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## RESEARCH ARTICLE

# CORRELATION OF SEVERITY OF PULMONARY REGURGITATION WITH RIGHT VENTRICULAR DIASTOLIC FUNCTION IN EARLY POST OPERATIVE PERIOD IN PATIENTS OF TATRALOGY OF FALLOT AFTER TOTAL CORRECTION

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**ABSTRACT**

**Objective:** To assess the occurrence of pulmonary regurgitation and right ventricular diastolic dysfunction in Tetralogy of Fallot after total correction and to correlate its severity with right ventricular diastolic dysfunction in early post operative period after total correction in TOF patients. **Methods:** We prospectively studied 38 TOF patients who has undergone total correction. Standard 2-Dimentional & doppler Trans thoracic echocardiographic assessment was done at seventh day , three month and six month after total correction . Pulmonary regurgitation severity, right ventricular diastolic dysfunction, right ventricular myocardial performance index, and tricuspid annular plane systolic excursion were assessed. **Results:** Most of the patients (50%) were < 5 year of age. 23 (60.5%) had none or mild pulmonary regurgitation while 15(39.5%) had moderate or severe pulmonary regurgitation. At 6 month follow up 86.8% patients had right ventricular diastolic dysfunction. Grade I, II and III right ventricular diastolic dysfunction was found in 31.6%, 31.6% and 23.7% respectively. Mean TAPSE and right ventricular myocardial performance index values at 6 month were 10.9±2.4mm and 39.07±7.8 respectively. The mean RVMPI was normal in none/mild pulmonary regurgitation severity group while it was abnormally high in mod/severe pulmonary regurgitation severity group. Spearman's rank order correlation coefficient value for pulmonary regurgitation severity group and RV diastolic dysfunction grade was 0.438, 0.50, and 0.447 on 7thday, three month and six month follow up respectively. **Conclusion:** PR severity had moderate positive correlation with right ventricular diastolic dysfunction in early post operative period after total correction in TOF patients.

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## INTRODUCTION

Tetralogy of Fallot is the commonest form of cyanotic congenital heart disease. It occurs in about four per 10,000 live births and accounts for up to one-tenth of all congenital cardiac lesions (Oswal *et al*., 2014). Surgical repair of Tetralogy of Fallot (TOF) has been successfully performed since 1955. Repair includes closure of the ventricular septal defect, and relief of right ventricular (RV) outflow tract obstruction that involves RV outflow tract infundibular muscle resection, pulmonary valvotomy or valvectomy, and commonly RV outflow augmentation with placement of a subvalvular or transannular patch.

The long-term outcome after surgical repair of TOF is excellent with survival rate of 86% at 30 years (Murphy *et al*., 1993; Foster, 1998) Chronic pulmonary valve regurgitation (PR) is the most common cardiovascular sequelae requiring reoperation in patients with repaired TOF (Oechslin *et al*., 1999). It has deleterious long-term effects on RV size and function, and has a recognized impact on late outcome. Chronic pulmonary insufficiency, ultimately leads to RV failure (Bouzas, 2005; Redington, 2006) Therefore, assessment of RV function is very important in the longitudinal follow-up of this patient population. Echocardiographic parameters like myocardial performance index or Tissue Doppler Imaging

(TDI) have obtained good correlations for right ventricular functions (Kaul, 1984; Schwerzmann *et al*., 2007) RV diastolic dysfunction is clinically useful because it serves as an early and more easily quantifiable marker of subclinical RV dysfunction. Multiple studies have shown that RV diastolic dysfunction is usually present before apparent systolic dysfunction and before RV dilatation. (Apitz, 2009; Redington, 2006). In this prospective study we tried to correlate the RV diastolic function by echocardiography with the severity of pulmonary regurgitation in early postoperative period after total correction in patient with Tetralogy of Fallot.

## MATERIALS AND METHODS

This was a prospective observational study conducted at PGIMER and Dr. Ram Manohar Lohia Hospital, New Delhi, a tertiary care hospital in India. Informed written consent was taken from all participants. Study protocol was approved by institutional review board and ethics committee. Post operative cases of classic Tetralogy of Fallot (TOF) who underwent total correction from september 2015 to march 2017 were included in this study. Patients who had other variants of the TOF (i.e. pulmonary atresia with ventricular septal defect (VSD), absent pulmonary valve, and double-outlet right ventricle ) were excluded. Each patient had undergone standard 2-Dimentional & doppler Trans thoracic echocardiography. Two dimensioal echocardiography was done using Philips Model Sonos 5500 machine and chamber dimensions, systolic and diastolic function, global/Regional wall motion abnormality and any valvular dysfunction were looked for. Severity of PR was assessed by colour and continuous Doppler studies in the parasternal short-axis view. The severity of pulmonary regurgitation was graded qualitatively according to the guidelines of the American Society of Echocardiography (Rudski *et al*., 2010). (Grade 0 - no regurgitation, grade 1 - mild, grade 2 - moderate, and grade 3 – severe.) Patients were divided into two groups – those having moderate or severe pulmonary regurgitation and those without regurgitation or mild regurgitation. Right ventricular diastolic function was assessed by right ventricular myocardial performance index and Tissue Doppler imaging(TDI) Doppler velocities of the transtricuspid flow (E, A, and E/A), tissue doppler velocities of the tricuspid annulus (E0, A0, E0/A0), deceleration time and Grading of RV diastolic dysfunction was done according to American society of echocardiography guidelines (Rudski *et al*., 2010). Right ventricular myocardial performance index was measured using continuous pulse wave Doppler of the pulmonary and tricuspid valves. Tricuspid annular plane systolic excursion (TAPSE) was measured by M-mode in the apical four-chamber view (Tei *et al*., 1996). After basal characterization, all patients received conventional treatment according to existing departmental protocol. Post hospital stay, study patients were called to attend cardiology outpatient department after discharge for post operative evaluation at one week, 3 month and at 6 months.

**Statistical analysis:** Statistical analysis was performed with the use of SPSS version 24. Data were expressed as mean ±SD. The Chi-square test was used to analyse categorical variables. Student's *t* test was used for continuous variables. The spearman's rank order correlation coefficient was used to find a correlation between diastolic dysfunction grading and pulmonary regurgitation severity. A probability value of $p<0.05$ was considered significant.

## RESULTS

**Study patients:** This study included 41 north Indian patients who were taken for total correction. 3 patients died within 6 months of surgery so they were excluded from this study. Mean age of the patients was 7.7 ± 7.20 years. 24 patients (63.2 %) were males and 14 patients (36.8%) were females. Out of 38 patients, 23 (60.5%) patients had none or mild pulmonary regurgitation while 15(39.5%) patients had mod or severe pulmonary regurgitation (Table 1). After total correction only 9(23.7%) patients had normal right ventricular diastolic function at 7$^{th}$ post operative day.10 (26.3%) patients had grade 1 ,14 (36.8%) patients had grade 2 ,and 5 (13.2%) patients had grade 3 right ventricular diastolic dysfunction **.** At 6 month follow-up normal right ventricular diastolic function was seen in 5 (13.2%) patients .12(31.6%) patients had grade 1, 12 (31.6%) patients had grade 2,and 9(23.7%) patients had grade 3 right ventricular diastolic dysfunction on 2D echocardiography (Table 1).

At 7$^{th}$ day after total correction mean right ventricular MPI was 38.9±4.4. At 3 month follow-up mean right ventricular MPI was 38.65±4.4. After 6 month of surgery the mean right ventricular MPI value was 39.07±7.8. (Table 1) After surgery mean TAPSE at 7$^{th}$ post operative day was 10.3±2.1 mm. Mean TAPSE value on 3 month and 6 month were 11.2±2.1 mm and 10.9±2.4 mm respectively. (Table 1) Mean TAPSE value at 7$^{th}$ post operative day was 10.89±1.95 mm in none-mild pulmonary regurgitation severity group vs. 9.40±2.11mm in mod-severe pulmonary regurgitation severity group. At 3 month and 6 month follow up mean TAPSE in none –mild Pulmonary regurgitation severity group were 11.91±1.97 mm and 11.87±2.48 mm vs. 10.133±2.03 mm and 9.700±1.7 mm in mod-severe pulmonary regurgitation severity group respectively. The difference in TAPSE between two groups was statistically significant in all follow-up visits. (P value<0.05) (Table 2). Mean RV MPI value at 7$^{th}$ post operative day was 37.91±4.5 in none-mild pulmonary regurgitation severity group vs. 40.5±3.9 in mod-severe pulmonary regurgitation severity group. At 3 month and 6 month follow-up mean RV MPI in none – mild pulmonary regurgitation severity group were 37.30±4.2 and 38.13±3.7 vs. 40.7±3.9 and 40.530±3.2 in mod-severe pulmonary regurgitation severity group respectively. The difference in right ventricular myocardial performance index between two groups was statistically significant at 3 month and six month follow-up visits. (P value <0.05) (Table 3). Correlation analysis of pulmonary regurgitation at 7$^{th}$ day of total correction was done with right ventricular diastolic dysfunction grade at 7$^{th}$ day, three month and six month visit. Spearman's rank order correlation coefficient value was 0.438, 0.50, and 0.447 at 7$^{th}$ day, three month and six month respectively. (Table 4)

## DISCUSSION

In this study 38 patients of Tetralogy of Fallot who underwent total correction were studied. Of 38 patients studied 63.2% were male and 36.8% were female. Mean age of the patients was 7.7 ± 7.2 years. Most of the patients (50%) were < 5 year of age. 23 (60.5%) patients had none or mild pulmonary regurgitation while 15(39.5%) patients had mod or severe pulmonary regurgitation. Most of the patients (76.3%) had right ventricular diastolic dysfunction after total correction.

**Table 1. Echocardiographic parameters at follow-up visits**

| Parameters | | Follow up Echocardiography | | |
|---|---|---|---|---|
| | | 7th day | 3 month | 6Month |
| | | No.of pts (percentage) | No.of pts (percentage) | No.of pts (percentage) |
| PR SEVERITY | None/Mild | 23(60.5%) | 23(60.5%) | 23(60.5%) |
| | Mod/severe | 15(39.5%) | 15(39.5%) | 15(39.5%) |
| Diastolic | Grade 0 | 9(23.7%) | 6(15.8%) | 5(13.2%) |
| dysfunction grade | Grade 1 | 10(26.3%) | 12(31.6%) | 12(31.6%) |
| | Grade 2 | 14(36.8%) | 12(31.6%) | 12(31.6%) |
| | Grade 3 | 5(13.2%) | 8(21.1.%) | 9(23.7%) |
| MYOCARDIAL PERFORMANCE INDEX mean±sd | | 38.9±4.4 | 38.65±4.4 | 39.07±7.8 |
| TAPSE mean±sd(mm) | | 10.3±2.1 | 11.2±2.1 | 10.9±2.4 |

**Table 2. Association between pulmonary regurgitation severity and TAPSE**

| | Tricuspid annular plane systolic excursion value | | | | | |
|---|---|---|---|---|---|---|
| PR severity | 7 day | | 3 month | | 6month | |
| | Mean± SD (mm) | P value | Mean± SD (mm) | P value | Mean± SD(mm) | P value |
| None/mild | 10.89±1.95 | 0.033 | 11.91±1.97 | .011 | 11.87±2.48 | 0.006 |
| Mod/severe | 9.40±2.11 | | 10.13±2.03 | | 9.700±1.7 | |

**Table 3. Association between pulmonary regurgitation severity and right ventricular myocardial performance index**

| | Rvmpi Value | | | | | |
|---|---|---|---|---|---|---|
| PR severity | 7 day | | 3 month | | 6month | |
| | Mean | P value | Mean | P value | Mean | P value |
| None/mild | 37.91±4.5 | 0.078 | 37.30±4.2 | .018 | 38.13±3.7 | 0.04 |
| Mod-severe | 40.5±3.9 | | 40.7±3.9 | | 40.530±3.2 | |

**Table 4. Correlation between pulmonary regurgitation severity with diastolic dysfunction**

| Time | Spearman correlation coefficient | Significance Level |
|---|---|---|
| 7 DAY | 0.438 | 0.006 |
| 3 MONTH | 0.50 | 0.001 |
| 6 MONTH | 0.447 | 0.005 |

At 6 month follow up 86.8% patients had right ventricular diastolic dysfunction. Grade I right ventricular diastolic dysfunction was found in 31.6% grade II in 31.6% and 23.7% had grade III right ventricular diastolic dysfunction. Most of the patients had lower mean TAPSE after surgery. Mean TAPSE at 7th post operative day and 6 month were 10.3±2.1 mm 10.9±2.4mm respectively. These lower mean values are suggestive of right ventricular systolic dysfunction after total correction. Patients with moderate/severe pulmonary regurgitation had lower TAPSE compared with patients with none/mild pulmonary regurgitation. Mean TAPSE value in moderate/severe pulmonary regurgitation group was 9.40±2.11mm and 9.700±1.7 on 7th post operative day and 6 month follow up respectively .Mean TAPSE was 10.89±1.95 mm and 11.87±2.48 mm in none/mild pulmonary regurgitation group on 7th post operative day and 6 month follow up respectively.

The difference in TAPSE value between the two groups was statistically significant. Mean Right ventricular myocardial performance index was normal in follow up period after surgical correction of Tetralogy of Fallot. On 7th day, three month and six month mean RVMPI were 38.9±4.4, 38.65±4.4, and 39.07±7.8 respectively. Patients with moderate/severe pulmonary regurgitation had higher right ventricular myocardial performance index compared with patients with none/mild pulmonary regurgitation. Mean RVMPI value in moderate/severe pulmonary regurgitation group was 40.5±3.9 and 40.530±3.2 on 7th post operative day and 6 month follow up period respectively.

Mean right ventricular myocardial performance index value was 37.91±4.5 and 38.13±3.7 in none/mild pulmonary regurgitation group on 7th post operative day and 6 month follow up period respectively. The mean RVMPI was normal in none/mild pulmonary regurgitation severity group while it was abnormally high in mod/severe pulmonary regurgitation severity group. The difference in RVMPI value between the two groups was statistically significant on three month and six month follow up period. A moderate correlation was found between pulmonary regurgitation severity and diastolic dysfunction grade in patients of TOF after total correction. Spearman's rank order correlation coefficient value was 0.438, 0.50, and 0.447 on 7th day; three month and six month follow up respectively. Previous studies also reported that pulmonary regurgitation (PR) is a common complication after surgical correction of Tetralogy of Fallot (Cheung *et al*., 2005) Similar finding was observed in our study also. We found that right ventricular diastolic dysfunction is common after surgical correction. Only a few studies have demonstrated right ventricular diastolic dysfunction after surgical correction of TOF. Munkhammar *et al*, studied right ventricular physiology in infancy. 47 patients with repaired TOF were evaluated by echocardiography. Restrictive RV physiology was noted in 13 patients (28%). Ten percent of patients repaired before 6 months of age demonstrated restrictive features at the time of follow-up, increasing to 38% with repair after 9 months (Munkhammar *et al*., 1998). Helbing *et al*, studied right ventricular diastolic function in TOF patients who had undergone surgical correction. Twelve healthy volunteers and 19 children with repair of Tetralogy of Fallot, all with residual

pulmonary regurgitation were studied. He demonstrated abnormalities in right ventricular diastolic function in young patients with residual pulmonary regurgitation after surgical correction of Tetralogy of Fallot. Impaired relaxation and restrictive right ventricular filling was found more commonly in patients group compared with control subjects (Helbing *et al*., 1996). There was no significant difference in pulmonary regurgitation severity between groups in this study. But in our study we found significant correlation of pulmonary regurgitation severity with diastolic dysfunction grading. D'Andrea *et al*. detected a correlation between myocardial performance assessed at rest via tissue Doppler (TD) and cardiac performance during physical effort in adult patients (21.4 ± 3.8 years). In their study, TD analysis showed lower Sa, Ea, Ea/Aa ratios in the corrected TOF patients compared to the normal group (D'Andrea *et al*., 2004). In contrast to our study, the corrected TOF patients of their study had no significant PR. Our study demonstrated combined systolic and diastolic dysfunction after surgical correction of Tetralogy of Fallot and pulmonary regurgitation severity moderately correlates with diastolic dysfunction grading severity. Since right ventricular function is strongly associated with clinical outcome, long term follow up of TOF patients after surgical correction is necessary.

**Conclusion**

This study concludes that pulmonary regurgitation is common after total correction of Tetralogy of Fallot. Right ventricular systolic and diastolic dysfunction is common after total total correction of Tetralogy of Fallot. Pulmonary regurgitation severity is correlated with right ventricular diastolic dysfunction. Larger studies with long term follow-ups are required in Tetralogy of Fallot patients after total correction and with significant pulmonary regurgitation to determine the exact role of serial assessment of right ventricular diastolic function predicting future cardiac events and intervention to reduce pulmonary regurgitation before significant right ventricular systolic dysfunction occurs.

**Limitations of study**

- Subjects were not compared with healthy control group.
- Limited numbers of patients were included and long term follow up was not done. Larger multi centre studies are required to further validate these results.

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**Conflict of Interest:** None

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