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Restrictive lung disease is an independent predictor of exercise intolerance in the adult with congenital heart disease

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Abstract

Background/Objectives—Following repair of congenital heart disease (CHD), adult patients are at risk for reduced exercise capacity. Restrictive lung disease (RLD) may contribute to reduced exercise capacity in this population. The aim of this study was to determine the prevalence of RLD and its impact on exercise tolerance in the adult with congenital heart disease.

Methods—One hundred consecutive adult patients with CHD, who underwent routine cardiopulmonary exercise testing with spirometry, were evaluated. Clinical data was obtained by retrospective chart review.

Results—Patients from 10 major diagnostic groups were identified. The median age for the cohort was 31 years (range 18–63) and included 43 males and 57 females. Most patients, 79%, had at least one previous surgical procedure. Based on spirometry and flow/volume loops, 50 patients were classified as normal pulmonary function, 44 patients had patterns suggestive of RLD, 4 suggestive of mixed (obstructive and restrictive), and 2 indeterminate. Risk factors associated with RLD include history of multiple thoracotomies (odds ratio=9.01, p=0.05) and history of atrial arrhythmias (odd ratio=4.25, p=0.05). Overall, 56% of the patients had abnormal exercise

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capacity. Spirometry suggestive of RLD was a significant risk factor for decreased exercise capacity (odds ratio=3.65, p=0.03). Patients with spirometry suggesting RLD also had lower exercise duration (p=0.004) and a higher New York Heart Association Functional Class (p=0.02). History of previous surgery and decreased heart rate reserve were also significant risk factors for decreased exercise capacity.

Conclusion—Abnormal spirometry suggestive of RLD is common in the adult with CHD and is a significant risk factor for decreased exercise tolerance in this population. Further studies, are needed to evaluate the relationship between RLD and exercise intolerance and its relationship to mortality in the adult with CHD.

Keywords

Congenital heart disease; Restrictive lung disease; Exercise capacity

Introduction

Recent data indicates that patients, after repair of congenital heart defects during infancy and childhood, have reduced exercise capacity once they reach adulthood.(1–6) Exercise intolerance in adults with congenital heart disease (CHD) is associated with an increased risk for hospitalization and death.(7) Decreased exercise capacity in this population is often attributed to an underlying cardiac etiology, including abnormal heart rate response to exercise and cardiac dysfunction. There are many studies, however, that have reported abnormal pulmonary function in adults with CHD, which may also contribute to reduced exercise capacity.(8–10) Spirometry measurements of lung function performed during cardiopulmonary exercise testing have suggested a higher incidence of restrictive lung disease (RLD).(11,12) Prior surgery during infancy and childhood, with subsequent lung scarring, chest deformities, and diaphragmatic palsy, are some of the many possible mechanisms for the abnormal pulmonary function observed in this population.

RLD may be a common, but under-recognized cause for long-term morbidity in adult survivors of congenital heart defects as it contributes to reduced exercise tolerance and decreased functional capacity. Treatment options for RLD, such as pulmonary rehabilitation, are effective in improving exercise endurance and the quality of life and in reducing hospital admissions in patients with RLD of various other causes.(13) These treatment options are likely underutilized in adults with CHD due to the fact that the true prevalence and etiology of abnormal pulmonary function in this diverse population is unknown. The aim of this study was to determine the prevalence of restrictive lung disease and its impact on exercise capacity in the adult with CHD.

Methods

Patient population

After receiving approval from the Children’s Hospital of Wisconsin and Medical College of Wisconsin institutional review board, the Wisconsin Adult Congenital Heart Disease Program (WAtCH) patient database was evaluated. One hundred consecutive adult (≥18-years-old) patients with a history of congenital heart disease, who had undergone treadmill

cardiopulmonary exercise stress testing with spirometry within the last 12 months, were identified. Patients with connective tissue disorders and muscular dystrophy were excluded. Clinical and exercise stress test data was obtained by retrospective chart review.

Exercise stress test

All cardiopulmonary exercise tests were performed at the Herma Heart Center outpatient congenital heart disease clinic using a standard Bruce protocol on a treadmill ergometer with incremental increases in speed and grade to voluntary exhaustion. Oxygen consumption (VO_2) was determined (CareFusion Corp., Yorba Linda, CA) and electronically recorded on a breath-by-breath basis. Maximal VO_2 was recorded. A test was considered maximal if the peak heart rate exceeded 90% predicted maximum, a plateau occurred in the VO_2 that did not rise with increasing work, or the respiratory quotient (RQ) exceeded 1.10. Peak oxygen consumption was expressed as a percent of predicted for stature, body mass, and age. Abnormal exercise capacity was defined as an indexed peak VO_2 < 80% predicted.

Spirometry (CareFusion Corp., Yorba Linda, Ca) was performed according to reviewed standards, with forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), peak expiratory flow rate (PEFR), and maximal mid-expiratory flow (FEF25-75) obtained.(14) Values were expressed as a percent predicted for stature, body mass, and age. Results of spirometry and flow/volume loops were reviewed by an independent pulmonologist blinded to the clinical data. Patients were classified categorically based on spirometry results into 4 groups: normal pattern (normal FEV1, FVC, and FEV1/FVC), pattern suggestive of restrictive lung disease (FVC less than 80% predicted, normal or increased FEV1/FVC, and convex shape of the expiratory limb on the flow-volume curve), pattern suggestive of obstructive lung disease (FEV1/FVC less than 80% predicted and concave shape of the expiratory limb on the flow-volume curve), and mixed pattern.(15)

Statistics

The primary outcome of interest was exercise capacity. This was evaluated for dependence on patient characteristics, primarily presence of RLD. Multivariate analysis was also used to evaluate factors associated with RLD. Statistical calculations were performed with SAS OnDemand Enterprise Guide 4.3 (SAS Institute, Cary, NC). Data are expressed as median with ranges or mean ± standard deviation. Comparisons between groups were performed with Fisher exact test. Univariate analysis was performed using Fisher exact test and multivariate analysis was performed with logistic regression. A p value of ≤0.05 was considered significant. Unadjusted and adjusted odds ratios are presented for significant factors.

Results

The median age for our cohort (n=100) was 31 years (range = 18–63 years), and included 43 male and 57 female subjects. Table 1 outlines the congenital heart diagnoses of the patients. The most common diagnosis for the cohort was coarctation of the aorta (n=19), followed by Tetralogy of Fallot (TOF) (n=17). The next most common diagnostic category was left ventricular outflow tract obstructive lesions not including coarctation of the aorta (n=12).

This group consisted of patients with aortic valve stenosis, subaortic stenosis, and supravalvular aortic stenosis. The remaining categories included septal defects (n=11), comprised of patients with history of an atrial septal defect, ventricular septal defect, or atrioventricular septal defect; single ventricle patients status post Fontan palliation (n=9); d-transposition of the great arteries {S,D,D} (d-TGA) status post the atrial switch procedure (n=9); congenitally corrected transposition of the great arteries {S,L,L} (ccTGA) (n=7); Ebstein anomaly (n=7); pulmonary valve stenosis (n=5); and d-TGA s/p arterial switch operation (ASO) (n=4).

Of the entire cohort, 79 patients had undergone at least one previous surgical intervention; 23 had undergone 2 previous surgeries; 15 had undergone 3 surgeries; and 7 patients had undergone 4 surgeries. Overall, 41 patients had undergone at least one previous thoracotomy, and 11 had undergone 2 previous thoracotomies. Medications at the time of evaluation included beta-blockers in 25, digoxin in 10, and anti-arrhythmic drugs in 7, of which 4 were taking amiodarone. Six patients had a history of obstructive sleep apnea and were being treated with continuous positive airway pressure. Four patients had a significant history of smoking tobacco and admitted to smoking cigarettes daily. Seven patients had a history of reactive airway disease and were on bronchodilators at time of evaluation. All 7 patients were administered their bronchodilator prior to starting their exercise stress test.

At time of evaluation, the majority of patients, 63%, were in New York Heart Association (NYHA) Functional Class I, 29% were in NYHA functional class II, and 8% were in NYHA functional class III. No patients were in NYHA functional class IV.

Twenty four of the 100 patients had a history of atrial arrhythmias. Six patients had a history of ventricular arrhythmias and all 6 had undergone previous implantation of a cardioverter-defibrillator. Fourteen patients had undergone previous implantation of a permanent pacemaker system.

At time of evaluation, 80% of the patients had normal systemic ventricular systolic function by echocardiography or cardiac magnetic resonance imaging (MRI); 13% had mildly reduced systolic function; and 7% had moderately reduced systolic function. No patient had severely reduced systemic ventricular function. Similarly, the majority of patients, 75%, had normal sub-pulmonic systolic function by echo or cardiac MRI; 12% had mildly reduced subpulmonic systolic function; and 5% had moderately reduced subpulmonic systolic function. No patient had severely reduced sub-pulmonic systolic function. Importantly, no one had significant pulmonary artery hypertension at time of evaluation.

Based on spirometry and flow/volume loops, 50 patients were classified as normal, 44 had patterns suggestive of RLD, 4 suggestive of mixed (obstructive and restrictive), and 2 indeterminate. Table 2 displays the number of patients with spirometry suggestive of RLD based on patient diagnosis. Patients with a single ventricle were most likely to have spirometry suggestive of RLD (8/9, 89%, p=0.03). Patients with TOF were also more likely to have spirometry suggestive of RLD (13/17, 76%, p=0.05). Patients with a history of Ebstein anomaly of the tricuspid valve and ccTGA were least likely to have abnormal spirometry suggestive of RLD.

Risk factors associated with spirometry suggestive of RLD are listed in Table 3. By univariate analysis, history of previous surgery ($p<0.0001$), history of atrial arrhythmias ($p=0.01$), history of amiodarone use ($p=0.01$), and having a permanent pacemaker ($p=0.03$) were all significant risk factors. However, by multivariate analysis, only atrial arrhythmias ($p=0.05$) and history of multiple thoracotomies ($p=0.05$) were significant risk factors. Age at initial surgery, length of follow-up, tobacco use, history of asthma, and history of only one previous thoracotomy were not significant risk factors.

Overall, 56% of the patients in the cohort had abnormal exercise capacity defined as a peak VO_2 index of < 80% predicted. Table 4 displays the percentage of patients with abnormal exercise capacity based on patient diagnosis and Table 5 demonstrates the mean and range of the different exercise variables evaluated for each cohort. Overall, the patients with single ventricles palliated with the Fontan procedure had the highest prevalence of abnormal exercise intolerance, with 100% of patients in this diagnosis group having abnormal exercise capacity. Patients with TOF were also statistically more likely to have abnormal exercise capacity ($p=0.02$). Patients with Ebstein anomaly were least likely to have abnormal exercise intolerance ($p=0.05$).

Risk factors associated with abnormal exercise capacity are listed in Table 6. Abnormal spirometry suggestive of RLD was significantly associated with decreased exercise capacity both by univariate ($p<0.001$) and multivariate analysis ($p=0.03$). Patients with spirometry suggesting RLD also had significantly lower exercise duration ($p=0.004$), and a higher NYHA functional class ($p=0.02$). Having a history of previous surgery was also a significant risk factor by multivariate analysis ($p=0.01$). Other predictors of abnormal exercise capacity included traditional risk factors such as lower chronotropic index and decreased heart rate reserve. Atrial arrhythmias, history of amiodarone use, and permanent transvenous pacemaker were significant factors by univariate, but not by multivariate analysis. Variables that were not predictive of exercise intolerance in our cohort included length of follow-up, patient age, and systemic ventricular dysfunction.

Discussion

To date, little has been published in regards to the prevalence and impact of RLD on the adult with CHD. This is in contrast to patients with acquired heart disease, where the relationship between abnormal lung function, exercise intolerance, and cardiovascular mortality is well established.(16) In a study by Sin et al. of 1,861 patients, even a modest decline in lung function was associated with a fivefold increase in deaths from ischemic heart disease, independent of baseline smoking status and other potential confounding factors such as age, gender, and Framingham risk scores.(16)

In the current study, we found that 44% of 100 consecutive patients who underwent cardiopulmonary stress testing as part of their annual evaluation at our institution had abnormal spirometry suggestive of RLD. This is markedly higher than the prevalence of spirometry-diagnosed RLD in the general adult population, which is reported to be around 9.2%.(17) Patients with history of Fontan palliation for single ventricle physiology and TOF were significantly more likely to have abnormal spirometry suggestive of RLD.

Our results are consistent with previously published studies of lung function measured at time of exercise testing in adults with CHD. Fredriksen et al. reported the results of cardiopulmonary exercise testing on 475 adults with various diagnoses of CHD, including ASD, ccTGA, Ebstein, Fontan and Mustards, and showed decreased mean FVC% predicted in all CHD diagnoses except patients with ASD.(1) Rigolin et al. also reported abnormal pulmonary function in 31 adults with CHD undergoing exercise stress testing, and noted both a reduced predicted FEV-1 of 73.2 ± 17.9% and a reduced predicted FVC of 76.6 ±17.6%, which are similar to values presented in this study.(10) A previous study has also suggested a high prevalence of restrictive lung disease in patients previously palliated with the Fontan procedure, with over 56% of the patients having abnormal spirometry suggestive of restrictive lung disease.(11)

Restrictive lung diseases are a group of conditions characterized by reduced lung volume, either because of an intrinsic cause, such as an alteration in lung parenchyma, or because of an extrinsic cause, such as a disease of the pleura, chest wall, or neuromuscular apparatus. The higher prevalence of restrictive lung physiology in adults with CHD may be secondary to extrinsic pulmonary causes, including diaphragmatic weakness, respiratory muscle weakness, and restrictive thoracic cage. Spinal deformities, including scoliosis and kyphosis, are significantly more common in patients with CHD, and may be related to previous thoracotomy or sternotomy.(18) This is supported by our results, which demonstrate that patients with abnormal lung function were more likely to have a history of multiple thoracotomies. In addition, patients in our series with the highest prevalence of abnormal spirometry were patients with single ventricle physiology and TOF, who are most likely to have undergone multiple previous surgeries, in particular multiple previous thoracotomies, either for repair or for placement of palliative systemic artery-to-pulmonary artery shunts.

RLD may also occur in adults with CHD as a result of intrinsic lung factors, such as that which may occur with lung toxicity from amiodarone use. In our study, we did find that all 4 patients being treated with amiodarone did have abnormal spirometry suggestive of RLD. This however did not reach significance by multivariate analysis. A history of atrial arrhythmias was also found to be a risk factor. We find this very interesting given many experts hypothesize that one of the major impacts of RLD on cardiac function is an abnormal interaction between the heart and lungs leading to elevated intracardiac filling pressures.(19)

In addition to finding a high prevalence of abnormal lung function in our population of adults with CHD, we also found that abnormal lung function was significantly associated with reduced exercise capacity. Along with traditional predictors such as decreased chronotropic index and heart rate reserve(20,21), we found that spirometry suggestive of RLD was a strong predictor of exercise intolerance by multivariate analysis with an odds ratio of 3.65 (p=0.03). While several exercise papers in the general population have been published discussing the impact of RLD on exercise(19,22), we believe that our paper is one of the first to demonstrate this relationship in adults with CHD. In this series, compared to patients with normal lung function, patients with abnormal lung function were more likely to have a lower peak VO_2 index, shorter exercise duration, and a higher NYHA functional class.

Factors that may contribute to decreased exercise tolerance among patients with RLD include increased dead space ventilation, decreased vital capacity, increased minute ventilation during exercise, reduced respiratory muscle strength from decreased thoracic or lung compliance, and abnormal gas exchange. In addition, there is concern for abnormal heart-lung interaction during exercise in patients with moderate RLD. Studies suggest that in the setting of RLD there is cardiac impairment and right ventricular dysfunction as a result of elevation in pulmonary artery pressures, and reduced compliance of the cardiac fossa from stiff lungs or chest wall resulting in restricted right ventricular diastolic filling during exercise.(19)

Limitations

This study was limited by the fact that it was a retrospective analysis and that the study cohort had a limited number of subjects. In addition, this study included patients followed at a single adult congenital heart disease center at a tertiary care medical center. Thus, subjects may reflect a more complex and fragile subset of adults with CHD, and may not be an accurate sample of the true adult congenital heart disease population. Finally, RLD was assessed in this study using spirometry. Spirometry may only be suggestive of a diagnosis of RLD. Pulmonary function testing with body plethysmography is needed to confirm the diagnosis of RLD by showing a reduction in total lung capacity.(23,24) Advantages of spirometry, however, are that it is low cost and typically performed during routine cardiopulmonary exercise testing, and therefore may be a very useful screening test in this population.

Conclusion

Abnormal spirometry suggestive of restrictive lung disease is common in the adult with congenital heart disease and is significantly associated with decreased exercise tolerance in this population. History of multiple previous thoracotomies during infancy or childhood may be a risk factor for developing restrictive lung physiology in adulthood. Further studies, are needed to evaluate the relationship between restrictive lung disease and exercise intolerance and its relationship to mortality in the adult with congenital heart disease.

References

1. Fredriksen PM, Veldtman G, Hechter S, Therrien J, Chen A, Warsi MA, Freeman M, Liu P, Siu S, Thaulow E, Webb G. Aerobic capacity in adults with various congenital heart diseases. Am J Cardiol. 2001; 87(3):310–314. [PubMed: 11165966]
2. Driscoll DJ, Offord KP, Feldt RH, Schaff HV, Puga FJ, Danielson GK. Five- to fifteen-year follow-up after Fontan operation. Circulation. 1992; 85(2):469–496. [PubMed: 1735145]
3. Fredriksen PM, Chen A, Veldtman G, Hechter S, Therrien J, Webb G. Exercise capacity in adult patients with congenitally corrected transposition of the great arteries. Heart. 2001; 85(2):191–195. [PubMed: 11156671]
4. Iserin L, Chua TP, Chambers J, Coats AJ, Somerville J. Dyspnoea and exercise intolerance during cardiopulmonary exercise testing in patients with univentricular heart. The effects of chronic hypoxaemia and Fontan procedure. Eur Heart J. 1997; 18(8):1350–1356. [PubMed: 9458430]
5. Paul MH, Wessel HU. Exercise studies in patients with transposition of the great arteries after atrial repair operations (Mustard/Senning): A review. Pediatr Cardiol. 1999; 20(1):49–55. [PubMed: 9861077]

6. Wessel HU, Paul MH. Exercise studies in tetralogy of Fallot: A review. Pediatr Cardiol. 1999; 20(1): 39–47. [PubMed: 9861075]
7. Diller GP, Dimopoulos K, Okonko D, Li W, Babu-Narayan SV, Broberg CS, Johansson B, Bouzas B, Mullen MJ, Poole-Wilson PA, Francis DP, Gatzoulis MA. Exercise intolerance in adult congenital heart disease: Comparative severity, correlates, and prognostic implication. Circulation. 2005; 112(6):828–835. [PubMed: 16061735]
8. Samanek M, Sulc J, Zapletal A. Lung function in simple complete transposition after intracardiac repair. Int J Cardiol. 1989; 24(1):13–17. [PubMed: 2759752]
9. Gilljam T, Sixt R. Lung function in relation to haemodynamic status after atrial redirection for transposition of the great arteries. Eur Heart J. 1995; 16(12):1952–1959. [PubMed: 8682032]
10. Rigolin VH, Li JS, Hanson MW, Sullivan MJ, Robiolio PA, Hearne SE, Baker WA, Harrison JK, Bashore TM. Role of right ventricular and pulmonary functional abnormalities in limiting exercise capacity in adults with congenital heart disease. Am J Cardiol. 1997; 80(3):315–322. [PubMed: 9264425]
11. Fredriksen PM, Therrien J, Veldtman G, Warsi MA, Liu P, Siu S, Williams W, Granton J, Webb G. Lung function and aerobic capacity in adult patients following modified Fontan procedure. Heart. 2001; 85(3):295–299. [PubMed: 11179270]
12. Pianosi PT, Johnson JN, Turchetta A, Johnson BD. Pulmonary function and ventilatory limitation to exercise in congenital heart disease. Congenital Heart Disease. 2009; 4(1):2–11. [PubMed: 19207396]
13. Naji NA, Connor MC, Donnelly SC, McDonnell TJ. Effectiveness of pulmonary rehabilitation in restrictive lung disease. J Cardiopulm Rehabil. 2006; 26(4):237–243. [PubMed: 16926688]
14. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten CP, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay R, Navajas D, Pedersen OF, Pellegrino R, Viegi G, Wanger J. ATS/ERS Task Force. Standardisation of spirometry. European Respiratory Journal. 2005; 26(2):319–338. [PubMed: 16055882]
15. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, Coates A, van der Grinten CP, Gustafsson P, Hankinson J, Jensen R, Johnson DC, MacIntyre N, McKay R, Miller MR, Navajas D, Pedersen OF, Wanger J. Interpretative strategies for lung function tests. European Respiratory Journal. 2005; 26(5):948–968. [PubMed: 16264058]
16. Sin DD, Wu L, Man SF. The relationship between reduced lung function and cardiovascular mortality: A population-based study and a systematic review of the literature. Chest. 2005; 127(6): 1952–1959. [PubMed: 15947307]
17. Mannino DM, Buist AS, Petty TL, Enright PL, Redd SC. Lung function and mortality in the United States: Data from the first National Health and Nutrition Examination Survey follow up study. Thorax. 2003; 58(5):388–393. [PubMed: 12728157]
18. Herrera-Soto JA, Vander Have KL, Barry-Lane P, Myers JL. Retrospective study on the development of spinal deformities following sternotomy for congenital heart disease. Spine. 2007; 32(18):1998–2004. [PubMed: 17700448]
19. Hsia CC. Cardiopulmonary limitations to exercise in restrictive lung disease. Medicine & Science in Sports & Exercise. 1999; 31(1 Suppl):S28–32. [PubMed: 9924727]
20. Diller GP, Dimopoulos K, Okonko D, Uebing A, Broberg CS, Babu-Narayan S, Bayne S, Poole-Wilson PA, Sutton R, Francis DP, Gatzoulis MA. Heart rate response during exercise predicts survival in adults with congenital heart disease. J Am Coll Cardiol. 2006; 48(6):1250–1256. [PubMed: 16979014]
21. Inuzuka R, Diller GP, Borgia F, Borgia F, Benson L, Tay EL, Alonso-Gonzalez R, Silva M, Charalambides M, Swan L, Dimopoulos K, Gatzoulis MA. Comprehensive use of cardiopulmonary exercise testing identifies adults with congenital heart disease at increased mortality risk in the medium term. Circulation. 2012; 125(2):250–259. [PubMed: 22147905]
22. Mascolo MC, Truwit JD. Role of exercise evaluation in restrictive lung disease: New insights between March 2001 and February 2003. Curr Opin Pulm Med. 2003; 9(5):408–410. [PubMed: 12904712]
23. Crapo RO. Pulmonary-function testing. N Engl J Med. 1994; 331(1):25–30. [PubMed: 8202099]

24. Aaron SD, Dales RE, Cardinal P. How accurate is spirometry at predicting restrictive pulmonary impairment? Chest. 1999; 115(3):869–873. [PubMed: 10084506]

Table 1

Descriptive data including diagnosis, age at time of spirometry testing, and gender distribution.

Diagnosis	# of Patients	Median Age (years)	Female
Coarctation of the aorta	19	28 (21–47)	10 (53%)
Tetralogy of Fallot	17	34 (18–55)	11 (65%)
LVOT obstructive lesion	12	24 (18–54)	5 (42%)
ASD, VSD, AVSD	11	38 (19–63)	7 (64%)
Single Ventricle s/p Fontan	9	34 (23–63)	4 (44%)
dTGA s/p Mustard	9	30 (19–52)	7 (78%)
ccTGA	7	42 (26–61)	5 (71%)
Ebstein anomaly	7	34 (20–44)	3 (43%)
Pulmonary valve stenosis	5	51 (21–60)	3 (60%)
dTGA s/p ASO	4	22 (19–28)	2 (50%)
Total	**100**	**31 (18–63)**	**57 (57%)**

ASD=Atrial septal defect, ASO=Arterial switch operation, AVSD=Atrioventricular septal defect, ccTGA=Congenitally corrected transposition of the great arteries, dTGA=d-transposition of the great arteries, LVOT=Left ventricular outflow tract, VSD=Ventricular septal defect

Table 2

Percentage of patients in each diagnosis category with abnormal spirometry suggestive of restrictive lung disease.

Diagnosis	# of Patients	Abnormal	Normal	p Value
Coarctation of the aorta	19	42%	58%	NS
Tetralogy of Fallot	17	76%	24%	0.05
LVOT obstructive lesion	12	25%	75%	NS
ASD, VSD, AVSD	11	36%	64%	NS
Single Ventricle s/p Fontan	9	89%	11%	0.03
dTGA s/p Mustard	9	44%	56%	NS
ccTGA	7	0%	100%	0.004
Ebstein anomaly	7	0%	100%	0.004
Pulmonary valve stenosis	5	60%	40%	NS
dTGA s/p ASO	4	25%	75%	NS
Total	**100**			

ASD=Atrial septal defect, ASO=Arterial switch operation, AVSD=Atrioventricular septal defect, ccTGA=Congenitally corrected transposition of the great arteries, dTGA=d-transposition of the great arteries, LVOT=Left ventricular outflow tract, NS= not significant (p>0.05), VSD=Ventricular septal defect

Table 3

Risk factors associated with abnormal spirometry suggestive of restrictive lung disease

Risk Factor	Unadjusted Odds Ratio	Univariate Analysis (p Value)	Adjusted Odds ratio	Multivariate Analysis (p Value)
History of > 1 thoracotomy	2.89	0.08	9.01	0.05
History of atrial arrhythmias	3.55	0.01	4.25	0.05
History of previous surgery	13.1	<0.0001	--	NS
History of amiodarone use	9.64	0.01	--	NS
Permanent pacemaker	3.94	0.03	--	NS
History of thoracotomy	1.99	0.10	--	NS

NS=not significant (p>0.05)

Table 4

Percentage of patients in each diagnosis category with exercise intolerance based on peak VO_2 index.

Diagnosis	# of Patients	Abnormal	Normal	p Value
Coarctation of the aorta	19	42%	58%	NS
Tetralogy of Fallot	17	82%	18%	0.02
LVOT obstructive lesion	12	25%	75%	NS
ASD, VSD, AVSD	11	36%	64%	NS
Single Ventricle s/p Fontan	9	100%	0	0.02
dTGA s/p Mustard	9	78%	22%	NS
ccTGA	7	43%	57%	NS
Ebstein anomaly	7	14%	86%	0.05
Pulmonary valve stenosis	5	80%	20%	NS
dTGA s/p ASO	4	75%	25%	NS
Total	100	56%	44%	

ASD=Atrial septal defect, ASO=Arterial switch operation, AVSD=Atrioventricular septal defect, ccTGA=Congenitally corrected transposition of the great arteries, dTGA=d-transposition of the great arteries, LVOT=Left ventricular outflow tract, NS=not significant (p>0.05), VSD=Ventricular septal defect

Table 5

Exercise results for each cohort displayed as means and ranges

Diagnosis	Exercise duration % predicted	VO2i % predicted	VE/VCO2 slope	RER	FEV1 %predicted	FVC % predicted	FEV1/FVC ratio	HRR (BPM)	Chronotropic Index
Coarctation of the aorta (n=19)	84% (75–94)	74% (64–85)	29 (25–33)	1.08	80% (72–87)	77% (69–84)	0.83 (0.8–0.86)	93 (81–104)	0.78 (0.69–0.87)
Tetralogy of Fallot (n=17)	77% (40–110)	62% (51–72)	34 (26–46)	1.08	72% (50–96)	70% (48–88)	0.81 (.68–.98)	88 (54–115)	0.77 (0.55–0.89)
LVOT obstructive lesion (n=12)	81% (43–110)	80% (61–97)	32.8 (24–43)	1.09	85 (53–114)	83 (50–110)	0.83 (.72–.93)	91 (31–142)	0.81 (0.35–1.07)
ASD, VSD, AVSD (n=11)	79% (51–106)	70% (37–96)	33 (27–39)	1.02	85 (72–107)	82 (66–99)	0.83 (.78–.91)	80 (31–112)	0.73 (0.3–1.02)
Single Ventricle s/p Fontan (n=9)	63% (38–83)	50% (31–70)	32 (29–37)	1.0	69% (44–89)	66% (40–87)	0.82 (.68–.90)	57 (36–85)	0.45 (0.3–0.66)
dTGA s/p Mustard (n=9)	82% (50–106)	65% (52–100)	35 (25–46)	1.1	84% (41–110)	80% (49–109)	0.84 (0.71–0.91)	95 (70–117)	0.8 (0.67–0.96)
ccTGA (n=7)	91% (58–118)	69% (35–93)	31 (29–32)	1.08	95% (74–109)	86% (77–96)	0.86 (.78–.93)	83 (63–120)	0.88 (0.62–1.06)
Ebstein anomaly (n=7)	79% (55–116)	70% (44–92)	32 (30–37)	1.15	95% (84–111)	100% (80–120%	0.81 (.67–.86)	90 (82–100)	0.81 (0.62–0.92)
Pulmonary valve stenosis (n=5)	88% (72–115)	63% (55–72)	36 (34–38)	1.06	72% (55–82)	74% (52–99)	0.81 (.70–.95)	83 (38–115)	0.7 (0.35–0.91)
dTGA s/p ASO (n=4)	81% (63–100)	72% (62–85)	31 (24–34)	1.12	85% (72–97)	80% (70–98)	0.87 (0.81–0.93)	103 (95–111)	0.77 (0.68–0.84)

ASD=Atrial septal defect, ASO=Arterial switch operation, AVSD=Atrioventricular septal defect, BPM=beats per minute, ccTGA=Congenitally corrected transposition of the great arteries, dTGA=d-transposition of the great arteries, FEV1=Forced expiratory volume in one second, FVC=Forced vital capacity, HRR=Heart rate reserve, LVOT=Left ventricular outflow tract, RER=Respiratory exchange ratio, VE/VCO2=Minute ventilation/carbon dioxide production, VO2i=Peak oxygen consumption index, VSD=Ventricular septal defect

Table 6

Risk factors associated with abnormal exercise capacity based on peak VO_2 index.

Risk Factor	Unadjusted Odds Ratio	Univariate Analysis (p Value)	Adjusted Odds Ratio	Multivariate Analysis (p Value)
Spirometry suggestive of restrictive lung disease	6.42	<0.001	3.65	0.03
History of previous surgery	9.58	<0.001	6.84	0.01
Low heart rate reserve (<70 bpm)	14.50	0.001	10.37	0.04
Low chronotropic index (<0.65)	13.32	0.002	--	NS
History of atrial arrhythmias	3.32	0.045	--	NS
History of amiodarone use	N/A*	0.024	--	NS
Permanent pacemaker	6.96	0.049	--	NS

*Unable to calculate odds ratio as 100% of patients with history of amiodarone use had abnormal exercise capacity,

NS=not significant (p>0.05).