Asymptomatic right ventricular dysfunction in surgically repaired adult tetralogy of fallot patients

Krishna Kumar Mohanan Nair, Sanjay Ganapathi, Bijulal Sasidharan, Anees Thajudeen, Harikrishnan Sivadasan Pillai, Jaganmohan Tharakan, Thomas Titus, Ajitkumar Valaparambil Kumaran, Sivasankaran Sivasubramonian, Kavassery Mahadevan Krishnamoorthy

Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India

ABSTRACT

Background : **Right ventricular (RV) dysfunction after surgical repair of Tetralogy of Fallot (TOF) is often asymptomatic and may be detected by tissue Doppler imaging (TDI). The severity of RV dysfunction is more after intracardiac repair with transannular patch (TAP).**

Methods : **One hundred seventy-three adult patients who have undergone surgical repair for TOF were prospectively analyzed for RV function using 2D echocardiography and TDI. RV function was compared between patients who have undergone intracardiac repair with and without TAP.**

Results : **In both the patient sub-groups, TDI derived myocardial performance index (MPI) and myocardial velocities were abnormal even when 2D echocardiography derived RV functional area change was normal. TDI derived MPI was significantly higher (0.5 ± 0.1 vs. 0.4 ± 0 $P < 0.001$) and Systolic tricuspid annular velocity (Sa) (9.2 ± 1.3 vs. 10.8 ± 1.6 $P < 0.001$) was significantly lower in the TAP group. Older age at surgery and severity of pulmonary regurgitation on follow-up were among the significant predictors of TDI derived MPI.**

Conclusions : **Asymptomatic RV dysfunction in surgically repaired adult TOF atients can be detected by TDI. Extent of RV dysfunction was significantly greater with patients requiring TAP, in those operated at older age, and in patients with severe pulmonary regurgitation.**

Keywords : RV function, tetralogy of fallot, tissue doppler imaging

INTRODUCTION

Tetralogy of fallot (TOF) is the most common cyanotic congenital heart defect with a prevalence of 0.5 per 1000 live births, and represents approximately 9% of all congenital heart defects.[1] With the advent of intracardiac repair, survival of patients with TOF into adulthood has become routine with a good long-term prognosis.[2] However, many patients have significant pulmonary regurgitation that can lead to Right ventricular (RV) dilatation and dysfunction, right heart failure, arrhythmias, and sudden cardiac death.[3] There is uniform agreement that these patients have mild to moderate impairment in exercise capacity with large individual variations.[4] Hence, assessment of RV function is crucial in the treatment of these patients as those with significant RV dilatation and symptoms may improve after pulmonary valve replacement.[5]

Access this article online	
Quick Response Code:	Website: www.annalspc.com
	DOI: 10.4103/0974-2069.107229

Objective measurement of RV function is not always easy to perform, especially when tricuspid regurgitation and pulmonary regurgitation are present.[6] Currently, cardiac magnetic resonance (CMR) imaging is the gold standard for evaluating RV volumes and ejection fraction, and for quantifying pulmonary regurgitation.[7] However, cardiac magnetic resonance is not widely available and many patients have contraindications to this modality. Echocardiography is widely available. However, the assessment of RV function is challenging because of its unusual shape and variability in filling with respiration. In recent years, tissue doppler imaging combining both

Address for correspondence: Dr. Sanjay Ganapathi, Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India. E-mail: drsanjayganesh@yahoo.com

systolic and diastolic time intervals and myocardial velocities has been reported to be a more reliable method for the assessment of RV dysfunction.[8,9]

The aim of the study was to determine the RV function in adult patients with repaired TOF using tissue doppler imaging and to assess whether there is any difference in the extend of RV dysfunction in patients undergoing intracardiac repair with transannular patch (TAP).

MATERIALS AND METHODS

Study population

Our study cohort comprised of 173 patients with repaired TOF (who have undergone surgical repair for tetralogy of Fallot, who were being followed up in our Institute). All patients were in NYHA functional class I at the time of study. No patient had residual ventricular septal defect or RV outflow tract obstruction. Mean age was 24.3 ± 7.8 years, ranging from 11 to 42 years. Their mean age at repair was 15.5 ± 8 years, ranging from 2 to 33 years.

RV function was compared between patients who have undergone intracardiac repair (ICR) with TAP or without TAP.

Echocardiography

Transthoracic echocardiography including tissue Doppler imaging (TDI) was performed with 3.5 Hz or 7 MHz probes (Vivid 7, General Electricals). Echocardiographic measurements of flow velocities and time intervals were taken as an average of three consecutive cardiac cycles.

2D echocardiography

Both M mode and planimetry were employed in determining the RV dimensions. M mode derived diastolic dimensions of the right ventricle were taken from parasternal long axis view. Planimetry derived end-diastolic and end-systolic areas of the right ventricle were obtained from apical 2-chamber view. M mode derived diastolic and systolic left ventricular dimensions were also taken.

RV fractional area change was calculated as follows:
RV fractional area change = (RV end-diastolic area - RV end-systolic area)/RV end-diastolic area[10])

Tissue doppler imaging

TDI images were obtained by activating the tissue doppler imaging mode of the machine. Filters were set to exclude high velocity signals. Gains were minimized to allow a clear tissue signal with minimal background noise. A 2 mm sample volume was placed at the lateral corner of tricuspid annulus. The resulting velocities, peak tricuspid annular velocity during systole (Sa), early diastole (Ea), and late diastole (Aa) were recorded at a sweep speed of 100 mm/s. Sa of <11.5 cm/s correlates well with an RV ejection fraction of less than 45% with a sensitivity of 90% and specificity of 85%.[11] The intervals were determined by 2 carefully placed vertical cursors that were moved with a track ball. The isovolumic contraction time (IVCT) was defined as the time period between onset of R wave on ECG and the beginning of the Sa-wave. The isovolumic relaxation time (IVRT) was defined as the time period between the end of the Sa-wave and the beginning of the Ea-wave. Ejection time (ET) was measured as the time interval between the onset and cessation of the systolic velocity. Echocardiographic measurements of flow velocities and time intervals were taken as an average of 3 consecutive cardiac cycles. The Myocardial Performance Index (MPI) was calculated according to the following equation:

Myocardial Performance Index[5] = (Isovolumic contraction time + isovolumic relaxation time)/Ejection time.

MPI of ≥ 0.28 ± 0.04 is taken as abnormal.[12]

Statistical analysis

Statistical analysis was done using the software SPSS version 10.0. Continuous variables are expressed as mean ± SD. Procedural results were compared using an unpaired Student's *t*-test. For comparison of group means, a *t*-test was used. Proportions were compared by use of the c^2 test and the Fisher exact test. $P < 0.05$ was considered as significant. Univariate and multivariate analysis were done using linear regression analysis.

RESULTS

Baseline characteristics were illustrated in Table 1. In the present study, out of the 173 patients, 97 (56%) needed transannular patch and 69 (40%) needed RV outflow tract patch. In 7 (4%) patients RV outflow tract repair was done by infundibular resection alone. Sixty-one (35%) had their primary repair done at the age of ≥ 18 years.

The TAP group consisted of 97 (56%) patients with a mean age of 21.8 ± 7.8 years ($P < 0.05$), who underwent surgery at a mean age of 12.7 ± 8.7 years ($P < 0.05$) and the non TAP group had 76 (44%) with a mean age of 27.1 ± 6.9 years ($P < 0.05$), who had surgery at a mean age of 18.5 ± 6.1 years ($P < 0.05$). The mean cardiopulmonary bypass time was 154.8 ± 22.5 min in the TAP group (vs. 148.2 ± 37.7; p: NS). Age at surgery was significantly higher in the non-TAP group. The cardiopulmonary bypass time was higher in the TAP group; but not significantly. All patients were in sinus rhythm at the time of surgery. QRS axis and duration were similar in both groups. Left ventricular internal dimension at diastole (LVIDd) and Right ventricular internal dimension at diastole (RVIDd) were significantly higher in the non-TAP group. Pulmonic stenosis gradient was similar in both the groups. Left ventricular internal dimension at systole (LVIDs) was comparable between the study groups.

Last follow-up

Mean age at last follow-up was significantly higher in the non-TAP group. The mean time to last follow-up after surgery was 9.1 ± 4.2 years in the TAP group and 7.8 ± 1 years in the non-TAP group (p: NS). All patients were in NYHA functional class I. No patient had right heart failure. No patient had residual ventricular septal defect or residual RV outflow tract obstruction. Clinical data on last follow-up is given in Table 2. All patients were in sinus rhythm. QRS axis was significantly more rightward in the transannular patch group. QRS duration was increased in both groups and this was greater in the TAP group, however the difference was not significant between the two groups.

LVIDd, LVIDs and RVIDd were not significantly different between the two groups on last follow-up. RV end-diastolic and end-systolic areas were significantly lower in the TAP group. RV functional area change was normal in both patient groups; yet it was lower in the TAP group (but the difference was not significant.)

Tissue doppler imaging on last follow-up

Tissue Doppler findings were compared between the TAP group and the non-TAP group. The findings were as in Table 3. Early diastolic tricuspid annular velocity (Ea) and late diastolic tricuspid annular velocity (Aa) were comparable between the two groups. Systolic tricuspid annular velocity, (Sa) was significantly lower in TAP group than non-TAP group. Ejection time was lower in the TAP group (but not significant). Isovolumetric relaxation time, isovolumetric contraction time and myocardial performance index values were significantly higher in TAP group than in non-TAP group.

Determinants of myocardial performance index

Age at surgery and time after surgery were the only demographic variables that determined the MPI on follow up. Among the 2D echocardiographic variables RV functional area change and pulmonary regurgitation were the important predictors of MPI [Table 4a and 4b].

Table 1: Comparison of baseline data

	Total	Non TAP	TAP	*P*
Age at surgery (years)	15.5±8.0	18.5±6.1	12.7±8.7	<0.05
QRS axis (degree)	103.4±18.6	105.5±16.1	101.4±20.7	NS
QRS duration (ms)	77±14.0	78.2±16.2	76±11.9	NS
LVIDd (mm)	31.4±7.3	34.5±6.5	28.6±7.0	<0.05
LVIDs (mm)	20±5.0	21.3±4.6	18.8±5.3	NS
RVIDd (mm)	21.8±6.6	23.7±6.7	20±6.1	<0.05
Pulmonic stenosis gradient (mm Hg)	73.4±12.8	73.6±13.1	73.2±12.7	NS

RVIDd: RV internal dimension at diastole, LVIDd: Left ventricular internal dimension at diastole, TAP: Transannular patch, LVIDs: Left ventricular internal dimension in systole

Table 2: Comparison at last follow-up

	Total	Non TAP	TAP	*P*
Age (on last follow-up)	24.3±7.8	27.1±6.9	21.8±7.8	<0.05
Time after surgery (years)	8.5±4.3	7.8±4.4	9.1±4.2	NS
QRS axis	71.8±29.1	61.6±32.7	81±22.4	<0.05
QRS duration (ms)	129.6±28.4	122.4±29.7	136.2±26.2	NS
LVIDd (mm)	40.4±5.9	41.9±5.8	38.9±5.8	NS
LVIDs (mm)	26.8±5.2	26.4±4.5	27±5.9	NS
RVIDd (mm)	31.7±12.3	32.5±16.7	31±6.3	NS
RV end-diastolic area	28.7±9.7	24.7±6.6	32.3±10.8	<0.05
right ventricular end-systolic area	17.4±6.7	14.4±3.9	20.1±7.6	<0.05
RV functional area change (%)	39.6±9	40.8±8.9	38.5±9.2	NS
Pulmonic stenosis (mm Hg)	15.6±5.5	15.3±5.2	15.8±5.9	NS

RVIDd: RV internal dimension at diastole, LVIDd: Left ventricular internal dimension at diastole, TAP: Transannular patch, LVIDs: Left ventricular internal dimension in systole

Table 3: Comparison of tissue doppler findings of non-transannular patch and transannular patch group

	Total	Non TAP	TAP	*P*
Systolic tricuspid annular velocity Sa (cm/s)	9.9±1.7	10.8±1.6	9.2±1.3	<0.001
Early diastolic tricuspid annular velocity Ea (cm/s)	12.7±2.7	12.5±2.7	12.8±2.7	NS
Late diastolic tricuspid annular velocity Aa (cm/s)	8.2±2.5	8.7±2.9	7.7±2.0	NS
Isovolumetric relaxation time (ms)	69.3±17.9	58.5±11.4	79±17.3	<0.001
Isovolumetric contraction time (ms)	60.9±18.4	51.6±10.4	69.2±20.1	<0.001
Ejection time (ms)	278±30.8	286.6±26	270.2±33.2	NS
Myocardial performance index	0.5±0.1	0.4±0.1	0.5±0.1	<0.001

TAP: Transannular patch

DISCUSSION

The overall survival of patients with repaired TOF is excellent. A 25-year survival of more than 94% has been reported.[13] However; concerns have been raised about the adverse long-term effect of chronic pulmonary regurgitation that is present almost in all of these patients. RV volume and pressure overload cause RV dysfunction and RV failure and may lead to the development of atrial and ventricular arrhythmias.[2-5]

Long-term volume overload in these patients with moderate or severe pulmonary regurgitation, a progressive RV dysfunction takes place in time.[1,2,7-10,13] For this reason, in patients with RV dilatation, pulmonary valve replacement (PVR) should be done before irreversible changes take place.[1-4,7,13] This study was performed to assess the RV function by using tissue doppler imaging.

The type of reconstruction of the RV outflow tract is a matter of controversy in the literature. Our surgical approach was in accordance with previous studies[4-6,14] which demonstrated the need for transannular patch

Table 4a: Determinants of myocardial performance index (Univariate analysis)

	Constant	B	*P*	R^2
Time after surgery (years)	0.387	0.011	<0.05	0.148
QRS duration on follow-up (ms)	0.308	0.001	<0.05	0.099
right ventricular end-diastolic area on last follow-up (cm^2)	0.354	0.004	<0.05	0.124
right ventricular end-systolic area on last follow-up (cm^2)	0.352	0.007	<0.05	0.168
Pulmonary regurgitation on follow-up	0.249	0.075	<0.05	0.471

Table 4b: Determinants of myocardial performance index (Multivariate analysis)

	B	Std. error	*P*	R^2
Cardiopulmonary bypass time	0.00	0.00	<0.05	0.8026
Age at surgery (years)	0.01	0.002	<0.001	
Time after surgery (years)	0.02	0.004	<0.001	
QRS duration on last follow-up (ms)	0.00	0.001	<0.05	
RVIDd (mm) on last follow-up	0.00	0.00	<0.005	
RV end-diastolic area on last follow-up (cm^2)	0.01	0.006	<0.05	
RV end-systolic area on last follow-up (cm^2)	-0.02	0.009	<0.05	
RV functional area change on last follow-up (%)	-0.01	0.003	<0.001	
Pulmonary regurgitation on follow-up	0.01	0.00	<0.05	

RVIDd:RV internal dimension at diastole

in approximately 24% of adult patients. Post-operative pulmonary valve insufficiency is common sequela of this approach. And all our patients who have needed transannular patch had free pulmonary regurgitation. Nollert and associates[6] have reported use of a transannular patch to be associated with significantly worse operative and 1-year mortality as compared with those without a transannular patch. The studies on the long-term outcomes of surgical correction of tetralogy in adulthood are limited with respect to interpretation of RV function. Although, postoperative functional class can provide an insight into the status of the RV function, two-dimensional echocardiography traditionally has been inaccurate in assessing the same.

Analysis of RV function using 2D echocardiography is likely to produce unreliable data.[9,10] In the present study we have used RV functional area change as the 2D echocardiography parameter for assessment of RV function. RV functional area change of <32% correlates with RV dysfunction. All our patients were on NYHA functional class I and had sinus rhythm at the time of study. All patients had normal RV function assessed by the 2D echocardiography parameter- RV functional area change. But the RV end-diastolic and RV end-systolic areas were significantly higher in the group who needed transannular patch.

RV function was also assessed by tissue Doppler imaging. The easily obtained and highly reproducible tissue doppler imaging indices clearly discriminated patients with repaired Tetralogy of Fallot from healthy individuals. This shows that repaired TOF patients, even if asymptomatic had RV dysfunction as shown by increased myocardial performance index and decreased myocardial velocities. Moreover, tissue Doppler imaging could unmask the RV dysfunction when 2D imaging showed normal RV functional area change in this patient group.

The extent of RV dysfunction was more in patients who needed a transannular patch. This remarkable decrease in systolic wall motion velocity occurred despite the presence of volume overload in all of our patients, because of the concomitant pulmonary regurgitation.[3,4] The fact that tricuspid annular velocities were decreased in our patients despite volume overload indicates that tissue Doppler imaging of the tricuspid annulus is able to unmask RV dysfunction in this category of patients (all were asymptomatic and had normal RV functional area change). Our results were similar to the results of Stella *et al.*, in which they have shown that patients with repaired Tetralogy of Fallot demonstrated reduced myocardial velocities: Systolic tricuspid annular velocity, Sa, 8.16 ± 1.15 versus 16.43 ± 1.15 cm/sec ($P < 0.001$).

Using both systolic and diastolic intervals during myocardial performance index calculation provides opportunity to assess global RV function.[3,4,15-17] It was shown that in the present study; all patients had asymptomatic RV dysfunction as assessed by tissue Doppler imaging. Ilker Cetin *et al.*, has shown that the myocardial performance index (MPI) (1.08 ± 0.35 vs. 0.58 ± 0.11, $P = 0.0001$) was higher in repaired TOF patients.

Abd El Rahman *et al.*,[18-21] in a study of 51 patients reported correlations between isovolumetric contraction time, isovolumetric relaxation time, and the degree of pulmonary regurgitation.[22,23] In their study, isovolumetric contraction time and isovolumetric relaxation time increased in accordance with the degree of pulmonary regurgitation.

When the determinants of MPI driven RV dysfunction were analysed it was found that age at the time of surgery and time after surgery were the only demographic variables that predicted the MPI. From this we can conclude that higher the age at surgery predicts RV dysfunction on follow-up. This may be attributed to the irreversible changes in the RV compliant properties that may be happening with prolonged RV outflow tract obstruction. Pulmonary regurgitation after surgery has been correlated to abnormal myocardial performance index in this study. The occurrence of free pulmonary regurgitation is increased after transannular patch and this may be the one of the reasons for the asymptomatic RV dysfunction in them.

Changes in the RV compliance due to persistent RV outflow tract obstruction, especially in those who had a surgery at relatively older age and the extend of pulmonary regurgitation after the surgery might have prominent role in the development of RV dysfunction in them, even if it is asymptomatic.

CONCLUSIONS

Subclinical RV dysfunction occurs in surgically repaired TOF patients as shown by decreased myocardial velocities and increased myocardial performance index. The magnitude of asymptomatic RV dysfunction assessed by myocardial performance index was more in patients who needed a transannular patch than those who did not. In patients who had significant pulmonary regurgitation, myocardial performance index was significantly high and systolic tricuspid annular velocity, Sa was significantly low, showing that pulmonary regurgitation is an important determinant of RV dysfunction.

REFERENCES

1. D'Andrea A, Caso P, Sarubbi BL. RV myocardial dysfunction in adult patients late after repair of tetralogy of Fallot. Int J Cardiol 2004;94:213-20.
2. Van Straten A, Vliegen HW, Hazekamp MG. RV function late after total repair of tetralogy of Fallot. Eur Radiol 2005;15:702-7.
3. Giannopoulos NM, Chatzis AC, Bobos DP. Tetralogy of Fallot: Influence of RV outflow tract reconstruction on late outcome. Int J Cardiol2004;97:87-90.
4. Gatzoulis MA, Elliott JT, Guru V. Right and left ventricular systolic function late after repair of tetralogy of Fallot. Am J Cardiol 2000;86:1352-7.
5. Redington AN. Determinants of short and long-term outcome in the surgical correction of tetralogy of Fallot. Curr Opin Pediatr 1993;5:619-22.
6. Maisel AS, Koon J, Krishnaswamy P. Utility of B-natriuretic peptide as a rapid, point-of-care test for screening patients undergoing echocardiography to determine left ventricular dysfunction. Am Heart J 2001;141:367-74.
7. Omland T, Aakvaag A, Vik-Mo H. Plasma cardiac natriuretic peptide determination as a screening test for the detection of patients with mild left ventricular impairment. Heart 1996;76:232-7.
8. Zhao XY, Yang YJ, Zhang J. The clinical value of B-type natriuretic peptide in the diagnosis of left heart failure. Zhonghua Yi Xue Za Zhi 2006;86:1165-9.
9. Ishii M, Eto G, Tei C. Quantitation of the global RV function in children with normal heart and congenital heart disease: A RV myocardial performance index. Pediatr Cardiol 2000;21:416-21.
10. Abd El Rahman MY, Abdul-Khalid H, Vogel M. Value of the new Doppler-derived myocardial performance index for the evaluation of right and left ventricular function following repair of tetralogy of Fallot. Pediatr Cardiol 2002;23:502-7.
11. Meluzin J, Spinarova L, Bakala J, Toman J, Krejci J, Hude P, *et al.* Pulsed Doppler tissue imaging of the velocity of tricuspid annular systolic motion: A new, rapid, and non-invasive method of evaluating RV systolic function. Eur Heart J 2001;22:340-8.
12. Tei C, Dujardin KS, Hodge DO, Bailey KR, McGoon MD, Tajik AJ, *et al.* Doppler echocardiographic index for assessment of global RV function. J Am Soc Echocardiogr 1996;9:838-47.
13. Lind L, Andren B, Arnlov J The Doppler-derived myocardial performance index is determined by both left ventricular systolic and diastolic function as well as by afterload and left ventricular mass. Echocardiography 2005;22:211-6.
14. Erdŏgan HB, Bozbŭga N, Kayalar N. Long-term outcome after total correction of tetralogy of Fallot in adolescent and adult age. J Card Surg2005;20:119-23.
15. Miller D, Farah MG, Liner A. The relation between quantitative RV ejection fraction and indices of tricuspid annular motion and myocardial performance. J Am Soc Echocardiogr 2004;17:443-7.
16. Amorim S, Cruz C, Macedo F. Tetralogy of Fallot: Prognostic factors after surgical repair. Rev Port Cardiol 2005;24:845-55.
17. Bouzas B, Kinler PJ, Gatzoulis MA. Pulmonary regurgitation: Not a benign lesion. Eur Heart J 2005;26:433-9.
18. Davlouros PA, Karatza AA, Gatzoulis MA. Timing and type of surgery for severe pulmonary regurgitation after repair of tetralogy of Fallot. Int J Cardiol 2004;97 Suppl 1:91-101.
19. Lillehei CW, Varco RL, Cohen M, Moller JH. The first open heart corrections of tetralogy of Fallot. A 26–31 year follow-up of 106 patients. Ann Surg 1986;204:490-502.
20. Mahle WT, McBride MG, Paridon SM. Exercise performance in tetralogy of Fallot: The impact of primary complete repair in infancy. Pediatr Cardiol 2002;23:224-9.
21. van Arsdell GS, Maharaj GS, Tom J, Rao VK, Coles JG, Freedom RM, *et al.* What is the optimal age for repair of tetralogy of Fallot? Circulation 2000;102:123-9.
22. Reddy VM, Liddicoat JR, McElhinney DB. Routine primary repair of tetralogy of Fallot in neonates and infants less than three months of age. Ann Thorac Surg 1995;60:S592-6.
23. Oechslin EN, Harrison DA, Harris L, Downar E, Webb GD, Siu SS, *et al.* Reoperation in adults with repair of tetralogy of fallot: Indications and outcomes. J Thorac Cardiovasc Surg 1999;118:245-51.

How to cite this article: Nair KK, Ganapathi S, Sasidharan B, Thajudeen A, Pillai HS, Tharakan J, *et al.* Asymptomatic right ventricular dysfunction in surgically repaired adult tetralogy of fallot patients. Ann Pediatr Card 2013;6:24-8.

Source of Support: Nil, **Conflict of Interest:** None declared