Cardiology in the Young

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The prevalence of abnormal spirometry in children with CHD

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Original Article

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Abstract

Background: The burden of pulmonary disease in children with CHD remains under-recognised. Studies have examined children with single ventricle and two ventricle heart disease and documented a decreased forced vital capacity. Our study sought to further explore the pulmonary function of children with CHD. *Methods:* A retrospective review was performed of spirometry in CHD patients over a 3-year period. Spirometry data were corrected for size, age, and gender and analysed using z-scores. *Results:* The spirometry of 260 patients was analysed. About 31% had single ventricle (n = 80, 13.6 years (interquartile range 11.5-16.8)) and 69% had two ventricle circulation (n = 180, 14.4 years (interquartile range 12.0-17.3)). Single ventricle patients were found to have a lower median forced vital capacity z-score compared to two ventricle patients ($p = 0.0133$). The prevalence of an abnormal forced vital capacity was 41% in single ventricle patients and 29% in two ventricle patients. Two ventricle patients with tetralogy of Fallot and truncus arteriosus had similar low forced vital capacity comparable to single ventricle patients. The number of cardiac surgeries predicted an abnormal forced vital capacity in two ventricle patients except tetralogy of Fallot patients. *Conclusion:* Pulmonary morbidity in patients with CHD is common with a decreased forced vital capacity noted in single ventricle and two ventricle patients. Forced vital capacity is lower in patients with single ventricle circulation; however, two ventricle patients with tetralogy of Fallot or truncus arteriosus have similar lung function in comparison to the single ventricle group. The number of surgical interventions was predictive of forced vital capacity z-score in some but not all two ventricle patients and not predictive in single ventricle patients suggesting a multifactorial to pulmonary disease in children with CHD.

Patients with single ventricle circulation who have undergone the Fontan procedure may have a variety of extracardiac complications. Some of the most critical organ systems impacted are the liver, intestines, and lungs.[1] From a pulmonary standpoint, a variety of complications have been described including plastic bronchitis and phrenic nerve injury leading to diaphragm paresis or paralysis. These complications are well-documented, yet recent evidence has begun to mount which suggests that at baseline these patients may have intrinsic restrictive or obstructive lung disease that may manifest in pulmonary function testing.[2]

Studies have shown that abnormal spirometry and decreased forced vital capacity are common following the Fontan procedure.[3–5] Lung function is an independent predictor of death among adults with all types of CHD.[6] One study examining patients with all types of CHD found that multiple cardiac surgeries were associated with decreased forced vital capacity.[7] One study investigating exercise capacity of adults with tetralogy of Fallot and adults with Fontan palliation found that both groups had decreased forced vital capacity compared to age-matched controls, and there was no abnormality in forced expiratory volume in the first second.[8] To further investigate the prevalence of abnormal spirometry and the aetiology of the abnormal forced vital capacity, we performed a retrospective analysis of spirometry data on patients with both single ventricle and two ventricle circulation.

Methods

The Children's Hospital Los Angeles Institutional Review Board approved a retrospective review of existing cardiopulmonary exercise and pulmonary function data in children with CHD. Children and adolescents with CHD who had a clinically indicated cardiopulmonary exercise test were included. Patients performed routine spirometry per American Thoracic Society guidelines immediately prior to exercise. Post-exercise spirometry was not done.

Children were screened to have the ability to perform cardiopulmonary exercise testing. Standard American Thoracic Society criteria were used for grading spirometry quality.[9] The attending physician supervising and interpreting the tests noted when there was premature termination of exhalation and poor reproducibility after four breathing trials. Per cent predicted (% predicted) and z-scores of the forced vital capacity, forced expiratory volume in the first second , and mid-expiratory flow rates ($FEF_{25-75\%}$) were calculated using the Global lung index calculator. Spirometry was corrected for age, gender, and height. A study found no evidence that race/ethnicity-based spirometry reference equations improved prediction of clinical events compared with race-neutral equations, and race-adjusted prediction equations for pulmonary function may have adverse consequences for patients of colour such as undertreatment,[10] so Caucasian was used for all patients for the calculations to reduce bias in the predicted values. There is no ethnic correction for Hispanic ethnicity in the Global lung index calculator. In all cases, z-scores were calculated from raw data values using the Global Lung Function Initiative and abnormal values were defined as z-score below −1.64.[11]

Data including spirometry, age at exercise testing, gender, body mass index, ethnicity, cardiac diagnosis, and the number of cardiac surgeries were extracted from the medical record. In all cases, demographic information was readily available; however, in 36 cases a patient's surgical history was not able to be verified due to lack of clear documentation in the medical record. In these cases, the number of cardiac surgeries was omitted. Of note, 10 patients performed multiple exercise tests. In these cases, the most recent study was used for analysis. Twenty patients had incomplete spirometry data. A total of four patients were also excluded if spirometry was not performed during the exercise study or if the patient's effort and ability were deemed poor. A total of 24 patients were excluded, leaving 260 patients for analysis. Body mass index z-score data were unavailable for patients age 20 and older. Median and interquartile range were used for descriptive statistics given that the variables were not normally distributed. Logistic regression analysis was done by selecting significant predictors. Body mass index z-score as a continuous variable and cardiac surgeries as a nominal variable were selected to be included in the model. Age was accounted for within the body mass index z-score variable itself.

Statistical analysis was performed using STATA 17.0 software (StataCorp, College Station, TX).[12]

Results

A total of 260 patients with CHD performed complete pulmonary function testing during the study period. The subjects had a median age of 14.2 years (interquartile range 12.0–17.2), and 65.4% were male. The median body mass index z-score was 0.33, and approximately 50% were of Hispanic ethnicity. Of the 260 patients, 80 (31%) had corrected single ventricle palliation with Fontan physiology and 180 (69%) had other forms of two ventricle CHD. There were no statistically significant differences between the groups in age, sex, body mass index, and ethnicity.

The median forced vital capacity z-score of the entire study population was −1.1 (interquartile range −2.0 to −0.3) with 33.1% of subjects exhibiting an abnormal forced vital capacity, suggesting a restrictive pattern (Table 1). The median forced expiratory volume in the first second/forced vital capacity was 89 (interquartile range 84–94) with 4.2% of subjects exhibiting an obstructive pattern with abnormal forced expiratory volume in the first second/forced vital capacity. Patients with single ventricle circulation had a lower forced vital capacity z-score in comparison to those with two ventricle circulation ($p = 0.0133$). Thirty-three (41.3%) patients with single ventricle circulation and 53 (29.4%) patients with two ventricle circulation had an abnormal forced vital capacity ($p = 0.062$). There were no significant statistical or clinical differences between these groups in regard to the per cent predicted forced expiratory volume in the first second, forced expiratory volume in the first second /forced vital capacity, and $FEF_{25-75\%}$.

Our primary aim was to study single ventricle and two ventricle populations based on spirometry values. However, we found subgroups within the two ventricle group with abnormal forced vital capacity. Post hoc subgroup analysis by individual diagnosis found 75% (n = 6) of patients with truncus arteriosus, and 43.8% (n = 21) of patients with tetralogy of Fallot had abnormal forced vital capacity (Table 2). The pulmonary function of these subgroups was compared directly against the forced vital capacity of the single ventricle group and the remainder of the two ventricle group. The tetralogy of Fallot and truncus arteriosus subgroups had forced vital capacity that did not differ significantly from that of the single ventricle group (−1.57 (interquartile range −2.47 to −0.61) and −1.92 (interquartile range −3.20 to −1.65), respectively). The truncus arteriosus group had a significantly lower per cent predicted forced vital capacity, forced expiratory volume in the first second, forced expiratory volume in the first second / forced vital capacity, and $FEF_{25-75\%}$ compared to the single ventricle group. The remainder of the two ventricle group, excluding tetralogy of Fallot and truncus arteriosus patients, had a lower percentage of patients with an abnormal forced vital capacity (21.6%, $p = 0.003$).

To investigate the aetiology of the abnormal spirometry in the population, surgical histories were obtained. Of the 260 patients analysed, a cardiac surgical history was obtained in 224 (86.1%). The median number of cardiac surgeries for the entire study population was 2. The single ventricle patients underwent a median of 3 (interquartile range 3–4) surgeries and two ventricle patients underwent 1 (interquartile range 0–2) surgery (Table 1). The two ventricle subgroup analysis demonstrated tetralogy of Fallot patients underwent two (interquartile range 1–2) surgeries, truncus arteriosus patients underwent three (interquartile range 1.5–3.5), and the remainder of two ventricle patients underwent a median of one (interquartile range 0–1) cardiac surgeries (Table 2). Three or more cardiac surgeries were associated with a higher rate of an abnormal forced vital capacity in both the single ventricle and two ventricle groups. Tetralogy of Fallot patients with 1–2 surgeries exhibited a higher rate of abnormal forced vital capacity compared to other two ventricle diagnoses, and there was a lower percentage of abnormal forced vital capacity in the tetralogy of Fallot group with four surgeries compared to three surgeries (Fig 1).

Logistic regression analysis of all patients revealed that increasing cardiac surgeries and lower body mass index was most predictive of an abnormal forced vital capacity. Analysis of the two ventricle group revealed that increasing cardiac surgeries was most predictive of an abnormal forced vital capacity (OR 2.25, $p < 0.001$) with a lower body mass index (OR 0.55, $p = 0.001$) as a slightly less significant predictor. In the single ventricle group, the number of cardiac surgeries did not reach significance as a predictor, while lower body mass index remained a significant predictor (OR 0.63, $p = 0.048$). Cardiac surgeries were not a significant predictor in the tetralogy of Fallot group ($p = 0.19$), whereas a lower body mass index ($p = 0.049$) was predictive of abnormal forced vital capacity. A logistic regression analysis could not be performed on the truncus arteriosus group due to small sample size.

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Table 1. Spirometry and surgical data of single and two ventricle populations.

	Total n = 260	Single Ventricle n = 80	Two Ventricle n = 180	p Value
FVC % pred, median (interquartile range)	87 (78–96)	84 (74–93)	89 (79–98)	0.012
FVC z-score, median (interquartile range)	−1.1 (−2.0 to −0.3)	−1.4 (−2.2 to −0.6)	−1.0 (−1.9 to −0.2)	0.013
Abnormal z-score FVC, n (%)	86 (33%)	33 (41%)	53 (29%)	0.062
FEV_{1sec} % pred, median (interquartile range)	89 (78–98)	86 (77–94)	91 (78–99)	0.085
FEV_{1sec} /FVC, median (interquartile range)	89 (84–94)	90 (86–93)	88 (83–94)	0.063
Abnormal z-score FEV_{1sec} /FVC, n (%)	11 (4.2%)	1 (1.3%)	10 (5.6%)	0.11
$FEF_{25-75\%}$ % pred, median (interquartile range)	92 ± 25	92 (77–107)	91 (73–108)	0.76
Cardiac surgeries*, median (interquartile range)	2 (1-3)	3 (3–4)	1 (0–2)	<0.001

*Cardiac surgery data not reported in 36 patients. FEV_{1sec} = forced expiratory volume in the first second; FVC = forced vital capacity.

Table 2. Spirometry and surgical data of one ventricle, tetralogy of Fallot, truncus arteriosus, and other two ventricle diagnoses.

	Single ventricle n = 80	Tetralogy of Fallot n = 48	Truncus arteriosus n = 8	Other 2V n = 125
FVC % pred, median (interquartile range)	84 (74–93)	82 (72–93) p* = 0.47	77 (63–81) p = 0.041	93 (82–100) p = 0.001
FVC z-score, median (interquartile range)	−1.4 (−2.2 to −0.6)	−1.57 (−2.47to −0.61) p = 0.43	−1.92 (−3.20 to −1.65) p = 0.067	−0.61 (−1.5 to −0.02) p = 0.001
Abnormal z-score FVC, n (%)	28 (41.3%)	21 (43.8%) p = 0.78	6 (75%) p = 0.068	27 (21.6%) p = 0.003
FEV_{1sec} % pred, median (interquartile range)	90.5 (77.8–99.1)	85.9 (74.8–95.6) p = 0.52	72.2 (60.9–79.5) p = 0.012	92.3 (82.1–101.0) p = 0.0027
FEV_{1sec} /FVC, median (interquartile range)	90 (86–93)	89.5 (83.5–94) p = 0.82	83.5 (81–86.5) p = 0.013	88 (83–94) p = 0.054
Abnormal z-score FEV_{1sec} /FVC, n (%)	1 (1.3%)	2 (4.2%) p = 0.29	1 (12.5%) p = 0.042	7 (5.6%) p = 0.12
$FEF_{25-75\%}$ % pred, median (interquartile range)	92.3 (76.7–107.2)	90.5 (72.6–106.7) p = 0.65	61.0 (52.2–66.2) p = 0.0024	94.1 (78.4–108.4) p = 0.77
Sternotomies, median (interquartile range)	3 (3–4)	2 (1–2) p < 0.001	3 (1.5–3.5) p = 0.068	1 (0–1) p < 0.001

*p Values are calculated from single ventricle data against either tetralogy of Fallot, truncus arteriosus, or other two ventricle. FEV_{1sec} = forced expiratory volume in the first second; FVC = forced vital capacity.

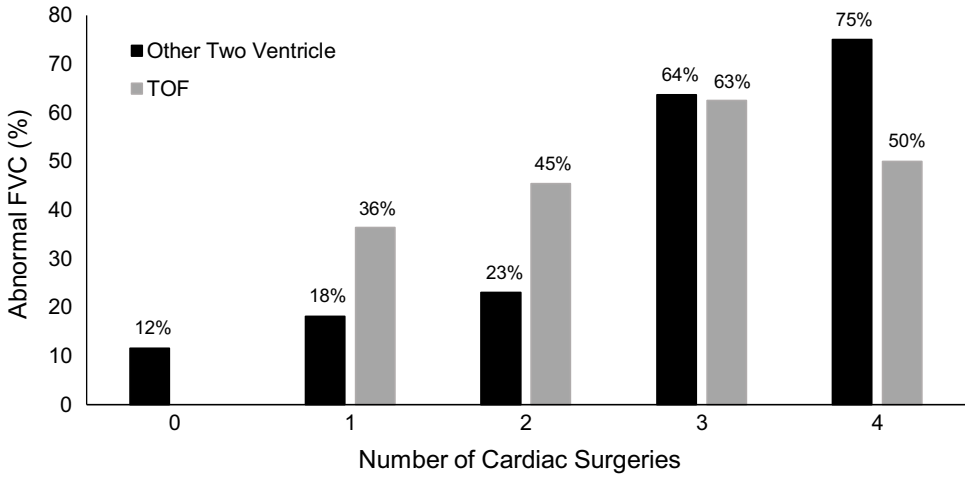

Figure 1. The percentage of individuals with an abnormal forced vital capacity based on the number of cardiac surgeries and diagnosis of either tetralogy of Fallot or another two ventricle circulation diagnosis.

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Discussion

Our study highlights that abnormal spirometry defined as an abnormal forced vital capacity is common in children with all types of CHD. While other studies have shown that single ventricle patients have abnormal lung function, our study demonstrated that approximately a quarter of two ventricle patients had an abnormal forced vital capacity. In subgroup analysis, approximately 40% of tetralogy of Fallot patients and 75% of truncus arteriosus patients possess an abnormal forced vital capacity. Our study found that patients with either tetralogy of Fallot physiology or truncus arteriosus possess a forced vital capacity that does not significantly differ from patients with palliated single ventricle disease. Abnormal spirometry is associated with increased mortality in adults with CHD.[6] While therapies for abnormal forced vital capacity in CHD have not been evaluated, the presence and possible progression of abnormal forced vital capacity may be an important clinical factor to follow longitudinally.

In investigating the predictive factors responsible for the forced vital capacity in these specific diagnostic groups, it was determined that surgical history is of minimal predictive influence in subgroup analysis of the single ventricle and tetralogy of Fallot subgroups as both these diagnoses require several surgical interventions, suggesting that factors not accounted for in the analysis were likely responsible for this finding. This was not the case for all other two ventricle patients analysed where the number of cardiac surgeries was highly predictive of an abnormal forced vital capacity. There was a dose-response relationship between number of cardiac surgeries and increasingly more patients with abnormal forced vital capacity in two ventricle patients, except in tetralogy of Fallot patients. This suggests that attention to cardiac surgical history is of utmost importance especially in children with different types of two ventricle disease. Our study found that lower body mass index was a significant predictor of abnormal forced vital capacity, suggesting low body mass index may be a predictor of poor health.

More recent studies in tetralogy of Fallot patients reveal a decreased total lung capacity in approximately a quarter of patients studied after complete intracardiac repair.[13,14] The mechanism of this is currently unclear, though one study analysing the spirometry of patients with tetralogy of Fallot postulated that abnormal spirometry may be secondary to right ventricular outflow tract obstruction leading to pulmonary hypoperfusion at birth.[15] Tetralogy of Fallot patients may also have pulmonary artery hypoplasia prior to repair in the perinatal period which can contribute to restrictive lung physiology. Right ventricular dilation may contribute to low forced vital capacity due to mass effect on the lung. Our study is unable to make conclusions regarding specific mechanism of low forced vital capacity in tetralogy of Fallot patients. Our study also may have been underpowered to truly detect differences in number of surgeries and forced vital capacity in tetralogy of Fallot patients. Similar studies have not been reported in Truncus Arteriosus patients.

One limitation of our study was the fact that total lung capacity, which requires plethysmography, is a better measure of lung volume than forced vital capacity. This is because forced vital capacity can be decreased by hyperinflation and restrictive diseases. Spirometry is advantageous in that it can be obtained quickly and is easy to perform, and our data suggest an absence of an obstructive component; thus, hyperinflation is less likely, and therefore, forced vital capacity is a reasonable screening test for restrictive disease. We have still been careful not to use the term restrictive lung disease in lieu of abnormal vital capacity and preserved forced expiratory volume in the first second/forced vital capacity. We did not report or correlate exercise data in this study but instead focused on characterising spirometry abnormalities as our exercise data were reported separately.[7] We did not separate sternotomies from thoracotomies in this study, though the majority of surgical interventions in CHD are performed via median sternotomy. As a single-centre retrospective study, there are sample size and bias limitations. There is particular interest in the tetralogy of Fallot, and truncus arteriosus patients though again those subgroups were small, thus limiting analysis.

Conclusion

Our study found that abnormal forced vital capacity was common in all patients with CHD, though more prevalent in patients with tetralogy of Fallot, truncus arteriosus, or single ventricle CHD. Number of past cardiac surgical interventions did not impact the prevalence of abnormal forced vital capacity in these 3 subgroups but did in the other two ventricle patients.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/S1047951123000550.

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Conflicts of interest. None.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the Helsinki Declaration of 1975, as revised in 2008, and its later amendments or comparable ethical standards have been approved by the Children's Hospital Los Angeles Institutional Review Board.

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