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Original Article

Exercise Limitation in Children after Tetralogy of Fallot repair Is Not related to Right Ventricular Dysfunction: Single Egyptian Center Experience

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Abstract:
Background: Tetralogy of Fallot (TOF) is one of the most prevalent cyanotic congenital heart diseases requiring surgery early in life.
Aim of work: Exercise capacity and right ventricular diastolic dysfunction in children after TOF repair.
Methods: Cross sectional descriptive study was conducted on 27 cases with TOF after total surgical repair. Cases were subjected to 12 leads ECG, chest X-ray, 6-minute walking test (6MWT) to assess the exercise capacity and transthoracic color Doppler echocardiography with assessment of right ventricle myocardial performance index (RVMPI) and pulmonary regurgitation index (PRi).
Results: The mean ± SD age of the our studied was TOF patients 6.59 ± 1.80 years. The mean ± SD age at operation was 2.46 ± 0.95 years. All had dilated right ventricle (right ventricle dilatation index RVDi > 0.5), and moderate to severe pulmonary regurge (PR) estimated by PRi (PRi <0.77). Impaired RVMPI (>0.32) was found in 6 (22%) patients. Exercise capacity measured by 6-MWT was significantly reduced compared to the normal population of the same age group (p= 0.001). Results of 6-MWT did not correlate with the RVMPI (p= 0.44, r= -0.077), the PRi (p= 0.83, r=0.006), QRS (p=0.31, r=0.066), or corrected QT interval (p=0.89, r= 0.169).
Conclusion: Exercise capacity was limited in our TOF patients after surgical repair, that was not related to right ventricular diastolic dysfunction as it did not correlate with RVMPI, degree of PR, QRS duration, nor corrected QT interval.

Level of Evidence of Study: IIA (*1*).
Keywords: Tetralogy of Fallot (TOF); right ventricular dysfunction; exercise capacity; 6-minute walking test; children.
Abbreviations: ACE: angiotensin converting enzyme; ECG: electrocardiography; ET: ejection time; HR: heart rate; ICT: isovolumetric contraction time; IRT: isovolumetric relaxation time; MHZ: megahertz; MPI: myocardial performance index; MWT: minute walk test; NYHA: New York heart association; PR: pulmonary regurgitation; PRi: pulmonary regurgitation index; QTc: corrected QT interval; RBBB: right bundle branch block; RV: right ventricle; RVDi: right ventricular dilatation index; RVMPI: right ventricle myocardial performance index; RVOT: right ventricular outflow tract; SO2: oxygen saturation; TOF: tetralogy of Fallot; VSD: ventricular septal defect.

Introduction

Tetralogy of Fallot (TOF) is a frequently occurring cyanotic congenital heart defect that requires early surgical repair. After primary surgery, pulmonary regurgitation (PR) is a common consequence because a transannular patch was used throughout the right ventricle outflow tract (RVOT) reconstruction process, as well as vigorous infundibulectomy, including the pulmonary valve annulus (*2*). Residual damage can result in the progressive right ventricle (RV) hypertrophy and malfunction, atrial and ventricular arrhythmias, exercise intolerance, heart failure, and sudden cardiac arrest (*3*). Exercise intolerance is multifactorial and has been proven to be associated with PR, poor lung function, and ventricular malfunction in most individuals with TOF (*4*). In this study, we measured the degree of PR by calculating the PRi, and myocardial performance index (MPI) by echocardiography and correlated it with our patients' exercise capacity, which was determined through a 6-minute walk test. The six-minute walk test (6-MWT) is a straightforward, practical, and safe submaximal exercise test for individuals with respiratory or cardiovascular disease (*5*). The 6-MWT is increasingly being utilized in young children, for whom doing cardiac exercise tests is particularly difficult. It requires a great level of coordination, cooperation, and motivation (*6*). We aimed to study exercise capacity and right ventricular diastolic dysfunction in children after TOF repair.

Subjects and Methods

This is a cross-sectional study wherein 27 patients with reconditioned TOF aged ≥4 years were enrolled over 6 months at Children's Hospital's Pediatric Postoperative Cardiac Surgery Clinic, Cairo University Hospitals, Egypt.

Participants

Patients with TOF variants (absent pulmonary valve, pulmonary atresia with ventricular septal defect, and double-outlet RV) and patients with significant postoperative residual abnormality or complication (VSD, valvular or peripheral stenosis, aneurysmal dilatation of the RVOT patch) were excluded. None of our patients had other diseases that may affect exercise ability e.g., coronary artery anomalies, associated joint disease or stroke. Each patient signed an informed consent.

Methods

A complete medical history was gathered for each patient, comprising age, gender, age at the time of surgical repair, and symptoms of heart failure. The NYHA (New York Heart Association) functional categorization was used to evaluate the stage of heart failure (*7*). A full Clinical examination was performed for each patient, including anthropometric measures, which were plotted to Egyptian growth curves (*8*), as well as a complete cardiac examination.

Electrocardiogram: Each patient was subjected to 12-leads ECG. The diagnosis of prolonged QRS was carried out after correlation with the patient age and sex. The corrected QT interval for heart rate (QTc) was determined utilizing Bazett's formula: $QTc = QT / \sqrt{RR}$. In children had 6 months and older, the normal QTc interval is (0.40 ±0.014) seconds with a normal upper limit of 0.44 seconds (*9*).

Trans-thoracic conventional and color Doppler echocardiography was performed as outlined by the American Society of Echocardiograph (*10*). The patients were investigated in a quiet, dark room in the left lateral decubitus using a (Hewlett-Packard 5500 SONOS phased array machine equipped with sector scanner 4,8 MHZ probes) to determine heart dimensions, detect residual RV outflow tract obstruction and VSD blockage, and detect valve regurgitation. The global functions of the RV were estimated by measuring the myocardial performance index (MPI) on the lateral tricuspid annulus utilizing the pulsed tissue Doppler approach as per the following expression: the product of the relaxation times and isovolumetric contraction (IRT and ICT) split by the ejection time (ET); and MPI equals (ICT+IRT)/ET. (*11*)

The normal mean value of RVMPI is 0.28±0.04 (*10*, *12–14*). We used RVMPI > 0.32 as a cut-off value to indicate global RV dysfunction in this study. Color and continuous Doppler imaging in the parasternal short-axis view and the ratio of the time of PR flow to the total diastolic time (PR index) were used to estimate the pulmonary regurgitation (PR) severity. PR index (PRi) more than or equal to 70% were regarded as mild PR, whereas values less than or equal to 70% were classified as moderate to severe PR (*15*).

For all individuals, the right ventricular dilatation index (RVDi) was measured. RVDi is the ratio of the RV end-diastolic dimension to the LV end-diastolic dimension (RVDi =RVEDD/LVEDD). RVDi less than or equal to 0.5 is considered normal (*16*).

6-Minute Walking Test: At a constant, uninterrupted, slow pace, it is the distance that an individual can walk in six minutes (*5*).

All 6 MWTs were conducted on a 50-meter-long corridor on flat, and firm ground. Before attempting the walk test, each child was given the exact same instructions. The children were instructed to stroll at their own pace without running or racing. To avoid competition, the tests were administered individually to each youngster. Every minute, the oxygen saturation and heart rate of the infant were determined using a portable pulse oximeter. The youngsters were encouraged (e.g., "Keep going", "You are doing well") and informed of the remaining time. We compared the results of 6-MWT to the normal values of published data in similar age group (4-11 years), the mean distance walked in 6 minutes was 470±59 m with range from 420±39 m to 512±41 m (*6*).

Statistical Analysis

The data were analyzed with IBM SPSS V.15. Categorical data were represented by percentages and frequencies, whereas continuous data were represented by the mean and standard deviation (SD). The Pearson Chi-Square was used to evaluate categorical data. The One-Way ANOVA and the independent-samples t-tests were employed to compare groups. P <0.0.5 was regarded as significant.

Results

Our study comprised 27 patients with completely repaired TOF, with a mean +/- SD age of 6.59 ± 1.80 years and a mean age at the time of surgery of 2.46 ± 0.95 years. The duration after surgical repair ranged from 2 to 9.5 years, with a mean of 4.9 ± 2.54 years. They were 17 (62.9%) males and 10 (37.03%) females.

Table1. Echocardiographic and ECG measurements of the studied cases.

	Range	**Mean± SD**
RVDi	0.54-8.33	0.99±1.47
RVMPI	0.09 – 0.53	0.21±0.11
PRi	0.38-0.94	0.69±0.13
QTc	0.41-0.57	0.47 ± 0.04
QRS duration	0.07-0.16	0.11± 0.02

RVDI: right ventricular diastolic index, RVMPI: right ventricular myocardial performance index, PRi: pulmonary regurgitation index, QTc: corrected QT interval.

Our cases were generally in good health as: majority of our patients 19 (70.4%) were NYHA class I, and 8 (29.6%) patients were NYHA class II, their mean weight centile was (22.20 ± 4.63), and their mean height centile was (42.76±24.73), and no abnormality could be detected in clinical examination except for features of dilated right ventricle, murmur of pulmonary regurgitation. Most of our patients, 22 (81.4%), were on anti-failure medications (diuretics, ACE inhibitors). Regular estimation of patients' electrolytes (sodium, potassium, calcium, magnesium) showed no abnormalities. All patients had dilated right ventricle (RVDi > 0.5), and abnormal right ventricular myocardial performance index (higher than 0.32) in 6 (22.2%) patients. Most of the studied cases (74%) showed a severe degree of pulmonary regurgitation (PRi <0.77). ECG findings included 19 (70.4%) cases had prolonged QRS and corrected QT interval as compared with the upper limit for age. All patients had normal sinus rhythm, and RBBB, and none had an arrhythmia. (Table 3).

The mean total length in the 6-MWT of the study group was significantly less than the mean total length in the 6-MWT of normal children (p= 0.001). (Table 4). There was no significant difference in 6-MWT distance between male and female patients (p =0.29). There was no statistically significant difference in the echocardiographic parameters (RVMPI, PRi) or ECG parameters (QTc, QRS duration) between cases with normal 6MWT and those with impaired 6MWT results (p value= 0.44, 0.83, 0.89, 0.31 respectively). (Table 5).

Table 2. Post-operative ECG findings of the studied cases

QRS Duration	Number of cases	%
< 0.08(sec)	8	29.6
>0.08(sec)	19	70.4
(QTc) Corrected QT interval		
<0.44(sec)	8	29.6
>0.44(sec)	19	70.4

ECG: electrocardiography, QTc: corrected QT interval.

Table 3. Six-minute walking test distances of the studied cases**.**

	Range	Mean ± SD
Total distance (m)	340 – 486	433.70 ± 39.42
Min1-HR (/min)	75 – 104	90 ± 8
Min1-SO2 (%)	96 – 99	97.85 ± 0.86
Min 6-HR(/min)	98 – 128	112 ± 8
Min 6-SO2 (%)	96 – 98	97.04 ± 0.80

Min: minute, HR: heart rate, SO2: oxygen saturation.

Table 4. Comparison between total length in 6-MWT in cases of TOF repair and published normal values for age.

	Age / Y							Total N= (27)
	5 (n=3)	6 (n=4)	7 (n=10)	8 (n=2)	9 (n=2)	10 (n=4)	11 (n=2)	
Distance/min (Study group)	364.6±23.0	426.5±10.2	435.9±38.3	438.5±20.5	469±24	450.5±37.1	467.0±15.5	433.7±39.4
Distance/min (Normal)	420±39	463±40	488±35	483±40	496±53	506±45	512±41	470±59
P value	0.05	0.006*	0.002*	0.20	0.35	0.05	0.15	0.001*

Table 5. 6-minute Walking distance classified and correlated according to different echocardiographic and electrocardiographic criteria.

		Number	%	6 min distance Mean ± SD	r value	P value
RVMPI	Normal <0.32	22	77.8	444.83 ± 16.12	-0.077	0.44
	Increased (0.34-0.53) Mean +/-SD= 0.39±0.29	6	22.2	430.52 ± 43.67		
PRi	Normal > 0.77	20	74.1	436.42 ± 34.39	0.006	0.83
	Decreased (0.38-0.75) Mean +/-SD= 0.49± 0.13	7	25.9	432.75 ± 41.68		
QTc	Normal <0.44 second	8	29.6	435.37 ± 40.00	0.169	0.89
	Prolonged (0.45-0.57) Mean +/-SD= 0.51± 0.08	19	70.4	433.00 ± 40.25		
QRS Duration	Normal < 0.08 second	8	29.6	438.78 ± 34.12	0.066	0.31
	Prolonged (0.09-0.16) Mean +/-SD= 0.13±0.04	19	70.4	421.62 ± 50.40		

PRi: pulmonary regurgitation index; QTc: corrected QT interval; RVMPI: right ventricle myocardial performance index.

Discussion

A moderate to severe degree of PR is a well-known, prevalent consequence in TOF patients after surgical repair and may occur in more than half of patients (*17–19*). This PR results in right ventricle continuous dilation and stretching, which lead to several adverse effects later in life, including decreased exercise capacity, right and left ventricular malfunction, electrocardiographic anomalies, and perhaps most significantly, the development of ventricular arrhythmias and sudden cardiac arrest (*17*).

We report that all our TOF patients had dilated RV (RVDi > 0.5), and moderate to severe PR estimated by PRi, impaired RVMPI (>0.32) in 6 (22%) patients and reduced exercise capacity measured by 6-MWT compared to the normal population of same age group. The results of 6-MWT did not correlate with the RVMPI, the PRi, QRS duration, nor QTc interval. We did not assess the 6-MWT prior to the surgery. We are not aware if the current post-operative 6-MWT has improved post-operatively or declined. Results of a preoperative 6MWT could be helpful to properly judge the improvement or decline in our patients, unfortunately these were not available. As the study was not a prospective one, so we are not aware if 6-MWT will improve with time for the studied cohort, or it will decline.

This continuous dilatation and stretch in RV may not manifest clinically in most TOF patients. Nonetheless, most TOF individuals report an acceptable level of exercise ability as a result of long-term adaptation (*20*). This explains the need to perform accurate measurements for the patients' exercise capacity. The 6-MWT in our studied population was carried out to assess exercise capacity. The mean total distance walked in our cases was statistically significantly lower than that reported for normal children (*5*). We preferred comparing our results to published data of normal children as these studies are carried out on large number of normal children giving more reliable normal estimates compared to the distances of a smaller control group. The limited exercise capacity in our studied cohort did not correlate with the diastolic dysfunction. It might be related to the sedentary life encouraged by the over worried parents after cardiac surgery, which may add to the physical limitations in our patients. Yet, accurate estimation of the patients' lifestyle was not estimated in our study. It is not clear if the life style of our studied cohort had influence on their exercise capacity.

This limited exercise capacity in our patients might be caused by the long term effects of hypoxemia which from which the patients suffered pre and intra operatively, dilated stretched RV secondary to pulmonary regurgitation, and longer QRS duration. Residuals and arrythmias might be other factors that contribute to the exercise limitation although it was not the case in our patients. Our results are in accordance with other authors who found that the exercise capacity in all patients was less than the minimum for age (*20*). However, it was contradictory to that reported by Kotby et al., who showed that the exercise performance was insignificantly reduced in patients in relation to the control group, probably because they used a different method to assess the exercise performance (the treadmill exercise stress test) (*21*).

We detected no correlation between RVMPI, and exercise capacity as measured by distance on the 6-MWT, which indicate that impaired exercise ability in our patients may be related to other factors. Possible factors responsible for the exercise limitation might be abnormal lung functions following cardiac surgery, secondary to intra and early postoperative factors e.g., duration of chest tube, and postoperative ventilation, that are known to limit exercise capacity (*22*). We did not asses the pulmonary functions as it was beyond the scope of this study.

The relation of exercise intolerance and right ventricle diastolic dysfunction is inconsistent, where some have reported that the diastolic dysfunction was responsible for the exercise limitation (*20)* and others (*21, 23)* including our work did not. This inconsistency might be related to the different right ventricle assessment methods, or how the exercise intolerance was assessed.

In our study, the QRS duration and corrected QT interval were prolonged in most of our patients (70%); however, both did not show statistically significant difference with the results of the 6-MWT ($p=0.31$, $r=0.066$, $p=0.89$, $r= 0.169$ respectively). Others reported a prolonged QRS and QT interval that were substantially longer in patients than in controls (*17*). QRS duration and QTc interval did not correspond with the distance walked in our study probably because they were prolonged secondary to the presence of RBBB.

Our study had several limitations, including small sample size, lack of specified physical activity questionnaire to assess lifestyle of the patients, lack of preoperative 6MWT, the absence of a tissue Doppler approach for MPI assessment, and the lack of the intra- and early postoperative periods data, which may affect the RVMPI, exercise capacity of the patients.

Conclusion

Most TOF individuals after surgical repair report an acceptable level of exercise ability because of long-term adaptation. This highlights the need to perform accurate but simple measurements for the patients' exercise capacity like 6MWT. As detected by 6-MWT, exercise capacity was significantly impaired in our TOF patients after surgical repair, but is not significantly related to RVMPI, PR degree, the QRS duration, nor corrected QT interval. We recommend regular follow up of diastolic functions of the RV. Further studies are needed to study effect of regular physical activity on their exercise capacity.

Author Contributions: This work was carried out in collaboration between all authors. Lamiaa Abdelrahman Ibrahim: managed the literature searches, wrote, edited the manuscript, and helped in the echocardiography. Fatma Alzahraa Mostafa: designed the study, reviewed the protocol and the manuscript. Gehan Hussien Ahmed: designed the study, reviewed the protocol and the manuscript. Abd El Rahamn MY: helped in the literature, revised the manuscript. Sherif Elmahdy: collected the cases, did the examination, 6MWT, helped in the statistics. Hanan Zekry: reviewed the protocol, did the echocardiography, and reviewed the data analysis and the manuscript. All authors have read and approved the final manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in connection with the reported study. Authors declare veracity of information.

References

1. S. Tenny, M. Varacallo, *Evidence Based Medicine*. (StatPearls Publishing; Treasure Island (FL), 2020; https://www.ncbi.nlm.nih.gov/books/NBK470182/).
2. M. Carminati, F. R. Pluchinotta, L. Piazza, A. Micheletti, D. Negura, M. Chessa, G. Butera, C. Arcidiacono, A. Saracino, C. Bussadori, Echocardiographic Assessment after Surgical Repair of Tetralogy of Fallot. *Front. Pediatr.* **3** (2015), doi:10.3389/fped.2015.00003.
3. N. Dłużniewska, P. Podolec, T. Miszalski-Jamka, M. Krupiński, P. Banyś, M. Urbańczyk, B. Suder, G. Kopeć, M. Olszowska, L. Tomkiewicz-Pająk, Effect of ventricular function and volumes on exercise capacity in adults with repaired Tetralogy of Fallot. *Indian Heart Journal*. **70**, 87–92 (2018).
4. S. Alborikan, B. Pandya, K. Von Klemperer, F. Walker, S. Cullen, S. Badiani, S. Bhattacharyya, G. Lloyd, Cardiopulmonary Exercise Test (CPET) in patients with repaired Tetralogy of Fallot (rTOF); A systematic review. *International Journal of Cardiology Congenital Heart Disease*. **1**, 100050 (2020).
5. B. Radi, A. M. Ambari, B. Dwiputra, R. E. Intan, K. Triangto, A. Santoso, B. Setianto, Determinants and Prediction Equations of Six-Minute Walk Test Distance Immediately After Cardiac Surgery. *Front. Cardiovasc. Med.* **8**, 685673 (2021).
6. A. E. Lammers, G.-P. Diller, D. Odendaal, S. Tailor, G. Derrick, S. G. Haworth, Comparison of 6-min walk test distance and cardiopulmonary exercise test performance in children with pulmonary hypertension. *Archives of Disease in Childhood*. **96**, 141–147 (2011).
7. S. D. Russell, M. A. Saval, J. L. Robbins, M. H. Ellestad, S. S. Gottlieb, E. M. Handberg, Y. Zhou, B. Chandler, New York Heart Association functional class predicts exercise parameters in the current era. *American Heart Journal*. **158**, S24–S30 (2009).
8. A. M. El Shafie, F. M. El-Gendy, D. M. Allahony, H. H. Hegran, Z. A. Omar, M. A. Samir, Z. A. Kasemy, A. N. El-Bazzar, M. A. Abd El-Fattah, A. A. Abdel Monsef, A. M. Kairallah, H. M. Raafet, G. M. Baza, A. G. Salah, W. S. Galab, S. H. Alkalash, A. A. Salama, N. A. Farag, W. A. Bahbah, Development of LMS and Z Score Growth References for Egyptian Children From Birth Up to 5 Years. *Front. Pediatr.* **8**, 598499 (2021).
9. Park MK., *Pediatric cardiology for Practitioners*. (Mosby Elsevier.Plos One., Philadelphia, ed. 7th, 2020).
10. W. W. Lai, T. Geva, G. S. Shirali, P. C. Frommelt, R. A. Humes, M. M. Brook, R. H. Pignatelli, J. Rychik, Guidelines and Standards for Performance of a Pediatric

Echocardiogram: A Report from the Task Force of the Pediatric Council of the American Society of Echocardiography. *Journal of the American Society of Echocardiography*. **19**, 1413–1430 (2006).
11. H. Z. A. Abuomara, O. M. Hassan, T. Rashid, M. Baraka, Myocardial performance index as an echocardiographic predictor of early in-hospital heart failure during first acute anterior ST-elevation myocardial infarction. *The Egyptian Heart Journal*. **70**, 71–75 (2018).
12. C. Tei, L. H. Ling, D. O. Hodge, K. R. Bailey, J. K. Oh, R. J. Rodeheffer, A. J. Tajik, J. B. Seward, New index of combined systolic and diastolic myocardial performance: a simple and reproducible measure of cardiac function--a study in normals and dilated cardiomyopathy. *J Cardiol*. **26**, 357–366 (1995).
13. A. F. AbdelMassih, F. Al. Zahraa Hassan, A. El-Gammal, M. Tawfik, D. Nabil, The overlooked left ventricle in persistent pulmonary hypertension of the newborn. *The Journal of Maternal-Fetal & Neonatal Medicine*. **34**, 72–76 (2021).
14. H. M. Agha, H. Ibrahim, I. A. El Satar, N. A. El Rahman, D. A. El Aziz, Z. Salah, S. El Saeidi, F. Mostafa, W. Attia, M. A. El Rahman, G. A. El Mohsen, Forgotten Right Ventricle in Pediatric Dilated Cardiomyopathy. *Pediatr Cardiol*. **38**, 819–827 (2017).
15. W. Li, P. A. Davlouros, P. J. Kilner, D. J. Pennell, D. Gibson, M. Y. Henein, M. A. Gatzoulis, Doppler-echocardiographic assessment of pulmonary regurgitation in adults with repaired tetralogy of Fallot: comparison with cardiovascular magnetic resonance imaging. *American Heart Journal*. **147**, 165–172 (2004).
16. A. Borowski, A. Ghodsizad, J. Litmathe, W. Lawrenz, K. G. Schmidt, E. Gams, Severe Pulmonary Regurgitation Late After Total Repair of Tetralogy of Fallot: Surgical Considerations. *Pediatr Cardiol*. **25**, 466–471 (2004).
17. A. Tanasan, R. Shabanian, M. Dadkhah, E. Mazloumi, The Accuracy of Myocardial Performance Index in the Diagnosis of Right Ventricular Dysfunction After Surgical Correction of Tetralogy of Fallot: A Narrative Review. *J. Pediatr. Rev.*, 161–168 (2019).
18. M. Y. Abd El Rahman, H. Abdul-Khaliq, M. Vogel, V. Alexi-Meskischvili, M. Gutberlet, R. Hetzer, P. E. Lange, Value of the New Doppler-Derived Myocardial Performance Index for the Evaluation of Right and Left Ventricular Function Following Repair of Tetralogy of Fallot. *Pediatr Cardiol*. **23**, 502–507 (2002).
19. N. P. V. K. Yantie, M. M. Djer, N. Advan, J. Rachmat, Outcomes of Tetralogy of Fallot repair performed after three years of age. *PI*. **56**, 176 (2016).
20. S. Demirpence, Pulmonary and ventricular functions in children with repaired tetralogy of Fallot. *Arch Turk Soc Cardiol* (2015), doi:10.5543/tkda.2015.52498.
21. A. A. Kotby, H. M. Elnabawy, W. M. El-Guindy, R. F. Abd Elaziz, Assessment of Exercise Testing after Repair of Tetralogy of Fallot. *ISRN Pediatrics*. **2012**, 1–4 (2012).
22. A. W. Powell, W. A. Mays, S. K. Knecht, C. Chin, Pulmonary effects on exercise testing in tetralogy of Fallot patients repaired with a transannular patch. *Cardiol Young*. **29**, 133–139 (2019).
23. J. C. Lu, T. B. Cotts, A. L. Dorfman, Diastolic Function and Patient-Reported Quality of Life for Adolescents and Adults With Repaired Tetralogy of Fallot: A Tissue Doppler Study. *Pediatr Cardiol*. **33**, 618–624 (2012).