6.8
	No	110	93.2
JET	Yes	20	16.9
	No	98	83.1

Abbreviations: RBBB, right bundle branch block; LAHB, left anterior hemiblock; LPHB, left posterior hemiblock; JET, junctional ectopic tachycardia

Table 3. The Frequency of Arrhythmias

Type of Arrhythmias		Frequency (n = 118)	Percentage (%)
Complete RBBB	Yes	83	70.3
	No	35	29.7
LAHB	Yes	28	23.7
	No	90	76.3
LPHB	Yes	8	6.8
	No	110	93.2
JET	Yes	20	16.9
	No	98	83.1

Abbreviations: RBBB, right bundle branch block; LAHB, left anterior hemiblock; LPHB, left posterior hemiblock; JET, junctional ectopic tachycardia

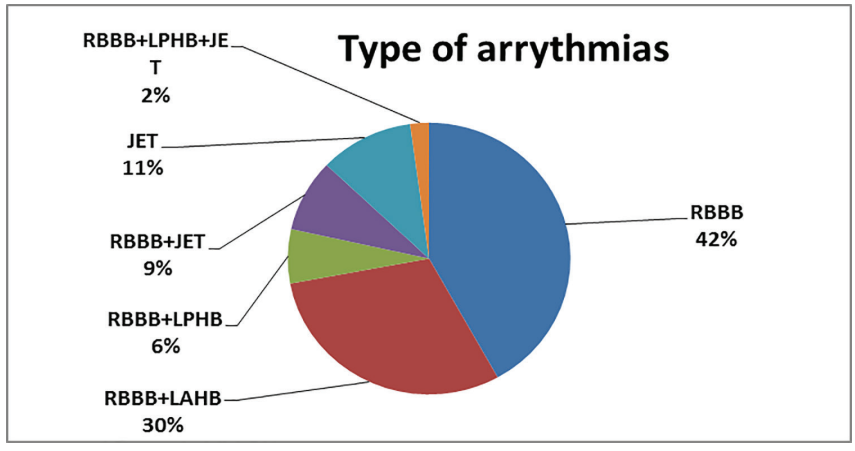

Figure 1. The Frequency of Arrhythmias Separately or in Combination

Table 4. The Associations between Different Variables amongst the Patients with and without Permanent Arrhythmias

Variables	Patients with Arrhythmia	Patients without Arrhythmia	P-value
Age below 1 year	29 (31.2%)	2 (8.0%)	0.021
Age above 1 year	64 (68.8%)	23 (92.0%)	
Anesthesia below 4 hours	31 (33.3%)	4 (16.0%)	0.138
Anesthesia above 4 hours	62 (66.7%)	21 (84.0%)	
CPBT below 90 minutes	49 (52.7%)	13 (52.0%)	1.000
CPBT above 90 minutes	44 (47.3%)	12 (48.0%)	
CCCT below 60 minutes	53 (57.0%)	13 (52.0%)	0.658
CCCT above 60 minutes	40 (43.0%)	12 (48.0%)	
Mild hypothermia (30 - 34 °C)	83 (89.2%)	25 (100.0%)	0.117
Moderate hypothermia (22 - 30 °C)	10 (10.8%)	0 (0.0%)	
Confluent pulmonary artery branches	87 (93.5%)	23 (92.0%)	0.676
Non-confluent pulmonary artery branches	6 (6.5%)	2 (8.0%)	
Previous shunt	9 (9.7%)	1 (4.0%)	0.686
No previous shunt	84 (90.3%)	24 (96.0%)	
Severe valvar pulmonary stenosis	87 (93.5%)	22 (88.0%)	0.397
Sub-valvar pulmonary stenosis	85 (92.6%)	20 (70.2%)	0.046
Supra-valvar pulmonary stenosis	32 (34.4%)	6 (24.0%)	0.470
Dopamine	34 (36.6%)	7 (28.0%)	0.486
Dobutamine	2 (2.2%)	0 (0.0%)	1.000
Epinephrine	82 (88.2%)	20 (80.0%)	0.326
Norepinephrine	2(2.2%)	1 (4.0%)	0.514
Milrinon	26(28.0%)	4 (16.0%)	0.304

Abbreviations: CPBT, cardiopulmonary bypass time; CCCT, cardiac cross clamping time

According to the results of univariate analysis, arrhythmia at the time of operation and in sub-valvar pulmonary stenosis ocurred more frequently in patients who were below one year old.

However, there were no statistically significant relationships between arrhythmias and other variables.

The two significant variables with $P < 0.05$ (age and sub-valvar pulmonary stenosis) were entered into multivariate model and the results have been shown in Table 5.

According to the results, 20 patients presented with JET. Among all inotropes, only milrinone was significantly associated with the presence of JET (Table 6).

Fortunately, none of the patients developed myocardial ischemia, infarction, or third degree atrioventricular block.

5. Discussion

Since early post-operative arrhythmias are associated with a higher rate of mortalities and morbidities, some researchers prefer to investigate arrhythmia and its risk factors early after total correction of TOF.

In the present study, nearly 78% of the patients showed one kind of permanent electrocardiographic abnormality early after TOF total correction. At the same time, ages less than one year at operation time had a great correlation with arrhythmias. In addition, severe subvalvar pulmonary stenosis (versus pink tetralogy with no severe stenosis) had a significant association with the occurrence of these permanent abnormalities. Besides, the most arrhythmia amongst the patients was cRBBB (70%) followed by LAHB (23.7%) and LPHB (6.7%).

In a previous study, the frequency of the three above-mentioned permanent arrhythmias was investigated in patients operated after the age of one year and the results indicated that 45% of the patients developed these three permanent arrhythmias and their manifestation was correlated to the duration of cardiopulmonary bypass time, but not to lower age at the time of surgery. However, age above two years was correlated to the occurrence

Table 5. Multivariate Analysis of the Variables with Significant Results

Variables	OR	95% CI
Age	5.21	1.085 - 22.64
Sub-valvar pulmonary stenosis	2.94	0.77 - 8.33

Abbreviations: OR, odds ratio; CI, confidence interval

Table 6. The Associations between the Variables among the Patients with and without JET

Variables	Patients with JET	Patients without JET	P-value
Age below 1 year	8 (40.0%)	23 (23.5%)	0.163
Age above 1 year	12 (60.0%)	75 (76.5%)	
Anesthesia below 4 hours	6 (30.0%)	29 (29.6%)	1.000
Anesthesia above 4 hours	14 (70.0%)	69 (70.4%)	
CPBT below 90 minutes	14 (70.0%)	48 (49.0%)	0.139
CPBT above 90 minutes	6 (30.0%)	50 (51.0%)	
CCCT below 60 minutes	14 (70.0%)	52 (53.1%)	0.218
CCCT above 60 minutes	6 (30.0%)	46 (46.9%)	
Mild hypothermia (30-34 C)	18 (90.0%)	90 (91.8%)	0.677
Moderate hypothermia (22-30 C)	2 (10.0%)	8 (8.2%)	
Confluent pulmonary artery branches	19 (95.0%)	91 (92.9%)	1.000
Non-confluent pulmonary artery branches	1 (5.0%)	7 (7.1%)	
Previous shunt	2 (10.0%)	8 (8.2%)	0.677
No previous shunt	18 (90.0%)	90 (91.8%)	
Valvar pulmonary stenosis	19 (95.0%)	90 (91.8%)	1.000
Sub-valvar pulmonary stenosis	18 (90.0%)	85 (86.7%)	1.000
Supra-valvar pulmonary stenosis	7 (35.0%)	31 (31.6%)	0.796
Dopamine	8 (40.0%)	33 (33.7%)	0.613
Dobutamine	1 (5.0%)	1 (1.0%)	0.311
Epinephrine	17 (85.0%)	85 (86.7%)	0.734
Norepinephrine	0 (0.0%)	3 (3.1%)	1.000
Milrinone	9 (45.0%)	21 (21.4%)	0.045

Abbreviations: CPBT, cardiopulmonary bypass time; CCCT, cardiac cross clamping time

of arrhythmias (31). Another study revealed that 80% of patients repaired with transannular patch method presented with cRBBB (28). Indeed, LAHB was seen in 10% of these patients aged more than one year. Thus, younger age and transannular and subvalvar patch insertion might be related to the occurrence of arrhythmia.

In the present study, 20 patients (17%) developed JET. The results indicated no direct relationships between the occurrence of JET and age, cardiopulmonary bypass time, cross-clamping time, hypothermia, and anesthesia time. Nonetheless, there was a significant relationship between milrinone and the occurrence of JET.

Dobutamine and norepinephrine were used with low frequency for the present study patients. Considering their paucity, their effects on JET could not be evaluated. Nonetheless, epinephrine was administered for a significant number of patients, but it did not show any prominent effects on induction of JET.

Batra et al. investigated 336 pediatric patients who underwent cardiac surgery and found that 8% of them developed JET. They stated that longer ischemic time was associated with JET (33). Moak J. P. et al. (34) also found that the incidence of JET increased with increased aortic cross-clamp time and cardiopulmonary bypass time. Regarding the use of milrinone as an inotrope, their results were in line with those of the present research, and they realized that the use of milrinone was associated with post-operative JET formation. They also found an association between the use of dopamine and JET. However, no statistically significant association was observed in this regard in the current study.

Makhoul M et al. (35) performed a matched case–control study on 54 patients with JET to identify its risk factors and a matched cohort study to compare the patients and controls regarding the outcome. After multivariate logistic regression analysis, cardiopulmonary bypass duration of more than 100 minutes and low operative weight were associated with the increased odds of developing JET. Another researcher (36) examined the possible factors resulting in JET after TOF repair and found no relationship between pulmonary artery trans-annular patch and JET arrhythmia, while all the patients underwent trans-annular patch for total repair. Another study (23) evaluated the association between JET and dopamine, milrinone, longer cardiopulmonary bypass time, and young age. The results showed that milrinone was associated with the occurrence of arrhythmias, which was consistent with the present research findings. However, the results of the current study indicated no significant relationships between dopamine and age below six months and the occurrence of arrhythmias.

5.1. Conclusion

The current study findings revealed age less than one year and severe subvalvar pulmonary stenosis as the main risk factors after TOF surgical total repair and milrinone as a major cause of developing JET. It appears that arrhythmias originate from multifactorial causes following cardiac surgery in pediatric patients with TOF. Although the study

might have not produced novel results, similar studies are recommended to be conducted on the issue considering different socioeconomic conditions, surgical experiences, and post-operative care services.

5.2. Study Limitations

This study had a retrospective design. Thus, further prospective studies with larger sample sizes are required to be conducted to achieve more precise results.

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Authors' Contribution

1- Study concept and design: MR E, 2- Acquisition of data, analysis and interpretation of data, and statistical analysis: M S, 3- Drafting of the manuscript and critical revision of the manuscript for important intellectual content: K K, 4- Study supervision: MR E and N M.

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