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Original Article

Additional mechanism for left ventricular dysfunction: chronic pulmonary regurgitation decreases left ventricular preload in patients with tetralogy of Fallot

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Abstract *Background:* Right ventricular dysfunction in patients with tetralogy of Fallot and significant pulmonary regurgitation may lead to systolic dysfunction of the left ventricle due to altered ventricular interaction. We were interested in determining whether chronic pulmonary regurgitation affects the preload of the left ventricle. In addition, we wanted to study whether severe chronic pulmonary regurgitation would alter the preload of the left ventricle when compared with patients having preserved pulmonary valve annulus. *Methods:* The study group comprised 38 patients with tetralogy of Fallot who underwent surgical repair between 1990 and 2003. Transannular patching was required in 21 patients to reconstruct the right ventricular outflow tract. Altogether, 48 age- and gender-matched healthy volunteers were recruited. Cardiac MRI was performed on all study patients to assess the atrial and ventricular volumes and function. *Results:* Severe pulmonary regurgitation (>30 ml/m^2) was present in 13 patients, of whom 11 had a transannular patch, but only two had a preserved pulmonary valve annulus. The ventricular preload volumes from both atria were significantly reduced in patients with severe pulmonary regurgitation, and left ventricular stroke volumes (44.1 ± 4.7 versus 58.9 ± 10.7 ml/m^2; $p < 0.0001$) were smaller compared with that in patients with pulmonary regurgitation <30 ml/m^2 or in controls. *Conclusions:* In patients with tetralogy of Fallot, severe pulmonary regurgitation has a significant effect on volume flow through the left atrium. Reduction in left ventricular preload volume may be an additional factor contributing to left ventricular dysfunction.

Keywords: Tetralogy of Fallot; pulmonary regurgitation; left ventricular preload; transannular patch

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Surgical treatment of tetralogy of Fallot has led to a growing number of adolescents and adults with cardiac defects. In the long term, these patients may demonstrate progressive pulmonary regurgitation with right ventricular dilation and dysfunction, which are known to be important determinants of their late outcome.[1–4] Impaired exercise tolerance, ventricular arrhythmia, and sudden death have all been reported as secondary complications of pulmonary regurgitation.[5–7] Left ventricular dysfunction has been reported to be present as a late sequel in 20% of tetralogy of Fallot patients.[8] On the other hand, patients with normal right ventricular ejection fraction were more likely to have normal left ventricular function.[8]

This concomitant dysfunction of the left heart appears to increase heart failure and mortality in these patients.[3,8–10] The reasons for left ventricular dysfunction in patients with tetralogy of Fallot have been under active examination. In one study, left ventricular dysfunction was shown to be affected by preoperative hypoxaemia.[11] Other possible causes are electromechanical asynchrony, shared septal myocardial fibres, the effect of ventricular septal defect, and adverse

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impact of the septal shift.[12–14] Our hypothesis was that, in postoperative patients of tetralogy of Fallot, severe chronic pulmonary regurgitation impedes the transpulmonary flow, which, by disturbing the preloading of the left ventricle, may be an additional factor affecting left ventricular performance.

Methods

The study group comprised 38 patients who had undergone surgical repair of tetralogy of Fallot between 1990 and 2003. The patients were referred for cardiac magnetic resonance by a paediatric cardiologist because their echocardiographic findings suggested significant pulmonary regurgitation and increased right ventricular size. The patients had undergone surgical correction for tetralogy of Fallot at the age of 1.3 years (with a range from 0.2 to 4.6). The postoperative follow-up period was 11.6 ± 2.9 years (with a range from 7.2 to 18.4 years). A transannular patch was used in 24 (53%) patients. In 17 patients, pulmonary valve annulus could be preserved at the primary repair. All corrective operations were performed on cardiopulmonary bypass with an aortic cross-clamp. The myocardium was protected with cold-blood cardioplegia. Table 1 summarises the baseline characteristics of patients with tetralogy of Fallot and those of healthy controls. There were no time-related trends in surgical techniques during the operative period from 1990 to 2003.

Postoperatively, 11 of our patients with a transannular patch had severe (>30 ml/m^2) pulmonary regurgitation (mean 30.8 ml/m^2 ± 10.2; range 16.7–59.4). Patients with preserved pulmonary valve annulus (15 patients) had mostly non-severe pulmonary regurgitation (mean 9.8 ml/m^2 ± 10.3; range 0–31.8) and only two patients had pulmonary regurgitation exceeding 30 ml/m^2. In controls, pulmonary regurgitation was negligible.

For the control group, 48 healthy age- and gender-matched paediatric and adolescent volunteers were recruited. They were eligible for the study if they had no medical history of any cardiovascular disease and no other pre-existing condition that would affect the cardiovascular system. An electrocardiogram was recorded and a paediatric cardiologist performed a morphological ultrasound to exclude possible latent cardiac problems.

Cardiac magnetic resonance was performed for all patients and controls. Cardiac MRI were obtained with a 1.5 Tesla Philips Achieva imager (Philips Healthcare, Amsterdam, The Netherlands) using a 5-channel cardiac coil. For right ventricular volume analysis, transaxial and left ventricle short-axis balanced turbo-field echo breath-hold cine images were obtained for the whole heart. The slice thickness was 5–8 mm depending on the patient's size, gap was 20%, and temporal resolution was 26–43 ms. For the ventricular volume measurements, both transaxial and left ventricular short-axis cine images were manually planimetered using the cardiac analysis tool of a Philips ViewForum workstation (Philips Healthcare, Amsterdam, The Netherlands). The pulmonary valve regurgitation fraction was calculated from volumetric measurements of both ventricles. The amount of tricuspid regurgitation was nonexistent or minimal in the controls, and it was minimal (n = 4) or mild (n = 40) within the patients.

For the atrial volume measurements, transaxial cine images were manually planimetered as described earlier.[15,16] Atrial volumetric measurements were used to calculate the cyclic volume change using the following formula: volume max – volume min. Conduit volume, which refers to diastolic blood flow to the chambers while the atrial pump remains passive, was assessed by subtracting cyclic volume change from the left ventricular stroke volume. The combined preload volumes from the atria for each ventricle were calculated by adding the cyclic volume change to conduit volume. Intraobserver variability was tested using the Bland–Altman method. The mean difference between two observations was

Table 1. Characteristics of the study population.

	Patients	Controls	p
n	38	48	
Male [n (%)]	23 (61%)	27 (56%)	–
Age (years)	12.9 ± 3.2	13.8 ± 3.4	ns
Age at TOF repair (years)	1.3 ± 1.3	–	–
Follow-up time from TOF repair (years)	11.8 ± 3.1	–	–
Weight (kg)	42.7 ± 14.7	50.5 ± 15.8	0.02
Height (cm)	152.2 ± 15.4	159.4 ± 16.2	0.03
Body surface area (m^2)	1.3 ± 0.3	1.5 ± 0.3	0.02
Plasma level of proBNP (ng/L)	152.8 ± 84.4	53.4 ± 36.2	<0.0001
Pulmonary regurgitation (ml/m^2)	24.2 ± 15.3	–	–
Aortic regurgitation (ml/m^2)	0.64 ± 1.3	–	–

proBNP = pro B-type natriuretic peptide; TOF = tetralogy of Fallot

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−1.7 ml with a standard deviation of 3.1 ml in right atrium and −1.2 ± 2.9 ml in left atrium.

Statistical analysis was performed using GraphPad Prism 5.0a (GraphPad Software, Inc., San Diego, California, United States of America). All results are reported as means and SD. Comparisons of continuous data between the groups were performed using an unpaired t-test. Correlations were calculated using linear regression. A two-tailed p-value of less than 0.05 was considered statistically significant.

The Ethics Committee of our hospital approved the study. Written informed consent was obtained from all participants and/or their parents.

Results

All patients in our study had pulmonary regurgitation. Pulmonary regurgitation was severe (>30 ml/m^2) in 13 patients (34%), of whom 11 had a transannular patch. In order to study the impact of pulmonary regurgitation on left ventricular preloading, left ventricular systolic function, and right ventricular volume and function, we compared these 13 patients with patients having non-severe regurgitation (n = 25) and with controls.

In tetralogy of Fallot patients, the maximum volume and cyclic volume change in the left atrium were significantly smaller than those in controls (Table 2). In addition, the conduit volumes were smaller in patients with severe pulmonary regurgitation, leading to diminished left ventricular preload volume. Consistently, these patients also had significantly smaller left ventricular end-diastolic volume, left ventricular stroke volume, and ejection fraction compared with controls. In comparison with controls, patients with non-severe regurgitation despite smaller left atrial cyclic volume change had similar conduit volumes and there was no significant difference in left ventricular preloading. Accordingly, the left ventricular end-diastolic volume, left ventricular stroke volume, and ejection fraction of these patients were similar to those of controls (Table 2).

In all patients with tetralogy of Fallot, the maximum volumes of the right atria were comparable to those of controls; however, the right atrial minimum volumes were increased in patients with tetralogy of Fallot, resulting in a reduced cyclic volume change (Table 3). The indexed right ventricular end-diastolic and end-systolic volumes of tetralogy of Fallot patients were significantly larger than those of controls, and the largest volumes were encountered in patients with severe pulmonary regurgitation (150.1 ± 22.0 ml/m^2 and 85.5 ± 27.8 ml/m^2). The right ventricular atrial preload was decreased in patients with severe pulmonary regurgitation compared with that in patients with non-severe pulmonary regurgitation (Table 3).

As the vast majority of patients with severe pulmonary regurgitation had undergone transannular patching, the patient material was divided according to the surgical method.

In comparison with controls, patients with a transannular patch had smaller left atrial maximum, cyclic, and conduit volumes, smaller left ventricular end-diastolic volume, smaller left ventricular stroke volume, and a smaller ejection fraction (Table 4). On the other hand, in patients with preserved pulmonary valve annulus, there was no difference in left ventricular preloading compared with that in controls. In patients with a transannular patch, the indexed right ventricular end-diastolic and end-systolic volumes (142.2 ± 20.2 ml/m^2 and 63.2 ± 15.3 ml/m^2, respectively) were significantly larger than those in controls. Consistently, in patients with a transannular

Table 2. The indexed volumes and function of left atrium and ventricle in patients and controls.

	Patients with PR > 30 ml/m^2 (n = 13)	Patients with PR ⩽ 30 ml/m^2 (n = 25)	Controls (n = 48)	p value (PR ⩽ 30 versus PR > 30)	p value (PR > 30 versus controls)	p value (PR ⩽ 30 versus controls)
Left atrium						
Minimum volume (ml/m^2)	17.7 ± 5.7	19.4 ± 6.6	22.2 ± 6.4	ns	0.04	ns
Maximum volume (ml/m^2)	40.3 ± 8.0	41.5 ± 9.5	48.5 ± 9.8	ns	0.01	0.008
Cyclic volume change (ml/m^2)	22.6 ± 4.7	22.0 ± 5.9	26.4 ± 5.1	ns	0.02	0.002
Conduit volume (ml/m^2)	22.3 ± 4.6	32.3 ± 9.4	32.7 ± 9.4	0.008	0.0003	ns
Left ventricle						
Ventricle preload from atria (ml/m^2)	44.1 ± 4.7	53.6 ± 8.8	58.9 ± 10.7	0.001	<0.0001	ns
Ventricle preload from AR (ml/m^2)	0.8 ± 1.3	0.7 ± 1.5	0	ns	ns	ns
End-diastolic volume (ml/m^2)	80.8 ± 8.5	90.9 ± 18.9	94.6 ± 15.9	ns	0.004	ns
End-systolic volume (ml/m^2)	35.9 ± 5.7	39.6 ± 9.6	35.7 ± 9.2	ns	ns	ns
Stroke volume (ml/m^2)	44.1 ± 4.7	53.6 ± 8.8	58.9 ± 10.7	0.0004	<0.0001	ns
Ejection fraction (%)	57.7 ± 5.8	59.3 ± 6.9	62.7 ± 6.9	ns	0.0008	ns

AR = aortic regurgitation; PR = pulmonary regurgitation

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Table 3. The indexed volumes and function of right atrium and ventricle in patients and controls.

	Patients with PR > 30 ml/m^2 (n = 13)	Patients with PR ⩽ 30 ml/m^2 (n = 25)	Controls (n = 48)	p value (PR ⩽ 30 versus PR > 30)	p value (PR > 30 versus controls)	p value (PR ⩽ 30 versus controls)
Right atrium						
Minimum volume (ml/m^2)	40.3 ± 11.5	37.5 ± 9.6	30.0 ± 10.5	ns	0.003	<0.0001
Maximum volume (ml/m^2)	60.7 ± 12.5	56.7 ± 10.6	60.3 ± 14.9	ns	ns	ns
Cyclic volume change (ml/m^2)	20.4 ± 4.4	19.2 ± 4.4	30.3 ± 7.4	ns	<0.0001	<0.0001
Conduit volume (ml/m^2)	27.7 ± 7.8	35.9 ± 6.9	29.3 ± 9.9	0.0014	ns	0.04
Right ventricle						
Ventricle preload from atria (ml/m^2)	44.9 ± 4.3	54.3 ± 8.0	58.9 ± 10.7	0.0004	<0.0001	ns
Ventricle preload from PR (ml/m^2)	37.0 ± 7.9	14.2 ± 10.6	1.2 ± 4.6	<0.0001	<0.0001	<0.0001
End-diastolic volume (ml/m^2)	150.1 ± 22.0	126.3 ± 21.7	102.0 ± 17.1	<0.0001	<0.0001	0.0004
End-systolic volume (ml/m^2)	85.5 ± 27.8	57.9 ± 15.9	43.1 ± 14.5	<0.0001	<0.0001	0.0001
Stroke volume (ml/m^2)	81.9 ± 10.8	68.4 ± 10.8	60.1 ± 10.8	0.0004	<0.0001	0.002
Ejection fraction (%)	55.4 ± 8.0	54.8 ± 5.5	59.2 ± 6.1	ns	ns	ns

PR = pulmonary valve regurgitation

patch, the right ventricular atrial preload was smaller than that in patients with a preserved pulmonary valve annulus. In fact, the right ventricular atrial preload of patients with preserved pulmonary valve annulus was similar to that of controls (Table 4).

Discussion

Our study shows that patients with tetralogy of Fallot and severe chronic pulmonary regurgitation have abnormal filling of the left ventricle resulting in smaller left ventricular end-diastolic and stroke volumes. The left atrial maximum volumes, cycling volume changes, and conduit volumes of our patients were smaller in comparison with those of controls. We propose that a significant pulmonary regurgitation among postoperative patients with tetralogy of Fallot results in reduced transpulmonary flow, affecting the left ventricular preloading, which may impede ventricular interaction and induce left ventricular dysfunction.

In the postoperative phase of repaired tetralogy of Fallot, chronic pulmonary regurgitation causes profuse diastolic filling of the right ventricle with dilation.[17,18] In these patients, despite normal right ventricular and left ventricular ejection fractions measured with ultrasound, disturbed postoperative pathophysiology can be teased out by exercise to demonstrate the defective contractile reserve of the left ventricle.[19] Marked pulmonary regurgitation and right ventricular dilation have recently been described to affect the left ventricle early-diastolic radial and circumferential strain rates,[17] and myocardial deformation imaging has demonstrated reduction in left ventricular systolic indices even in patients with preserved left ventricular ejection fraction.[20,21] Accordingly, as many as 20% of late survivors of tetralogy of Fallot develop a concurrent left ventricular dysfunction, making it an important factor in the patient's late outcome.[8] An important finding of the present study is that, despite successful surgical repair carried out in our patients with tetralogy of Fallot, left atrial function was impaired. This was especially remarkable in patients with severe pulmonary regurgitation in whom florid regurgitation was associated with defective atrial filling and left ventricular diastolic function due to reduced transpulmonary flow. In other recent studies on patients with CHD, similar changes in left ventricular filling have been linked to chronic reduction in left ventricular diastolic performance despite corrective surgery, suggesting that prenatal and postnatal haemodynamic factors present before the surgery may affect the left atrial filling and the left ventricular preload.[22] We have demonstrated that left ventricular preload volume is defective in tetralogy of Fallot, which may be an important factor, in addition to the substantial pulmonary regurgitation, contributing to disturbed ventricular interaction and the consequent dysfunction and reduction in the reserves of the left ventricle.

Finally, it is noteworthy that severe pulmonary regurgitation, disturbed left atrial function, and filling of the left ventricle were encountered especially in patients with a transannular patch compared with patients with preserved pulmonary valve annulus and controls.[23–27]

To allow proper postoperative remodelling of the enlarged right ventricle, intervention to correct pulmonary regurgitation is considered appropriate when the right ventricle has dilated up to 150 ml/m^2, even in patients without symptoms. Interestingly, despite gains in exercise tolerance and NYHA functional class after pulmonary valve replacement following repair of tetralogy of Fallot,[23,24] objective improvements in systolic and diastolic function of both ventricles have

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Table 4. The volume and function of left and right atria and ventricles of patients with transannular patch (TAP), patients with preserved pulmonary valve annulus (PPVA), and healthy controls.

	Patients with TAP (n = 21)	Patients with PPVA (n = 17)	Controls (n = 48)	p value (TAP versus PPVA)	p value (TAP versus controls)	p value (PPVA versus controls)
Left atrium						
Minimum volume (ml/m^2)	17.1 ± 5.2	20.6 ± 7.1	22.2 ± 6.4	ns	0.005	ns
Maximum volume (ml/m^2)	39.7 ± 7.7	42.0 ± 10.7	48.5 ± 9.8	ns	0.001	0.04
Cyclic volume change (ml/m^2)	22.6 ± 5.8	21.4 ± 5.5	26.4 ± 5.1	ns	0.01	0.001
Conduit volume (ml/m^2)	25.6 ± 9.5	33.7 ± 6.2	32.7 ± 9.4	0.005	0.005	ns
Left ventricle						
Ventricle preload from atria (ml/m^2)	47.2 ± 8.2	54.8 ± 7.5	58.9 ± 10.7	0.005	<0.0001	ns
Ventricle preload from AR (ml/m^2)	1.0 ± 1.6	0.3 ± 1.1	0	ns	ns	ns
End-diastolic volume (ml/m^2)	82.5 ± 18.9	93.5 ± 11.2	94.6 ± 15.9	0.04	0.008	ns
End-systolic volume (ml/m^2)	37.9 ± 7.8	38.4 ± 9.8	35.7 ± 9.2	ns	ns	ns
Stroke volume (ml/m^2)	48.2 ± 7.4	55.1 ± 7.1	58.9 ± 10.7	0.006	<0.0001	ns
Ejection fraction (%)	57.7 ± 5.8	59.3 ± 6.9	62.7 ± 6.9	ns	0.004	ns
Right atrium						
Minimum volume (ml/m^2)	40.3 ± 11.5	37.5 ± 9.6	30.0 ± 10.5	ns	0.0001	0.004
Maximum volume (ml/m^2)	60.7 ± 12.5	56.7 ± 10.6	60.3 ± 14.9	ns	ns	ns
Cyclic volume change (ml/m^2)	20.4 ± 4.4	19.2 ± 4.4	30.3 ± 7.4	ns	<0.0001	<0.0001
Conduit volume (ml/m^2)	27.7 ± 7.8	35.9 ± 6.9	29.3 ± 9.9	0.002	ns	0.01
Right ventricle						
Ventricle preload from atria (ml/m^2)	48.2 ± 7.4	55.1 ± 7.1	58.9 ± 10.7	0.006	<0.0001	ns
Ventricle preload from PR (ml/m^2)	30.8 ± 10.2	9.8 ± 10.3	1.2 ± 4.6	<0.0001	<0.0001	<0.0001
End-diastolic volume (ml/m^2)	142.2 ± 20.2	121.7 ± 22.8	102.0 ± 17.1	0.006	<0.0001	0.0004
End-systolic volume (ml/m^2)	63.2 ± 15.3	56.74 ± 17.5	43.1 ± 14.5	ns	<0.0001	0.003
Stroke volume (ml/m^2)	79.0 ± 10.8	64.9 ± 8.5	60.1 ± 10.8	0.0001	<0.0001	ns
Ejection fraction (%)	56.2 ± 5.8	54.0 ± 6.2	59.2 ±6.1	ns	ns	0.004

AR = aortic regurgitation; PR = pulmonary regurgitation

not been uniformly demonstrated.[25–27] It would be important to find out whether pulmonary valve replacement in addition to correcting the preloading of the right ventricle has a beneficial effect on left ventricular preloading.

Conclusions

In patients with tetralogy of Fallot, transpulmonary flow is affected by an abundant pulmonary regurgitation, leading to volume impediment of the left atrial filling and defective left ventricular preload volume. Our observation may be an important additional mechanism contributing to disturbed ventricular interaction causing dysfunction and reducing the reserves of the left ventricle.

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Conflicts of Interest

None.

References

1. Redington AN. Determinants and assessment of pulmonary regurgitation in tetralogy of Fallot: practice and pitfalls. Cardiol Clin 2006; 24: 631–639; vii.
2. Owen AR, Gatzoulis MA. Tetralogy of Fallot: late outcome after repair and surgical implications. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2000; 3: 216–226.
3. Geva T, Sandweiss BM, Gauvreau K, et al. Factors associated with impaired clinical status in long-term survivors of tetralogy of Fallot repair evaluated by magnetic resonance imaging. J Am Coll Cardiol 2004; 43: 1068–1074.
4. Therrien J, Marx GR, Gatzoulis MA. Late problems in tetralogy of Fallot – recognition, management, and prevention. Cardiol Clin 2002; 20: 395–404.
5. Wessel HU, Cunningham WJ, Paul MH, et al. Exercise performance in tetralogy of Fallot after intracardiac repair. J Thorac Cardiovasc Surg 1980; 80: 582–593.

6. Rowe SA, Zahka KG, Manolio TA, et al. Lung function and pulmonary regurgitation limit exercise capacity in postoperative tetralogy of Fallot. J Am Coll Cardiol 1991; 17: 461–466.
7. Gatzoulis MA, Balaji S, Webber SA, et al. Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot: a multicentre study. Lancet 2000; 356: 975–981.
8. Broberg CS, Aboulhosn J, Mongeon FP, et al. Prevalence of left ventricular systolic dysfunction in adults with repaired tetralogy of fallot. Am J Cardiol 2011; 107: 1215–1220.
9. Ghai A, Silversides C, Harris L, et al. Left ventricular dysfunction is a risk factor for sudden cardiac death in adults late after repair of tetralogy of Fallot. J Am Coll Cardiol 2002; 40: 1675–1680.
10. Knauth AL, Gauvreau K, Powell AJ, et al. Ventricular size and function assessed by cardiac MRI predict major adverse clinical outcomes late after tetralogy of Fallot repair. Heart 2008; 94: 211–216.
11. Hausdorf G, Hinrichs C, Nienaber CA, et al. Left ventricular contractile state after surgical correction of tetralogy of Fallot: risk factors for late left ventricular dysfunction. Pediatr Cardiol 1990; 11: 61–68.
12. Helbing WA, Roest AA, Niezen RA, et al. ECG predictors of ventricular arrhythmias and biventricular size and wall mass in tetralogy of Fallot with pulmonary regurgitation. Heart 2002; 88: 515–519.
13. Anderson RH, Ho SY, Redmann K, et al. The anatomical arrangement of the myocardial cells making up the ventricular mass. Eur J Cardiothorac Surg 2005; 28: 517–525.
14. Weyman AE, Wann S, Feigenbaum H, et al. Mechanism of abnormal septal motion in patients with right ventricular volume overload: a cross-sectional echocardiographic study. Circulation 1976; 54: 179–186.
15. Jarvinen VM, Kupari MM, Poutanen VP, et al. A simplified method for the determination of left atrial size and function using cine magnetic resonance imaging. Magn Reson Imaging 1996; 14: 215–226.
16. Jarvinen VM, Kupari MM, Poutanen VP, et al. Right and left atrial phasic volumetric function in mildly symptomatic dilated and hypertrophic cardiomyopathy: cine MR imaging assessment. Radiology 1996; 198: 487–495.
17. Friedberg MK, Fernandes FP, Roche SL, et al. Impaired right and left ventricular diastolic myocardial mechanics and filling in asymptomatic children and adolescents after repair of tetralogy of Fallot. Eur Heart J Cardiovasc Imaging 2012; 13: 905–913.
18. Tobler D, Crean AM, Redington AN, et al. The left heart after pulmonary valve replacement in adults late after tetralogy of Fallot repair. Int J Cardiol 2012; 160: 165–170.
19. Roche SL, Grosse-Wortmann L, Friedberg MK, et al. Exercise echocardiography demonstrates biventricular systolic dysfunction and reveals decreased left ventricular contractile reserve in children after tetralogy of Fallot repair. J Am Soc Echocardiogr 2015; 28: 294–301.
20. Nakamura A, Horigome H, Seo Y, et al. Right ventricular remodeling due to pulmonary regurgitation is associated with reduced left ventricular free wall strain in surgically repaired tetralogy of fallot. Circ J 2014; 78: 1960–1966.
21. Kempny A, Fernandez-Jimenez R, Orwat S, et al. Quantification of biventricular myocardial function using cardiac magnetic resonance feature tracking, endocardial border delineation and echocardiographic speckle tracking in patients with repaired tetralogy of Fallot and healthy controls. J Cardiovasc Magn Reson 2012; 31: 14–32.
22. Marcondes LD, Galati JC, Jones BO, et al. Abnormal left ventricular diastolic function at late follow-up after repair of total anomalous pulmonary venous drainage: the impact of altered ventricular loading in utero. J Thorac Cardiovasc Surg 2014; 148: 238–244.
23. Frigiola ATV, Bull C, Coats L, et al. Biventricular response after pulmonary valve replacement for right ventricular outflow tract dysfunction: is age a predictor of outcome? Circulation 2008; 118: 182–190.
24. Discigil BDJ, Puga FJ, Schaff HV, et al. Late pulmonary valve replacement after repair of tetralogy of Fallot. J Thorac Cardiovasc Surg 2001; 121: 344–351.
25. Warner KG, O'Brien PK, Rhodes J, et al. Expanding the indications for pulmonary valve replacement after repair of tetralogy of fallot. Ann Thorac Surg 2003; 76: 1066–1071.
26. Eyskens BRT, Bogaert J, Dymarkowsky S, et al. Homograft insertion for pulmonary regurgitation after repair of tetralogy of fallot improves cardiorespiratory exercise performance. Am J Cardiol 2000; 85: 221–225.
27. Ghez OTV, Frigiola A, Coats L, et al. Right ventricular outflow tract reconstruction for pulmonary regurgitation after repair of tetralogy of Fallot. Preliminary results. Eur J Cardiothorac Surg 2007; 31: 654–658.