EARLY AND LATE OUTCOMES IN REPAIRED TETRALLOGY OF FALLOT

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ABSTRACT

Background

Background: Tetralogy of Fallot is the most common cyanotic congenital heart disease which needs surgical repair usually during 1st year of life. Numerous early and late complications arise postoperatively such as right ventricular failure, arrhythmias, pulmonary valve and branch stenosis and regurgitation and VSD patch residual leak and dehiscence. The 2D, wave and color Doppler-echocardiography reveal an important tool not only in the diagnosis of children with such disease and its complications, but also in their follow up post operatively in whom further therapy can be provided

Objective

This study aims to detect an early (within the 1st year) and late (after the 1st year) post surgical repair complications using 2D echo, wave and color Doppler-echocardiography and ventricular performance index. Correlate between type of operation performed and the type, time and severity of the complications that might appear. Find out the percentage, type, onset of post-surgical repair complications.

Patients and Methods

Children and adolescent of either sex suffered with TOF operated upon, or waiting for operation had been subjected to medical history, clinical examination, oxygen saturation, ECG, chest x-ray and Doppler-echocardiography. However, these tests had been done in Sulaimani Pediatric Teaching Hospital/ Pediatric Cardiology Department.

Results

This study shows that there is a significant increase in SpO^2 after operation (P-value= 0.0001), RBBB show high incidence in group 2 (P-value = 0.0001), Pulmonary valve regurgitation shows high incidence in group 2 (P-value of (0.0001)), tricuspid regurgitation was also significant (P-value = 0.029), EF shows significant correlation with BSA (P-value = 0.0001) and Z-score of -2.62. MPI of the right ventricle of the two groups show the RVESD show significant finding (P-value = 0.042).

Conclusion

Patients with TOF operated upon are suspected to have several complications that need to be evaluated serially to illustrate their progression and if they need further intervention. The echocardiography is a non invasive, bedside, available and relatively cheap investigation of benefit in assessing these patients and their follow up.

Keywords: *Echocardiography, Tetralogy of Fallot, MPI.*

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INTRODUCTION

Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart disease, affects both sexes equally, and accounts for 10% of congenital heart diseases (CHD) [1]

This anomaly is characterized by: right ventricular outflow obstruction, ventricular septal defect, right ventricular hypertrophy, and dextroposition of the aorta. Etienne-Louis Fallot, a French physician, first described that the condition could be diagnosed in patients and it is now known as the Tetralogy of Fallot.

From a physiological point of view TOF requires the first two anomalies:

A malaligned VSD large enough to equalize systolic pressures in both ventricles (as large as the aortic valve).

A stenosis of the right ventricular outflow tract (RVOT) in the form of infundibular stenosis, valvular stenosis, or both [2].

The clinical features of the disease includes the following: cyanosis which depends on the degree of the right ventricular outflow tract obstruction (RVOTO), and may not be present at first leading to what is sometimes termed as: (pink TOF). The cyanosis will typically increase with age and exercise and sometimes may be associated with: hypoxic spells (or Tet spells), which is an emergency condition and requires rapid intervention to prevent death [3, 4], failure to thrive, digital clubbing, and erythrocytosis are seen frequently. Stroke may occur and the risk is increased with iron deficiency anemia, but is rare. The actual cause of cyanosis is decreased pulmonary blood flow (PBF). The PBF is kept balanced by keeping the systemic vascular resistance high thus more blood will be pushed through the RVOTO. If there is a reduction in the systemic resistance (as in crying, exercise, dehydration etc.), the PBF will drop leading to profound cyanosis and hypoxic spells [5]. Thus surgical repair is mandatory to decrease morbidity and mortality [6].

The survival rate of patients who have TOF and have had operative repair is increased when compared to the unrepaired population. However those whose operative repair resulting in a residual lesion of pulmonary insufficiency were found to have changes in RV function and size. These changes led to increase the interest to the right ventricular function and suggesting protocols to handle the problems that these patients may suffer from; therefore many investigations are available now to evaluate the right ventricular function including MRI, CT, 3 D- echo, and even percutanous catheterization. Each of these aforementioned techniques has its advantages and disadvantages but all cannot be frequently used either because of their cost or because of their side effects; therefore 2-D echo has emerged as the first line imaging modality for assessment of RV function [7].

The Doppler derived myocardial performance index (MPI, also known as TEI- Doppler index), a fairly new index of combined systolic and diastolic function, is defined as the sum of isovolumic contraction time and isovolumic relaxation time divided by the ejection time [8]. It could be used to measure the function of both ventricles. This type of index will demonstrate the diastolic dysfunction of the ventricle in concern and in case of RV it will be of great value since estimation of EF will reflect systolic function only; and it is difficult to get an accurate measurements because of the difficulty in determining the volume of the RV because its anatomical shape. The evaluation of diastolic ventricular function requires analysis of the flow signals across the AV valve and within the proximal central venous system (either pulmonary veins for the LV or systemic veins for the RV). For all signals the Doppler beam must be aligned as closed to parallel as possible with the interrogated flow [9].

PATIENTS AND METHODS

This study involves two groups of TOF patients referred from operating centers or pediatricians for cardiological assessment in the echocardiographic unit/Sulaimani Pediatric Teaching Hospital. The (Group 1) consists of 40 patients who have TOF and are status post complete repair; 20 males, and 20 females with a mean age of (6.99 ± 3.6) years. The other group (Group 2) consists of 20 patients with TOF waiting for operation; 9 males and 11 females with a mean age of (4.12 ± 2.47).

All patients were subjected to: medical history, clinical examination, Demographic measures (weight in (kg) and height in (cm)) to calculate the body surface area (BSA) by the Mosetellar equation.

Pulse oximetry to assess arterial oxygen saturation, ECG to estimate rhythm, regularity, rate, intervals (PR, QRS, and cQT by the equation cQT= QT/$\sqrt{R-}$), axis, ventricular hypertrophy, and conduction abnormalities; chest X-ray, and echocardiography using Two dimensional, and Doppler (spectral and color) by echocardiography machine with 3V2C and 7V3C MHz transducers (adjusted according to examinations were obtained for each patient chest wall thickness) using a commercial Accuson Cypress , USA made, supplied by Siemens Company. The echo measurements were recorded according to the standards recommended by the American Society of Echocardiography [(10)].

In addition to the standard measures, we measured the RVESD, RVEDD via the 2-D in the apical 4-chamber view by measuring the maximum transverse diameter of the RV between the upper 1/3 and the lower 2/3 [(11)]. RVOT pressure gradient was measured by spectral Doppler technique. Color Doppler application was used to detect; VSD residual shunt, PR jet, TR jet, and AR and if any valvular regurgitation presented its severity was measured by spectral Doppler. Since the right ventricular ejection fraction (EF) could not be accurately measured directly as the left ventricle EF due to the position of the RV, its complex anatomy and the heavy trabeculations makes the direct estimation of the volume of the inner side of RV inaccurate, so we used indirect method to estimate the RV EF that's by accounting the fractional shortening of the RV by the equation: *FS= ((EDD_ESD)/EDD)*100 [(18)] EF≈ FS*1.7*

Z-score of EF, RVEDD and RVESD were calculated from the measures we obtained by echocardiography and BSA by using the above measures in a special software programmed calculation (special hospital type Z-score software).

MPI was performed by recording the tricuspid inflow waves from the apical 4-chamber view with the pulse wave Doppler sample volume positioned at the tip of the tricuspid leaflets at the diastole. The RV ejection time was measured from parasternal short axis scan plane with a pulse wave Doppler signal placed at pulmonary valve annulus in RV outflow tract.

Calculation of isovolumic contraction time (ICT) demonstrated in figure 2, isovolumic relaxation time (IRT) intervals and RVMPI are demonstrated in figure 3. To account for slight variations in R-R cycle length, each time intervals was measured on three consecutive beats and then averaged.

MPI is calculated by using the equation:
MPI= (ICT+IRT)/ET
Thus MPI= a-b/b. [7] , normal MPI for RV is 0.32± 0.03

Statistics

Data were processed and analyzed by using the SPSS statistic program version 11 for windows, (SPSS Inc., Chicago, Illinois).

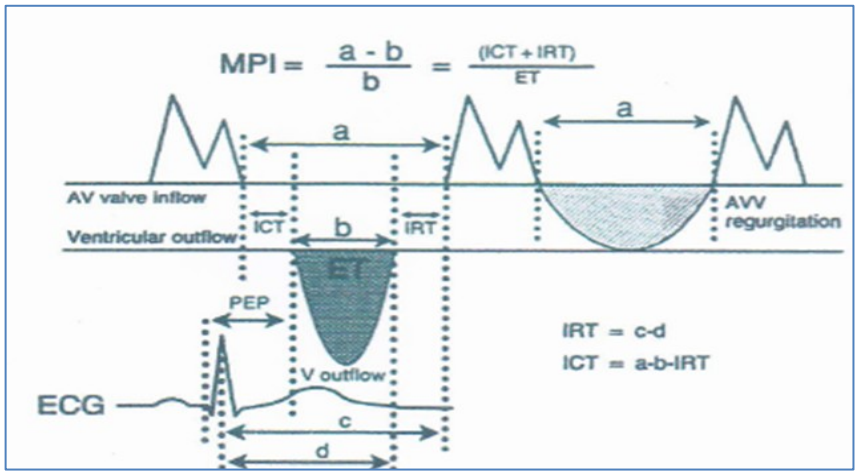

Figure 1. The calculation of the MPI (Eidem, Cetta, and O'Leary; 2010)[(9)].

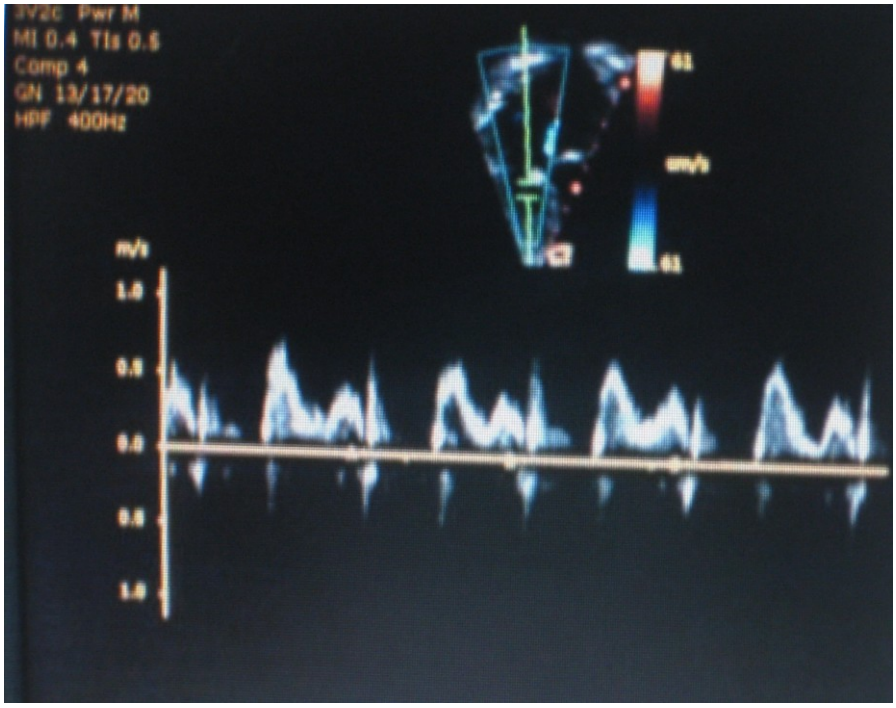

Figure 2. Pulsed wave Doppler applications in the apical four-chamber view at the level of tricuspid valve leaflets. The duration of ICT+ IRT is measured from the cessation of tricuspid valve inflow to the onset of the tricuspid valve inflow (from the end of the A wave to the beginning of the E wave). This represents the (a) variable in the equation.

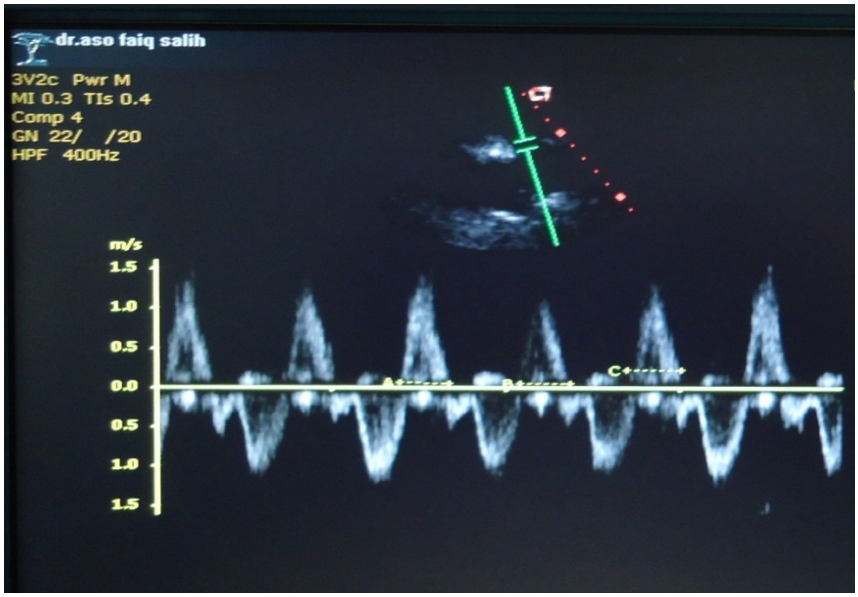

Figure 3. The measurements of the RV isovolumic relaxation time by using the pulse wave Doppler at the tip of the pulmonary valve.

RESULTS

Regarding the ECG findings demonstrated in table 1 and 2; table 1 demonstrate some ECG finding between Group 1 and 2 of patients by Chi square test. The rhythm and regularity shows no statically significant changes (P= 0.476, 0.156 respectively). The axis also shows no significant change still right axis deviation in both group with (p=0.381), the right ventricular hypertrophy percentage is decreased (95% to 72.5%) but its reduction has no statistical significance (p=0.12) but only the conduction defect is highly significant (p=0.0000).

Table 2 shows comparison between the two groups in regards the types of conduction defects which illustrated that there was a significant prolongation in PR and QRS intervals, with *p*-value of (0.0111, 0.0000) respectively, RBBB show highly increased rates in Group 1of a (*p*-value 0.000).

Echocardiography finding demonstrated in table 3, showed incidence of pulmonary regurgitation and to less extend tricuspid regurgitation; with p-value of (0.000, 0.029) respectively in which means that both kinds of regurgitation with incidence post operatively especially PR which had bad consequence on RV function especially if its moderate to severe.

Table 4 shows echocardiographic finding of repaired heart as residual RVOTO, which occurred in 40% of patients with varying degree of severity in which there is 60% no residual RVOT gradient which means the majority had good results. VSD patch residual shunt occurring in 22.5% of patient also of varying degree of sizes and severity in which in majority there is restrictive residual VSD shunt which is thermodynamically non significant.

Regarding RV function; this study showed that the ejection fraction of the RV is less than predictable for BSA with p-value of 0.000, the MPI proved this result although the systolic function of the RV was fair enough to increase the arterial oxygen saturation to significant levels in comparison with the Group 2 with a *p*-value of 0.000.as shown in table 5.

Table 1. Some of ECG comparison between the two groups using chi square test. Values were expressed as numbers and percentages, p-values less than 0.05 were considered as statistically significant.

parameters		Group 2 (n=20)		Group 1 (n=40)		P value
		Frequency	%	Frequency	%	
Rhythm	**Sinus**	20	100.0	39	97.5	0.476
	Pacemaker	0	0.0	1	2.5	
Regularity	**Regular**	16	80.0	37	92.5	0.156
	Irregular	4	20.0	3	7.5	
Axis	**Normal**	2	10.0	3	7.5	0.381
	Right	18	90.0	36	90.0	
	Left	0	0.0	1	2.5	
Ventricular hypertrophy	**No**	1	5.0	10	25.0	0.12
	Right	19	95.0	29	72.5	
	Left	0	0.0	1	2.5	
Conductive defects	**No**	16	80.0	5	12.5	0.0001
	RBBB	4	20.0	34	85.0	
	CBBB	0	0.0	1	2.5	

Table 2. Some ECG findings comparison between the two groups using T test. Values were expressed as mean ± SD, P-values less than 0.05 were considered as statistically significant.

Parameters	GROUP 2 (n=20)	GROUP 1 (n=40)	P value
Rate (beats/min)	115.3±27.76	97.05±21.68	0.0151
PR interval (sec)	0.14±0.02	0.16±0.03	0.0111
QRS (sec)	0.1±0.03	0.14±0.03	0.0001
CQT (sec)	0.42±0.04	0.45±0.05	0.0846

Table 3. Comparison of some echocardiography findings between the two groups using chi square. Values were expressed as numbers and percentages, values less than 0.05 were considered as statistically significant, TR=tricuspid regurgitation, PR= pulmonary regurgitation.

Parameters		Preoperative (n=20)		Postoperative(n=40)		P value
		Frequency	%	Frequency	%	
TR	**No**	20	100.0	26	65.0	0.029
	Mild	0	0.0	10	25.0	
	Moderate	0	0.0	3	7.5	
	Severe	0	0.0	1	2.5	
PR	**No**	20	100.0	13	32.5	0.0001
	Mild	0	0.0	20	50.0	
	Moderate	0	0.0	7	17.5	

Table 4. Some postoperative echocardiographic finding. Values were expressed as numbers and percentages, RVOTO (right ventricular outflow tract obstruction), VSD (ventricular septal defect). (The gradients were used to determine the PS or shunt was mild or non restrictive if its 20-40mmhg, moderate if its 40-60mHg or severe or restrictive if it's more than 60mmHg).

Parameters		Group 1 (n=40)	
		Frequency	%
RVOTO (PS)	**No**	24	60.0
	Mild	13	32.5
	Moderate	3	7.5
Residual VSD Patch Shunt	**No shunt**	31	77.5
	Restrictive	6	15.0
	Non restrictive	3	7.5

Table 5. The RV function in correlations and p-value. RV=right ventricle, MPI= myocardial performance index, RVESD= right ventricular end systolic diameter, EF= ejection fraction, BSA= body surface area. p- value less than 0.05 were considered significant.

Parameters	r value	p value
RV MPI & RVESD z-score	-0.323	0.042
EF & BSA	0.999	0.000
RV MPI and EF Z score	0.893	0.000

DISCUSSION

The physiological importance of the right ventricle (RV) has been underestimated; the RV was considered mainly as a conduit whereas its contractile performance was thought to be haemodynamically unimportant. Now the contractile function of the RV is well established to maintain adequate pulmonary perfusion under varying circulatory and loading conditions and to prevent tissue and organ congestion by maintaining a low systemic venous pressure but when the RV dilated so the systemic venous pressure will rise.

At the last two decades special concern was paid to the evaluation of the function of the right heart due to increased life spectrum of children born with congenital heart diseases after the possibility of surgical repair. Hence, there was a more considerable insight into the right ventricular function and pulmonary system since they consequently will affect the global cardiac function and eventually the patient's life.

Patients with Tetralogy of Fallot, who should be treated surgically during the first year of life, need serial follow up to evaluate the postoperative complications, such as right ventricular dysfunction, arrhythmias, pulmonary valve and branch stenosis and/ or regurgitation, VSD patch residual leak and dehiscence, and tricuspid regurgitation [(12)].

Since cardiac arrest and serious ventricular arrhythmias were the most common causes of death in adults with surgically repaired TOF, [(13-15)] special concern was made to ECG changes in this study. Results were expressed in table 1 showing that the rhythm and regularity were not affected so does the axis which remains with right deviation that's because of RVH in Group 2 patients and the RBBB in Group 1 patients. The RVH shows a reduction (95-72.5) but still of no statistical significance, the RVH in Group 1 mainly because of PR; while the RBBB show high incidence (p value of 0.0001) that's because of the iatrogenic injury to the RB during surgery even with the modern transannular approach. Also part of ECG finding show significant reduction in rate postoperatively that's because of increased pulmonary blood flow will improve oxygen saturation thus reducing hypoxia in addition the postoperative patient group are older than the preoperative group (heart rate decreases with age which is the physiological phenomenon) as shown in table 2.

The PR interval shows significant prolongation in postoperative group (Group 1) due to right side enlargement and dysfunction which will occur postoperatively. QRS complex is also significantly prolonged that's because of RBBB occurring in 85% due to iatrogenic injury to the Purkinje fibers of the right ventricle during surgery.

Prolongation of the PR interval and RV dysfunction which results also from the pulmonary regurgitation in 67.5% and stenosis in 40%, these results were similar to the study done by Scherptong, *et al.*; 2010 [(15)], and Waien, *et al.*; 1992 [(12)] respectively. While cQT (is a sum of depolarization and repolarization of the ventricle) is not affected because it reflects the AV node conduction (which lies at the atrial wall) downward to the AV bundle [(16)].

Regarding valvular function and integrity this study shows that there's a high incidence of pulmonary regurgitation 67.5% of all surgical patients. Patients who underwent a transannular approach their percentage increases up to 85%. Tricuspid regurgitation was also significantly

increased (35%) and a p value of 0.029 also due to surgery.

In this study Residual RVOTO was 40% of varying degree of severity, the residual VSD patch shunt in 22.55% with varying degree of severity; these values depend on surgical skilling and patient's original condition.

The accurate assessment of RV size and function is important because indications for pulmonary valve replacement following TOF repair include the development of RV dysfunction or progressive RV dilation [17-19]. However unlike the left ventricle there are many inherent limitations in the ability to assess the RV size and function with a two-dimensional echocardiography these are: the complex shape of the RV (crescent in short axis view), the heavy trabeculation of its endocardium, the three parts of the RV (the inlet, the body and the outlet (infundibulum) are typically not imaged together in any of the echocardiographic views and the proximity of the RV to the anterior chest wall, makes inherent limitation in image resolution due to near-field effects. This limited resolution particularly affects evaluation of the anterior wall of the RV [11]. These entire factors make the classical evaluation of LV function is inapplicable to estimate the RV function. Thus multiple parameters have been suggested to quantify the systolic function of the RV. In this study we used EF and MPI (myocardial performance index) to estimate the RV function.

The EF estimated by measuring the fractional shortening which describes the systolic function in absence of abnormal ventricular wall contraction. As we mentioned above, the measurement fractional area shortening by planimetry of the area of the right ventricle, is unreliable thus in this study the RV diameter was measured at the end systole and at the end diastole (RVESD, RVEDD respectively), these measures show statistical importance in which they are used to estimate shortening fraction and eventually EF which showed here that the systolic function is less than the predictable for BSA; with statistically significance value (p= 0.000) as expressed in Table 5.

The reduction in RVEF (RV systolic dysfunction) recorded in this study was similar to the study done by Davlouros, *et al.*:2002.[2]

Thus in this study the myocardial performance index (MPI) which describes both systolic and diastolic ventricular function was more reliable to assess the RV function. The results of MPI in postoperative group in correlation with RVESDZ-score was significantly correlated (*P*= 0.042) The correlation between RVESD Z-score and RVEDD Z-score was statistically significanct (*P* = 0.000), that's because the RV remodeling after surgery and the presence of residual PS will result in impaired systolic RV function more than the diastolic impairment. These results were similar to the results done by Davlouros, *et al.*:2002 [2].

CONCLUSION:

The results of this study provide evidences that:

Post operative improved SPo2 due to increase PBF and improved symptoms. Conduction defect with PR, QRS prolongation presented in high percentage of postoperative patients due to RBBB which is inevitable because of the surgery. Valvular function is affected in pulmonary and tricuspid valves also due to surgical procedure. RV function assessment showed decreased systolic function of the RV this assessed by EF and MPI but MPI does measure systolic and diastolic function. Thus serial regular echocardiography examination is essential for these patients to assess valve function and its effect on ventricular function by using MPI to determine the need for further evaluation by other ways for evaluating RV such as MRI.

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