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Pulmonary and ventricular functions in children with repaired tetralogy of Fallot

Düzeltilmiş Fallot tetralojili çocuklarda akciğer ve ventrikül fonksiyonları

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ABSTRACT

Objective: This study aimed to evaluate biventricular function, brain natriuretic peptide levels, respiratory function test and 6 minute walking test (6MWT) in children with repaired tetralogy of Fallot (TOF), and analyse the correlation between these variables and clinical status.

Methods: Twenty-five children (14 boys, 11 girls; aged 6 to 17 years) with repaired TOF (Group 1) and 25 age-sex matched healthy controls (Group 2) were enrolled in the study. Tissue Doppler echocardiography, respiratory function test, 6MWT distance and brain natriuretic peptide levels were measured.

Results: Mean ages of the children at TOF corrective surgery and at study time were 5.1±3.5 years and 11.6±2.7 years respectively. The duration between palliative operation and corrective surgery was 4.3±2.0 years, and the follow-up period after corrective surgery was 6.3±3.0 years. The right ventricular and left ventricular myocardial performance indices (MPIs), and isovolumic relaxation and contraction times were significantly higher in Group 1 than in Group 2 ($p<0.01$). Spirometry displayed significantly reduced forced vital capacity (FVC), forced expiratory volume in one second (FEV1), forced expiratory flow 25–75% (FEF25–75) and inspirational capacity in Group 1 compared to Group 2 ($p<0.01$). In Group 1, 6MWT distances were significantly lower than in Group 2 ($p=0.001$). Right ventricular MPI is correlated with FEV1, FVC and 6MWT distance in the current study.

Conclusion: The children with repaired TOF had impaired ventricular and pulmonary functions. Hence, right ventricular MPI along with FEV1, FVC and 6MWT distance may be useful in the follow-up of children with repaired TOF.

ÖZET

Amaç: Bu çalışmada, Fallot tetralojisi (TOF) nedeniyle ameliyat edilen çocuklarda, 6 dakika yürüme testi, solunum fonksiyon testi, beyin natriüretik peptid düzeyi ve biventriküler fonksiyonları değerlendirildi.

Yöntemler: Çalışmaya TOF nedeniyle ameliyat edilen 25 çocuk (14 erkek, 11 kız; yaş dağılımı 6–17 yıl) (Grup 1) ve yaş-cinsiyet açısından uyumlu 25 sağlıklı kontrol grubu (Grup 2) dahil edildi. Doku Doppler ekokardiyografi, solunum fonksiyon testi yapıldı; 6 dakika yürüme testi mesafesi ve beyin natriüretik peptid düzeyleri ölçüldü.

Bulgular: Çalışma grubunda ortanca yaş 11.6±2.7 yıl, düzeltici cerrahi yaşı 5.1±3.5 yıl, palyatif operasyon ile düzeltici cerrahi arasındaki süre 4.3±2.0 yıl, düzeltici cerrahi sonrası takip süresi 6.3±3.0 yıl idi. Sağ ventrikül ve sol ventrikül miyokart performans indeksi (MPİ), izovolumik gevşeme zamanı ve izovolumik kasılma zamanı Grup 1'de, Grup 2'ye göre anlamlı yüksek bulundu ($p<0.01$). Spirometre ölçümleri Grup 1 ile Grup 2 ile karşılaştırıldığında zorlu vital kapasite (FVC), birinci saniye sonundaki zorlu ekspiryum hacmi (FEV1), zorlu ekspiratuvar akım %25–75 (FEF 25–75) ve inspiratuvar kapasitenin anlamlı azalmış olduğunu gösterdi ($p<0.01$). Grup 1'de 6 dakika yürüme mesafesi Grup 2'ye göre anlamlı olarak daha düşüktü ($p=0.001$). Bu çalışmada sağ ventrikül MPİ'nin FEV1, FVC ve 6 dakika yürüme mesafesi ile korele olduğu gösterildi.

Sonuç: Fallot tetralojisi tamiri uygulanan çocuklarda ventrikül ve akciğer fonksiyonları bozulmuştur. Sağ ventrikül MPİ'nin yanısıra FEV1, FVC ve 6 dakika yürüme mesafesi, düzeltici cerrahi uygulanan TOF'li çocukların takibinde yararlıdır.

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While surgical repair of tetralogy of Fallot (TOF) is possible, and has a low mortality and favorable long-term outcome,[1] the right ventricle (RV) is susceptible to functional compromise following this surgical repair.[2,3] This vulnerability is strongly attributed to pulmonary regurgitation (PR), which can cause RV dilatation and dysfunction.[2] Besides pulmonary regurgitation, suboptimal relief of the obstructed RV outflow tract and residual pulmonary artery stenosis may lead to a status of chronic pressure strain.[4] These abnormalities may not cause clinical symptoms in a majority of TOF patients, and careful evaluation of ventricular functions and exercise capacity are necessary to show cardiac and pulmonary abnormalities in some.[5] Nevertheless, the majority of TOF patients mostly report their exercise capacity as acceptable due to long-term adaptation.[6] Assessment of RV function by echocardiography is also difficult due to its atypical form and alteration of filling due to respiration.[3] However, newer modalities such as Doppler tissue imaging (DTI) allow for direct measurement of myocardial velocities, and it has been used to evaluate RV function in patients with congenital heart disease.[7] Analysis of biomarkers that indicate clinical functional status and ventricular function is possibly a convenient alternative approach.[8]

The objective of the current study was to evaluate biventricular function, respiratory function test, 6 minute walk test and brain natriuretic peptide (BNP) levels in children with repaired TOF and investigate the association between these variables and clinical status, and to suggest utilization of these markers in follow-up of patients with repaired TOF.

METHODS

Thirty-six patients who had undergone TOF surgery were randomly selected for this cross-sectional study. The parents of six patients did not give consent for the analysis. Two patients who had acute infection and chronic lung disease at the time of analysis, and three who were using beta blocker or angiotensin enzyme inhibitor agents were excluded from the study. Therefore, Group 1 comprised 25 patients (14 boys, 11 girls). The age range of Group 1 was 6.1–16.7 years, while that of the control group (Group 2) was 6.7–16.7 years. This age group allowed adequate cooperation from children for pulmonary function and exercise tests. The following data were collected: age, gender, prior palliative surgery, type of surgery, follow-up period since operation and history of arrhythmia. Group 2 comprised 25 age-sex matched subjects (14 boys, 11 girls). These were healthy children who were followed up in the Pediatric Cardiology Outpatient Clinic for nonspecific palpitations and chest pain. Body weight and height were measured, and the body surface area was calculated for all participants according to the DuBois formula.[9] All participants and parents were provided with information on the study and informed consent was obtained. The study protocol was reviewed and approved by the Institutional Ethics Committee.

Abbreviations:

6MWT	*The six-minute walking test*
BNP	*Brain natriuretic peptide*
FEV1	*Forced expiratory volume in one second*
FVC	*Forced vital capacity*
LV	*Left ventricular*
MPI	*Myocardial performance indices*
PR	*Pulmonary regurgitation*
RV	*Right ventricle*
RVED	*Right ventricular end-diastolic*
RVEDA	*Right ventricular end-diastolic area*
RVEF	*Right ventricular ejection fraction*
RVES	*Right ventricular end-systolic*
RVESA	*Right ventricular end-systolic area*
TOF	*Tetralogy of Fallot*

Electrocardiography

Standard electrocardiography with 12 derivations was obtained for all subjects after 15 minutes of resting. QRS and PR duration were measured. Any arrhythmia or bundle branch block were recorded. The duration of the QT interval was corrected using Bazett's formula.[10]

Echocardiography

Comprehensive transthoracic echocardiography was performed using the Vivid S6 machine (General Electric's Healthcare, Milwaukee, WI, USA). The average of measurements from 3 cardiac cycles was used for statistical analyses. Apical and subcostal 4-chamber views were obtained to assess Simpson's right ventricular ejection fraction (RVEF). Based on these views, distance from the atrioventricular valve to the right ventricular apex, atrioventricular diameter and midventricular dimension at the end-diastole were measured, as reported previously.[11] The Simpson's rule method was used to measure RV volumes. Tracings of the RV endocardium at systole and end-diastole were done by either recognizing tricuspid valve opening and closure or by visually evaluating the smallest and largest RV size.[11] Measured RV systolic and diastolic volumes were indexed to the body surface area.

RV systolic and diastolic pressures were measured with the modified Bernoulli equation, using the peak systolic tricuspid regurgitation and end-diastolic pulmonary regurgitation velocity. Pulsed-wave Doppler echocardiography was done to obtain peak tricuspid and mitral velocities at early (E wave) and late diastole (A wave), E/A ratios and deceleration times. Tissue Doppler echocardiographic images were obtained from an apical 4-chamber view at the right ventricular free wall, the ventricular septum, and the left ventricular (LV) free wall. Nyquist limits were modified to 15–20 cm/s, gains were minimized to allow for less background noise, as described previously.[12] Sample volume was adjusted to 2 mm and systolic myocardial velocity (Sm), early diastolic myocardial velocity (Em), and late diastolic myocardial velocity (Am) were measured. The myocardial performance indices (MPI) for the RV, LV and interventricular septum were calculated as the sum of isovolumic contraction and relaxation times divided by ejection time.[12] MPI parameters were measured using TDI and tracings were recorded at a speed of 100 mm.s^{-1} in all patients.

Six minute walking test

The six-minute walking test (6MWT) was performed on a 30-m path in a straight clinic passageway. All subjects were directed to walk the greatest possible distance in 6 minutes. The distance was recorded with a lap counter. The entire distance covered was calculated by multiplying the number of laps by 60 m and then summing up the extra meters of the last incomplete lap. Oxygen saturation was measured using a pulse oximeter (OxiMax n-560, Nellcore, Hayward, CA) before and after the 6MWT.

Spirometry

Spirometry was performed using Cosmed Pony FX equipment on all subjects before the 6MWT. Reference values regarding spirometric parameters in children are changing quietly between countries, with certain formulas and equations according to height and age.[13] All individuals were given standardized instructions on the technique of performing forced expiratory maneuvers by a respiratory technician before testing. Forced vital capacity (FVC), forced expiratory volume in one second (FEV1), FEV1/FVC, Forced expiratory flow 25–75% (FEF25–75), peak expiratory flow (PEF) were measured and interpreted according to the European Respiratory Society Standards.

Brain natriuretic peptide measurement

Venous blood samples were obtained from all subjects before and after the 6MWT. Plasma BNP level was measured using the triage BNP immunoassay (Biosite Diagnostics Inc., San Diego, California, USA). At a cut-off value of 100 pg/ml, the assay showed 82% sensitivity and 99% specificity for differentiating heart failure from normal cardiac function.[14]

Statistical Analysis

Results are presented as mean±SD unless otherwise specified. Values of $p<0.05$ were considered statistically significant. Initially, Kolmogorov-Smirnov tests were performed for equality of distribution relating to all variables. Comparison of demographic, clinical, and echocardiographic data between the two groups were made using Fisher's exact test for categorical variables and Mann-Whitney U test and student's t test for continuous variables. Pearson or Spearman correlation tests were used for correlation analyses. We used SPSS 17.0 (SPSS; Chicago, Illinois, USA) for statistical analysis.

RESULTS

The baseline clinical characteristics of all participants in the study are given in Table 1. The two groups were of similar age, sex distribution and body weight. All patients were classified as New York Heart Association functional Class I at the time of enrollment. In Group 1, 10 (40%) patients had palliative shunts (a modified Blalock-Taussig [mBT shunt]) before corrective surgery, 19 (76%) patients had a transannular patch, 4 (16%) patients had corrective surgery with a jugular bovine valve (Contegra), and 1 (4%) patient had a pulmonary homograft. Age at corrective surgery ranged from 1 to 14 years (median 11.6±2.7), duration between palliative operation and corrective surgery ranged from 2 to 9 years, and follow-up period after corrective surgery ranged from 2 to 12 years. Heart rates were significantly lower in Group 1 compared to Group 2 (95±10 /min *vs.* 108±16 /min respectively). The QRS duration and corrected QT interval were significantly higher in Group 1 than in Group 2 (125±21 ms *vs.* 89±9 ms; 438±32 ms *vs.* 408±10 ms respectively). In Group 1, 18 (72%) patients had a complete right bundle branch block, one patient an incomplete right bundle branch block and another a first degree atrioventricular block. There were no arrhythmias or blocks in Group 2.

Table 1. Clinical characteristics and respiratory function test parameters in both groups*

Variables	Patients (n=25)	Controls (n=25)	*p*
Age (years)	11.6±2.7	12.3±2.3	0.41
Sex male, n (%)	14 (56)	11 (44)	0.94
Body weight (kg)	38.3±13.6	44±13	0.24
Resting heart rate (beats/min)	95±10	108±16	0.011
Oxygen saturation at rest (%)	97.3±1.4	98.2±0.6	0.038
QRS duration (ms)	125±21	89±9	0.011
QTc duration (ms)	438±32	408±10	0.011
Forced vital capacity (%)	76±13	91±13	0.005
Forced expiratory volume in one second (%)	79±15	92±15	0.005
Forced expiratory volume in one second/Forced vital capacity (%)	105±9	102±9	0.259
Peak expiratory flow (%)	87±22	98±22	0.083
Forced expiratory flow$_{25–75}$ (%)	2.3±0.6	3.1±0.6	0.004
Inspiration capacity (L)	0.96±0.38	1.64±0.38	0.005

*Data are expressed as mean±SD or number unless otherwise indicated.

Spirometric variables

Spirometry displayed significantly reduced FVC (76±13 *vs*. 91±13 respectively, p=0.005), FEV1 (79±15 *vs*. 92±15 respectively, p=0.005), FEF25–75 (2.3±0.6 *vs*. 3.1±0.6 respectively, p=0.004) and inspirational capacity (0.96±0.38 *vs*. 1.64±0.38 respectively, p=0.005) in Group 1 compared to Group 2 (Table 1). In Group 1, a mild restrictive pattern was evident in 10 (40%) patients; an obstructive pattern in 3 (12%), a mild mixed restrictive and obstructive pattern in 1 (4%), a mixed obstructive and restrictive impairment in 4 (16%), with the remaining 7 patients having normal spirometry data. In Group 2, a mild restrictive pattern was noted in only 3 (15%) patients.

Neurohormonal variables

Only one patient had an abnormal level of BNP measured before the 6MWT. There were no significant differences between the levels of brain natriuretic peptide before and after the 6MWT in Group 1, (39.1±33.6, 30.9±22.4 respectively, p>0.05). Comparison of brain natriuretic levels after the 6MWT in Group 1 revealed that patients who had an mBT shunt before corrective surgery had significantly higher levels compared to patients with no history of mBT shunt (44.6±20.9, 21.8±18.8 respectively, p=0.013).

Six minute walking test

All subjects finished the 6MWT. In Group 1, 6MWT distance was significantly shorter than in Group 2 (441±60 m. *vs*. 571±101 m respectively, p=0.001). Although there was no abnormal oxygen saturation level before and after the test in either group, mean oxygen saturation levels were significantly lower in

Table 2. Comparison of six minute walking distance test variables in patients and healthy control subjects*

Variables	Patients (n=25)	Controls (n=25)	*p*
Six minute walking test distance (m)	441±60 (330–564)	571±101 (432–720)	0.001
Oxygen saturation before six minute walking test (%)	97±1.6 (94–99)	98±0.6 (97–99)	0.002
Oxygen saturation after six minute walking test (%)	97±1.6 (94–99)	98±0.6 (97–99)	0.002

*Data are expressed as mean±SD (range).

Table 3. Echocardiographic data of patients and healthy subjects*

Variables	Patients (n=25)	Controls (n=25)	*p*
	Mean±SD (range)	Mean±SD (range)	
LVEDD (mm)	3.84±0.56 (2.9–5.0)	4.30±0.41(3.6–4.8)	0.017
LVESD (mm)	2.50±0.37 (1.9–3.2)	2.77±0.28 (2.2–3.2)	0.022
Ejection fraction (%)	64±3 (58–80)	67±3 (60–71)	0.035
Fractional shortening (%)	34±4 (29–48)	37±2 (32–41)	0.015
Tricuspid Sm (m/s)	0.10±0.02 (0.07–0.17)	0.14±0.02 (0.10–0.20)	<0.001
Tricuspid Em (m/s)	0.11±0.03 (0.06–0.18)	0.16±0.02 (0.12–0.21)	<0.001
Tricuspid Am (m/s)	0.07±0.02 (0.05–0.13)	0.10±0.01 (0.08–0.13)	0.003
Tricuspid Em/Am	1.51±0.45 (0.67–2.57)	1.6±0.27 (1.23–2.22)	0.541
Mitral Sm (m/s)	0.09±0.02 (0.06–0.15)	0.12±0.01 (0.10–0.17)	0.004
Mitral Em (m/s)	0.14±0.03 (0.05–0.22)	0.19±0.02 (0.16–0.24)	0.001
Mitral Am (m/s)	0.06±0.01 (0.04–0.10)	0.07±0.01 (0.05–0.10)	0.04
Mitral Em/Am	2.2±0.49 (0.63–3.0)	2.5±0.51 (2.0–3.6)	0.11
RVEDA (cm^2)	23.4±5.8 (13.7–34.5)	16.1±3.6 (11.6–23.9)	<0.001
RVEDV index (ml/m^2)	65.9±21.9 (33–113)	36.7±12.1 (22–63)	<0.001
RVESA (cm^2)	7.2±3.8 (9.9–25.9)	10.1±2.3 (6.7–14)	<0.001
RVESV index (ml/m^2)	39.8±10.9 (20–63)	18.3±5.8 (9–27)	<0.001
Right ventricular EF^ (%)	38.3±7.9 (24–49)	49±6.7 (38–59)	<0.001
Right ventricular MPI	0.51±0.08 (0.36–0.70)	0.41±0.06 (0.28–0.52)	0.002
RV IVCT	71.3±11.5 (52–89)	59±11.2 (44–78)	0.004
RV IVRT	57.9±11.8 (33–81)	44±8.1(30–55)	0.001
Left ventricular MPI	0.49±0.11 (0.3–0.75)	0.36±0.05 (0.28–0.45)	0.001
LV IVCT	70.6±15.3 (44–110)	51.9±10.6 (37–67)	0.001
LV IVRT	56±11.3 (37–74)	43.8±8 (30–55)	0.002
Septal MPI	0.46±0.07 (0.33–0.59)	0.35±0.06 (0.27–0.48)	<0.001

*Data are expressed as mean±SD (range). Am: Late diastolic myocardial velocity; Em: Early diastolic myocardial velocity; Sm: Systolic myocardial velocity; IVCT: Isovolumic contraction time; IVRT: Isovolumic relaxation time; LVEDD: Left ventricular end diastolic diameter; LVEDS: Left ventricular end systolic diameter; MPI: Myocardial performance index; RVEDA: Right ventricular end diastolic area; RVEDV index: Right ventricular end diastolic volume indexed; RVESA: Right ventricular end systolic area; RVESV index: Right ventricular end systolic volume indexed ^ measured using Simpson method.

Group 1 when compared to Group 2 (p=0.002) (Table 2).

Echocardiographic data

Systolic and diastolic diameters of the left ventricle and systolic function parameters in Group1 were lower compared to Group 2 (Table 3). Mean values of right ventricular end-diastolic (RVED) volume, end-systolic (RVES) volume, end-diastolic area (RVEDA) and end-systolic area (RVESA) were significantly higher in Group 1 than in Group 2 (p<0.001) (Table 3). RVEF in Group 1 was lower than in Group 2 (38.3±7.9 *vs*. 49±6.7, p<0.001). RVED volume indexed to body surface area was significantly higher Group 1 than in Group 2 (65.9±21.9 ml/m^2, 36.7±12.2 ml/m^2 respectively, p<0.001). Group 1 had a higher LV eccentricity index (p<0.001), higher tricuspid A wave velocity (p=0.001), a lower E/A ratio (p<0.001), lower tricuspid (p<0.001) and mitral (p=0.004) annular Sm velocities and lower tricuspid (p<0.001, p=0.003; respectively) and mitral (p=0.001, p=0.004; respectively) annular Em and Am velocities (Table 3). The RV and LV MPI and isovolumic relaxation and contraction times were significantly higher in Group 1 (p<0.01) (Table 3). Group 1 had significantly higher RV systolic pressure than Group 2 (15.2±5 *vs*. 7±2,

Table 4. Relation between age at total repair and right ventricle function, left ventricular function, ECG, pulmonary function test and six minute walking test data

	r	*p*
Heart rate	0.089	0.674
QRS	0.150	0.473
QTc	–0.047	0.824
Forced vital capacity	–0.266	0.199
Forced expiratory volume in one second	–0.176	0.401
Forced expiratory flow, 25%–75%	-0.026	0.901
Inspiratory capacity	0.129	0.537
Six minute walking test distance	–0.195	0.351
Brain natriuretic peptide level before exercise	0.182	0.383
Brain natriuretic peptide level after exercise	0.485	0.014
Right ventricular myocardial performance index	–0.308	0.134
Left ventricular myocardial performance index	0.112	0.596
Septum myocardial performance index	0.104	0.622
Tricuspid annular planar systolic excursion	0.114	0.586
Right ventricular ejection fraction	0.213	0.305
Right ventricular end systolic area	–0.073	0.727
Right ventricular end diastolic area	–0.060	0.774

r: Pearson correlation coefficient; p: p value.

p=0.005). No patient in Group 1 had severe tricuspid regurgitation, significant pulmonary outflow obstruction or residual ventricular septal defect. Pulmonary regurgitation was mild in 5 patients, moderate in 19 and severe in 5.

Correlation Analyses

A significant correlation was found between BNP level after 6MWT and age at operation (r=0.485, p=0.014). Age at operation correlated with RVED volume index (r=0.400, p=0.04) and RVES volume index (r=0.445, p=0.02). There was a significant correlation between follow-up duration after corrective surgery and RVED volume index (r=0.425, p=0.03). RV MPI had a significant correlation with 6MWT distance, BNP levels after the 6MWT, FVC and FEV1 (Fig. 1). There were no significant correlations between age at total repair and heart rate, QRS duration, QTc duration, FVC, FEV1, FEF25–75, inspiratory capacity, 6MWT distance, RV MPI, LV MPI, septum MPI, TAPSE, RVEF, RVESA and RVEDA. There was significant positive correlation (r=0.485, p=0.014) between operation age and BNP level after exercise (Table 4). The analysis of subtypes according to type of total correction including transannular patch (76%), Contegra conduit (16%) and pulmonary homogreft (4%) revealed no

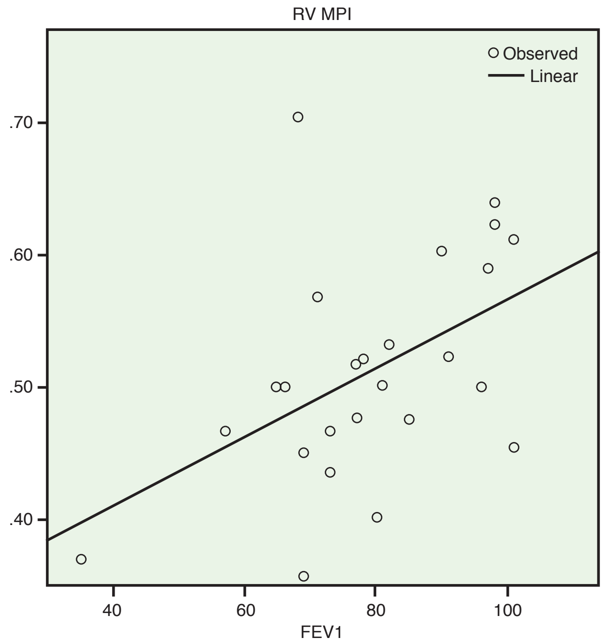

Figure 1. Association of right ventricular MPI and FEV1 levels (r=0.490, p=0.013).

significant correlation between the technique of total correction and RVEF, RVEDA, RVESA, TAPSE, RV MPI, LV MPI, septum MPI, 6MWT distance, FVC, FEV1 and BNP level before exercise test. There was a positive correlation only between the type of total repair and BNP level after the exercise test (p=0.029).

DISCUSSION

In the present study, it was found that children with repaired TOF had impaired pulmonary function and decreased 6MWT duration. 6MWT distance and oxygen saturation levels were lower in the patient group before and after the test. One novel element of the current study is the finding of reduced FVC, FEV1, FEF25–75 and inspirational capacity in children with repaired TOF. These findings confirmed previous studies.[15,16] Gaultier et al.[15] reported that children with TOF repaired after the age of two have impaired lung function, and alterations in lung function became worse with palliation preceding complete repair, possibly due to abnormal vascular growth. Zapletal et al.[16] reported that there was a regression in smaller airway obstruction, and lung hyperinflation occurred after complete repair in patients with TOF after intracardiac repair. They further reported abnormal spirometric findings after exercise in these patients, suggesting a sign of long-term sequelae of early lung damage associated with abnormal pulmonary hemodynamics.

The finding that the RV MPI is correlated with FVC and FEV1 is consistent with the hypothesis that the MPI in children with repaired TOF is associated with an impaired pulmonary function test. Current study data regarding pulmonary function parameters are consistent with those of Cetin et al.[17] They showed that corrected values of FVC and FEV1 were significantly lower in children with repaired TOF. Alterations in the pulmonary vasculature, intraoperative factors such as cardiopulmonary bypass, and positive airway pressure ventilation may lead to a detrimental effect in the respiratory system.[18] Habre et al.[19] demonstrated that children with TOF had increased airway resistance after surgery. In the current study, none of the patients had residual RV outflow obstruction or peripheral pulmonary arterial stenosis. Abnormalities in lung perfusion—mostly in the left lung—have been described in TOF using cardiac catheterization.[20]

In the current study, mean RV and LV MPI values (0.46±0.07, 0.49±0.11, respectively) in children with repaired TOF were higher compared to the healthy subjects, demonstrating biventricular dysfunction. The decreased mitral and tricuspid tissue Doppler velocities, and increased MPIs of the right and left ventricular dysfunction in the current study are consistent with the findings of Samman et al.,[21] who revealed an association between biventricular dysfunction (increased MPI levels) and limited exercise capacity in adults with repaired TOF. In the current study, we also found a correlation between RV MPI and the 6MWT distance and BNP level after the 6MWT. To date, no such association has been reported in children with repaired TOF.

In the current study, no association was found between BNP levels at rest and tissue Doppler echocardiographic parameters of RV and LV. However, RV MPI, mitral Sm velocity and septal MPI correlated well with BNP levels after the 6MWT. Brain natriuretic peptide is secreted by the atria and ventricles in response to volume and pressure overload.[22] Several studies have addressed the inverse correlation between BNP levels and RVEF, and increased plasma levels of BNP levels with RV dysfunction.[23,24] Oosterhof et al.[24] have shown CMR-obtained RVEF to be an independent predictor of plasma BNP level. Ishii et al.[25] demonstrated significant negative association between increases in BNP levels and changes in tricuspid Sm velocity and RV dp/dt during exercise. The study population in our investigation did not have severe pulmonary regurgitation. Therefore, we did not find such increases in BNP levels after the 6MWT. Our study demonstrated that patients who had an mBT shunt before corrective surgery had significantly higher BNP levels after 6MWT than those with no history of mBT shunt. This finding might be explained by the observation that palliative systemic venous shunts leading to LV volume overload result in LV dysfunction and diminished exercise tolerance.[26]

Among the several limitations of this study is its cross-sectional character, which means that serial changes in BNP levels and RV MPI values in patients were not obtained.

The current study showed that children with repaired TOF had decreased respiratory functions. The findings suggest that children with repaired TOF might have impaired RV MPI along with BNP level after the 6MWT. Further larger studies are needed to elucidate the role of these parameters in the follow-up of these patients.

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Keywords: Natriuretic peptide, brain; tetralogy of Fallot; tissue Doppler echocardiography; six minute walking test; respiratory function test.

Anahtar sözcükler: Beyin natriüretik peptid; Fallot tetralojisi; doku Doppler ekokardiyografi; altı dakika yürüme testi; solunum fonksiyon testi.