Relationship between ventricular function assessed by tissue Doppler imaging and exercise capacity in patients after repair of tetralogy of Fallot: an observational study

Tam düzeltme ameliyatı yapılan Fallot tetralojili hastalarda doku Doppler ekokardiyografi ile değerlendirilen ventrikül fonksiyonlarının egzersiz kapasitesi ile ilişkisi: Gözlemsel bir çalışma

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ABSTRACT

Objective: The present study aims to study the relationship between tissue Doppler echocardiography (TDE) indices of right ventricle and exercise capacity in patients after total correction for tetralogy of Fallot (ToF).
Methods: This cross-sectional observational study included 20 patients, after undergoing total correction procedure for ToF diagnosed with mild/moderate pulmonary regurgitation and 30 age-matched healthy children. In the postoperative period, patients were invited to hospital for evaluation of the ventricular functions by 2D, M-mode, Doppler (DE) echocardiography and TDE and exercise testing to evaluate the effort capacity. Statistical analysis was performed using Mann-Whitney U and Chi-square tests, and Pearson correlation analysis.
Results: Compared with the controls; the mitral annular peak systolic flow velocity (Sm) value was significantly lower, while isovolumic contraction time (IVCT), isovolumic relaxation time (IVRT) and myocardial performance index (MPI) values obtained at the tricuspid and mitral (MV) valves were significantly higher (p<0.05 for all) in patients after ToF repair. There was a negative correlation between the exercise period and the total correction age (r=-0.20, p=0.015) and the same negative correlation existed between the exercise period and METS (r=-0.25, p=0.010). MV IVCT with DE and TDE was found to be correlated with METS (r=-0.45, p=0.04). Left ventricular MPI was found to be correlated with maximum heart rate (r=-0.20, p=0.03). By DE, tricuspid valve deceleration time and Sm peak flow velocity with TDE were significantly correlated with METS (r=-0.30, p=0.04; r=-025, p=0.005, respectively). MPI calculated with TDE was correlated with maximum heart rate (r=-0.15, p<0.01).
Conclusion: Even if patients, undergone total correction surgery for ToF were asymptomatic or had minimal clinical symptoms, MPI index assessed by pulse wave TDE and exercise testing may allow early diagnosis of right ventricle dysfunction.
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Key words: Echocardiography, exercise test, tetralogy of Fallot, cardiovascular surgery procedures, ventricular function

ÖZET

Amaç: Tam düzeltme ameliyatı yapılan Fallot Tetralojili hastalarda doku Doppler yöntemi ile elde edilen sağ ventrikül fonksiyonları ve egzersiz kapasitesi arasındaki ilişkiyi çalışmayı amaçladık.
Yöntemler: Enine kesitli-gözlemsel çalışmaya, Fallot Tetralojisi tanısı ile tam düzeltme operasyonu uygulanmış, hafif-orta derecede pulmoner regürjitasyonu olan 20 hasta ile kontrol grubu olarak 30 sağlıklı çocuk dahil edildi. Hastalar, ameliyat sonrası dönemde 2D, M mod, Doppler ekokardiyografi ve doku Doppler ekokardiyografi ile ventrikül fonksiyonları, egzersiz testi ile efor kapasiteleri değerlendirilmek üzere hastaneye çağrılmıştır. İstatistiksel analiz Mann-Whitney U ve Ki-kare testi ve Pearson korelasyon analizi ile yapıldı.
Bulgular: Kontrol grubu ile karşılaştırıldığında, Fallot tetralojili hasta grubunda mitral annüler pik sistolik akım hız (Sm) değeri belirgin olarak düşük, triküspit ve mitral (MV) kapaktan elde edilen izovolümik relaksasyon zamanı (IVRT), izovolümik kontraksiyon zamanı (IVCT) ve miyokart performans indeksi (MPI) değerleri daha yüksek idi (tümü için p<0.05). Egzersiz süresi ile total düzeltme yaşı arasında negatif korelasyon saptandı (r=-0.20, p=0.015), aynı korelasyon egzersiz süresi ile METS arasında da mevcut idi (r=-0.25, p=0.010). Pulse ve doku Doppler ile elde

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edilen MV IVCT, METS ile korele bulundu (r=-0.45, p=0.04). Sol ventrikül MPI maksimum kalp hızı ile korele bulundu (r=-0.20, p=0.03). Triküspit kapak deselerasyon zamanı ve doku Doppler Sm değeri METS ile korele (sırayla; r=-0.30, p=0.04; r=-025, p=0.005); doku Doppler MPI, maksimum kalp hızı ile korele (r=-0.15, p<0.01) bulundu.

Sonuç: Tam düzeltme operasyonu olan hastalar asemptomatik veya klinik bulguları çok az bile olsa doku Doppler ekokardiyografi ile ölçülen MPI değeri ile egzersiz testi sağ ventrikül disfonksiyonunun erken tanısında kullanılabilir. *(Anadolu Kardiyol Derg 2012; 12: 490-7)*

Anahtar kelimeler: Ekokardiyografi, egzersiz testi, Fallot tetralojisi, kardiyovasküler cerrahi işlemleri, ventriküler fonksiyon

Introduction

Tetralogy of Fallot (ToF) is a cyanotic congenital heart disease characterized by an underdeveloped right ventricular outflow tract (RVOT), RVOT stenosis (caused by the anterolateral misplacement of the infundibular septum), large malalignment type ventricular septal defect and overriding of the aorta (1). Total correction of ToF refers to the closure of the ventricular septal defect with a patch and correction of the RV outflow tract stenosis (2-4).

The patients with ToF usually have left ventricular (LV) dysfunction before surgery and there is no further deterioration after surgery (5-8). On the other hand, right ventricular (RV) volume increases and ejection fraction decreases after surgery. These post-operative alterations have been attributed to pulmonary insufficiency, pre-operative hypoxia and ventriculotomy (8-12). Restrictive physiology is defined as antegrade blood flow to the pulmonary artery during late diastole. It has been proposed that this physiology protects against RV dilation after total correction of ToF (9-14).

The complex geometry of the right ventricle, limits the usefulness of conventional echocardiography (14, 15). Magnetic resonance imaging (MRI) and radionuclide ventriculography are the reference methods to evaluate the ventricle functions, but they are costly, and time-consuming (16, 17). Measurement of myocardial velocities by tissue Doppler imaging (TDI) is useful for assessing LV and RV function (17, 18). Pulsed TDI of the tricuspid annulus is noninvasive and has recently been shown to be a reliable method of assessing RV function compared to the gold standard of magnetic resonance imaging (19). Since diastolic dysfunction starts before systolic dysfunction, early diagnosis of diastolic dysfunction by tissue Doppler echocardiography may be helpful (20, 21).

The determination of exercise capacity would indicate the necessity of surgical intervention, catheter angiography or re-evaluation in congenital heart diseases (20). However, exercise test (ET) is subjective and it cannot be performed at every age group. In patients with ToF, any increase in end-diastolic volume can cause deterioration of right heart functions, which may even worsen during exercise (22, 23).

The present study aims to study the relationship between tissue Doppler indices of right ventricular function and exercise capacity in patients after TOF repair.

Methods

Study design

This cross-sectional observational study was approved by the local Ethics Committee of Dr. Behçet Uz Pediatrics and Pediatric Surgery Research and Education Hospital, where the study was conducted. Written informed consent was obtained from the participants and their parents.

Study population

Between the years 2009-2010, 20 patients who were diagnosed with mild or moderate pulmonary regurgitation in the department of tertiary pediatric cardiology unit after undergoing total correction procedure for ToF and 30 age-matched healthy children were included in the present study. Four children with ToF (20%) received palliative treatment before total correction procedure, which was performed after an average period of 2.8±0.5 years. All of the participants were clinically evaluated by physical examination, telecardiography and electrocardiography.

Variables

Baseline demographic, clinical and laboratory parameters are; gender, age, heart rate, tension arterial, and hemoglobin; primary outcome variables are tissue Doppler RV and LV function parameters, secondary outcome variable is exercise capacity.

Study protocol

The follow-up period of the patients was mean 4.5±2.7 years (range: 1.0-13.0 years). All children underwent clinical evaluation, electrocardiographic, echocardiographic and exercise test study.

Echocardiography

All of the patients and healthy controls were assessed by a Vivid 3 echocardiography device with 3 and 5 mHz probes (General Electric, NE, USA) under electrocardiographic monitoring. The same pediatric cardiologist performed two-dimensional echocardiography, color Doppler, pulse wave Doppler, continuous wave Doppler and pulse wave tissue Doppler examinations.

Two-dimensional echocardiograms of the parasternal short-axis view at the level of the aortic root were obtained and the RVOT was visualized. M-mode recordings of the RVOT were obtained and dimensions were measured at end- diastole (onset of the Q wave) and end-systole (end of T-wave) using endocardial leading edge methodology. RV fractional shortening was calculated as the percentage fall in RVOT diameter in systole with respect to that in diastole. RV long -axis function was recorded from the apical four-chamber view with the M-mode cursor positioned at the free wall angle of the tricuspid valve annulus. Total RV long -axis excursion amplitude was taken from end-systole to end-diastole (13).

RVOT SF: [(RVOTd-RVOTs)/RVOTd]x100

For assessment of the degree of enlargement of the RV, the RV end-diastolic diameter (RVEDD) was indexed to the LV end-diastolic diameter (LVEDD), finally given as RV dilatation index (RVDI=RVEDD/LVEDD). RV size was classified as normal when RVDI was equal or less than 0.5 (24).

Tricuspid regurgitation (TR) was assessed on a scale from 1 to 3, grade 1 for trivial, grade 2 for mild, and grade 3 for severe.

To evaluate LV mass index, Devereux Formula is used (25)

LV mass: $1.04([LVID+PWT+IVST]^3-([LVID]^3-13.6$ g

The tricuspid valve Doppler signals were recorded in the apical 4-chamber view, with the Doppler sample volume placed at the tip of the valve. Peak early filling velocity (E wave), peak atrial systolic velocity (A wave), early-to-late diastolic flow ratio (E/A), deceleration time (dTE), isovolumic relaxation time (IVRT) and isovolumic contraction time (IVCT) were measured for the tricuspid valve (26). Tricuspid annular plane systolic excursion (TAPSE) was calculated with 2-dimensional echocardiograph-guided M-mode recordings from the apical 4-chamber view with the cursor placed at the free wall of the tricuspid annulus (27). Care was taken in aligning the sample volume as vertical as possible with respect to the cardiac apex. Maximal TAPSE was determined by the total excursion of the tricuspid annulus from its highest position after atrial ascent to the lowest point of descent during ventricular systole.

Tissue Doppler echocardiography (TDE) was performed from the apical four-chamber view. Myocardial velocity profiles of the lateral tricuspid annulus were obtained by placing the sample volume at the junction of the tricuspid annulus and the RV free wall, respectively. With this modality, the values recorded were the early (Em) and late (Am) diastolic mitral annular velocity, and the ratio of Em/Am (28).

The myocardial performance index (MPI) was calculated according to the following equation: MPI=(IVCT + IVRT)/ET.

The mean values were recorded by averaging the results of five consecutive measurements.

Exercise test

Exercise Test (ET) was performed on a treadmill (LE 200 CE, h/p/Cosmos sports&medical GmbH, Nussdorf-Traunstein, Germany) according to modified Bruce protocol. The heart rate and electrocardiographic changes were monitored continuously; blood pressure was measured every minute with an indirect automatic manometer throughout the test. ST elevation or depression, negative T-waves, maximum blood pressure, heart rate, and if present, symptoms were noted, QRS duration and QTc were calculated during exercise.

Treadmill test depends on the principle of walking or running on either a speed and slope adjustable rolling band. In compliance with modified Bruce protocol, treadmill test was terminated whenever target heart rate was achieved and/or there was exhaustion, shortness of breath or serious ventricular arrhythmia. Maximum heart rate, maximum blood pressure, metabolic equivalents (METs) and exercise period were recorded. The test was regarded as suboptimal for patients in whom target heart rate was not achieved.

Table 1. Demographic and clinical features of patients and control groups

Variables	Patient (n=20)	Control (n=30)	*p
Sex, male, %	60%	56.6%	
Age, years	8.05±3.00 (5-14)	8.93±2.87 (5-15)	NS
Heart rate, beats/min	86.1±8.52 (74-116)	87.67±6.35 (70-121)	NS
BP systolic, mmHg	88.95±5.26	88.83±6.90	NS
BP diastolic, mmHg	48.75±8.71	44.83±6.75	NS
Hb, g/dL	12.1±0.90 (11-13)	11.9±0.90 (11-13)	NS

Data are presented as mean±SD, (min-max.) values and percentage
*Mann- Whitney U and Chi-square tests
BP - blood pressure, Hb - hemoglobin, NS - not significant

Statistical analysis

Collected data were analyzed by Statistical Package for Social Sciences version 12.0 (SPSS Inc, Chicago, IL, USA). All variables are presented as mean±standard deviation; and minimum-maximum values. Comparison between patients and controls was performed using Mann-Whitney U and Chi-square tests, while Pearson test was utilized to specify the correlations. A $p<0.05$ was accepted to be statistically significant.

Results

Baseline characteristics (Table 1)

The present study included 20 patients (8 females, 12 males) and 30 healthy controls (13 females, 17 males). Both the patients and controls were statistically similar in aspect of mean age, body weight, systolic blood pressure and diastolic blood pressure.

The follow-up period of the patients was 4.5±2.7 years in average (range: 1.0-13.0 years). Four children with ToF (20%) received palliative treatment before total correction procedure was performed after an average period of 2.8±0.5 years. The mean age was 3.5±1.5 years (range: 1.0-7.0) at the time of total correction. Two patients with ToF had transatrial surgery whereas transventricular surgery was preferred in 18 patients. Transannular patch was placed in four patients in whom transventricular intervention was accomplished. The mean duration of intensive care unit stay and hospitalization were respectively 3.0±3.1 days and 9.5±7.1 days. All patients' electrocardiographic evaluation showed sinus rhythm with QRS time increase (the mean QRS time was 145±15 msec) and right bundle block accompanied by right axis deviation. Mean cardiothoracic index on telecardiography was 0.50±0.05.

Echocardiography (Tables 2-4)

The patient and control groups were statistically significantly different in the following aspects: LVEDD was lower

Table 2. 2D ve M-Mode echocardiographic parameters

Variables	Patient (n=20)	Control (n=30)	*p
Septal wall, mm	6.5±0.12 (5.7-6.5)	5.9±0.09 (4.8-6.4)	0.096
LV posterior wall, mm	7.7±0.13 (6.7-8.3)	8.3±0.17 (6.3-9.6)	0.169
LVEDD, mm	32.6±4.2 (30-34.6)	37.1±6.5 (34-37.6)	0.008
LVESD, mm	20.8±3.7 (14.2-21.2)	23.4±4.9 (18.2-27.3)	0.054
LV EF, %	69.9±6.5 (62.1-71.2)	67.16±7.4 (60.2-74.2)	0.188
LVSV, mm^3	41.03±7.8 (33.2-48.2)	43.24±11.9 (32.1-54.1)	0.474
LV mass diastole	50.47±5.89 (43.2-57.3)	59.62±19.6 (38.1-80.3)	0.049
SF_{RVOT}, %	26±1.2 (24-28)	48±2.0 (36-62)	<0.001
TR diameter, mm	36.6±0.43 (32-38.2)	25.6±0.68 (22.1-27.2)	<0.001
RV long axis diameter diastolic, mm	63.1±1.11 (56.1-68.2)	49.8±1.31 (44.2-56.4)	<0.001
RV long axis diameter systolic, mm	53.4±0.95 (42.1-58.9)	38.3±1.09 (32.1-44.2)	<0.001
RVEDD, mm	30.6±0.41 (28.2-34.1)	22.0±0.46 (18.2-32.1)	<0.001
RVESD, mm	26.4±0.30 (22.1-28.3)	17.4±0.31 (15.2-18.3)	<0.001
RVDI	0.96±0.20	0.61±0.23	<0.001
TAPSE	0.41±0.21 (0.3-0.51)	0.47±0.29 (0.21-0.49)	0.481

Data are presented as mean±SD and (min-max.) values
*Mann- Whitney U test
LVEDD-LVESD - left ventricular end-diastolic-end-systolic diameters, LVEF - ejection fraction, LVSV - systolic volume, RVEDD - right ventricular end-diastolic diameter, RVESD - right ventricular end-systolic diameter, RVDI - right ventricular dilatation index, SFRVOT - right ventricular outflow tract shortening fraction, TAPSE - tricuspid annular plane systolic excursion, TR diameter - tricuspid ring diameter

(p=0.008), RVOT fraction shortening (SF_{RVOT}) and LV mass were decreased (p<0.0001 and p=0.049), while tricuspid ring diameter (TR diameter), RV diastolic long -axis diameter, RV systolic long -axis diameter, RVEDD, RV end systolic diameter (RVESD) and RVDI parameters were increased (p<0.001 for all) in patient group. No statistical significance was found in tricuspid annular plain systolic excursion (TAPSE) values. Two patients had tricuspid insufficiency, that the TR velocity was 2.3 and 3.5 m/sec. The RVOT gradient was 26 and 54 mmHg.

Table 3 summarizes the pulse Doppler and pulse tissue Doppler measurements obtained from tricuspid valve. Accordingly, with pulse wave Doppler echocardiography, the patient and control groups had statistically significant differences in tricuspid valve A velocity, tricuspid valve E/A flow velocity ratio, and IVRT (p<0.001, <0.001, p=0.029, respectively). When compared with the healthy controls; the pulse tissue Doppler parameters such as Sm value was significantly lower while IVCT, IVRT and MPI values were significantly higher in patients with ToF (p=0.007, p=0.035, p=0.004, and p<0.001, respectively)

Table 4 demonstrates the pulse Doppler and pulse tissue Doppler measurements obtained from mitral valve. Compared with the control group; MV deceleration time was lower

Table 3. Transtricuspid pulse wave Doppler and tricuspid annulus tissue Doppler echocardiographic parameters

Variables	Patient (n=20)	Control (n=30)	*p
E peak, m/sec	0.68±0.18 (0.50-0.72)	0.66±0.11 (0.56-0.72)	0.64
A peak, m/sec	0.75±0.15 (0.62-0.78)	0.51±0.10 (0.42-0.60)	<0.001
E/A ratio	0.82±0.44 (0.62-0.89)	1.34±0.34 (1.10-1.80)	<0.001
DTE, m/s	277.80±36.0 (232-305.6)	287.06±96.23 (182.3-360.7)	0.683
IVCT, msec	215.75±62.83 (148.2-320.1)	217.63±33.03 (172.1-264.5)	0.891
IVRT, msec	199±34.43 (150.2-244.8)	165.06±61.10 (151.2-224.4)	0.029
RV MPI	0.13±0.03 (0.11-0.14)	0.15±0.04 (0.12-0.16)	0.16
Em peak, m/sec	0.14±0.02 (0.10-0.16)	0.16±0.03 (0.12-0.17)	0.166
Am peak, m/sec	0.07±0.03 (0.06-0.072)	0.06±0.02 (0.05-0.07)	0.668
Em/Am ratio	2.59±1.16 (1.89-2.79)	2.84±1.67 (1.86-2.98)	0.562
Sm peak, m/s	0.10±0.02 (0.08-0.12)	0.11±0.01 (0.10-0.12)	0.007
tDE IVCT, msec	105.5±37.35 (65.3-142.1)	85.30±28.48 (56.2-112.1)	0.035
tDE IVRT, msec	117.75±39.74 (76.2-157.5)	86.76±32.40 (54.2-115.4)	0.004
tDE RV MPI	0.73±0.059 (0.56-0.70)	0.51±0.034 (0.44-0.64)	<0.001

Data are presented as mean±SD and (min-max.) values
*Mann- Whitney U test
A - late diastolic flow velocity, Am-tricuspid annulus late diastolic flow velocity, DtE - deceleration time E, E - early diastolic flow velocity, Em - tricuspid annulus early diastolic flow velocity, IVCT - isovolumic contraction time, IVRT - isovolumic relaxation time, MPI - myocardial performance index, RV - right ventricle, Sm - tricuspid annulus peak systolic flow velocity, tDE - tissue Doppler echocardiography

Table 4. Transmitral pulse wave Doppler and mitral annulus and tissue Doppler echocardiographic parameters

Variables	Patient (n=20)	Control (n=30)	*p
E peak, m/sec	1.19±0.19 (1.01-1.15)	1.16±0.15 (1.08-1.18)	0.48
A peak, m/sec	0.69±0.18 (0.54-0.78)	0.60±0.13 (0.50-0.72)	0.049
E/A ratio	1.78±0.35 (1.05-1.89)	1.95±0.41 (1.09-2.12)	0.137
DtE, msec	298±64.2 (231-386.1)	363±124 (201-452.1)	0.036
IVCT, msec	89.4±11.3 (86.2-92.1)	65.9±8.5 (62.1-74.2)	<0.001
IVRT, msec	175±41.08 (132.1-224.7)	154.10±71.49 (68.2-220.1)	0.242
LV MPI	0.05±0.02 (0.02-0.072)	0.07±0.06 (0.012-0.12)	0.23
Em peak, m/sec	0.13±0.02 (0.09-0.15)	0.18±0.03 (0.14-0.22)	<0.001
Am peak, m/sec	0.05±0.019 (0.28-0.66)	0.06±0.03 (0.02-0.10)	0.22
Em/Am ratio	3.34±1.79 (1.3-4.9)	3.52±1.13 (2.8-5.1)	0.67
Sm peak, m/s	0.07±0.01 (0.05-0.08)	0.12±0.09 (0.021-0.21)	0.105
tDE IVCT, msec	103.90±49.87 (51.2-162.1)	79.86±26.18 (54.2-112.1)	0.031
tDE IVRT, msec	106.55±46.63 (54.6-164.3)	85.00±22.77 (52.3-112.5)	0.034
tDE LV MPI	0.60±0.44 (0.11-1.23)	0.50±0.32 (0.20-0.92)	<0.001

Data are presented as mean±SD and (min.-max.) values
*Mann-Whitney U test
A - late diastolic flow velocity, Am - mitral annulus late diastolic flow velocity, DtE - deceleration time E, E - early diastolic flow velocity, Em - mitral annulus early diastolic flow velocity, IVCT - isovolumic contraction time, IVRT - isovolumic relaxation time, LV - left ventricle, MPI - myocardial performance index, Sm - mitral annulus peak systolic flow velocity, tDE - tissue Doppler echocardiography

Table 5. The results of the exercise test

Variables	Patients
Maximum heart rate, beats/min	132.5±13.3 (110-156)
Maximum BP systolic, mmHg	110±9.86 (96.3-124.2)
METS value	6.9±1.49 (5.2-8.3)
Exercise time, min	13±2.99 (9.1-17.2)

Data are presented as mean±SD and (min.–max.) values
BP - blood pressure, METs - metabolic equivalents

Table 6. Correlation between parameters of the exercise test and left ventricular function

Variables	MAX HR	MAX BPs	METs
	p	p	p
E peak, m/sec	0.37	0.72	0.92
A peak, m/sec	0.53	0.25	0.60
E/A ratio	0.94	0.24	0.78
DTE, m/s	0.26	0.69	0.10
IVCT, msec	0.01	0.02	0.04 (r=-0.45)
IVRT, msec	0.53	0.15	0.09
LV MPI	0.03 (r=-0.20)	0.20	0.80
Em peak, msec	0.19	0.11	0.95
Am peak, msec	0.83	0.93	0.65
Em/Am ratio	0.71	0.88	0.70
Sm peak, msec	0.52	0.53	0.85
tDE IVCT, msec	0.01 (r=-0.10)	0.02 (r=0.20)	0.04 (r=-0.30)
tDE IVRT, msec	0.21	0.02 (r=-0.12)	0.81
tDE LV MPI	0.01 (r=-0.15)	0.21	0.98

Pearson correlation analysis
A- late diastolic flow velocity, Am-mitral annulus late diastolic flow velocity, BPs - blood pressure systolic, DtE - deceleration time E, E - early diastolic flow velocity, Em-mitral annulus early diastolic flow velocity, HR - heart rate, IVCT - isovolumic contraction time, IVRT - isovolumic relaxation time, LV - left ventricle, max - maximum, METs - metabolic equivalents, MPI - myocardial performance index, Sm - mitral annulus peak systolic flow velocity, tDE - tissue Doppler echocardiography

(p=0.036), MV A, and MV IVCT were higher group (p=0.049, p<0.001, respectively) in patients after ToF repair. Similarly, tissue Doppler echocardiography MV IVCT, IVRT and MPI values were significantly higher in patients with ToF (p=0.031, p=0.034, p<0.001, respectively) as compared with controls.

Exercise test (Table 5)

Exercise test could not be performed in one patient who was unable to cooperate. Moreover, another patient was unable to complete the exercise test due to exhaustion. The exercise test was regarded to be suboptimal in 12 of 19 patients (63.1%). Maximum heart rate was 132.5±13.3 bpm. METS value was found to be 6.9±1.49. There was negative correlation between the exercise period and the total correction age (r=-0.20, p=0.015) and the same negative correlation existed between the exercise period and METS (r=-0.25, p=0.010).

Table 7. Correlation between parameters of the exercise test and right ventricular function

Variables	MAX HR	MAX BPs	METs
	p	p	p
E peak, m/sec	0.60	0.90	0.10
A peak, m/sec	0.40	0.87	0.87
E/A ratio	0.79	0.81	0.13
DTE, msec	0.55	0.62	0.04 (r=-0.30)
IVCT, msec	0.08	0.56	0.18
IVRT, msec	0.32	0.23	0.39
RV MPI	0.01 (r=-0.20)	0.06	0.45
Em peak, m/sec	0.33	0.09	0.48
Am peak, m/sec	0.99	0.24	0.24
Em/Am ratio	0.01 (r=-025)	0.56	0.13
Sm peak, m/s	0.16	0.65	0.005 (r=-0.25)
tDE IVCT, msec	0.20	0.03 (r=0.20)	0.25
tdE IVRT, msec	0.32	0.04 (r=-0.20)	0.42
tDE RV MPI	<0.001 (r=-0.15)	0.02 (r=-0.15)	0.36

Pearson correlation analysis
A - late diastolic flow velocity, Am - tricuspid annulus late diastolic flow velocity, BPs - blood pressure systolic, DtE - deceleration time E, E - early diastolic flow velocity, Em-tricuspid annulus early diastolic flow velocity, HR - heart rate, IVCT - isovolumic contraction time, IVRT - isovolumic relaxation time, max - maximum, METs - metabolic equivalents, MPI - myocardial performance index, RV - right ventricle, Sm - mitral annulus peak systolic flow velocity, tDE - tissue Doppler echocardiography

Correlation between tissue Doppler and exercise test variables (Tables 6, 7)

MV IVCT by pulse Doppler echocardiography was found to be correlated with METS (r=-0.45, p=0.04). Tissue Doppler MV IVCT was correlated with METS (r=-0.45, p=0.04), LV MPI was found to be correlated with maximum heart rate (r=-0.20, p=0.03).

Yet by Doppler echocardiography, exercise test parameters especially METS was significantly correlated with tricuspid valve deceleration time (r=-0.30, p=0.04); while MPI calculated with tissue Doppler echocardiography was correlated with maximum heart rate (r=-0.15, p<0.01), and Sm peak flow velocity with METS score (r=-025, p=0.005) (Table 7).

Discussion

In this study; we observed that even if patients, undergone total correction surgery for ToF were asymptomatic or had minimal clinical symptoms, MPI index assessed by PW TDE and exercise testing may allow early diagnosis of right ventricular dysfunction. Compared with the controls; the mitral Sm value was significantly lower while IVCT, IVRT and myocardial performance index values obtained at the tricuspid and mitral valves were significantly higher. There was negative correlation between the exercise period and the total correction age and the same negative correlation existed between the exercise period and METs. Transthoracic and tissue Doppler MV IVCT was found to be correlated with METs. LVMPI was found to be correlated with maximum heart rate. Tricuspid valve deceleration time and Sm peak flow velocity were significantly correlated with METs.

Many patients with ToF following successful operations reach adolescent and adult ages. The overall survival rate of patients with repaired ToF is good, with mortality of less than 6% at 25 years after corrective surgery (29).

RV systolic and diastolic dysfunction commonly occurs after total correction surgery for ToF is performed. It has been hypothesized that the problems encountered during the follow-up of patients who underwent ToF repair are related with the RV physiology. Pre-operative hypoxia and hypertrophy, intra-operative myocardial damage and postoperative pulmonary regurgitation (PR) may participate in the etiopathogenesis of RV dysfunction (22, 23).

Both PR and TR are seen frequently in patients with TOF after repair. The prognosis is good; however, because of long-term volume overload, in patients with moderate or severe regurgitation, progressive RV dysfunction takes place in time (18, 19). It is impossible to assess RV dysfunction according to the clinical findings. PR and TR are well-tolerated by the patients. In the presence of severe regurgitation, especially PR, the risk for arrhythmia, heart failure, and sudden death increases (30). In our study, two patients had severe tricuspid regurgitation that the TR velocity was 2.3-3.5 m/sec. and the RVOT gradient was 26-54 mmHg.

The studies indicate that the Doppler pulse echocardiography usually shows the reduction in tricuspid valve E/A ratio and prolongation of IVRT, which indicate restrictive pattern in the RV. Chaturvedi et al. (31) presented prolonged relaxation time and decreased E/A ratio in these category of patients. In our study, we also found that TV IVRT was significantly higher compared to the control group.

On the other hand, it was shown that age, heart rate, sample volume position, RV preload and function might affect Doppler time intervals (32). Cullen et al. (20) confirmed the existence of restrictive pattern in the RV by showing that tricuspid valve E/A ratio did not vary with inspiration and expiration in ToF patients who had total correction surgery. We also found that TV E/A values were significantly lower when compared with the control group. This result can be explained by increased A wave, and restrictive physiology of the ventricle.

Due to the complex geometry of the RV, the utilization of conventional echocardiographic techniques (such as two-dimensional or M-mode pulse wave Doppler) is insufficient to diagnose RV dysfunction (16).

MPI overall reflects the systolic and diastolic functions of the ventricles. It has been recently reported that MPI can be efficiently used to evaluate the global RV functions in patients who developed valve insufficiency after surgery (33).

Lindqvist et al. (13) reported that the systolic functions of the RV can be assessed by measuring RVOT end-diastolic and end-systolic diameters obtained by two-dimensional M-mode echocardiography throughout the parasternal short- axis. Yasuoka et al. (34) stated that MPI assessed by tissue Doppler echocardiography (rather than pulse wave Doppler echocardiography) successfully pointed out the RV functions of the patients who developed PR after total correction of ToF. The present study also showed that LV and RV MPI values obtained by pulse tissue Doppler were significantly increased in the patients with ToF.

Patient with ToF had statistically significant increase in mitral valve A, mitral valve deceleration time, and IVCT values as assessed by pulse wave Doppler echocardiography. When compared with the healthy controls, the patients with ToF had significantly lower Em peak velocity whereas significantly higher IVCT, IVRT and MPI as evaluated by pulse wave tissue Doppler echocardiography.

Evaluation of the tricuspid valve by pulse Doppler echocardiography resulted in statistically significant differences in tricuspid valve A, tricuspid valve E/A, and IVRT values. When compared with the healthy controls, the patients with ToF had significantly lower Sm values whereas significantly higher IVCT, IVRT and MPI values assessed by tissue Doppler echocardiography.

Not only decreased Sm, but also increased MPI measured with tissue Doppler echocardiography indicate that both systolic and diastolic functions of the RV are impaired and increased IVRT, IVCT and MPI of LV assessed with TdE demonstrated diastolic dysfunction in the LV.

MRI and radionuclide ventriculography are the reference methods but they are costly, and time-consuming (16, 17). Measurement of myocardial velocities by tissue Doppler imaging is useful for assessing left and RV function (18). Pulsed TDI of the tricuspid annulus is noninvasive and has recently been shown to be a reliable method of assessing RV function compared to the gold standard of MRI (19). The present study also shows significant changes, among TDI parameters such as LV MPI and RV MPI.

The patients who have total correction surgery for ToF should undergo annual exercise test in order to determine the maximum heart rate, blood pressure response and any arrhythmias provoked during physical stress.

D'Andrea reported that Em flow rate values less than 0.13 msec (as measured at the tricuspid annulus by pulse wave tissue Doppler echocardiography) can predict submaximal exercise test with 90% sensitivity and 93% specificity (35). The present study showed that exercise test was suboptimal in twelve patients and two of these patients had Em flow velocity rate less than 0.13 msec (0.10-0.11 m/sec). Moreover, there were statistically significant correlations between tricuspid valve Em/Am flow velocity ratio, deceleration time, MPI and IVCT parameters.

The exercise test parameters were found to be unrelated with the measurements obtained by two-dimensional echocardiography. In addition, these parameters did not correlate with the systolic and diastolic measurements of the LV obtained by either pulse Doppler or pulse tissue Doppler echocardiography except IVRT and IVCT. There was no correlation between left and RV MPI values.

Harada et al. (36) reported that an insufficient increase in Sm suggests impaired response to exercise of RV in patients with ToF. We found a negative correlation between Sm and METS index (r=-0.25). Cheung reported that RV MPI correlated inversely with exercise duration (r=-0.45, p=0.013) and peak oxygen consumption (r=-0.56, p= 0.001). Increased MPI is a reflection of reduced exercise capacity in patients after TOF repair (37). In our study, we observed negative correlation between TV deceleration time, RV Sm peak velocity and METS (r=-0.30, -0.25, respectively). After the examination of LV, we found negative correlation between IVCT, both measured with pulse Doppler and pulse tissue Doppler, and METS (r=-0.45, -0.30)

Study limitations

The limitation is the number of the study group. These patients were all operated just in one pediatric cardiac surgery unit and follow-up made by only our department to minimize the observer variability. That is why these results may not indicate a satisfactory answer, we thought this study as a midterm result and we will continue to evaluate new ToF patients.

Conclusion

Pulse wave tissue Doppler echocardiography can be used to determine the left and RV dysfunction in patients who has undergone total correction surgery for ToF within a short-to-moderate postoperative period. Even if these patients were asymptomatic, MPI index assessed by pulse wave tissue Doppler echocardiography may allow early diagnosis of RV dysfunction. For further diagnostic workup; tricuspid deceleration time, Sm peak velocity, Em/Am flow velocity ratio, MPI and IVCT parameters can be considered whenever the evaluation of exercise capacity is a necessity and exercise test cannot be performed.

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