Optimal timing of pulmonary valve replacement in tetralogy of Fallot

Straten, A. van

7

Time Course of Diastolic and Systolic Function Improvement after Pulmonary Valve Replacement in Adult Patients with Tetralogy of Fallot

A van Straten

HW Vliegen

HJ Lamb

SD Roes

EE van der Wall

MG Hazekamp

A de Roos

J Am Coll Cardiol. 200;46:1559-64

Abstract

Background

To assess right ventricular diastolic and systolic function before and after pulmonary valve replacement (PVR) in adult patients after repair of tetralogy of Fallot.

Background: Pulmonary valve replacement (PVR) in adult patients late after repair of tetralogy of Fallot leads to rapid improvement of right ventricular systolic function.

Methods

Sixteen patients and 8 healthy subjects were included. Median age at initial repair was 4.9 (0.9 - 13.1) years and mean age at PVR was 28.7 (19.5 – 45.6) years. Cardiac magnetic resonance imaging was performed before and 8 and 22 months after PVR. Right ventricular volumes and function as well as RV in- and outflow patterns were assessed.

Results

The volume of the early filling of the right ventricle (Evol) increased from 49.8±14.7 ml to 53.8±19.3 ml (not significant) and 62.0±18.9 ml respectively ($P<0.05$), while the volume of the atrial contraction (Avol) remained unchanged. Consequently the Evol/Avol ratio increased from 1.4±0.7 before PVR to 1.6±0.7 (not significant) and 2.3±1.2 at 22 months ($P<0.01$). The Evol/Avol ratio was not significantly different from the healthy subjects at 22 months, indicating late recovery of diastolic function. Systolic function improved rapidly after PVR; the indexed RV end-systolic volume decreased from 93.7±33.0 to 60.9±18.4ml ($P<0.01$) and 54.8±21.0ml ($P<0.01$).

Conclusion

In adult patients late after total repair of Fallot, PVR leads to late improvement of diastolic function. We speculate that the rapid volume unloading after PVR increases systolic performance, whereas improvement in diastolic function requires long-term remodeling.

Introduction

Longstanding pulmonary regurgitation (PR) after total repair of tetralogy of Fallot in infancy is frequently encountered and may lead to enlargement of the right ventricle [1-4] and consequently deterioration of systolic and diastolic function [3-7]. This right ventricular failure may ultimately require replacement of the pulmonary valve. Evaluation of the haemodynamic effects of pulmonary valve replacement (PVR) in patients with severe PR has shown that volume unloading of the right ventricle leads to a rapid improvement of systolic function [8-11].

Recent studies on right ventricular diastolic function in Fallot patients using cardiac magnetic resonance imaging have revealed that impaired relaxation and restriction of the right ventricle are relatively common findings in the long-term follow-up [6,7]. However, the haemodynamic effects of PVR on right ventricular diastolic function in Fallot patients have not been studied previously. Lamb et al. found a short-term deterioration of left ventricular diastolic function following aortic valve replacement for aortic regurgitation [12]. The authors speculated that concentric remodeling of the left ventricle after rapid volume unloading leads to a relatively increased hypertrophy and consequently deterioration of ventricular stiffness and relaxation disturbances. However, the late effects of aortic valve replacement on left ventricular diastolic function are largely unknown. In analogy to these observations in patients after aortic valve surgery, similar changes might be expected for the right ventricle after PVR.

Accordingly, the purpose of this study was to assess the time course of changes in right ventricular diastolic and systolic function in the short-term and mid-term follow-up after PVR in patients late after repair of Fallot.

Methods

Study group

Sixteen patients with repaired tetralogy of Fallot and 8 healthy subjects were studied. All patients underwent cardiac magnetic resonance examinations before and 7.9 ± 2.0 and 21.7 ± 3.6 months after PVR. The characteristics of patients and healthy subjects are

listed in table 7.1. Median age at total repair was 4.9 years (range 0.9 to 13.1 years). Four patients (25%) had received a trans-annular patch during initial repair and 7 patients (43.8 %) had undergone palliation before primary repair. This study has been approved by the local medical ethical committee and informed consent was obtained from all patients. The present study group is a subset of the cohort studied before [8,13].

Table 7.1. *Baseline and surgical characteristics of patients and healthy subjects.*

Variables Characteristics (n (%))	**NRPR group** **N=14**	**RPR group** **N=11**
Gender (male)	8 (32%)	7 (28%)
Previous palliation	7 (28%)	4 (16%)
Total repair		
RV patch	3 (12%)	3 (12%)
Transannular patch	5 (20%)	4 (16%)
Arrhythmias	4 (16%)	1 (4%)
QRS duration >180 msec	3 (12%)	4 (16%)
Pulmonary stenosis	2 (8%)	3 (12%)
NYHA (mean ± SD)	2.0 ± 0.7	2.0 ± 0.6
Age at repair (median, range)	5.0 (1.8 – 21.0)	4.9 (2.0 – 9.2)
Age at PVR (median, range)	32.8 (18.4 – 45.6)	25.0 (17.0 – 42.1)

Surgical procedures

The mean age at the time of PVR was 28.7 years (range 19.5 to 45.6 years). All patients were operated using a median sternotomy with normothermic or moderately hypothermic cardiopulmonary bypass. Pulmonary valves were inserted on the beating heart. Cannulation of femoral vessels was performed if considered necessary. The proximal pulmonary artery was longitudinally opened and the incision was slightly extended across the former pulmonary annulus if necessary. Cryopreserved pulmonary homografts were used in all patients and inserted in the orthotopic pulmonary position with one proximal and one distal end-to-end running suture. Calcified outflow tract patch material was

resected as much as possible. Additional procedures performed during the same session are listed in table 7.1.

Magnetic Resonance Imaging

MRI studies were performed with a 1.5 Tesla system (NT15 Gyroscan, Philips Medical Systems, Best, the Netherlands), according to our clinical protocol. A multiphase, ECG triggered, multishot echoplanar gradient echo (GRE) technique was used to acquire short axis images. Images were acquired during breath holds, each lasting 10 to 15 seconds. The scout images were used to acquire 10-12 sections that covered both ventricles in the transverse plane; slice thickness was 10 mm with a 0.8-1.0-mm section gap. The flip angle was 30°, and the echo time was 5-10 msec. Eighteen to 25 frames resulted in a temporal resolution of 22-35 msec. Velocity mapping was performed with the use of a velocity-encoded phase contrast sequence. Section thickness was 8 mm, the flip angle was 20°, and the echo time was 12 msec. For velocity mapping of the pulmonary artery a plane perpendicular to the vessel was used. Pulmonary flow measurements were performed halfway between the pulmonary valve and the bifurcation. The sequence was encoded for through-plane velocities up to 200 cm/s. A temporal resolution of 25-35 msec was achieved. The MR examinations lasted 45-60 minutes. No sedation was used in any of the patients.

Post-processing

The studies were quantitatively analyzed on a Solaris workstation (SUN Microsystems Inc., Mountain View, California USA), using FLOW and MASS software packages which were developed at our institution. All contours were drawn manually. The inter- and intraobserver variability is well documented [14,15]. The FLOW analytical software package was used to analyze the velocity maps [16] (Figure 7.1).

A region of interest was manually traced along the inner borders of the tricuspid orifice or pulmonary artery wall in each time frame during the cardiac cycle, by the same observer. For every time frame, spatial averages and spatial maximum flow velocity within the region of interest were automatically measured by a computer algorithm. The instantaneous volume flow was calculated by multiplying the region of interest area and spatial average flow velocity. Pulmonary regurgitant fraction was calculated by the formula: (regurgitant flow / systolic forward flow) * 100. The presence of end-diastolic

forward flow in the main pulmonary artery (EDFF), a marker for restriction of the right ventricle, was noted and EDFF volume was calculated. Flow versus time curves of the tricuspid flow were analyzed using Microsoft Excel (version 2000) for the following parameters of diastolic function: E peak filling rate (Epfr), A peak filling rate (Apfr), E/A peak flow ratio, E wave volume (Evol), A wave volume (Avol), Evol/Avol ratio. The Evol and Avol were calculated by integration of the flow curves.

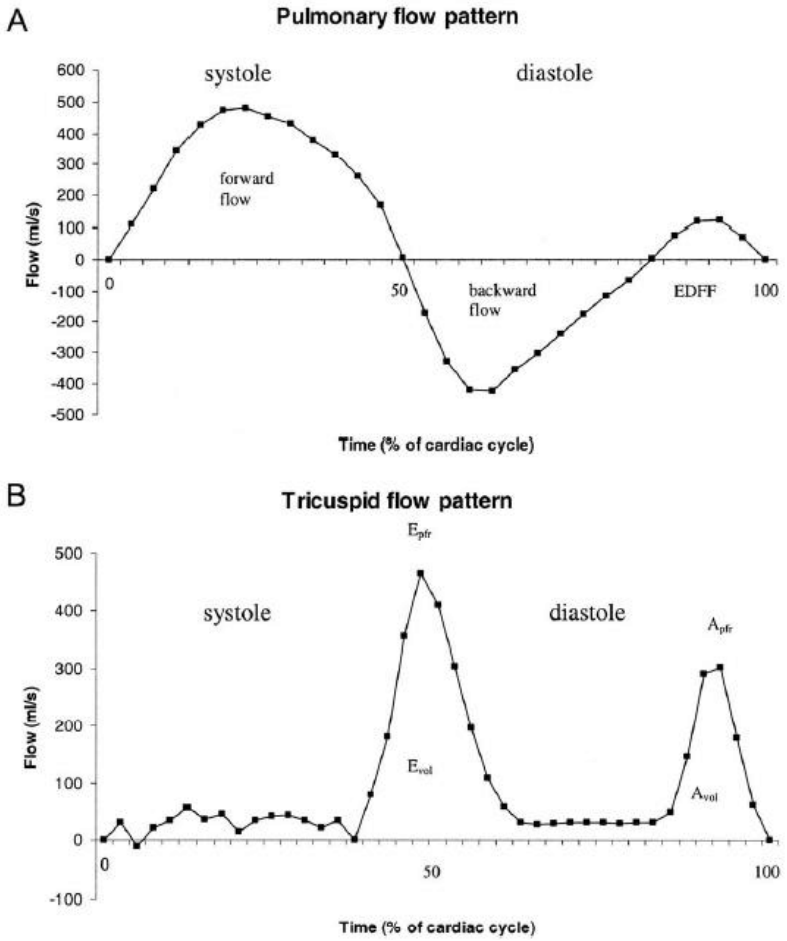

Figure 7.1. *Examples of flow curves of blood flow through pulmonary* ***(A)*** *and tricuspid* ***(B)*** *valve. The pulmonary flow curve shows severe pulmonary regurgitation and a small amount of end-diastolic forward flow in the main pulmonary artery (EDFF), the latter being a marker of restriction of the right ventricle. The tricuspid flow curve shows a normal flow pattern with the early filling, peak flow rate (E_{pfr}), slightly higher than the atrial contraction, peak flow rate (A_{pfr}), and no tricuspid regurgitation. A_{vol} = atrial contraction, volume; E_{vol} = early filling, volume.*

The short axis gradient echo sequences of the ventricles were analyzed using the MASS software package [16]. The endocardial contours were manually drawn in the images of all slices of the end-diastolic and end-systolic phase. Right ventricular end-diastolic volumes indexed for body surface area (BSA) according tot the Haycock formula (BSA (m^2) = Wt (kg) 0.5378 x Ht (cm) 0.3964 x 0.024265) (RV-EDV-I) and right ventricular end-systolic volumes indexed for body surface area (RV-ESV-I) were measured. Stroke volume and right ventricular ejection fraction were calculated from the end-diastolic and end-systolic volumes of the right ventricle. The ejection fraction corrected for regurgitation was calculated by dividing the net pulmonary flow (forward flow minus diastolic regurgitant flow) by the RV-EDV-I.

Statistical Analysis

The SPSS for Windows Software (version 10.0, SPSS, Chicago, Illinois) was used for data analysis. Data are expressed as mean ± standard deviation unless otherwise stated. We used a linear mixed model analysis with LSD criterion for post-hoc comparisons for all MRI parameters on 8 respectively 22 months versus baseline (pre-PVR). Predicted values scatter plots showed no conspicuous deviation from the usual distribution assumptions (e.g. normality). P values of less than 0.05 were considered statistically significant.

Table 7.2. *Right Ventricular Function Before and After Pulmonary Valve Replacement*

	baseline		**7 months**		**19 months**	
MRI	**NRPR group N=14**	**RPR group N=11**	**NRPR group N=14**	**RPR group N=11**	**NRPR group N=14**	**RPR group N=11**
PR (%)	47.9±11.3‡	41.9±8.5‡	0.8±2.2‡*	8.6±10.3‡§*	0.1±0.5*	15.0±12.3§*
TR (%)	1.6±3.0*	7.0±9.0*	1.8±2.4	3.0±4.9	3.2±4.0	3.2±5.0
RV-EDV-I (ml/m^2)	170.5±43.3‡	162.0±40.5‡	111.1±19.0‡‖	116.7±51.0‡	99.4±19.9‖	122.6±56.3
RV-ESV-I (ml/m^2)	95.2±34.7‡	102.4±40.7†	58.3±16.3‡§	73.9±50.7†	50.6±12.8§	75.2±54.4
RV-EF (%)	45.9±8.9	38.7±11.4	47.2±9.7	40.6±11.9	51.4±9.4*	41.6±11.6*
$RV\text{-}EF_{cor}$ (%)	25.2±8.8‡	24.6±6.1†	48.9±9.3*‡	38.3±12.5*†	49.8±5.8*	38.4±13.1*
Clinical						
NYHA class	2.0±0.7	2.0±0.6	1.2±0.3	1.5±0.6	1.1±0.2	1.5±1.0

PR, TR, RV-EF and $RV\text{-}EF_{cor}$ *as percentage (%), RV-EDV-I and RV-ESV-I as indexed volume* (ml/m^2).
*A = atrial contraction; E = Early filling; EDFF = end-diastolic forward flow; pfr = peak flow rate; PR = pulmonary regurgitation; PVR = pulmonary valve replacement; RV-EDV-I = right ventricular end-diastolic volume, indexed for body surface; RV-EF = right ventricular ejection fraction; RV-ESV-I = right ventricular end-systolic volume, indexed for body surface; vol = volume. * Not assessed.*

Results

All haemodynamic parameters are shown in table 7.2. Mean PR before surgery was 47.9 ± 10.2 %. None of the healthy subjects had PR. At follow-up, almost no residual PR was found.

Diastolic function

The Evol/Avol ratio and Epfr/Apfr ratio before PVR were lower in the patient group compared to the healthy subjects (Evol/Avol ratio 1.4 ± 0.7 and 2.7 ± 0.8 respectively ($P<0.01$) and Epfr/Apfr ratio respectively 1.1 ± 0.4 and 1.6 ± 0.3 respectively ($P<0.01$)). After PVR, the Evol/Avol ratio remained essentially unchanged at 1.6 ± 0.7 at 8 months (not significant), followed by an increase to 2.3 ± 1.2 at 22 months ($P < 0.01$). Furthermore, the Epfr/Apfr ratio did not increase at 8 months (1.2 ± 0.4 (not significant)), but increased to 1.5 ± 0.6 at 22 months ($P < 0.05$). These results indicate a late improvement of diastolic function after surgery. The Epfr was 320.3 ± 115.8 ml/s before PVR and did not change at 8 and 22 months after PVR. However, the Apfr decreased from 322.8 ± 89.5 ml/s before PVR to 291.0 ± 78.0 ml/s (not significant) and 252.8 ± 78.4 ml/s ($P<0.05$) at 8 and 22 months respectively. The Apfr in the patients at 22 months was similar to the Apfr in the healthy subjects (252.8 ± 78.4 ml/s and 222.6 ± 81.0 ml/s respectively (not significant)). Consequently, the Epfr/Apfr ratio did not increase at 8 months (1.2 ± 0.4 (not significant)), but increased to 1.5 ± 0.6 at 22 months ($P < 0.01$), which was comparable with the Epfr/Apfr ratio in the healthy subjects. Moreover, the same recovery patterns were observed for the Evol, Avol and Evol/Avol ratio as for the Epfr, Apfr and Epfr/Apfr ratio respectively.These results indicate that the late improvement of both E/A peak flow ratios and E/A volume ratios can be explained by an increase in volume of the early diastolic filling a decrease of the peak flow rate and volume of the atrial contraction respectively.

Restriction

Before PVR, significant EDFF was detected in 8 patients, while 8 patients did not have EDFF. At follow-up, EDFF was not found in any patient. Patients with EDFF had a mean volume of EDFF of 5.3 ± 4.2 % (range 1.7 to 14.9 ml) of right ventricular stroke volume. E/A volume and peak flow ratios did not differ between patients with and without EDFF at baseline. Furthermore, an equal improvement in both diastolic and systolic function was found in both groups.

Systolic function

Mean RV-EDV-I decreased from 164.2 ± 42.8 ml/m^2 before PVR to 112.7 ± 26.2 ml/m^2

(P<0.01) at 8 months follow-up, while no further change was observed at 22 months (107.1 ± 35.8 ml/m^2 (not significant)). The RV-ESV-I followed the same recovery pattern. Furthermore, the RV-EF corrected for regurgitation improved significantly from 23.6 ± 4.8 % to 46.0 ± 11.1 % (P<0.01) and remained essentially unchanged at 47.6 ± 7.1% (not significant) respectively.

Left ventricular end-diastolic volume was within normal ranges in all patients before PVR. Following PVR, the end-diastolic volume remained unchanged. Moreover, the left ventricular EF did not change after PVR. However, 6 patients had a preoperative left ventricular EF of less than 50%, while after PVR, 4 of these 6 patients had a left ventricular EF of more than 50%. In one patient the left ventricular EF had increased from 28 to 42% (P<0.001), while in another patient the left ventricular EF remained essentially unchanged (45% before and 47% at the last follow-up).

Discussion

In the present study, we found a delayed normalization of diastolic function parameters in adult Fallot patients who underwent PVR, as compared to the rapid improvement of systolic function. Possibly different mechanisms play a role in the improvement of diastolic and systolic function after valve replacement.

Diastolic function

Left ventricular diastolic function in patients and healthy volunteers has been studied extensively [17-20]. Analysis of mitral flow velocity curves acquired using echo-Doppler have contributed to the understanding of ventricular filling characteristics. Nowadays, there is growing recognition that an abnormal left ventricular diastolic function is an important risk factor for the development of systolic dysfunction and congestive heart failure [21]. Filling characteristics of the right ventricle have been assessed in healthy subjects by means of tricuspid flow velocity patterns derived form echo-Doppler imaging [22] and by cardiac magnetic resonance flow mapping [23]. In patients with congenital heart disease affecting the right ventricle, diastolic dysfunction is a common finding. Helbing et al. found impaired relaxation and restriction to filling in children with repaired tetralogy of Fallot [7]. In several other studies, abnormal right ventricular filling patterns

have been demonstrated in patients with different cardiac conditions, such as pulmonary stenosis [24,25], myocardial infarction [26] and restrictive cardiomyopathy [27]. To our knowledge, the effects of PVR on right ventricular diastolic function have not been studied before. In our group, only small volumes of EDFF were found (the largest volume was 14.9 % of right ventricular stroke volume in one patient). In the study by Helbing et al the authors found a correlation between small amounts of EDFF and diminished exercise capacity. The amount of EDFF in their patients was comparable to our patients with a mean of 3.6 ± 3.5% [7]. In another study, Gatzoulis et al. reported less cardiomegaly in patients with restrictive physiology. They speculate that this phenomenon reflects the limited right ventricular end-diastolic volume they found in these patients. However, in the present study, patients with EDFF in the main pulmonary artery, a marker for restrictive physiology of the right ventricle, showed the same recovery pattern as patients without EDFF. Furthermore, baseline characteristics between patients with and without EDFF did not differ.

Concentric remodeling

In a recent study, Lamb et al. studied the effects of aortic valve replacement in patients with either aortic valve stenosis or regurgitation [12]. They found a discrepancy in the recovery patterns between both groups. Patients operated for aortic valve stenosis showed rapid diastolic function improvement following surgery, while in patients with preoperative aortic regurgitation, a deterioration of diastolic function was observed at up to 9 months follow-up. The authors concluded that this discrepancy is most likely caused by concentric remodeling of the left ventricle, due to the slow decrease of left ventricular mass reduction compared to the rapid decrease of left ventricular dilatation. In the present study, we found a lack of early improvement of diastolic function parameters, followed by a late improvement of E/A volume and peak flow ratios. Concentric remodeling is by definition not possible in the right ventricle, since the right ventricular morphology is not concentric. It is not clear whether some form of remodeling plays a role in the time course of recovery of right ventricular diastolic function after valve replacement. However, the lack of early improvement of diastolic function parameters in our study is in accordance with the findings of Lamb et al. Furthermore, the late normalization of E/A volume and peak flow ratios could be the result of a late decrease of right ventricular

mass. However, right ventricular mass was not quantified in the present study, since accurate delineation of the borders of the right ventricular wall using standard gradient echo sequences is difficult to appreciate in patients in whom no wall can be visualized due to (severe) RV dilatation.

Systolic function

The rapid improvement of systolic function of the right ventricle is in accordance with previous studies. Bove et al. found an improvement of right ventricular ejection fraction in 11 patients who underwent PVR for pulmonary regurgitation or stenosis [28]. In a recent study by our group in 26 adult Fallot patients undergoing PVR for severe regurgitation, we found a dramatic increase in right ventricular ejection fraction when corrected for regurgitation from 25.2 ± 8.0% to 43.3 ± 13.7% ($P<0.001$) [8]. We speculate that diminishing the PR fraction and thus unloading of the right ventricle leads to increased systolic performance. The left ventricular systolic function as expressed by the EF did not change following PVR. In previous studies it was found that severe RV dysfunction could lead to impairment of left ventricular function [29]. In our group six patients had a left ventricular EF of less than 50% and one patient had a preoperative EF of 28%. These patients showed an improvement of EF at 22 months follow-up, however EF remained below 50%. Further studies are required to evaluate the left ventricular function late after PVR.

Conclusion

This study shows that right ventricular diastolic function normalizes after PVR in patients late after primary repair of Fallot. However, in contrast to the rapid improvement of systolic function, the improvement of diastolic function is delayed, possibly due to the rapid volume unloading after PVR leading to a relative hypertrophy of the right ventricle. Furthermore, restriction to filling of the right ventricle before operation did not seem to hamper the improvement of diastolic function after PVR. Therefore, PVR should be considered in patients with severe PR in combination with diastolic and/or systolic dysfunction.

References

1 Gatzoulis MA, Elliott JT, Guru V et al. Right and left ventricular systolic function late after repair of tetralogy of Fallot. Am J Cardiol 2000;86:1352-7.

2 Murphy JG, Gersh BJ, Mair DD et al. Long-term outcome in patients undergoing surgical repair of tetralogy of Fallot. N Engl J Med 1993;329:593-9.

3 Marie PY, Marcon F, Brunotte F et al. Right ventricular overload and induced sustained ventricular tachycardia in operatively "repaired" tetralogy of Fallot. Am J Cardiol 1992;69:785-9.

4 Zahka KG, Horneffer PJ, Rowe SA et al. Long-term valvular function after total repair of tetralogy of Fallot. Relation to ventricular arrhythmias. Circulation 1988;78:III14III19.

5 Wessel HU, Cunningham WJ, Paul MH et al. Exercise performance in tetralogy of Fallot after intracardiac repair. J Thorac Cardiovasc Surg 1980;80:582-93.

6 Gatzoulis MA, Clark AL, Cullen S et al. Right ventricular diastolic function 15 to 35 years after repair of tetralogy of Fallot. Restrictive physiology predicts superior exercise performance. Circulation 1995;91:1775-81.

7 Helbing WA, Niezen RA, Le Cessie S et al. Right ventricular diastolic function in children with pulmonary regurgitation after repair of tetralogy of Fallot: volumetric evaluation by magnetic resonance velocity mapping. J Am Coll Cardiol 1996;28:1827-35.

8 Vliegen HW, Van Straten A, de Roos A et al. Magnetic resonance imaging to assess the hemodynamic effects of pulmonary valve replacement in adults late after repair of tetralogy of Fallot. Circulation 2002;106:1703-7.

9 Warner KG, Anderson JE, Fulton DR et al. Restoration of the pulmonary valve reduces right ventricular volume overload after previous repair of tetralogy of Fallot. Circulation 1993;88:II189-II197.

10 Oechslin EN, Harrison DA, Harris L et al. Reoperation in adults with repair of tetralogy of Fallot: indications and outcomes. J Thorac Cardiovasc Surg 1999;118:245-51.

11 Yemets IM, Williams WG, Webb GD et al. Pulmonary valve replacement late after repair of tetralogy of Fallot. Ann Thorac Surg 1997;64:526-30.

12 Lamb HJ, Beyerbacht HP, de Roos A et al. Left ventricular remodeling early after aortic valve replacement: differential effects on diastolic function in aortic valve stenosis and aortic regurgitation. J Am Coll Cardiol 2002;40:2182-8.

13 van Straten A, Vliegen HW, Hazekamp MG et al. Right ventricular function after pulmonary valve
replacement in patients with Tetralogy of Fallot. Radiology 2004; 233:824-8

14 Pattynama PM, de Roos A, van der Wall EE et al. Evaluation of cardiac function with magnetic resonance imaging. Am Heart J 1994;128:595-607.

15 Pattynama PM, Lamb HJ, Van der Velde EA et al. Reproducibility of MRI-derived measurements of right ventricular volumes and myocardial mass. Magn Reson Imaging 1995;13:53-63.

16 van der Geest RJ, Reiber JH. Quantification in cardiac MRI. J Magn Reson Imaging 1999;10:602-8.

17 Nishimura RA, Housmans PR, Hatle LK et al. Assessment of diastolic function of the heart: background and current applications of Doppler echocardiography. Part I. Physiologic and pathophysiologic features. Mayo Clin Proc 1989;64:71-81.

18 Nishimura RA, Abel MD, Hatle LK et al. Assessment of diastolic function of the heart: background and current applications of Doppler echocardiography. Part II. Clinical studies. Mayo Clin Proc 1989;64:181-204.

19 Hanrath P, Mathey DG, Siegert R et al. Left ventricular relaxation and filling pattern in different forms of left ventricular hypertrophy: an echocardiographic study. Am J Cardiol 1980;45:15-23.

20 Eichhorn P, Grimm J, Koch R et al. Left ventricular relaxation in patients with left ventricular hypertrophy secondary to aortic valve disease. Circulation 1982;65:1395-404.

21 Zile MR, Brutsaert DL. New concepts in diastolic dysfunction and diastolic heart failure: Part I: diagnosis, prognosis, and measurements of diastolic function. Circulation 2002;105:1387-93.

22 Zoghbi WA, Habib GB, Quinones MA. Doppler assessment of right ventricular filling in a normal population. Comparison with left ventricular filling dynamics. Circulation 1990;82:1316-24.

23 Mostbeck GH, Hartiala JJ, Foster E et al. Right ventricular diastolic filling: evaluation with velocity-encoded cine MRI. J Comput Assist Tomogr 1993;17:245-52.

24 Vermilion RP, Snider AR, Meliones JN et al. Pulsed Doppler evaluation of right ventricular diastolic filling in children with pulmonary valve stenosis before and after balloon valvuloplasty. Am J Cardiol 1990;66:79-84.

25 Vermilion RP, Snider AR, Bengur AR et al. Long-term assessment of right ventricular diastolic filling in patients with pulmonic valve stenosis successfully treated in childhood. Am J Cardiol 1991;68:648-52.

26 Isobe M, Yazaki Y, Takaku F et al. Right ventricular filling detected by pulsed Doppler echocardiography during the convalescent stage of inferior wall acute myocardial infarction. Am J Cardiol 1987;59:1245-50.

27 Hatle LK, Appleton CP, Popp RL. Differentiation of constrictive pericarditis and restrictive cardiomyopathy by Doppler echocardiography. Circulation 1989;79:357-70.

28 Bove EL, Kavey RE, Byrum CJ et al. Improved right ventricular function following late pulmonary valve replacement for residual pulmonary insufficiency or stenosis. J Thorac Cardiovasc Surg. 1985; 90:50-55.

29 Niezen RA, Helbing WA, Der Wall EE et al. Left ventricular function in adults with mild pulmonary insufficiency late after Fallot repair. Heart 1999; 82:697-703.