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## Assessment of right ventricular function in significant pulmonary regurgitation by 2d echocardiography after repair of tetralogy of fallot

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### Abstract

**Background:** Tetralogy of Fallot (TOF) is a genetic cardiac defect that arises during embryonic development and is characterized by the presence of pulmonary valve regurgitation. The echocardiogram is widely regarded as the preferred diagnostic method for the identification of TOF. The objective of this research was to evaluate the function of the right ventricle (RV) after the surgical correction of TOF.

**Methods:** A cross-sectional research was conducted on a group of thirty individuals who had undergone surgical correction for TOF. Patients were categorized into two groups: group one: less than ten years after the repair and group two more than or equal to ten years after the repair. Following the surgical treatment of TOF, a comprehensive evaluation of RV systolic function was conducted on all patients using two-dimensional (2D) echocardiography (ECG).

**Results:** Using variables such as age, RV size, body mass index (BMI), and the distal and proximal diameters of the RV outflow tract, Ring of the lungs, and Pulmonary artery diameters (right and left), Group One had considerably worse myocardial performance index (MPI) than Group two. Palpitation, heart rate (HR), and cardio-thoracic ratio <0.5, RA End systolic area <18 cm<sup>2</sup> and Inferior vena cava (IVC) diameter <2.1 cm, S wave, fractional area change, and tricuspid annular plane systolic excursion TAPSE was significantly elevated in group one than group two. Wide Quality Rating System and Right axis deviation, RA ESA and IVC diameter were significantly higher in group two than in group one. Univariate regression study found that age, cardiothoracic index, RV basal diameter, and RV mid diameter were all significant predictors of RV impairment, but multivariate regression analysis found no such relationship.

**Conclusions:** Following the surgical repair of individuals diagnosed with TOF for a duration exceeding ten years, there is a notable decline in right RV function. This decline may be evaluated by the use of ECG.

**Keywords:** Right ventricular function, pulmonary regurgitation, 2d echocardiography, repair of tetralogy of fallot

### Introduction

Congenital heart disease manifests in around 0.9% of live births. Notably, advancements in the fields of pediatrics, cardiology, surgery, and resuscitation have contributed to a significant increase in the survival rate of affected individuals, with approximately ninety % now reaching maturation. Among what are commonly called “grown-up congenital heart diseases” (GUCHs) or, more recently, “adult congenital heart diseases” (ACHDs), tetralogy of Fallot (TOF) has a preponderant place, because of because it is possible to have corrective surgery and its relatively high prevalence, leading to almost normal physiology and anatomy in maturity. Long-term follow-up studies have provided evidence indicating that the health state of individuals is exceptional, characterized by a notably low death rate [1].

TOF is a congenital heart defect that manifests during the early stages of embryonic development [2]. TOF is well recognized as a prevalent etiology of cyanotic heart disease in early infancy, with an incidence rate of three per ten thousand live births. It accounts for around seven% to ten% of all congenital defects.

It is one of the most common causes of cyanotic heart disease beyond the neonatal age. There is a somewhat higher prevalence of men being impacted compared to females. The etiology of the condition is considered to be multifaceted, with many factors having been linked to its development. These factors include maternal consumption of retinoic acid, phenylketonuria, and untreated maternal diabetes. Chromosomal anomalies including trisomy's twenty-one, eighteen, and thirteen have also been associated with TOF. More frequent, however, are microdeletions of chromosome twenty-two. There is also an association between Alagille syndrome with JAG1 mutations and TOF [3].

The objective of this study was to evaluate the right ventricular function after the surgical correction of TOF.

### Methods and Patient

Cross-sectional research was undertaken on a cohort of thirty patients who had been diagnosed with surgically corrected Fallot tetralogy. The investigation was carried out at the Cardiology Department of the Faculty of Medicine at Tanta University. The study was done after approval from the Ethical Committee Tanta University Hospitals. An informed written consent was obtained from the patient.

The exclusion criteria include individuals who exhibit alternative sources of right ventricular failure, patients who are not in sinus rhythm throughout the evaluation, and patients who are clinically unstable. Patients were categorized into two groups: Group one (n=twelve): Patients underwent surgical repair of FOT less than ten years after the repair. Group two (n=eighteen): Patients underwent surgical repair of FOT more than ten years after the repair. All patients were subjected to chest x-ray history taking, general clinical examination, for cardiomegaly (RA and RV enlargement), twelve-lead ECG, 2D transthoracic ECG, with detailed assessment of RV functions (parasternal long-axis view (PLAX), parasternal short-axis view (PSAX), apical four-chamber view, subcostal views).

### 2D Echocardiography

Tissue Doppl ECG for measurement of: RV MPI (Tei index), s wave. The percentage RV FAC was calculated by the formula (End-diastolic area-end-systolic area)/end-diastolic area). The measurement of TAPSE was conducted using M-mode ECG. This included setting the 2D cursor at the tricuspid lateral annulus and measuring the distance of systolic annular RV excursion along a longitudinal line. The end of systole was defined as the point when the T wave in the ECG concluded [4]. Color Doppler ECG was done for detection of (residual ventricular septal defect (VSD) leak, tricuspid regurgitation, degree of pulmonary incompetence). RA area was traced at the end of ventricular systole (largest volume) from the lateral aspect of the tricuspid annulus to the septal aspect, excluding the area between the annulus and leaflets, following the RA endocardium, excluding the IVC and SVC and RA appendage [4]. The diameter of the IVC should be measured in the subcostal view with the patient in the supine, using the long-axis view. For accuracy, The measurement should be conducted in a perpendicular

manner with respect to the long axis of the inferior vena cava (IVC).

RV dimensions measured as the RV focused apical 4-chamber view (a dedicated view which keeps the LV apex in the center and displays the largest basal RV diameter should be used. o

The RVOT diameter can be measured in the parasternal short-axis views, proximal to the pulmonary valve, as well as from a PLAX angled superiorly [5]. Pulmonary annulus of artery and size branches diameters were also measured.

### Statistical analysis

The statistical analysis was conducted using version twenty-five of the SPSS (Statistical Package for the Social Sciences) software, developed by IBM Inc. in Chicago, IL, USA. Histograms and Shapiro-Wilks normality test were used to examine the quantitative variables distribution to choose accordingly the statistical testing sort: nonparametric or parametric. The parametric variables were represented by the SD and mean and their comparison across the three groups was conducted using the F test. Subsequently, a post hoc (Tukey) test was used to assess each pair of groups. The paired T test was employed to compare two variables within the same group. The non-parametric variables were assessed using the Kruskal-Wallis's test, with their representation being based on the IQR and mean. Additionally, a further analysis was conducted using the Mann-Whitney (U) test to compare each pair of groups. The Wilcoxon test was employed to compare two variables within the same group. The categorical variables were represented as percentages and frequencies, and their statistical analysis was conducted using the Chi-square test. A two-tailed P value of less than or equal to 0.05 is considered to be statistically significant.

### Results

There was an important difference regarding BSA and age and no important difference regarding gender, syncope, exertional dyspnea, fatigue, and residence between the studied groups. As shown in table one, Palpitation was important elevated in group one more than group two ( $p=0.01$ ).

Group one had more patients with RA ESA eighteen cm<sup>2</sup> and higher HR, IVC 2.1 cm and worse CTR than group two, whereas group two had more patients with RA ESA, IVC diameter, RVOT proximal and distal diameters, SBP, and DBP. Table two Wide QRS and RAD were significantly elevated in group two than in group one ( $p=0.024$  and  $0.045$  respectively). There was no significant variance in RBBB and RAE between the studied groups. Table 3

Pulmonary annulus, RPA, and LPA diameters were significantly higher in group two than group one ( $p<0.001$ ). S wave, FAC, and TAPSE were significantly higher in group one than group two ( $p<0.001$ ). MPI was significantly lower in group one than group two ( $p<0.001$ ). Table four.

In Multi variate regression analysis, age, cardio thoracic index, RA ESC, RV basal diameter and RV mid diameter were insignificant predictors of RV impairment Table five.

**Table 1:** Demographic characteristics and Symptoms distribution among the studied group

		Group one (n =twelve)	Group two (n =eighteen)	P value
Age (years)		5.25±2.53	16.11±3.22	<0.001*
Gender	Male	5 (41.67%)	6 (33.33%)	0.712
	Female	7 (58.33%)	12 (66.67%)	
BSA (m <sup>2</sup> )		0.91±0.14	1.54±0.15	<0.001*
Residence	Urban	9 (75.00%)	10 (55.56%)	0.442
	Rural	3 (25.00%)	8 (44.44%)	
Palpitation	Present	12 (100%)	10 (55.56%)	0.01*
	Absent	0 (0.00%)	8 (44.44%)	
Fatigue	Present	7 (58.33%)	16 (88.89%)	0.084
	Absent	5 (41.67%)	2 (11.11%)	
Exertional dyspnea	Present	8 (66.67%)	15 (83.33%)	0.391
	Absent	4 (33.33%)	3 (16.67%)	
Syncope	Present	0 (0.00%)	0 (00.00%)	0.255
	Absent	12 (100%)	18 (100%)	

Data are demonstrated as average± SD, frequency (%). BSA, \*statistically significant as p value ≤0.05.

**Table 2:** Comparison of HR and blood pressure, RA end systolic area and IVC diameter, RV dimensions and RVOT diameters between the studied groups

		Group one (n =twelve)	Group two (n =eighteen)	P value
HR (bpm)		106.92 ±10.45	88.61±4.42	<0.001*
SBP (mmHg)		103.08±5.07	120.78±5.7	<0.001*
DBP		62.58±4.7	76.94±6.59	<0.001*
CTR	<0.5	10 (83.33%)	1 (5.56%)	<0.001*
	>0.5	2 (16.67%)	17 (94.44%)	
RA ESA (cm <sup>2</sup> )		12.04±3.11	17.22±2.67	0.007*
RA ESA (cm <sup>2</sup> )	<18	10 (83.33%)	6 (33.33%)	0.011*
	≥18	2 (16.67%)	12 (66.67%)	
IVC diameter (cm)		1.13±0.2	1.92±0.44	<0.001*
IVC diameter (cm)	<2.1	12 (100%)	8 (44.44%)	0.002*
	≥2.1	0 (0%)	10 (55.56%)	
RV basal diameter (cm)		3.72±0.36	5.21±0.6	0.009*
RV mid diameter (cm)		3.22±0.35	4.36±0.64	0.036*
RV longitudinal diameter (cm)		6.98±1.14	8.74±0.28	0.004*
RVOT proximal (cm)		2.86±0.13	4.13±0.39	<0.001*
RVOT distal (cm)		2.05±0.33	3.06±0.27	<0.001*

Data are shown as average± SD or frequency (%), HR, SBP, DBP, CTR: Cardio- thoracic ratio, RVOT, RV, RA: RV. ESA: End systolic area, IVC\*statistically significant as p value ≤0.05.

**Table 3:** ECG results between the studied groups

		Group one (n =twelve)	Group two (n =eighteen)	P value
Wide QRS >120 ms	Present	3 (25.00%)	13(72.22%)	0.024*
	Absent	9 (75.00%)	5 (27.78%)	
RAD	Present	5 (41.67%)	15(83.33%)	0.045*
	Absent	7 (58.33%)	3 (16.67%)	
RBBB	Present	3 (25.00%)	10(55.56%)	0.141
	Absent	9 (75.00%)	8 (44.44%)	
RAE	Present	2 (16.67%)	5 (27.78%)	0.121
	Absent	10 (83.33%)	13(72.22%)	

Data are demonstrated as average± SD or frequency (%), ECG: Electrocardiograph, RAD, RBB, RAE, \*statistically significant as p value ≤0.05.

**Table 4:** RV function and pulmonary artery and pulmonary branch diameters by 2D echo cardiography between groups.

	Group one (n =twelve)	Group two (n =eighteen)	P value
Pulmonary annulus (cm)	2.03±0.08	2.45±0.21	<0.001*
RPA diameter (cm)	1.09±0.11	2.47±0.57	<0.001*
LPA diameter (cm)	0.99±0.33	2.73±0.55	<0.001*
S wave (cm/s))	10.71±1.48	8.19±0.87	<0.001*
MPI	0.37±0.16	0.58±0.06	<0.001*
FAC (%)	36.67±1.87	33±3.07	<0.001*
TAPSE (cm)	1.96±0.28	1.51±0.24	<0.001*

Data are demonstrated as average± SD, MPI, RPA, LPA: Left pulmonary artery, \*statistically significant as p value ≤0.05. FAC: Fraction area change, TAPSE: tricuspid annular plane systolic excursion, \*statistically significant as p value ≤0.05.

**Table 5:** Prediction of RV impairment using univariate and multivariate logistic regression of several factors.

	Univariate analysis		Multi variate analysis	
	OR (95% CI)	P value	OR (95%CI)	P value
Age (years)	1.29 (1.07 – 1.56)	0.006*	1.22 (0.82– 1.82)	0.311
Cardio thoracic index (>0.5)	14.22 (2.32 –87.03)	0.004*	1.76 (0.07– 39.34)	0.721
Wide QRS	0.33 (0.07 – 1.55)	0.163	-	-
RBBB	0.33 (0.07 – 1.68)	0.184	-	-
Right atrial enlargement	0.21 (0.02 – 2.10)	0.187	-	-
RA ESA	1.38 (1.08 – 1.78)	0.011*	1.09 (0.74– 1.62)	0.645
RV basal diameter	5.10 (1.48 –17.52)	0.009*	1.48 (0.19– 11.39)	0.704
RV mid diameter	3.66 (1.01 –13.38)	0.049*	0.53 (0.05– 5.40)	0.591
RV longitudinal diameter	1.66 (0.84 – 3.32)	0.144	-	-

Data are shown as average $\pm$  SD or percentage (%), RBBB, RA, ESA, RV, \*statistically significant as p value  $\leq$ 0.05.

## Discussion

TOF is the prevailing manifestation of cyanotic congenital heart disease, constituting around seven-1ten% of the overall prevalence of congenital cardiac abnormalities [6]. The complete correction of TOF has been a viable treatment option for almost six decades, with positive results in the majority of patients [7].

Pulmonary regurgitation that is acquired subsequent to a surgical procedure for TOF findings in a persistent increase in volume inside the right ventricle, leading to a chronic state of overload. This condition often leads to a gradual decline in the ventricle's functional capacity over time [8]. The potential benefits of pulmonary valve replacement in enhancing right ventricular hemodynamics have been seen, while there is controversy over the optimal scheduling for this procedure. Hence, the evaluation of RV function and pulmonary insufficiency function over an extended period of time is of crucial significance in the management of individuals who have had surgical repair for TOF [9]. Therefore, the evaluation of RV function and pulmonary insufficiency over an extended period of time is of crucial significance in the management of individuals who have had surgical repair for TOF [10].

Over time, the persistent pulmonary stenosis resulting from the conservative surgical method and the regurgitation of blood caused by the transannular patch (TAP) graft used to expand the right ventricular outflow tract give rise to two distinct pathophysiological conditions in the right ventricle, which differ significantly from each other. dilation RV and hypertrophy [11].

ECG is a valuable diagnostic technique that is non-invasive in nature. [104] ECG is a diagnostic imaging technique that provides measurements of both the functional and structural RV characteristics. These variables include the RV fractional area of change, RV Tei index tricuspid and annular plane systolic excursion (TAPSE) [12].

ECG seems to be the most suitable modality for longitudinal monitoring of postoperative patients with tetralogy of TOF, given its cost-effectiveness and widespread accessibility across various healthcare settings [13]. Too far, a range of echocardiographic modalities have been used for the evaluation of right ventricular volumes and function, and their findings have been compared to measures acquired using CMR imaging [14-16].

In our research, With respect to the RVs size among the categories under investigation. The basal, mid, and longitudinal diameters of the RV, as well as the IVC and RAESA diameter, exhibited statistically significant increases in group two compared to group one. Patients with RA ESA  $\geq$ eighteen cm<sup>2</sup> and IVC diameter > 2.1 cm was significantly elevated in group two than group (p =0.011,

and =0.002 respectively). Also, regarding the RV systolic function: the S wave, FAC and TAPSE were elevated in group one than group two while the MPI was elevated in group two than group one.

In our research, as regards TAPSE, S wave and FAC were significantly elevated in group one than group two (p<0.001). MPI was found to be considerably lower in group one compared to group two (p< 0.001).

In our research, In the context of univariate regression analysis, the variables of cardio thoracic index, RA ESC, basal diameter, RV, and RV mid diameter exhibited statistical significance as predictors of RV impairment. In the context of Multi variate regression analysis, it was shown that variables such as age, cardio thoracic index, RV basal diameter, and RV mid diameter did not provide significant predictive power in relation to RV impairment. Ayabakan *et al.* [17] conducted research whereby they conducted ECG follow-up to assess the RV function after to TOF procedure. A cohort of sixty-six individuals had surgical procedures at an average age of 14.4 $\pm$ 9.3 months. Subsequently, these patients were subjected to a follow-up period of 7.2 $\pm$ 4.3 years. They found a similar rise in RVOT diameter, RV area, and length after 7.2 $\pm$ 4.3 years, and a gradual increase in TEI with time, and they found that RV function was damaged, but he demonstrated that by RV EF and CMRI, so they classified the patients into those who required PVR and those who did not.

In contrast to our findings, they detected no substantial time-to-time variation in cardiac velocity (S wave) in the tricuspid valve lateral annulus. Myocardial lateral tricuspid annulus and trans-esophageal echo (TAPSE) velocities did not vary or correlate with treatment by ECG. The authors hypothesized that this may be due to a local malfunction in the pattern of cardiac contraction after TOF surgery that does not manifest itself in systemic ventricular activity. TAPSE depends on ventricular load rather than the right ventricular ejection fraction (RVEF) [17].

In agreement with our research. Dłużniewska *et al.* (2018) conducted research on patients with TOF to investigate the long-term effects of surgery. They observed substantial changes in RV dysfunction and dilatation. The researchers categorized their sample of eighty-three patients into two groups: group one consisted of patients who had repair less than twenty-five years ago, while group two included patients who underwent repair more than twenty-five years ago. Also, their finding as ours regarding: RA area, RBBB and RVOT prox a were in group two > group one while S wave and TAPSE were in group one >group two but, Alternative approaches, such as CPET and MRI and were used for the assessment of RV function.

In contrast, Rana *et al.* (2019) shown via the use of tissue doppler imaging that early onset of right ventricular dysfunction might manifest after surgical repair. In their investigation, with an intermediate post operative follow-up of three months, 54.16% of the patients had RV dysfunction immediately following ICR. The elevated frequency seen in their investigation may be attributed to the following factors. The use of a TAP has been seen to exhibit an association with the manifestation of significant pulmonary regurgitation, subsequently resulting in right ventricular dysfunction<sup>[20, 21]</sup>. The use of tissue Doppler, in conjunction with 2D pulse Doppler, for the evaluation of RV function has shown sensitivity that matches the findings of our investigation.

Furthermore, Cetin *et al.*<sup>[22]</sup> conducted an assessment of RV function using tissue doppler imaging around ten years post-repair of TOF. The research included a cohort of twenty-five individuals who had an average age of 14.1±4.4 years and had undergone surgical correction for TOF at an average age of 4.9±years. The researchers conducted a comparative analysis between the subjects and a control group, demonstrating that there exists a positive correlation between the degree of PR following repair and the reduction in S wave as measured by tissue Doppler. Additionally, there was a positive correlation observed between the increase in RVEDD and MPI, which suggests the presence of RV dysfunction<sup>[22]</sup>.

Contrary to the findings of our investigation, Abd El Rahman *et al.*<sup>[23]</sup> reached the conclusion that there was no correlation between the duration of the repair or the duration of the follow-up period and MPI. It has been shown that the use of a non-compliant RV may lead to a reduction in the duration of the RV isovolumetric relaxation period, thereby leading in a MPI. The potential outcome of this intervention is a decline in the index's ability to accurately identify individuals who have developed RV dysfunction subsequent to corrective surgery for TOF. It was shown that only 14.5% of the total sample size of fifty-one patients had severe PR, with this manifestation often occurring about 17±11 years subsequent to the first repair procedure.

Similarly with our findings, Mercer-Rosa *et al.* (2015) conducted an assessment of right ventricular function in individuals who had undergone surgical repair for TOF, with an average time passed since the procedure of 11.5 years (range: 9.1-14.5 years). The researchers reached the conclusion that the quantitative assessment of RV function using ECG revealed a moderate inverse relationship between RVEF and RV MPI. The RV MP) was found to be significantly greater in individuals with impaired RV systolic function compared to those with normal function. There was no significant link seen between the systolic annular velocity of the tricuspid valve (S') and the RVEF ( $r=0.006$ ;  $P=0.94$ ).

Over a period of ten years, wilder *et al.*<sup>[25]</sup> observed a comparable higher frequency of catheter-based re-interventions in the group of patients who received stents in the RVOT compared to those who had neonatal repair. Also, in research conducted by Uebing *et al.*<sup>[26]</sup>, the authors examined the relationship between the degree of and RVED and PR dimensions in a cohort of sixty seven individuals diagnosed with TOF. The purpose of the study was to evaluate the correlation at an average follow-up period of 4.8 years after the surgical procedure. The degree of PR after TOF repair is associated with the size of the pulmonary

annulus after surgery, and contrary to our observations, it is strongly linked with RV enlargement. A possible explanation for the variation from our results might be attributed to the very short duration of the follow-up period in their investigation. Shehata *et al.*<sup>[11]</sup> was in agreement with our research, their research was carried on thirty individuals underwent surgical repair of TOF. They were followed up 5±2 years after the repair. This research included MRI, 2D ECG and tissue doppler in some cases. The researchers demonstrated that the RV function was compromised in the individuals under investigation, as shown by the presence of extended MPI, reduced S wave velocity, and diminished TAPSE value.

Limitations: The size of sample was relatively small. The research was in a single centre. The research study did not include a comparison with a control group consisting of individuals who were in good condition.

### Conclusions

Following the surgical repair of individuals diagnosed with TOF for a duration exceeding ten years, there is a notable decline in right RV function. This decline may be evaluated by the use of ECG.

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**Conflict of Interest:** Nil

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