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The Impact of Pulmonary Insufficiency on the Right Ventricle: A Comparison of Isolated Valvar Pulmonary Stenosis and Tetralogy of Fallot

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Abstract

Introduction—Pulmonary insufficiency (PI) is associated with right ventricular (RV) dilation, dysfunction and exercise intolerance in patients with tetralogy of Fallot (TOF). We sought to compare RV function and exercise performance in patients with valvar pulmonary stenosis (VPS) following pulmonary balloon valvuloplasty to those with repaired TOF with similar degrees of PI.

Methods—We performed a cross-sectional study of patients with VPS and TOF. Cardiac magnetic resonance (CMR) and exercise stress test (EST) were performed. Subjects were matched by time from initial procedure and severity of PI using propensity scores.

Results—After matching, there were 16 patients with VPS and 16 with TOF for comparison, with similar demographics. Time from initial procedure was 14 years (12; 16), p= 0.92, and pulmonary regurgitant fraction was 19 % (6; 31), p= 0.94, Patients with TOF had lower ejection fraction [58 % (53; 66) vs. 65 % [60; 69], p= 0.04] and more RV hypertrophy [69 g/m2 [52; 86] vs. 44 g/m2 [32; 66], p=0.04] compared to those with VPS. Aerobic capacity was worse in patients with TOF [68 ± 19% mVO2 (56; 84) vs. 82 ± 9.2 % (74; 89) in VPS, p=0.01], with a trend for less habitual physical activity [0.9 (0; 12) vs. 8 hours/ week (4; 12), p= 0.056], respectively.

Conclusions—With similar degrees of PI, patients with TOF demonstrate worse RV function and aerobic capacity as compared to patients with just VPS. Habitual exercise may in part explain differences in exercise performance and should be further explored.

Keywords

Tetralogy of Fallot; Pulmonary stenosis; Outcome; Pulmonary insufficiency; Exercise; Congenital Heart Disease

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Introduction

The adverse effects of pulmonary insufficiency (PI) are well characterized in tetralogy of Fallot (TOF). Ensuing right ventricular (RV) enlargement and dysfunction are associated with exercise intolerance, propensity for serious arrhythmias and increased risk of sudden cardiac death. [1, 2] Nonetheless, the RV remodeling in TOF, i.e., changes in size (dilation), shape (hypertrophy) and function, is quite variable, such that RV dysfunction and symptoms develop at inconsistent times following surgery, and the timing for restoring pulmonary valve competency varies from patient to patient.[3] Surgical repair for TOF involves placing a transannular patch in most patients as well as a ventriculotomy in some. Therefore, it is likely that a combination of factors, including ventriculotomy, non-contractile outflow tract, hypoplastic pulmonary arteries, and sternotomy, influences RV remodeling.

Isolated valvar pulmonary stenosis (VPS) treated via percutaneous balloon dilation (BD) can also result in PI, and although long-term results after BD for VPS are excellent with relatively low re-intervention rates, the impact of PI on outcome in this population has not been extensively described.[4] VPS can serve as a model for understanding the independent effect of PI on the RV apart from other surgery-related factors in TOF. Therefore, the rationale for this study was to compare RV function, morphology, and exercise performance in two clinical scenarios characterized by PI. We hypothesized that for the same degree and length of exposure to PI, ventricular function and exercise performance would be worse in TOF patients than in those with isolated VPS.

Material and Methods

Study population and data collection

We performed a cross sectional study at The Children's Hospital of Philadelphia (CHOP) of subjects with TOF or VPS, ages 8-18 years. Subjects underwent protocol-based cardiac magnetic resonance (CMR) and exercise stress testing (EST). Echocardiograms were available for the TOF group only. Testing was performed at most within three months in the TOF group and on the same day on all subjects with VPS. Subjects also completed a validated written questionnaire assessing habitual exercise.[5] The number of hours per week of physical activity was recorded for each patient. The VPS group included patients who underwent BD. The TOF group included patients operated for TOF. Subjects were identified from clinical, catheterization, and surgical databases at our institution. For those with VPS, inclusion criteria included history of isolated VPS status post BD and no evidence of a genetic syndrome. For TOF, patients with genetic syndromes other than 22q11.2 deletion were excluded.

This study was approved by the Institutional Review Board for the Protection of Human Subjects at CHOP. All subjects provided written informed consent prior to participating in the study.

Cardiac Magnetic Resonance—CMR studies were performed on a 1.5-T Avanto Whole Body Magnetic Resonance System (Siemens Medical Solutions, Erlanghen, Germany) with a 6-channel body-array coil scanner using a standard imaging protocol, as previously described by our group. [6] All CMRs were read by an experienced physician (MF) who was blinded to patient's clinical information. Briefly, RV volumes were calculated. The RV end-systolic and end-diastolic volumes and RV mass were indexed to body surface area (m^2) and corresponding Z-scores were calculated using published normative data. [7, 8] Phase contrast velocity mapping with a flow-sensitive gradient-echo sequence was performed in the main pulmonary artery. Forward, regurgitant, and net flows were then automatically calculated from the resulting time-volume curves. PI was measured as pulmonary regurgitant fraction (RF). The RF through a region of interest is defined as follows: RF (%) = (reverse flow/forward flow) X 100. Residual pulmonary stenosis was defined by the velocity in the main pulmonary artery and graded as greater than mild if >3 m/sec.

Exercise Stress Test—Patients exercised to maximal ability using an electronically braked cycle ergometer (SensorMedics, Yorba Linda, CA). The exercise protocol has been previously described. [6] We used a respiratory exchange ratio (RER) ≥1.1 to identify subjects who achieved maximum effort on EST. The percent of predicted maximum VO2 (%mVO2) was calculated for each patient, according to normative values for age, gender and body size. Exercise performance was defined by percent mVO2 and defined as abnormal if less than 85% of the predicted value.[9-11]

Echocardiogram—A complete echocardiogram was performed in the TOF group, following a standard research protocol in our laboratory. Echocardiogram data was used to obtain the estimated RV pressure using the tricuspid regurgitation jet, to estimate the association between RV pressure and RV mass.

Statistical Analysis

To examine differences given comparable degrees of PI, propensity score matching was used to match patients in the VPS to the TOF groups. First, a logistic model with group as dependent variable and years of PI and pulmonary regurgitation as predictors was used to calculate the propensity scores. Then, each VPS patient was matched on a TOF patient based on the propensity scores in order to achieve the balance between two groups according to duration of PI (years of exposure) and severity of pulmonary regurgitation (measured as RF).

After matching, continuous variables are presented as mean and standard deviation (SD) or as median with inter-quartile ranges (IQR), as appropriate. Categorical variables are described using count and percentages. The differences between the VPS and TOF groups were tested with Students' paired *t test* or the signed rank test for continuous variables according to the distribution. The McNemar's test or Fisher's exact test was used for categorical variables. Associations between covariates were compared with Pearson's correlation coefficient. Statistical significance was reached if p-values were < 0.05 (2-sided tests). All analyses were performed using Stata/IC statistical software version 11.2 (College Station, TX) or SAS version 9.2 (Cary, NC).

Results

Patient characteristics

Our study cohort consisted of 19 cases with VPS and 176 cases with TOF, from which 16 cases of each were matched for RF and length of exposure to PI for intergroup comparison. By study design, the groups had comparable age. There was no difference in age at the time of the initial procedure (p=0.11) There was a predominance of males and Caucasians **(Table 1).**

Valvar PS Group Characteristics

In the VPS group (n=19), only one patient had greater than mild residual pulmonary valve stenosis. Although the right ventricular end-diastolic dimension was normal on average (Z score = 0.7 ± 2.7, range −3.2 to + 6.8), there were six subjects with dilated RVs (RV end-diastolic volume Z scores ≥2). Eight patients had greater than mild PI (>20% RF) and consequently more dilated RVs as compared to those with less than mild PI (RV end-diastolic volume Z score +2.5 ± 2.5 vs. −0.64±2.1, p=0.009). However, those 8 patients had comparable RV function (ejection fraction) and aerobic capacity to those with less than mild PI (RVEF 62±5 vs. 67±9%, p=0.21 and mVO2 79±8 and 83±11%, p=0.42, respectively). There was a strong linear association between PI and RV enddiastolic volume (r= 0.63, p=0.003), and a moderate association between PI and age at balloon dilation (r=−0.51, p= 0.043), but no association between PI and RVEF (r=−0.37, p=0.11), RV mass (r=0.08, p=0.75), or years from BD (r=0.12, p=0.59).

On EST, most VPS subjects (74%) exercised to maximal effort (RER >=1.1), achieving a maximum heart rate of 193±10 bpm. Aerobic capacity was mildly decreased [%mVO2 = 84 % (74; 89)] **(Table 2**). Oxygen consumption was not associated with oxygen pulse, even when limited to those achieving a maximum exercise test, but it had a moderate negative correlation with PI, indicating that subjects with more severe PI had lower percent predicted mVO2 (r=-0.52, p=0.04).

Habitual exercise questionnaires were available for 14 VPS subjects. Overall they performed 7.4 (2.2; 12.1) hours of exercise per week. Habitual exercise was moderately associated with percent predicted mVO2 and with RV function (RVEF) (r= 0.56, p =0.02 and r=0.61, p= 0.013, respectively).

TOF Matched Group Characteristics

For this analysis, of the 176 available TOF patients, 16 subjects were matched to the VPS group by RF and length of exposure, and constitute the sample for comparison with the VOS group . Given the degree of PI in the VPS group, matching resulted in mild PI in the TOF study group, with RF = 21% (6; 32). There was significant RV hypertrophy with RV mass = 67 ± 24 g/m^2, with corresponding RV mass Z score = +6.7 (+3.9; +10.3) **(Table 2).** Six subjects had dilated RVs (RV end-diastolic Z score ≥ +2).

Similar to the VPS group, there was a moderate positive correlation between PI and RV end-diastolic volume (r= 0.68, p=0.004), but no significant correlation between PI and age at surgical repair (r=0.15, p=0.60), RVEF (r=0.001, p=0.99), RV mass (r=0.43, p=0.09), or years from surgery (r=0.12, p=0.59).

Like the VPS group, on EST, most subjects with TOF (74%) exercised to maximal effort. Aerobic capacity was decreased on average [%mVO2 = 66 (IQR 56; 84)] % of predicted for age and gender). There was no significant correlation between PI and percent-predicted mVO2 (r= 0.51, p= 0.06). Questionnaires with habitual exercise information were available for ten TOF patients. Overall, they performed less than one hour/ week of physical activity [0.9 hours/week (0; 12)]. Unlike the VPS group, there were no associations between habitual exercise (hours/week) and percent of predicted mVO2 (r= 0.42, p= 0.22), or RVEF (r = −0.21, p= 0.56) in this small subset of patients.

Echocardiographic estimate of RV pressure using the tricuspid regurgitation jet was available in 12 subjects, for whom the RV pressure was calculated at 37% systemic (32; 43). There was no association between RV pressure ratio and indexed RV mass (r= -0.44, p= 0.16).

Between Group Comparisons

Given that subjects were matched by RF and years of exposure to PI, the overall PI was mild in both groups (driven by mild PI in the VPS patients). Because three of the VPS patients had RF=0, only 16/19 were matched to TOF patients. There was mild or less residual pulmonary stenosis overall and no statistically significant difference in the groups. Likewise, ventricular volumes were comparable in the two groups **(Table 2**). Although RV function was preserved overall in both groups, the TOF group had lower RV ejection fraction as compared to the VPS patients [58% (54; 66) vs. 65 % (60; 69), p=0.04, respectively] and more RV hypertrophy [RV mass 69 (52; 86) vs. 44 (32; 66) g/m^2, p=0.04, respectively] **(Table 2).** The TOF group performed worse on exercise testing as compared to the VPS cases with significantly lower %mVO2 [66 (56; 84) vs. 84 (74; 89), p=0.01] **(Table 2).** Duration of exposure to PI was not associated with RF in either group, although there was a tendency towards significance in the TOF group [r= 0.47, p=0.07 (TOF) and r= 0.34, p=0.19 (VPS)].

Discussion

In this study, we sought to investigate differences in RV function and exercise performance in two groups of patients exposed to similar PI severity, while also examining the clinical status of patients with VPS after BD. As such, we used the subjects with VPS who underwent BD as a model of PI in an otherwise unoperated heart in comparison to the operated heart in TOF.

Clinical Status of Patients with VPS

Our results suggest that residual PI can be significant in a group of children and adolescents with VPS after BD. Although on average the degree of PI was mild in the VPS group, 42% demonstrated moderate PI (RF greater than 20%) with corresponding RV dilation. At this intermediate age of follow up, VPS subjects demonstrated preserved RV function but abnormal aerobic capacity on average. Oxygen consumption was associated with worse PI and increased habitual exercise and RV function. These findings support the need for long term follow up of this population since they already demonstrate physiologic abnormalities in adolescence and could potentially develop symptoms in adulthood.[12]

In some aspects our findings are similar to those reported by Harrild et al (2009), who found a comparable degree of PI and consequent RV dilation in a larger group of patients (n= 41) with a wider age range.[13] In that study, however, there was an association between peak VO2 and regurgitant fraction, whereby patients with >15 % RF had lower VO2 as compared to those with <15% RF. We did not find such an association, possibly due to the difference in age range or the smaller sample size in our study.

However, habitual exercise was associated with oxygen consumption in our VPS group. Similar to our results, others have demonstrated an association between daily physical activity and mVO2. Furthermore, Fredriksen et al (2000) demonstrated improvements in mVO2 on exercise testing after an exercise intervention program in children and adolescents with congenital heart disease, thus providing further evidence that daily physical activity is associated with mVO2.[14-16] In our study, the mVO2 was abnormal in the face of overall mild residual disease. This finding was unexpected in this group, particularly given the young age range; however, patients with congenital heart disease are known to have decreased aerobic capacity and to be less active than their peers. Whether their lower aerobic capacity results from deconditioning, hemodynamic or other factors remains to be elucidated.[17-19] In addition, we were not able to ascertain whether more physical activity leads to better RVEF and mVO2 or alternatively, whether lower RVEF and mVO2 result in less habitual exercise.

We found a moderate association between age at BD and severity of PI, indicating, similar to others, that patients in whom BD was performed at a younger age have more severe PI, possibly due to more severe disease at presentation.[20, 21] Garty et al (2005) reported that PI increased in severity over time and showed that half of the patients in a large series had moderate to severe PI at a mean follow up of 12 years.[20] Although we were not able to ascertain whether PI was progressive over time due to the cross sectional design of our study, our study group demonstrated overall mild residual PI in a median follow up of 15 years.

Comparison with TOF

Matching for severity and duration of PI resulted in a relatively healthy group of TOF with preserved RV function and mild PI, none of which necessarily reflect the full spectrum of TOF disease. Nonetheless, for a relatively well group with seemingly mild residual disease, the matched TOF subset fared worse in terms of RV function (lower RVEF), RV hypertrophy (increased RV mass), aerobic capacity, and hours of habitual exercise than the VPS group. Therefore, as one would predict, PI does not appear to be the sole determinant of long-term RV remodeling and exercise capacity in TOF. In particular, although normal on average and despite matching for PI, the RVEF was statistically significantly lower in the TOF group as compared to the VPS study group. Because of the significant difference in RV mass that was independent from increased RV pressure in the TOF group, we postulate that there is intrinsic RV disease in TOF. This could be secondary to several factors, including:

post-natal exposure of the RV myocardium to cyanosis, surgical factors such as ventriculotomies and transannular patches, and abnormalities of the distal pulmonary artery tree. In addition, genetic factors appear to influence the RV's remodeling and reverse remodeling patterns in TOF. [22, 23]

We also found that patients with TOF have worse exercise performance when compared to VPS subjects matched by duration and severity of PI. Several studies have explored exercise performance in TOF and its determinants appear to be multifactorial. Proposed etiologies include cardiovascular factors, restrictive pulmonary function, deficient habitual exercise and chronotropic impairment. All of these can be associated with decreased aerobic capacity identified in the TOF group, which was present but to a lesser extent in the VPS after BD group. [24, 25] Although we were not able to test this hypothesis in our study, it is possible that patients with VPS perform better on EST than those with TOF because they exercise more and feel well enough to do so. Moreover, patients with TOF might be less encouraged to exercise and as such are less conditioned and perform worse on EST as compared to those with VPS.

Limitations

We acknowledge limitations to our study. We analyzed a small sample of patients with VPS, although testing was performed on the same day using study protocols, lending more reliability to the associations we identified. We might have found stronger associations in a larger sample size or if we had identified VPS subjects with more severe PI. Because we found only mild to moderate PI in this study cohort, our results can only be generalized to patients with similar a degree of PI in both subgroups. Catheterization data was not available for all subjects enrolled and thus we could not correlate the conduct of the BD with outcomes. However the objective of this study was to describe the clinical status of children and adolescents with VPS, and to isolate the effect of PI on the unoperated heart in comparison to TOF. Finally, exercise data were self-reported, relying on the parents and/or participants to remember the level of physical activity in the previous year, therefore subjecting our study to recall bias. However, if error is present and if it is non-differential, it would bias our results towards the null.

In conclusion, our study suggests that RV remodeling in TOF, in particular increased RV mass and decreased RV ejection fraction, is not solely dependent on the degree of PI. Although the patients with VPS performed better on EST, they nonetheless demonstrate abnormal aerobic capacity. Thus future studies are needed to better understand RV remodeling in response to PI and to explore novel therapeutic strategies. Finally, while, it is possible that better RV function in the VPS group permits greater participation in exercise and improved aerobic capacity as compared to the TOF group, it is likely that habitual exercise is associated with improved aerobic capacity in both groups. As such there may be added benefits to encouraging rather than restricting safe, habitual exercise.

References

1. Zahka KG, Horneffer PJ, Rowe SA, Neill CA, Manolio TA, Kidd L, Gardner TJ. Long-term valvular function after total repair of tetralogy of fallot. Relation to ventricular arrhythmias. Circulation. 1988; 78:III14–19. [PubMed: 3180393]
2. Carvalho JS, Shinebourne EA, Busst C, Rigby ML, Redington AN. Exercise capacity after complete repair of tetralogy of fallot: Deleterious effects of residual pulmonary regurgitation. Br Heart J. 1992; 67:470–473. [PubMed: 1622697]
3. Frigiola A, Hughes M, Turner MS, Taylor AM, Marek J, Giardini A, Hsia TY, Bull K. Physiologic and phenotypic characteristics of late survivors of tetralogy of fallot repair who are free from pulmonary valve replacement. Circulation. 2013; 128:1861–1868. [PubMed: 24065608]
4. Harrild DM, Powell AJ, Tran TX, Geva T, Lock JE, Rhodes J, McElhinney DB. Long-term pulmonary regurgitation following balloon valvuloplasty for pulmonary stenosis risk factors and relationship to exercise capacity and ventricular volume and function. J Am Coll Cardiol. 55:1041–1047. [PubMed: 20202522]
5. Kriska AM, Sandler RB, Cauley JA, LaPorte RE, Hom DL, Pambianco G. The assessment of historical physical activity and its relation to adult bone parameters. Am J Epidemiol. 1988; 127:1053–1063. [PubMed: 3358406]
6. Mercer-Rosa L, Yang W, Kutty S, Rychik J, Fogel M, Goldmuntz E. Quantifying pulmonary regurgitation and right ventricular function in surgically repaired tetralogy of fallot: A comparative analysis of echocardiography and magnetic resonance imaging. Circ Cardiovasc Imaging. 2012; 5:637–643. [PubMed: 22869820]
7. Sarikouch S, Peters B, Gutberlet M, Leismann B, Kelter-Kloepping A, Koerperich H, Kuehne T, Beerbaum P. Sex-specific pediatric percentiles for ventricular size and mass as reference values for cardiac mri: Assessment by steady-state free-precession and phase-contrast mri flow. Circ Cardiovasc Imaging. 2010; 3:65–76. [PubMed: 19820203]
8. Robbers-Visser D, Boersma E, Helbing WA. Normal biventricular function, volumes, and mass in children aged 8 to 17 years. J Magn Reson Imaging. 2009; 29:552–559. [PubMed: 19243036]
9. Ross RM. Ats/accp statement on cardiopulmonary exercise testing. Am J Respir Crit Care Med. 2003; 167:1451. author reply 1451. [PubMed: 12738602]
10. Cooper DM, Weiler-Ravell D, Whipp BJ, Wasserman K. Aerobic parameters of exercise as a function of body size during growth in children. J Appl Physiol Respir Environ Exerc Physiol. 1984; 56:628–634. [PubMed: 6706770]
11. Howley ET, Bassett DR Jr. Welch HG. Criteria for maximal oxygen uptake: Review and commentary. Med Sci Sports Exerc. 1995; 27:1292–1301. [PubMed: 8531628]
12. Shimazaki Y, Blackstone EH, Kirklin JW. The natural history of isolated congenital pulmonary valve incompetence: Surgical implications. Thorac Cardiovasc Surg. 1984; 32:257–259. [PubMed: 6207619]
13. Harrild DM, Powell AJ, Tran TX, Geva T, Lock JE, Rhodes J, McElhinney DB. Long-term pulmonary regurgitation following balloon valvuloplasty for pulmonary stenosis risk factors and relationship to exercise capacity and ventricular volume and function. J Am Coll Cardiol. 2010; 55:1041–1047. [PubMed: 20202522]
14. Muller J, Hess J, Hager A. Daily physical activity in adults with congenital heart disease is positively correlated with exercise capacity but not with quality of life. Clin Res Cardiol. 2012; 101:55–61. [PubMed: 21935655]
15. Fredriksen PM, Kahrs N, Blaasvaer S, Sigurdsen E, Gundersen O, Roeksund O, Norgaand G, Vik JT, Soerbye O, Ingjer E, Thaulow E. Effect of physical training in children and adolescents with congenital heart disease. Cardiol Young. 2000; 10:107–114. [PubMed: 10817293]
16. Ubeda Tikkanen A, Opotowsky AR, Bhatt AB, Landzberg MJ, Rhodes J. Physical activity is associated with improved aerobic exercise capacity over time in adults with congenital heart disease. Int J Cardiol. 2013; 168:4685–4691. [PubMed: 23962775]
17. Ubeda Tikkanen A, Opotowsky AR, Bhatt AB, Landzberg MJ, Rhodes J. Physical activity is associated with improved aerobic exercise capacity over time in adults with congenital heart disease. Int J Cardiol. 2013

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18. Duppen N, Takken T, Hopman MT, Ten Harkel AD, Dulfer K, Utens EM, Helbing WA. Systematic review of the effects of physical exercise training programmes in children and young adults with congenital heart disease. Int J Cardiol. 2013
19. Dua JS, Cooper AR, Fox KR, Graham Stuart A. Physical activity levels in adults with congenital heart disease. Eur J Cardiovasc Prev Rehabil. 2007; 14:287–293. [PubMed: 17446809]
20. Garty Y, Veldtman G, Lee K, Benson L. Late outcomes after pulmonary valve balloon dilatation in neonates, infants and children. J Invasive Cardiol. 2005; 17:318–322. [PubMed: 16003007]
21. Poon LK, Menahem S. Pulmonary regurgitation after percutaneous balloon valvoplasty for isolated pulmonary valvar stenosis in childhood. Cardiol Young. 2003; 13:444–450. [PubMed: 14694939]
22. Mital S, Chung WK, Colan SD, Sleeper LA, Manlhiot C, Arrington CB, Cnota JF, Graham EM, Mitchell ME, Goldmuntz E, Li JS, Levine JC, Lee TM, Margossian R, Hsu DT. Renin-angiotensin-aldosterone genotype influences ventricular remodeling in infants with single ventricle. Circulation. 2011; 123:2353–2362. [PubMed: 21576655]
23. Jeewa A, Manickaraj AK, Mertens L, Manlhiot C, Kinnear C, Mondal T, Smythe J, Rosenberg H, Lougheed J, McCrindle BW, van Arsdell G, Redington AN, Mital S. Genetic determinants of right-ventricular remodeling after tetralogy of fallot repair. Pediatr Res. 2012; 72:407–413. [PubMed: 22797143]
24. Meijboom F, Szatmari A, Deckers JW, Utens EM, Roelandt JR, Bos E, Hess J. Cardiac status and health-related quality of life in the long term after surgical repair of tetralogy of fallot in infancy and childhood. J Thorac Cardiovasc Surg. 1995; 110:883–891. [PubMed: 7475153]
25. Friedberg MK, Fernandes FP, Roche SL, Slorach C, Grosse-Wortmann L, Manlhiot C, Fackoury C, McCrindle BW, Mertens L, Kantor PF. Relation of right ventricular mechanics to exercise tolerance in children after tetralogy of fallot repair. Am Heart J. 2013; 165:551–557. [PubMed: 23537972]

Table 1

Demographic characteristics of matched groups

	VPS[a]	TOF[b]	P-value
Number of subjects	19	16	
Age at testing	15.3 ± 3.6	14.3 ± 2.8	0.40
Males (%)	63	56	0.72
Race White (%)	75	94	0.14
Age at procedure (years)[c]	1.2 ± 1.5	0.5 ± 0.41	0.11
Years of exposure to PI[c]	14 ± 4.1	14 ± 2.7	1.0

[a]VPS = valvar pulmonary stenosis

[b]TOF = tetralogy of Fallot

[c]Non-significant P values reflect adequate matching by years of exposure to PI.

Table 2

Cardiac Magnetic Resonance and Exercise Stress Test Characteristics Comparing VPS to TOF Matching for Duration of PI and Pulmonary Regurgitant Fraction

	VPS[a] N=16	TOF[b] N=16	P-value
CMR[‡]			
Pulmonary Regurgitant Fraction (%)	19 (9; 26)	21 (6; 32)	0.73
Main pulmonary artery velocity (m/sec)	1.7 (±0.8)	1.9 (±0.7)	0.34
RV end-diastolic volume (mL/m^2)[c]	87 (72; 113)	97 (73; 119)	0.46
RV end-diastolic volume Z score	0.99 ± 2.8	1.5 ± 2.5	0.50
RV end-systolic volume (mL/m^2)	35 (21; 45)	35 (26; 53)	0.21
RV Ejection Fraction (%)	65 (60; 69)	58 (54; 66)	0.04
Indexed RV mass (grams/m^2)	44 (32; 66)	69 (52; 86)	0.04
EST[d]			
RER >=1.1 (%)[e]	69 % (11 of 16)	73 % (11 of 15)	0.78
Indexed Oxygen pulse (mL/O_2/beat/m^2)	11.2 ± 4.8	8.6 ±3.3	0.71
mVO2 (mL/Kg/min)[f]	32 (29; 37)	25 (21; 34)	0.10
%mVO2[g]	84 (74; 89)	66 (56; 84)	0.01
Habitual Exercise			
Hours/ week of exercise	8 (4; 12)	0.9 (0; 12)	0.038

[a]VPS = valvar pulmonary stenosis

[b]TOF = tetralogy of Fallot

[‡]CMR = cardiac magnetic resonance

[c]RV = right ventricle

[d]EST = exercise stress test

[e]RER = respiratory exchange ratio

[f]mVO2 = maximum oxygen consumption

[g]%mVO2 = percent of predicted VO2