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ASSESSMENT OF RIGHT VENTRICULAR INEFFICIENCY USING ENERGY TRANSFER RATIO IN REPAIRED TETRALOGY OF FALLOT

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ABSTRACT

Pulmonary insufficiency (PI) induces pulmonary regurgitation and often leads to right ventricular (RV) enlargement and RV pressure overloading in repaired Tetralogy of Fallot (rTOF) patients. The appropriate timing of surgical treatments to renormalize RV function remains uncertain due to lack of suitable clinical diagnostic parameters. An energy transfer ratio (e_{MPA}) between the net energy (E_{net}) transferred at main pulmonary artery (MPA) from RV and stroke work (SW) by RV was calculated using RV volume and pressure data for subjects in two study groups: the rTOF patient group (n=7) and the control group (n=7). Statistical analysis was performed to determine the difference of e_{MPA} between the two groups. The mean e_{MPA} for rTOF patients (0.64) was significantly lower (60.2%, $p<0.05$) than that of controls (1.61).

INTRODUCTION

Tetralogy of Fallot (TOF) is a common cyanotic syndrome of congenital heart defects which involves four ailments: 1) PA stenosis: a narrowing of the pulmonary valve; 2) ventricular septal defect: a hole in the wall that separates the two lower chambers of the heart; 3) overriding aorta: aorta overrides RV; 4) RV hypertrophy; RV enlargement and stiffening associating with pressure overloading in RV [1].

Adult repaired TOF (rTOF) often develop gradually deteriorating RV myocardial dysfunction due to pulmonary insufficiency (PI). Although good long-term survival of young children has been shown after surgery, a risk of late postoperative mortality still exists resulting in sudden death from congestive heart failure [2].

PV replacement surgery (PVR) is performed to prevent permanent RV myocardial dysfunction. The appropriate timing for PVR and the quantifiable clinical criteria to base the decision upon still remains unclear.

Recently, clinicians have been using RV volumes, end-diastolic volume (EDV) and end-systolic volume (ESV), and RV pressures, end-diastolic pressure (EDP) and end-systolic pressure (ESP) to assess the deterioration and progression of RV dysfunction [3,4]. For this research, the methodology developed by Das et al., 2010 [5] was used to calculate energy transfer ratio (e_{MPA}) of rTOF patients and control subjects. Statistical analysis was performed to confirm our hypothesis that e_{MPA} in dysfunctional RV of rTOF patients was significantly lower than that of RV with normal condition. The long term goal of this research was to investigate the appropriate clinical diagnostic endpoint to discern the prognosis of PI and RV dysfunction in rTOF patients.

METHOD

Seven rTOF patients (age: 12.4±12.0 years, BSA: 1.2±0.5 m^2, heart rate: 83.4±21.5 bpm) were retrospectively analyzed for this study. Seven subjects (age: 14.9±7.5 years, BSA: 1.6 ± 0.6 m^2, heart rate: 74.3±14.3 bpm) with native and healthy RV and PA physiology were selected as the control group. Both the groups show similar physical characteristics. Values shown above are means and standard deviations.

RV Cardiac Magnetic Resonance (CMR) images of each subject were analyzed to assess RV volume with the semi-automated computer software (QMASS version 7.2, Medis Medical Imaging Systems, Leiden, the Netherlands). RV pressure was measured by *cardiac catheterization* with general endotracheal anesthesia technique. RV pressure variation over time during the cardiac cycle at RV was recorded with the ECG tracing curve. Clinically, simultaneous MRI and cardiac catheterization is difficult. RV volume versus time data and RV pressure versus time data need to be *co-registered* since RV volume and RV pressure data were non-simultaneously measured. Co-registration procedures were done using electrocardiographic (ECG) curve. RV pressure-volume loop was obtained from RV pressure versus time and RV volume versus time data.

The e_{MPA} was calculated as dividing the net energy transferred at MPA (E_{net}) by RV stroke work (SW). The net energy transferred at MPA (E_{net}) over one cardiac cycle (T) can be computed by integrating the rate of total energy transferred to MPA ($\dot{E_m}$) over T [5].

$$e_{MPA} = E_{net}/SW, \quad E_m = \left(p_m + \frac{1}{2}\rho v_m^2\right) Q_m \tag{1}$$

where p_m is the MPA pressure, ρ the density of blood, v_m the mean MPA velocity of blood, and Q_m is the MPA flow rate of blood. RV SW was calculated by computing the area enclosed by the pressure-volume loop [5],

$$SW = \oint pdV, \quad SW_I = SW/BSA \tag{2}$$

The Shapiro-Wilk test and Kolmogorow-Smirnov test was performed to determine normality of the distribution for all endpoints. Then, the two sample Student -*t* test and the two-tailed Wilcoxon two sample test were used to compare the statistical difference of RV pressure and volumetric measurements, RV SW_I and e_{MPA} between the two groups were compared using SAS 9.2 package (SAS Institute, Cary, NC)

Table 1. Right ventricular (RV) pressure and volumetric data

RV pressure and volumetric data	rTOF	control
End-systolic pressure, ESP (mmHg)*	55.0±8.4	26.7±7.5
End-diastolic pressure, EDP (mmHg)	4.7±2.8	3.7±3.9
End-diastolic volume index , EDV_I (ml/m^2)	101.4±25.4	79.0±17.0
End-systolic volume index, ESV_I (ml/m^2)	50.2±20.1	33.7±9.6
Regurgitation fraction (%)*	29.2±14.3	0.0±0.0
Ejection fraction (%)	51.9±6.9	58.5±7.2
RV mass index, $RVmass_I$ (g/m^2)*	33.1±13.3	20.2±4.2
Peak ejection rate (EDV/s)*	2.1±0.5	3.0±0.7
Stroke work index, SW_I (J/m^2)*	0.187±0.044	0.092±0.035
Energy ratio, e_{MPA}*	0.64±0.42	1.61±0.82

Values are means and standard deviations. The endpoints with star mark (*) have a statistically significant difference ($p<0.05$) between the two groups.

RESULTS AND DISCUSSION

Measured RV pressure and volume data for both the rTOF group and control group are shown in Table 1. The mean ESP of rTOF patients (55.0±8.4mmHg) was significantly higher (106.2%, $p<0.05$) compared to that of controls (26.7±7.5 mmHg), whereas there was no statistical significance in the mean EDP between the two groups. This confirms *RV pressure overloading* in rTOF patients.

The mean EDV_I of the rTOF group (101.4±25.4 ml/m^2) was higher (28.4%) than that of control group (79.0±17.0 ml/m^2). Similarly, the mean ESV_I of rTOF group (50.2±20.1 ml/m^2) was higher (49.0%) than that of control group (33.7±9.6 ml/m^2). Both EDV_I and ESV_I were not significantly different between the two groups due to large variation. These show *RV volume overloading* in rTOF patients.

Further, rTOF patients had significantly large (29.2±14.3%, $p<0.05$) pulmonary regurgitation fraction, a ratio between backward flow and forward flow, compared to controls due to the presence of PI. Moreover, ejection fraction, a ratio between stroke volume (=EDV-ESV) and EDV, in rTOF patients (51.9±6.9%) was lower (11.2%) than that of controls (58.5±7.2%) but it was not significantly different between the two groups due to large standard deviation. rTOF patients had higher $RVmass_I$ (64%, $p<0.05$), BSA indexed RV mass, and lower peak ejection rate (30.2%, $p<0.05$) compared to controls. Hypertrophic RV in rTOF patients resulting from RV pressure overloading may cause increased RV mass and reduced ejection fraction and peak ejection rate that are indicative of impairment of RV systolic function.

As noted in preceding paragraph, RV volume and pressure overloading as well as RV systolic dysfunction were observed in rTOF patients. These do not occur independently. Generally, they follow one another. Therefore, *energy based endpoint* such as e_{MPA}, can be used for more accurate diagnosis of the disease.

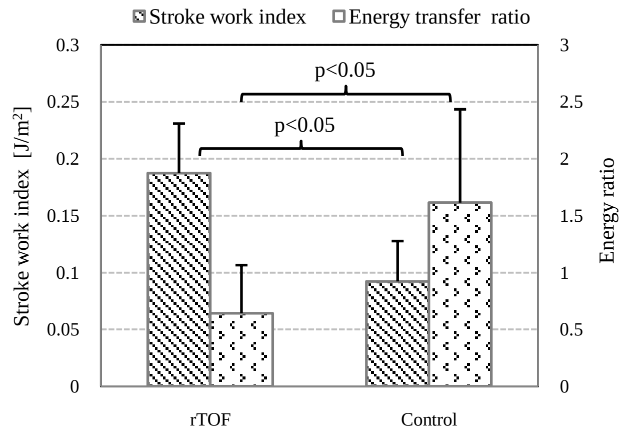

Figure 1. The comparison of energy transfer ratio (e_{MPA}) and RV stroke index (SW_I) between rTOF patients and controls. RV SW_I are significantly higher ($p<0.05$) in rTOF patients than controls, whereas significantly lower e_{MPA} ($p<0.05$) in rTOF patients was observed compared to controls.

The e_{MPA} has an advantage that it accounts for both RV and MPA blood flow conditions. Also, it utilizes both RV pressure and volume data via RV SW. Our data shows that the mean RV SW_I, BSA indexed SW, in rTOF patients (0.187±0.044 J/m^2) was significantly higher (103.3%, $p<0.05$) than controls (0.092±0.035 J/m^2). However, *the mean e_{MPA} in rTOF patients (0.64±0.42) was significantly lower (60.2%, $p<0.05$) than controls (1.61±0.82)* in Table 1 and Fig.1. It indicates that although the required RV SW in rTOF was higher than controls, the efficiency of RV was significantly reduced by RV systolic dysfunction due to PI in rTOF patients.

CONCLUSION

In this study, we have used a methodology to compute e_{MPA} by using non-simultaneously measured RV volume and pressure data. The result confirmed that rTOF patients with RV dysfunction had significantly lower e_{MPA} (60.2%, $p<0.05$) than controls. Therefore, e_{MPA} can be a useful diagnostic endpoint to assess RV inefficiency in rTOF patients.

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