

# Relationship of Tissue Doppler-Derived Myocardial Velocities to Peak Systolic Right-to-Left Ventricular Pressure Ratio in Repaired Tetralogy of Fallot

Ujjwal Kumar Chowdhury<sup>1\*</sup>, Aandrei Jha<sup>1</sup>, Suruchi Hasija<sup>2</sup>, Lakshmi Kumari<sup>1</sup>, Mani Kalaivani<sup>3</sup>, Vishwas Malik<sup>2</sup>

<sup>1</sup>Department of Cardiothoracic and Vascular Surgery, AIIMS, New Delhi, India

<sup>2</sup>Department of Cardiac Anesthesia, AIIMS, New Delhi, India

<sup>3</sup>Department of Biostatistics, AIIMS, New Delhi, India

\*Corresponding author: Ujjwal K. Chowdhury, Department of Cardiothoracic and Vascular Surgery, All India Institute of Medical Sciences, New Delhi 110029, India. Tel: +911126594835; Fax: +911126588663; Email: [ujjwalchow@rediffmail.com](mailto:ujjwalchow@rediffmail.com); [ujjwalchow-dhury@gmail.com](mailto:ujjwalchow-dhury@gmail.com)

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## Abstract

**Background:** This study was designed to analyze the specific evolution of postoperative peak systolic right-to-left ventricular pressure ratio (Prv/Plv) and its relationship to Tissue Doppler Imaging (TDI) variables of the Right Ventricle (RV) in patients undergoing intracardiac repair of Tetralogy of Fallot (TOF).

**Method:** Two hundred and eight-five patients undergoing intracardiac repair of TOF between January 2010 and December 2016 underwent serial TDI studies. The intraoperative post repair pressure measurements showed a Prv/Plv ratio  $>0.7$  in 134 (47%) patients (group I) and  $<0.7$  in 151 (53%) patients (group II). Age was 18 months to 28 years (mean, group I:  $8.45 \pm 6.34$ ; group II:  $9.75 \pm 6.16$  years). Generalized estimating equation was used to test the evolution of Prv/Plv ratio and its relationship to TDI-derived variables.

**Results:** Despite the occurrence of an increased incidence of low cardiac output in patients with higher Prv/Plv, there was no difference in reoperation and actuarial survival (Hazard ratio:  $0.69 \pm \text{SD } 0.33$ ; 95% CI: 0.27-1.75;  $p=0.4$ ). Group I patients exhibited significant reduction of Prv/Plv late postoperatively. There was significant improvement of tricuspid annular plane systolic excursion, isovolumic acceleration, isovolumic contraction, peak myocardial velocity during systole and early diastolic basal wall lengthening of RV except late diastolic relaxation of right ventricular free wall ( $a'$ ).

**Conclusions:** An immediate postoperative Prv/Plv ratio  $>0.7$  in patients with stable hemodynamics without residual surgical lesions undergo significant postoperative reduction without any adverse effect on mortality. All TDI-derived variables except  $a'$  improve over time along with a significant reduction of Prv/Plv.

**Keywords:** Echocardiography; Tetralogy of Fallot; Tissue Doppler Imaging

## Abbreviations

$a'$	:	Diastolic Basal Wall Lengthening of Right Ventricle in Late Diastole
CCF	:	Congestive Cardiac Failure
CHB	:	Complete Heart Block
CI	:	Confidence Interval

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e'	:	Diastolic Basal Wall Lengthening of Right Ventricle in Early Diastole
IVA	:	Isovolumic Acceleration
IVC	:	Isovolumic Contraction
LCOS	:	Low Cardiac Output Syndrome
LV	:	Left Ventricle
MAPCAs	:	Major Aortopulmonary Collateral Arteries
Prv/Plv	:	Right-to-Left Ventricular Systolic Pressure Ratio
PR	:	Pulmonary Regurgitation
RV	:	Right Ventricle
RVOTO	:	Right Ventricular Outflow Tract Obstruction
s'	:	Peak Myocardial Velocity During Systole
TAP	:	Transannular Patch
TAPSE	:	Tricuspid Annular Plane Systolic Excursion
TDI	:	Tissue Doppler Imaging
TEE	:	Transesophageal Echocardiography
TOF	:	Tetralogy of Fallot
TTE	:	Transthoracic Echocardiography
VSD	:	Ventricular Septal Defect
VSD	:	Ventricular Septal Defect

## Introduction

The wide spectrum of Right Ventricular Outflow Tract Obstruction (RVOTO) and pulmonary artery anatomy encountered in TOF clearly necessitates an individualized surgical approach. The morphology of the pulmonary valve and the method of RVOT reconstruction are arguably the most important determinants of later pulmonary valve incompetence [1-4]. The ideal RVOT reconstruction involves finding the delicate balance, whereby the surgeon avoids both inadequate resection and excessive transannular patching. It remains a surgical challenge, however, to adequately relieve RVOT obstruction without inducing significant pulmonary regurgitation.

The postoperative course is usually straight forward in most patients after intracardiac repair of TOF. However, several investigators including ourselves have shown that some patients experience a prolonged troublesome postoperative recovery with low cardiac output in the absence of any residual surgical lesions [1-4]. The primary decision-making on the requirement of Transannular Patch (TAP) is indeed the size of the pulmonary valve ring. Postoperative Prv/Plv can guide the surgeons in borderline cases [1-4]. Despite having complete relief of RVOTO in the

absence of a residual correctable surgical lesion i.e. RVOTO or a Ventricular Septal Defect (VSD), a subset of patients with repaired TOF exhibits a higher postoperative Prv/Plv which may or may not improve over time and may or may not be responsible for early or late postoperative mortality and/or morbidity [1-7].

Based on the above observations, we hypothesized that a subset of patients undergoing intracardiac repair of TOF have abnormalities of RV function, hyperdynamic state of the myocardium in the immediate postoperative period and/or have an extreme deviation of the infundibular septum which may be responsible for higher postoperative Prv/Plv in the absence of residual RVOTO or other surgical lesions. It has been shown that Doppler tissue echocardiographic parameters like right ventricular systolic and early diastolic velocities are abnormal in 50% of patients with repaired TOF despite normal RV function on conventional echocardiograms [8-14].

To test this hypothesis, we conducted this study with the primary objective to identify the relationship between Tissue Doppler-Derived Myocardial Velocities (TDI) and postoperative Prv/Plv in patients with repaired TOF.

The secondary objectives were:

- identify the subset of patients requiring revision surgery;
- analyze the evolution of Prv/Plv in repaired TOF;
- elucidate the significance of elevated postoperative Prv/Plv ( $\geq 0.8$ ) with respect to adverse outcomes like Congestive Cardiac Failure (CCF), Low Cardiac Output Syndrome (LCOS), prolonged inotropic requirement, reoperation, sudden death and arrhythmias and compare the same with patients with Prv/Plv  $< 0.8$ .

## Methods

### Patients and Study Design

**Selection criteria:** To enhance homogeneity of the population, selection criteria included survivors of repaired TOF more than one year after surgery undergoing tissue Doppler imaging without i) residual intracardiac shunting and (ii) pulmonary stenosis (Doppler gradient  $\geq 30$  mmHg) and (iii) significant ventricular arrhythmias (Low grade  $> 2$ ). Exclusion criteria included patients with TOF and pulmonary atresia, double outlet right ventricle, complete atrioventricular septal defect, Complete Heart Block (CHB), and those dying in the preoperative perioperative and late postoperative period.

This study conforms to the principles outlined in the declaration of Helsinki and was approved by the Institutional Ethics Committee. Patients were enrolled in the study protocol after obtaining informed written consent from parents / guardians.

Between January 2010 and December 2016, two hundred and eighty-five consecutive patients underwent intracardiac repair of TOF by a single surgeon (corresponding author). Of these, 18 patients dying in the perioperative and late postoperative period and those requiring permanent pacemaker implantation ( $n=2$ ) were excluded from the study. Thus, two hundred and sixty-five survivors underwent serial tissue Doppler-derived myocardial velocity studies and peak systolic right-to-left ventricular pressure ratio (Prv/Plv) measurements and underwent data analysis. However, for group comparison and actuarial estimates of survival all patients ( $n=285$ ) were taken into consideration.

Age at operation of the entire study group was 18 months to 28 years with 28% ( $n=80$ ) patients being younger than 3 years of age. Their demographic and clinical profiles are depicted in table E1. Echo cardio graphically, 149 (52.3%) patients had aortic override  $\geq 50\%$  and 67 (23.5%) underwent coil embolization for significant MAPCA's. Cardiac catheterization and angiocardiology were performed in all patients to confirm the diagnosis, to define coronary artery anatomy, and to identify Major Aortopulmonary Collateral Arteries (MAPCAs). Ninety (31.6%) patients have severe pulmonary annular and main pulmonary artery hypoplasia. None had branch pulmonary artery hypoplasia. The examiners were blind to demographic, procedural and hemodynamic data. Based on postoperative Prv/Plv measurements the patients were allocated to two groups: Group I ( $n=134$ , Prv/Plv  $\geq 0.7$ ) and group II ( $n=151$ , Prv/Plv  $< 0.7$ ). There was no significant difference between age, sex distribution, hematocrit, history of previous palliation and the presence of significant MAPCAs between the two groups (Table E1).

Variables	Group I (n=134) No. (%)	Group II (n= 151) No. (%)	p value	OR (95%CI)
<b>Age at operation, no. (%)</b>				
- $\leq 3$ years,	38 (28.4)	42 (27.8)	0.92	1.03 (0.59, 1.78)
- $> 3$ years	96 (71.6)	109 (72.2)		
<b>Age at operation (years)</b>	8.45 $\pm$ 6.34	9.75 $\pm$ 6.16	0.92	1.03 (0.59, 1.78)
<b>mean<math>\pm</math>SD (range)</b>	(18 months-26 years)	(24 months-28 years)		
<b>Sex</b>				
- Male	101 (75.4)	111 (73.5)	0.72	1.10 (0.63, 1.95)
- Female	33 (24.6)	40 (26.5)		
<b>Preoperative oxygen saturation (%)</b>				
- $\leq 80\%$	83 (61.9)	110 (72.8)	0.05	0.61 (0.35, 1.03)
- $> 80\%$	51 (38.1)	41 (27.2)		

Hematocrit (%)				
- ≥45%	73 (54.5)	80 (52.9)	0.80	1.06 (0.65, 1.74)
- <45%	61 (45.5)	71 (47.1)		
Aortic override				
- ≥50%	104 (77.6)	45 (29.8)	<0.001	8.17 (4.62, 14.48)
- <50%	30 (22.4)	106 (70.2)		
Previous modified Blalock-Taussig shunt				
- Yes	6 (4.5)	13 (8.6)	0.163	0.49 (0.15, 1.46)
- No	128 (95.5)	138 (91.4)		
Major aortopulmonary collateral arteries				
- Present	38 (28.4)	29 (19.2)	0.069	1.67 (0.92, 3.01)
- Absent	96 (71.6)	122 (80.8)		
In-Hospital and late deaths				
- Hospital death	8 (5.9)	6 (3.9)	0.453	1.44 (0.49, 4.34)
- Late death	2 (1.5)	2 (1.3)		
- Alive	124 (92.5)	143 (94.7)		
Perioperative supraventricular and ventricular arrhythmias			<0.001	4.13 (2.09, 8.48)
- Yes	42 (31.3)	15 (9.9)		
- No	92 (68.7)	136 (90.1)		
Transannular patch				
- Yes	91 (67.9)	77 (50.9)	0.004	2.03 (2.09, 8.48)
- No	43 (32.1)	74 (49.1)		
Pulmonary regurgitation				
- Present	91 (67.9)	77 (51)	0.004	2.03 (2.09, 8.48)
- Absent	32 (32.1)	74 (49%)		
Low cardiac output (immediate postoperative)				
- Present	82 (61.2)	52 (34.4)	<0.001	3.0 (1.80, 5.01)
- Absent	52 (38.8)	99 (65.6)		
Reoperation for poor hemodynamics				
- Yes	6 (4.5)	2 (1.3)	0.108	3.5 (0.61, 35.8)
- No	128 (95.5)	149 (98.6)		
Inotropic requirement (hours)	52.05±26.4	36.88±8.0	0.001	
Mean ± SD				
Mean(±SD) duration of hospitalization (days)	9±5	6±3	<0.001	
OR= Odds Ratio, SD= Standard deviation, CI= Confidence interval.				

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**Table E1:** Demographic, operative and perioperative details of two groups of patients of the study group (n=285).

Standard cardiopulmonary bypass, modified ultrafiltration and myocardial preservation techniques were used in all patients. Intracardiac repair was performed with a trans atrial, transpulmonary approach in 193 (67.7%) patients and a trans right atrial approach in 92 (32.3%) patients. In 168 (58.9%) patients, a TAP was used. In this series, the decision to perform transannular patching of the RVOT was based on the determination of z-value. [15] Our protocol was to avoid both ventriculostomy and/or transannular patching in patients with a pulmonary annulus z-score  $>-3$ , to preserve both RV and pulmonary valve function. Whenever possible, we used the trans atrial+transpulmonary approach accepting postoperative Prv/Plv ratio even higher than  $\geq 0.7$ , when we were quite sure that residual obstruction was due to the small pulmonary annulus, or extreme cephalad deviation of the infundibular septum (and not due to residual infundibular stenosis or residual VSD) and always, in the presence of stable hemodynamics. Intraoperatively, after pulmonary arteriotomy, pulmonary valvular commissurotomy, muscle resection of the RVOT, the adequacy of RVOT muscle resection was assessed using Hegar's dilator, and matched with nomogram, thereby excluding hemodynamically significant RVOTO [15].

After surgery, pressures in the right and left ventricles were measured and two-dimensional Trans Esophageal Echocardiography (TEE) was performed. We considered the repair satisfactory in the presence of stable hemodynamics and no significant residual defects on TEE. We went back on bypass and either revised the transannular patch (n=5) or performed a more aggressive muscle resection (n=2).

Transesophageal and transthoracic Two Dimensional (2D), color flow, Doppler echocardiography and Tissue Doppler Imaging (TDI) was performed using a Phillips iE33 with 2.0 to 5.0 MHZ transducer and HP Sonos 5500; Hewlett Packard, Andover, MA machine [14]. Before discharge, patients underwent Doppler echocardiography and parameters pertaining to RV function, residual pulmonary stenosis / regurgitation and Tricuspid Regurgitation (TR) were recorded.

TDI was performed at specific intervals in preoperative (t=0), immediate postoperative (t=1), prior to discharge (t=2), at 6 months (t=3) and at one-year (t=4) intervals. The first two readings (at t=0 and t=1) were obtained by Transesophageal Echocardiography (TEE) and the rest of the postoperative readings were taken by Transthoracic Echocardiography (TTE). The parameters recorded were TAPSE, e', a', s', IVA and IVC (Definitions – electronics).

**Postoperative studies:** Between January 2010 and December 2016 (closing interval), 265 patients underwent clinical examination, electrocardiogram and echocardiography at discharge, six months and at 1 year with minimum of 12 months follow-up. The functional class at follow-up, need for cardiac medications and late complications were noted and was merged to form two groups:

“good” functional class I/II, (n=261) and “poor” functional class (class III/IV, n=4). They were followed up prospectively for development of adverse outcomes. Using standard statistical tools, significance was sought between adverse outcomes and Prv/Plv in short and medium-term follow-up.

## Statistical Analysis

Statistical analysis was carried out using Stata 11.0 (College Station, Texas, USA). Continuous data were presented as mean  $\pm$  standard deviation, whereas categorical variables were presented as frequency distribution and percentage. Qualitative data were analyzed by using  $\chi^2$  test. Normality assumptions for continuous variables were assessed using Shapiro-Wilks test. For quantitative variables, comparisons between two groups were done using t-test. Echocardiographic parameters over a period between the groups were tested using generalized estimating equation population-averaged model with exchangeable correlation analysis.

Mortality rates were calculated depending on the total number of years of follow-up for each patient. Actuarial estimates were calculated using the Kaplan-Meier technique and the log-rank test was performed to analyze statistically the difference of survival between patients of both groups. Baseline predictors of hospital mortality were identified by univariate logistic regression analysis initially performed on candidate variables. Multivariate logistic regression analysis was performed on the feasible independent variables. The results were reported as odds ratio (95% confidence interval).  $P < 0.05$  was considered as statistically significant.

## Results

### Group Comparison

Pairwise comparison revealed that patients in group I were more likely to have significant degree of aortic override ( $>50\%$ ) ( $p < 0.001$ ), greater systemic arterial desaturation ( $p = 0.05$ ), increased likelihood of TAP requirement ( $p = 0.004$ ) and significant postoperative PR ( $p = 0.004$ ) (Table E1).

### Early Results

There were 14 (4.6%; group I: n=8; group II: n=6) perioperative deaths and 8 (2.7%; group I: n=6; group II: n=2) patients underwent redo procedures.

In group I, five patients were reoperated for poor hemodynamics within 12 hours post-operatively due to significant stenosis at the annular level with no additional muscle bundles in RVOT and TAP was revised. One of these patients died in the immediate postoperative period due to intractable LCOS. The sixth patient underwent balloon pulmonary arthroplasty and pulmonary artery stenting at the level of previous Blalock-Taussig shunt at 2 months for right pulmonary artery stenosis. In group I, the other perioperative deaths were due to massive pulmonary hemorrhage



(n=3), intractable ventricular arrhythmias (n=2) and LCOS and multiorgan failure (n=2) (Table E1).

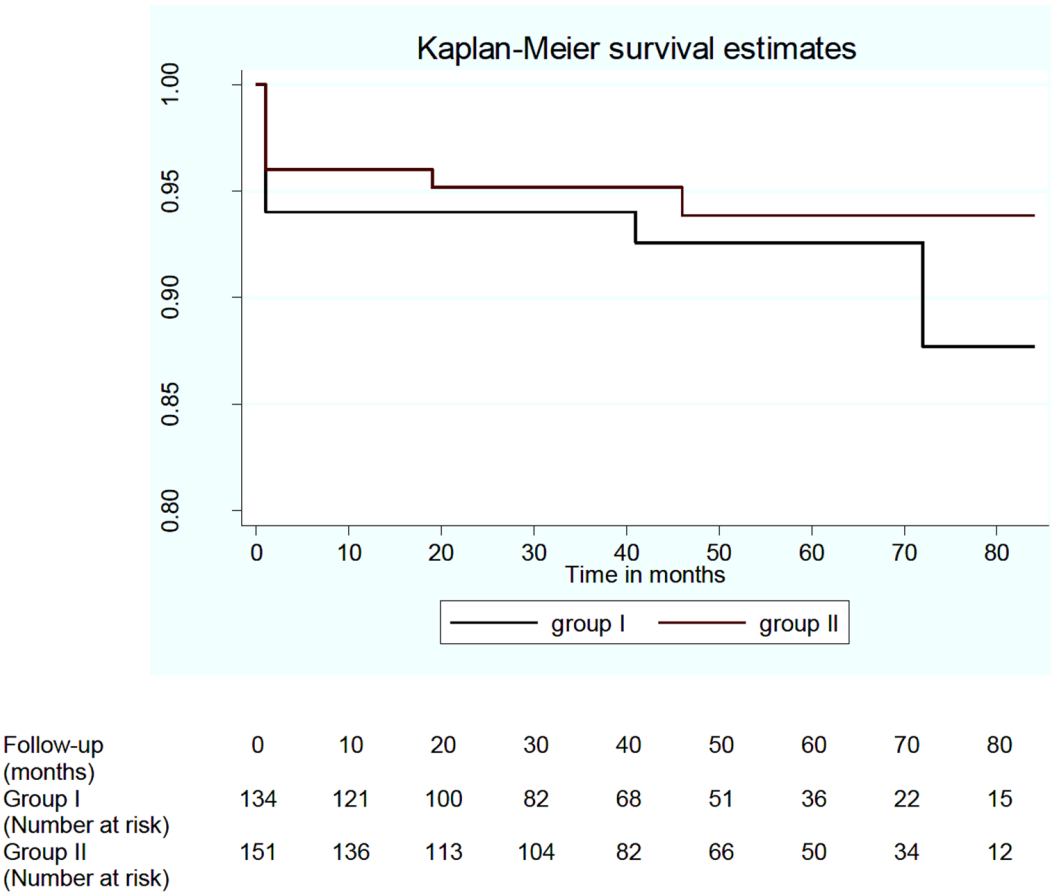
In group II, there were 6 perioperative deaths due to massive pulmonary hemorrhage (n=2), intractable ventricular arrhythmias (n=2), LCOS and multiorgan failure (n=2). Two patients underwent reoperation for residual muscular obstruction. Mean duration of hospitalization was 9±5 and 6±3 days in group I and II respectively (p<0.001) (Table E1). Although, pairwise comparison did not reveal any difference in peri-operative and late mortalities, group I patients were more likely to have postoperative LCOS and prolonged inotropic requirement (>24 hours) (p<0.001).

All patients were routinely started on dopamine (4µg.kg.min<sup>-1</sup>) to increase renal perfusion and sodium nitroprusside (0.5µg.kg.min<sup>-1</sup>) to reduce afterload. Patients considered to have LCOS (n=134) required dopamine, dobutamine, epinephrine and milrinone either isolated or in combination. Mean duration of

inotropic requirement was 52.05 (± 26.4) hours for group I and 36.88 (±8.0) hours for group II patients (p=0.001). Forty-two (31.3%) patients of group I and 15 (9.9%) patients of group II had postoperative supraventricular arrhythmias and premature ventricular contractions and was treated medically (p<0.001).

**Late Outcomes**

There were 4 (1.5%; group I, n=2; group II, n=2) late deaths due to ventricular arrhythmias (n=2) and late onset CHB (n=2). Follow-up was 100% complete (range, 1 month to 84 months) and yielded 968 patient-years of data with a mean follow-up time of 43.52 months [SE± 2.08; 95% confidence interval (CI): 39.41 to 47.64]. The actuarial survival at 43.52 months was 94.03%±0.02% in group I, and 96.03%±0.01% in group II [Hazard ratio: 0.69; ±SD 0.33; 95% confidence interval (CI): 0.27-1.75; p=0.4; Figure 1]. At their last follow-up 99.1% (122/123) and 99.2% (141 of 142) survivors were in NYHA class I/II.



**Figure 1:** Actuarial survival curves (Kaplan-Meier) of two groups of patients undergoing intracardiac repair of tetralogy of Fallot [Group I: n=134 (Prv/Plv ≥0.7); Group II: n=151 (Prv/Plv <0.7)].

Thirty-seven (13.8%) patients had complete right bundle branch block and left axis deviation. Two (0.7%) patients required permanent pacemaker implantation. The LVEF was normal ( $\geq 0.5$ ) in 151 (53%) and depressed (LVEF  $< 0.5$ ) in 134 (47%) patients. One hundred and eight (37.9%) patients had mild and 60 (21%) had moderate PR. Fifteen (5.3%) patients had mild tricuspid regurgitation. No patient had residual anatomical problems.

### Data Analysis and Study Interpretation

All patients dying in the perioperative and late postoperative period (n=18) and those requiring permanent pacemaker (n=2) were excluded from the study. Thus, 123 patients in group I and 142 patients in group II received full follow-up echocardiographic evaluation at designated time intervals.

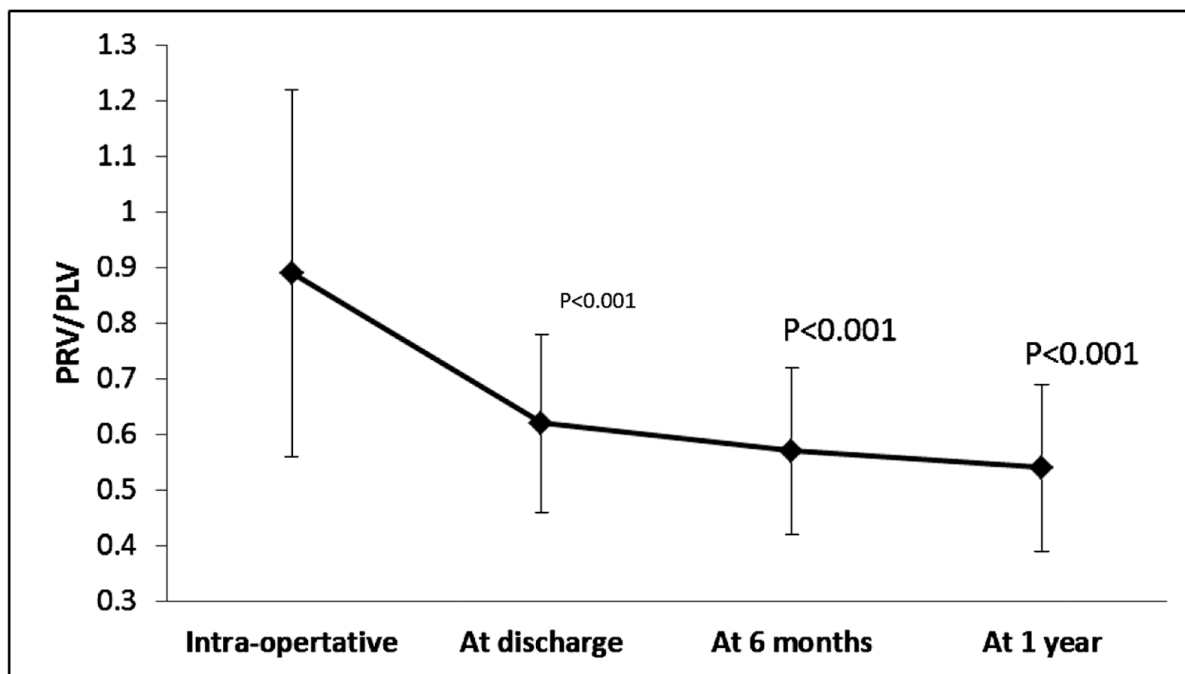
### Evolution of Prv/Plv

The Prv/Plv ratio was assessed on operation table after stabilization of hemodynamics and administration of protamine

by direct needle puncture. Intraoperatively, this directly measured pressure was interrelated with transesophageal echocardiography (t=1) and using transthoracic echocardiography at t=2 (discharge), t=3 (six months) and t=4 (12 months).

In all patients, the median Prv/Plv ratio as measured in the operating room was 0.62 (range, 0.3-1.3) with a median pressure gradient in RVOT of 19.6 mmHg (range 15-26). One hundred and thirty-four (47%) patients had a Prv/Plv ratio  $\geq 0.7$  ranging from 0.7-1.3 (group I).

After a mean follow-up of 43.52 (SE  $\pm 2.08$ ) months, Prv/Plv decreased from  $0.89 \pm 0.33$ , range: 0.3-1.3 to  $0.54 \pm 0.15$ , range: 0.2-0.92 (t1-t4,  $p < 0.001$ ) in the study cohort; in group I, the reduction was from  $0.80 \pm 0.52$  to  $0.44 \pm 0.27$  ( $p = 0.001$ ) and in group II, it was from  $0.51 \pm 0.18$  to  $0.42 \pm 0.26$  ( $p = 0.18$ ). In group I, there was statistically significant decrease in Prv/Plv at all points of time with overall significant decrease over one year in the postoperative period ( $p < 0.001$ ; Figure 2).



**Figure 2:** Line graph showing evolution of postoperative peak systolic right-to-left ventricular pressure ratio (Prv/Plv) during the designated follow-up period of survivors of repaired TOF undergoing data analysis (n=265).

### Relationship between TDI-derived Variables and Prv/Plv

Tables E2-E7 provide between group and within group TDI-derived at designated time intervals (t=0, t=1, t=2, t=3 and t=4). Generalized estimating equation with exchangeable correlation analysis revealed:

**Tricuspid annular plane systolic excursion (TAPSE; cm):** Preoperatively, there was no difference in the values between the two groups ( $p = 0.29$ ). Postoperatively, the values were statistically significant at all levels of measurement from t1 to t4 (Table E3). Within group comparison of the pattern of change revealed overall significant increase in TAPSE readings across four points of time

spread over one year in group II ( $p<0.001$ ). Within group I, the increase was significant between 6 months ( $p=0.04$ ) and one year ( $p=0.001$ ) after surgery (Table E2).

TAPSE	Group I (n=123) mean±SD (range)	Group II (n=142) mean±SD (range)	Difference: 95% confidence interval	p value
t=0	9.17±3.83 (1.7-18.8)	8.31±3.33 (4-18)	0.86 (0.73, 2.45)	0.29
t=1	9.18±2.84 (2.6-13.98)	11.62±3.4 (4.5-23)	-2.45 (-3.88, -1.01)	0.001
t=2	0.95±2.86 (3.2-15.6)	11.42±3.17 (4-22.98)	-1.47 (-2.84, -0.1)	0.03
t=3	10.36±2.68 (3.8-15.21)	11.66±3.08 (4.1-20)	-1.29 (-2.6, 0.02)	0.05
t=4	11.43±3.23 (4-18)	12.91±2.93 (4.5-19)	-1.47 (-2.8, -0.1)	0.03
Group II: t0 vs t1, t2, t3, t4; $p<0.001$ , statistically significant				
Group I: t0 vs t3, $p=0.04$ ; t0 vs t4, $p=0.001$ , statistically significant				

**Table E2:** Tricuspid Annular Peak Systolic Excursion (TAPSE, cm) recorded in both groups of patients with repaired TOF.

IVA	Group I (n=123) mean±SD (range)	Group II (n=142) mean±SD (range)	Difference: 95% confidence interval	p value
t=0	8.23±5.67 (3.12-28.2)	7.23±3.42 (3.4-18.5)	0.99 (-1.02, 3.02)	0.3
t=1	9.59±6.86 (2.07-31.2)	9.90±4.4 (4.6-21.1)	-0.35 (-2.85, 2.15)	0.7
t=2	9.69±6.66 (2.5-37.1)	9.8±3.6 (4.6-18.98)	-0.11 (-2.42, 2.19)	0.9
t=3	9.60±6.11 (2.8-27.9)	10.31±3.92 (4.6-20.2)	-0.71 (-2.94, 1.52)	0.5
t=4	9.99±5.52 (2.9-27.45)	10.42±3.75 (4.7±20.56)	-0.42 (-2.48, 1.63)	0.7
Group II: t0 vs t1, t2, t3, t4; $p<0.001$ , statistically significant				
Group I: t0 vs t1, $p=0.02$ ; t0 vs t3, $p=0.01$ ; t0 vs t4, $p=0.001$ , statistically significant				

**Table E3:** Isovolumic acceleration (IVA, cm/sec<sup>2</sup>) recorded in both groups of patients with repaired TOF.

**Isovolumic acceleration (IVA; cm/sec<sup>2</sup>):** Myocardial acceleration during isovolumic contraction (IVA), as assessed by TDI did not reach statistical significance between the two patient groups at any given time (Table E3). Within group comparison revealed overall significant increase in IVA readings across four points of time spread over one year in group II ( $p<0.001$ ). However, within group I, the increase was significant immediate postoperatively, at 6 months ( $p=0.01$ ) and one year ( $p=0.001$ ; Table E3).

**Isovolumic contraction (IVC; cm/sec):** The shortening of basal right ventricular wall during Isovolumic Contraction (IVC) between the two groups was significant at all points except t=0. Patients in the higher Prv/Plv group had lower IVC recordings always except at t=0 (Table E4). From table E4, it is seen overall change in group II was significant during the designated follow-up period t1 to t4 ( $p<0.001$ ). In group I, the change was significant at 6 months ( $p=0.04$ ) and at one year ( $p=0.002$ ) after surgery.



IVC	Group I (n=123) mean±SD (range)	Group II (n=142) mean±SD (range)	Difference: 95% confidence interval	p value
t=0	7.77±3.22 (2.8-15.7)	7.25±2.35 (3.2-13.57)	-0.51 (-0.7, 1.75)	0.4
t=1	8.40±2.91 (1.5-16.34)	10.35±2.85 (5.17-15.98)	-1.94 (-3.2, -0.65)	0.003
t=2	8.58±2.92 (1.8-14.7)	10.09±2.5 (5.4-15)	-1.49 (-2.7, -0.3)	0.01
t=3	8.63±2.79 (1.9-14.2)	10.18±2.55 (4.7-15)	-1.54 (-2.74, -0.35)	0.01
t=4	9.32±3.0 (2.8-15.8)	10.8±2.46 (6-14.78)	-1.47 (-2.69, -0.62)	0.01
Group II: t0 vs t1, t2, t3, t4; p<0.001, statistically significant				
Group I: t0 vs t3, p=0.04; t0 vs t4, p=0.002, statistically significant				

**Table E4:** Isovolumic contraction (IVC, cm/sec) recorded in both groups of patients with repaired TOF.

**Peak myocardial velocity during systole (s', cm/sec):** The right ventricular systolic function available by peak myocardial velocity during systole (s') was lower in group I than patients in group II at all points of time and the difference approached statistical significance throughout the postoperative period at t=1, 2, 3, 4 (Table E5). From table E5, it is seen that overall change in both groups was significant during the designated follow-up period (t 0-4; p<0.001).

s'	Group I (n=123) mean±SD (range)	Group II (n=142) mean±SD (range)	Difference: 95% confidence interval	p value
t=0	6.15±2.2 (3.1-13.1)	6.73±2.83 (3.1-15)	-0.58 (-1.74, 0.58)	0.3
t=1	7.29±2.08 (3.9-12.89)	9.42±2.9 (4.6-15.9)	-2.12 (-3.3, -0.96)	0.001
t=2	7.70±2.5 (3.9-14.4)	9.66±2.84 (4.8-15.15)	-1.95 (-3.17, -0.73)	0.002
t=3	8.0±2.56 (4-14.87)	9.86±2.85 (4.5-15.88)	-1.84 (-3.07, -0.61)	0.003
t=4	8.6±2.9 (4.8-16)	10.32±2.97 (4.8-15.62)	-1.7 (-3.1, -0.36)	0.01
Group II: t0 vs t1, t2, t3, t4; p<0.001, statistically significant				
Group I: t0 vs t1, t2, t3, t4; p<0.001, statistically significant				

**Table E5:** Peak myocardial velocity during systole (s', cm/sec) recorded in both groups of patients with repaired TOF.

## Right Ventricular Diastolic Function

**Diastolic basal wall lengthening of right ventricle in early diastole (e', cm/sec):** Pulmonary arterial antegrade flow coincident with atrial systole on Doppler, characterizing restrictive ventricular physiology was present in all patients in the preoperative period.

The peak myocardial velocity in early diastole (e') was lower in group I at all points of time (t=0, 1, 2, 3, 4), compared to group II. As is evident in table E6, there was overall significant increase in e' within both groups (group I: p=0.001 and group II: p=0.001) with progression over time (t=0-4).

e'	Group I (n=123) mean±SD (range)	Group II (n=142) mean±SD (range)	Difference: 95% confidence interval	p value
t=0	5.89±2.1 (1.4-12.07)	6.48±1.83 (3.1-10)	-0.58 (-1.46, 0.28)	0.1
t=1	7.24±2.36 (3-13.99)	8.37±1.66 (5.2-12)	-1.12 (-2.0, -0.24)	0.01
t=2	7.16±1.93 (3.38-11.11)	8.52±1.8 (4.78-12.75)	-1.36 (-2.19, -0.53)	0.001
t=3	7.42±2.35 (4-12.69)	8.84±2.05 (4.9-14)	-1.42 (-2.4, -0.45)	0.005
t=4	8.36±3.01 (4-15)	9.29±2.35 (5-14.6)	-0.93 (-2.12, 0.26)	0.12
Group II: t0 vs t1, t2, t3, t4; p<0.001, statistically significant				
Group I: t0 vs t1, t2, t3, t4; p<0.001, statistically significant				

**Table E6:** Early diastolic basal wall lengthening of right ventricle (e', cm/sec) recorded in both groups of patients with repaired TOF.

**Diastolic basal wall lengthening of right ventricle in late diastole (a', cm/sec):** The diastolic basal wall lengthening of RV in late diastole (a') was lower always in group I compared to group II, but the difference reached statistical significance only preoperatively (t=0; p=0.004). Overall change in group II was statistically significant at all points of follow-up from t1 to t4 (p<0.001). However, in group I, the change was statistically insignificant at all points of designated follow-up period (t1 to t4; Table E7).

a'	Group I (n=123) mean±SD (range)	Group II (n=142) mean±SD (range)	Difference: 95% confidence interval	p value
t=0	8.23±3.36 (3-16.7)	6.53±1.77 (4.24-10.87)	1.71 (0.55, 2.85)	0.004
t=1	8.65±2.75 (4.1-16)	8.77±2.62 (5-15.4)	-0.12 (-1.32, -1.08)	0.8
t=2	8.1±2.44 (3-13)	8.49±2.36 (4.9-14.5)	-0.41 (-1.5, 0.67))	0.45
t=3	8.14±2.32 (3.9-13.9)	8.94±2.37 (4.7-14.9)	-0.8 (-1.85, 0.26)	0.14
t=4	8.18±2.37 (4-13.8)	8.87±2.69 (0.9-15)	-0.7 (-1.84, 0.46)	0.24
Group II: t0 vs t1, t2, t3, t4; p<0.001, statistically significant				
Group I: t0 vs t1 (p=0.25), t0 vs t2 (p=0.68), t0 vs t3 (p=0.81), t0 vs t4 (p=0.91); statistically insignificant				
t=0 (preoperatively), t=1 (immediate postoperative), t=2 (at discharge), t=3 (at six months) and t=4 (at one year).				

**Table E7:** Late diastolic relaxation of right ventricular free wall (a', cm/sec) recorded in both groups of patients with repaired TOF.

**Analysis of adverse outcomes:** Baseline predictors of perioperative and late mortalities of both groups of patients were identified by univariate and multivariate logistic regression analysis (Table E8). The risk of death in repaired TOF with Prv/Plv >0.7 was 9.42 times higher (95% CI: 1.37-64.59; p=0.02) in patients aged ≤36 months and 37.60 times higher (95% CI: 3.27-431.21; p=0.004) in patients

having perioperative supraventricular and ventricular arrhythmias on multivariate analysis (Table E9). The risk of death in repaired TOF with Prv/Plv <0.7 was 18.85 times higher (95% CI: 2.16-163.96; p=0.008) in patients having perioperative supraventricular and ventricular arrhythmias on multivariate analysis (Tables E10, E11).

Variables	No. of patients	Odds ratio 95% confidence interval	P value
Age			
- ≤3 years	38	4.31 (1.14-16.26)	0.001
- >3 years	96		
Systemic arterial oxygen saturation			
- ≤80%	83	1.47 (0.36-5.97)	0.001
- >80%	51		
Hematocrit			
- ≥45%	73	0.53 (0.14-1.97)	0.001
- <45%	61		
Aortic override			
- ≥50%	104	2.74 (0.33-22.60)	0.35
- <50%	30		
Previous modified Blalock-Taussig shunt			
- Yes	6	7.5 (1.18-47.32)	0.001
- No	128		
Major aortopulmonary collateral arteries			
- Present	38	4.31 (1.14-16.26)	0.03
- Absent	96		
Supraventricular and ventricular arrhythmias			
- Yes	42	24.82 (3.02-203.5)	0.001
- No	92		
Transannular patch			
- Yes	91	4.61 (0.56-37.61)	0.001
- No	43		
Pulmonary regurgitation			
- Present	91	4.61 (0.56-37.61)	0.001
- Absent	43		
Low cardiac output			
- Present	82	2.70 (0.55-13.25)	0.001
- Absent	52		
Reoperation			
- Yes	6	2.64 (0.27-25.12)	0.001
- No	128		

**Table E8:** Univariate predictors of 0- to 7-years mortality in repaired tetralogy of Fallot with Prv/Plv ≥0.8 (group I; n=134).

Variables (Covariate adjusted)	Odds ratio (95% confidence interval)	p value
Age (less than 36 months)	9.42 (1.37-64.59)	0.02
Perioperative supraventricular and ventricular arrhythmias	37.60 (3.27-431.21)	0.004

**Table E9:** Predictors of 0- to 7-year mortality by logistic regression analysis applied to all 134 patients with repaired tetralogy of Fallot with Prv/Plv  $\geq 0.8$  (group I).

Variables	No. of patients	Odds ratio 95% confidence interval	p value
Age			
- $\leq 3$ years	42	0.83 (0.16-4.27)	0.001
- $> 3$ years	109		
Systemic arterial oxygen saturation			
- $\leq 80\%$	110	0.35 (0.83-1.46)	0.001
- $> 80\%$	41		
Hematocrit			
- $\geq 45\%$	10	2.12 (0.23-19.22)	0.001
- $< 45\%$	141		
Aortic override			
- $\geq 50\%$	45	1 (Omitted)	
- $< 50\%$	106		
Previous palliation			
- Yes	13	28.12 (5.68-139.19)	0.001
- No	138		
Major aortopulmonary collateral arteries			
- Present	29	1 (Omitted)	
- Absent	122		
Supraventricular and ventricular arrhythmias			
- Yes	15	44.66 (7.86-253.67)	0.001
- No	136		
Transannular patch			
- Yes	77	1 (Omitted)	
- No	74		

Pulmonary regurgitation			
- Present	77	1 (Omitted)	
- Absent	74		
Low cardiac output			
- Present	52	1 (Omitted)	
- Absent	99		
Reoperation			
- Yes	2	1 (Omitted)	
- No	149		

**Table E10:** Univariate predictors of 0- to 7-years mortality in repaired tetralogy of Fallot with Prv/Plv <0.8 (group II; n=151).

Variables (Covariate adjusted)	Odds ratio (95% confidence interval)	p value
Previous modified Blalock-Taussig shunt	4.39 (0.54-35.96)	0.167
Perioperative supraventricular and ventricular arrhythmias	18.55 (2.16-163.96)	0.008

**Table E11:** Predictors of 0- to 7-year mortality by logistic regression analysis applied to all 151 patients with repaired tetralogy of Fallot with Prv/Plv <0.8 (group II).

## Discussion

As far as we could establish, there are limited studies in the English literature addressing specifically the evolution of postoperative peak systolic right-to-left ventricular pressure ratio and its relationship to postoperative outcome and TDI-derived variables of the right ventricular myocardium [3, 6].

### The Principal Findings of this Investigation Include:

- Because the TAP was limited, 47% of patients with repaired TOF continued to exhibit higher Prv/Plv  $\geq 0.7$ . A high postoperative Prv/Plv was accepted in the presence of stable hemodynamics without residual VSD and RVOTO because of hypercontractile state of the hypertrophied myocardium in the immediate postoperative period and extreme cephalad deviation of infundibular septum causing dynamic right ventricular outflow tract obstruction.
- A significant reduction of Prv/Plv in the whole cohort and in the group of patients with higher Prv/Plv ( $p=0.001$ ).
- Despite the occurrence of LCOS in patients with higher Prv/Plv, there was no difference in surgical mortality between the two groups.
- The occurrence of lower pre - operative late diastolic wall lengthening of basal RV in late diastole (a') in patients with a

higher Prv/Plv as compared to group II.

- Consistent occurrence of lower RV systolic and diastolic function i.e TAPSE, IVC, e' and s' values with higher Prv/Plv at varying points of time in the postoperative period.
- A significant occurrence of impaired RV systolic and early diastolic function in all patients with repaired TOF despite having a variable Prv/Plv. It is noteworthy that among all TDI-derived variables, TAPSE, IVA, IVC, s' and e' continued to improve to a greater degree among patients with lower postoperative Prv/Plv (<0.8).
- The absence of improvement of the late diastolic relaxation of RV free wall (a') in patients with higher post-operative Prv/Plv.

Decisions made at the time of intracardiac repair of TOF have a definite impact on the performance of repair over the subsequent 20-30 years and beyond [1-7]. Although the primary decision-making on the requirement of TAP is indeed the size of the pulmonary valve ring, postoperative Prv/Plv can guide the surgeons in borderline cases. Many surgical centres will consider using a TAP if immediate post repair Prv/Plv is  $\geq 0.7$ . Increased postoperative Prv/Plv is widely accepted as a risk factor for adverse postoperative outcomes as well as long-term mortality [1-5]. A postoperative Prv/Plv between 0.8 to 1.0 without TAP and

>0.85 with TAP adversely affects survival [1-7].

**Bony Boni** and colleagues documented that pulmonary valve sparing procedure with Prv/Plv up to 0.9 may be acceptable provided the infundibular resection is adequate and the pulmonary annulus has a Z-score >-0.4. They demonstrated significant reduction of Prv/Plv late postoperatively due to ensuing infundibular relaxation. Katz and colleagues in 1982 did not find TAP to be a risk factor for late mortality but did find high Prv/Plv to be associated with late events including death [7].

In this study, because the transannular patch was limited, Prv/Plv continued to remain  $\geq 0.7$  in 47% (n=134) patients undergoing intracardiac repair of TOF in the absence of a residual VSD, residual RVOTO or MAPCAs. We have accepted a maximum Prv/Plv upto 1.3 because we believed that the annulus was in the recommended limit, the muscular resection was deep enough, and the great majority were late presenters with hypertrophied heart. These patients were more likely to have significant degree (>50%) of aortic override ( $p<0.001$ ) and there was increased likelihood of requirement of TAP [ $p=0.004$ , OR (95% CI): 2.03 (2.09-8.48)] and significant PR [ $p=0.004$ , OR (95% CI): 2.03 (2.09-8.48)]. The postoperative course of patients operated on with a higher Prv/Plv with or without TAP could be a complicated one since the recently operated RV is still facing a high afterload at the annular level. These patients with higher Prv/Plv  $\geq 0.7$ , were more likely to have postoperative LCOS [ $p<0.001$ , OR (95% CI): 3.0 (1.8-5.0)], prolonged inotropic requirement (>24 hours,  $p<0.001$ ) and supraventricular arrhythmias [ $p<0.001$ , OR (95% CI): 4.13 (2.09-8.48)]. There was no difference in surgical mortality and reoperation for poor hemodynamics in this group of patients with higher Prv/Plv (Table E1). The risk of death in repaired TOF with Prv/Plv  $\geq 0.7$  was 9.42 times higher (95% CI: 1.37-64.59;  $p=0.02$ ) in patients aged  $\leq 36$  months and 37.60 times higher (95% CI: 3.27-431.21;  $p=0.004$ ) in patients having perioperative supraventricular and ventricular arrhythmias (Table E9). At a mean follow-up of 43.52 months (SE  $\pm$  2.08; 95% CI: 39.41-47.64), there was no difference in actuarial survival between two groups of patients (group I: 94.03% $\pm$ 0.02%, group II: 96.03% $\pm$ 0.01%; Hazard ratio: 0.69;  $\pm$ SD 0.33; 95% CI: 0.27-1.75;  $p=0.5$ ; Figure 1). After a mean follow-up of 43.52 (SE  $\pm$ 2.08) months, Prv/Plv decreased from 0.89 $\pm$ 0.33 (range: 0.3-1.3) to 0.54 $\pm$ 0.15 (range, 0.2-0.92; t1-t4;  $p<0.001$ ) in the study cohort (in group I, the reduction was from 0.80 $\pm$ 0.52 to 0.44 $\pm$ 0.27;  $p=0.001$  and in group II, it was from 0.51 $\pm$ 0.18 to 0.42 $\pm$ 0.26;  $p=0.18$ ). In group I, there was significant decrease in Prv/Plv at all points of time with overall significant decrease over one year in the postoperative period ( $p<0.001$ ; Figure 2).

Careful analysis of the published literature substantiates a significant incidence of LCOS following intracardiac repair of TOF [1-7,11,15]. The culprit pathophysiological mechanisms

responsible for LCOS in repaired TOF although not specifically addressed or analyzed is multifactorial in nature. In this study, although it is impossible to relate directly a LCOS state to a specific tissue Doppler-derived variable, such a relation is suggested in patients with higher postoperative Prv/Plv exhibiting absence of improvement of late diastolic relaxation of RV free wall (a').

Significant diastolic dysfunction of the RV after intracardiac repair of TOF may produce a restrictive physiology in which the stiff RV demonstrates true filling and behaves as an almost passive conduit for pulmonary blood flow. Its prevalence in the literature ranges from 28% to 52% [16-18] Several investigators including ourselves have demonstrated the presence of myocardial hypertrophy, endocardial thickening and perivascular / interstitial fibrosis in late presenters of TOF [19-21] The additional adverse effects of right ventriculostomy, interposition of interventricular septal patches, placement of transannular patch, myocardial oedema secondary to the effects of extracorporeal circulation, cardioplegia, hypothermia and RVOTO might be expected to influence the diastolic performance of the ventricle in early and late postoperative period [1-7,11-13,15].

The mean age of the patients in this series was between 8 and 9 years. Because late presentation of congenital heart disease is not unusual in the developing world, it is not uncommon to be faced with the grown-up patients with tetralogy physiology without previous palliation. In our previous investigation, we demonstrated that the great majority of myocardial tissues in cyanotic TOF indicate pre-existing ultrastructural hypertrophy and degenerative changes. [19] The changes are more pronounced in older patients subjected to long-standing cyanosis and pressure overload and may account for or may coexist with the higher incidence of myocardial dysfunction and ventricular arrhythmia [19].

The systolic function is usually normal in these patients. Abnormalities of right ventricular diastolic function in the immediate postoperative period have been incriminated to this clinical behavior. [16,17] Using tissue Doppler interrogation, another marker of diastolic impairment, we could show diastolic dysfunction was already present preoperatively in all patients in this study, worsened significantly in all of them immediately after surgery and remained reduced at late assessment particularly in patients with higher postoperative Prv/Plv ( $\geq 0.7$ ).

The strongest predictor of restrictive physiology was the requirement of TAP which was significantly higher in patients with Prv/Plv  $\geq 0.7$  [ $p=0.004$ ; OR (95% CI): 2.03 (2.09, 8.48)]. During the study period, although all patients exhibited significant reduction of Prv/Plv late postoperatively, the restrictive physiology (diastolic basal wall lengthening in late diastole a') resolved only in patients with lower Prv/Plv <0.7. Among all TDI-derived variables, TAPSE, IVA, IVC, s', e' continued to improve to a greater degree in patients with lower Prv/Plv. Although, the study group because of late



presentation selects out all the TOF variants were severe annular and/or PA branch hypoplasia and represent the most favorable spectrum of TOF disease, the myocardium has been subjected to long-standing cyanosis and pressure overload and may account for higher incidence of myocardial dysfunction.

## Potential Relevance and Clinical Implications of TDI Measurements

Tissue Doppler imaging has high temporal and spatial resolution and is thus suited for accurately measuring velocities of myocardium at specific locations. Literature is rife with investigators comparing TDI with radionuclide studies and magnetic resonance imaging in patients with TOF [22]. Unlike a conventional TTE, most TDI-derived variables are preload independent.

Among the TDI-derived variables, TAPSE and  $s'$  have been shown to correlate well with global systolic RV function [8-11].  $s'$  ( $<10$  cm/sec) is an independent predictor of RV dysfunction and reduced exercise capacity in repaired TOF.<sup>13</sup> It has been shown by Shan and colleagues that systolic ( $s'$ ) early ( $e'$ ) and late ( $a'$ ) of the left heart measured by TDI are dependent on myocardial fibrosis and  **$\beta$ -adrenoreceptor density** [23]. In the setting of various degrees of preload independent TDI variables, postoperative pulmonary regurgitation, IVA, has been found useful in assessment of RV contractile function [24,25].

## Study Limitations

The mean age (8-9 years) is substantially older than standard practice in most countries. This may limit the applicability of the study findings. TDI as a technique for assessment of RV Function is currently evolving as measurements continue to get validated. Achilles' heel of TDI is that it analyses one segment at a time, the projection of which to the entire myocardium may not be appropriate because of non-uniform distribution of myocardial histopathological changes in TOF. Some indices maybe affected by loading conditions (e.g. tricuspid annular peak systolic excursion) whereas others may have significant interobserver variability, may be difficult to perform with technical issues like poor alignment, poor windows and a learning curve, each of which may have an impact on TDI readings.

## Definitions (Electronics)

### Echocardiographic studies and measurements

Pulsed DTI of RV was performed from the apical 4 chamber view by placing 5 mm sample volume at the tricuspid annulus (free wall). Peak myocardial velocities during systole ( $s'$ ), early diastole ( $e'$ ) and late diastole ( $a'$ ) were measured. Other systolic indices of RV function (IVA, IVC and TAPSE) were also recorded. All measurements were performed three times and the mean value was used for analysis. These velocities were recorded for five

consecutive cardiac cycles at a sweep speed of 100 mm/sec.

Tricuspid regurgitation was assessed semi-quantitatively as grade 1+ to 4+. Tricuspid regurgitation was considered severe if there was a jet more than 30 mm from the annulus or a ratio of regurgitation jet area-to-right atrial area more than 33% on Doppler echo [14]. Pulmonary regurgitation was assessed from both continuous-wave Doppler trace and color-flow mapping. Pulmonary regurgitation was classified as mild when the retrograde pressure drop was maintained throughout diastole, moderate when equilibration between pulmonary artery and right ventricular pressures occurred in late diastole, and severe when it met the baseline in middiastole or earlier [14]. Persistent (residual) pulmonary valvular stenosis was considered present when the peak systolic RVOT gradient was  $\geq 30$ mmHg [14].

### Tricuspid Annular Plane Systolic Excursion, (TAPSE)

It is also known as Tricuspid Annular Motion (TAM) and is simplest to obtain and most widely studied Doppler tissue echocardiographic variable as a marker of right ventricular function in systole. From an apical four chamber view, it measures the longitudinal systolic apical descent of the tricuspid valve annulus (taken along right ventricular free wall) with obvious surmise that greater the descent, better the right ventricular function. It has been shown to correlate well with magnetic resonance imaging and has low intra-observer variability [22]. However, it lacks extensive validation studies and it maybe preload dependent. Lower reference value for impaired right ventricular function is taken as 16 mm [9,10,14].

**$e'$  (cm/sec):** It denotes diastolic basal wall lengthening of right ventricle in early diastole, representing the early passive filling of the right ventricle [14].

**$a'$  (cm/sec):** It denotes diastolic basal wall lengthening of right ventricle in late diastole, representing atrial contraction i.e. the active filling [14].

**Isovolumic contraction (IVC) cm/sec:** It is the shortening of basal right ventricular wall during isovolumic ventricular contraction [14].

**Isovolumic acceleration (IVA) cm/sec<sup>2</sup>:** Is the acceleration of basal right ventricular wall during isovolumic ventricular contraction. It is apparently less dependent on loading conditions [14] than other ejection period indices. It varies with heart rate and is age dependent. Lower reference values are suggested as 2.2 m/sec<sup>2</sup>.

**$s'$  (cm/sec):** It denotes peak myocardial velocity during systole. It correlates directly with right ventricular force of contraction. It is measured via an apical four chambered view with pulsed doppler volume placed on lateral tricuspid annulus. It has been shown to be an independent predictor of exercise capacity in operated patients

of tetralogy of Fallot.<sup>10</sup> Although its use has been validated in population-based studies, it is less reproducible, and values less than 10 cm/sec suggest right ventricular dysfunction, especially in a young adult [14].

### Low cardiac output Syndrome (LCOS)

Low cardiac output syndrome in repaired tetralogy of Fallot (TOF) patient was diagnosed if the patient required inotropic support (dopamine at 4-10 µg/[kg · min]), dobutamine at 5-10 µg/[kg · min], epinephrine at 0.01-0.1 µg/[kg · min] either isolated or in combination in the operating room or in the intensive care unit, to maintain stable hemodynamics in the absence of residual structural lesions and mechanical external compression after correction of all electrolytes or blood gas abnormalities and after adjustment of the preload to its optimal value. Low-output syndrome was also diagnosed if there was an increasing requirement of the above-mentioned inotropes with or without intra-aortic balloon counter pulsation along with afterload reduction with sodium nitroprusside. Patients who received less than 4 µg/ (kg · min) dopamine to increase renal perfusion were not considered to have low output syndrome.

Accordingly, under the definition of low output syndrome after repair of TOF, an integration of relevant clinical, laboratory and bedside echocardiographic criteria were used. The criteria for diagnosis were as follows: cold extremities, absent pedal pulses, decreased toe temperature, reduced systolic pressure, impaired renal function and oliguria (<1.0 mL.kg<sup>-1</sup>.h<sup>-1</sup>), metabolic acidosis, increased serum lactate levels ≥2.0 mmol/L, ≥2 hours), low mixed venous oxygen saturation (≤50%), and blunt sensorium [19].

**Arrhythmias:** Patient with complete heart block requiring permanent pacemaker insertion (n=2) were not included as they were more of a surgical complication rather than being related to disease per se. Patients with supraventricular (paroxysmal supra ventricular tachycardia, ventricular tachycardia, atrial fibrillation) and ventricular (frequent ventricular premature contractions, sustained ventricular tachycardia) arrhythmias were included for comparison between the two groups.

### Conclusions

Our results demonstrate that despite performing an adequate intracardiac repair, a subset of patients will have an immediate postoperative Prv/Plv ≥0.7. Although, there is an increased likelihood of LCOS, requirement of a TAP and significant postoperative pulmonary regurgitation in this subset of patients, there is no difference in surgical mortality, reoperation and actuarial survival between two groups.

A high Prv/Plv may be acceptable in the presence of stable hemodynamics as it reduces significantly over time. All TDI-derived variables excepting a' improves late postoperatively. The

absence of improvement of late diastolic relaxation of RV free wall (a') may be the causative factor for higher incidence of LCOS in these patients.

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