A Comparative Study: Right Ventricular Assessment in Post-Repaired Tetralogy of Fallot Patients by Echocardiogram with Cardiac Magnetic Resonance Imaging

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Background: *Post-repaired Tetralogy of Fallot (TOF) patients require comprehensive evaluation of the right ventricular (RV) size and function. Currently, cardiac magnetic resonance imaging (CMR) is considered to be the gold standard for RV function assessment. Echocardiogram (ECHO) is the most useful non-invasive tool for RV assessment. However, correlations of ECHO and CMR findings for this particular group of patients require further evaluation.*
Objective: *The first objective is to assess the correlation between RV size/function, measured by ECHO and CMR. The second objective is to investigate ECHO parameters that correlate best with RV end diastolic volume index (RVEDVi) of 160 mL/m^2 from CMR.*
Material and Method: *The present study recruited 20 TOF patients (mean age 14$\pm$2 years) who underwent right ventricular outflow tract reconstruction and/or pulmonary valve replacement for at least 5 years, from June 2011 to March 2012. The RV was initially evaluated with CMR, followed by ECHO within 3 months. ECHO parameters measured were tricuspid annular plane systolic excursion (TAPSE), fractional area change (FAC), area of right ventricular end diastole index (area RVEDi), RV free wall myocardial performance index (RVMPI), and qualitative assessment of pulmonary valve regurgitation (PR). All ECHO parameters were compared with CMR measurements of right ventricular ejection fraction (RVEF), RVEDVi and quantitative assessment of PR. Comparative analysis were assessed by Pearson's sample correlation coefficient, Kappa, and sensitivity and specificity of RVEDi area from ROC curve analysis.*
Results: *Results showed significant correlations between RVEDVi and area RVEDi (R = 0.768, p<0.01), RVEF with FAC (R = 0.759, p<0.01), and RVEF with TAPSE (R = 0.688, p<0.01). Hundred percent correlation was found in moderate to severe PR assessment by ECHO and CMR (Kappa = 0.912). Abnormal RVMPI was not correlated with NYHA FC, CXR and ECG (Kappa = -0.10, 0.15, -0.04). The area RVEDi $\geq$20.43 cm^2/m^2 correlated well with RVEDVi $\geq$160 mL/m^2 (sensitivity 64%, specificity 83%) from ROC curve analysis.*
Conclusion: *ECHO is an effective tool for RV evaluation in post-repaired TOF with PR. FAC, TAPSE and severity of PR from ECHO correlated well with CMR parameters. Measurement of area RVEDi from ECHO is the best parameter to predict RVEDVi from CMR.*

Keywords: *Tetralogy of fallot, Pulmonary valve regurgitation, Right ventricular function, Echocardiogram, Cardiac magnetic resonance imaging*

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Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart disease and must be surgically treated in all patients. However, progressive pulmonary valve regurgitation (PR) usually occurs several years after surgery. PR in progressive right ventricular (RV) dilatation leads to the development of ventricular arrhythmia, RV dysfunction, and sudden death[1,2]. Establishing appropriate time for pulmonary valve replacement (PVR) is important to prevent irreversible deterioration of the right ventricle.

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Cardiac magnetic resonance imaging (CMR) is currently the gold standard to assess RV function, anatomy of pulmonary artery, and degree of pulmonary valve stenosis (PS)/PR. Indications for PVR are as follows[3]:

1) Moderate or severe PR (PR fraction ≥25% on CMR) with two or more of the following criteria: RV end-diastolic volume index (RVEDVi) ≥160 mL/m^2 (Z score >5), RV end-systolic volume index (RVESVi) ≥70 mL/m^2, Left ventricular end-diastolic volume index (LVEDVi) ≥65 mL/m^2, RV ejection fraction (RVEF) ≤45%, RV outflow tract aneurysm, or clinical criteria such as exercise intolerance, symptoms and signs of heart failure, cardiac medications, syncope, and sustained ventricular tachycardia.

2) Presence of other hemodynamically significant lesions.

3) For patients who have undergone TOF repair at age ≥3 years, PVR may be indicated earlier in the presence of less severe RV dilatation or dysfunction due to a higher risk of adverse clinical outcomes.

Echocardiographic assessment is less invasive and is universally available in all cardiac centers. Recently, several parameters have been developed to evaluate RV function after TOF repair[4-7]. However, there are limitations in applying these particular parameters in the Asian population. The objectives of this study were to assess the correlation of RV size and function measured by echocardiography and CMR, and to investigate echocardiographic parameters that correlate best with RVEDVi of 160 mL/m^2.

Material and Method

The authors conducted a comparative study from June 2011 to March 2012, on 20 post-surgical repaired TOF patients, who had undergone RV outflow tract reconstruction and/or PVR, for at least 5 years at Queen Sirikit National Institute of Child Health (QSNICH). New York Heart Association functional class and clinical symptoms of syncope or palpitation, QRS duration from 12-lead electrocardiogram (ECG) and cardio-thoracic ratio (CT-ratio) were evaluated. CMR was performed in all patients using CINE FIESTA technique in axial, 4-chamber, 3-chamber, 2-chamber, short axis LV, long axis LV, coronal and sagittal, and right ventricular outflow tract (RVOT) views. Phase contrast cineangiography was performed at the aorta, pulmonary arteries, and tricuspid and mitral valves. Contrast magnetic resonance angiography was performed at the aorta and pulmonary arteries. Two-dimensional myocardial contrast delayed enhancement was performed in short axis, 4-chamber, and RVOT views. The right ventricular end systolic and diastolic volume (RVESV, RVEDV), the RVEDVi, RVEF, and degree of PR were calculated. Presence of pulmonic regurgitation fraction (PRF) less than 20% is defined as mild PR, PRF from 20 to 40 % is defined as moderate PR, and PRF more than 40 % defined as severe PR. All parameters were evaluated by a radiologist who was blinded to the patients' conditions.

Echocardiogram (ECHO) was then performed 4-12 weeks after CMR by an echocardiographer, blinded to the CMR results. Echocardiographic parameters were evaluated following the guidelines for the echocardiographic assessment of the right heart[8]. This assessment included tricuspid annular plane systolic excursion (TAPSE) (Fig. 1), fractional area change (FAC) (Fig. 2), tissue Doppler imaging (TDI) (Fig. 3), and

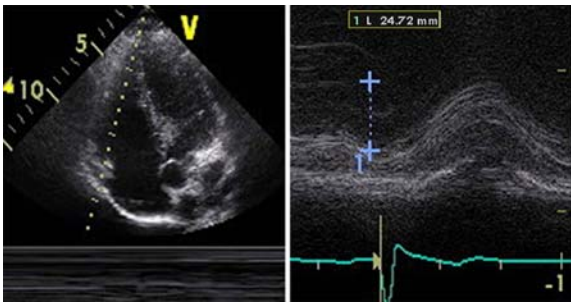

Fig. 1 Measurement of the Tricuspid Annular Plane Systolic Excursion (TAPSE) in apical four-four chamber view[8].

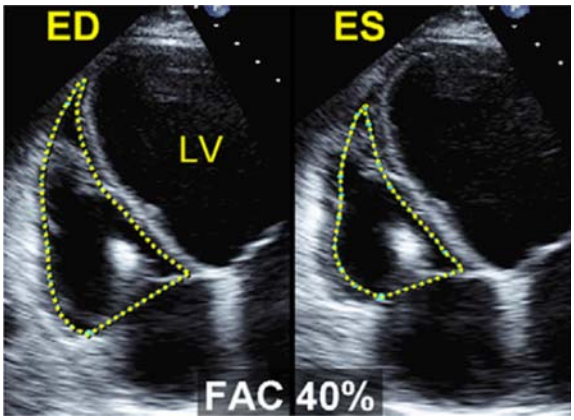

Fig. 2 Measurement of the Fractional Area Change (FAC) in apical four-chamber view[8] FAC = 100 x [end diastolic area (Area RV ED)-end systolic area (Area RV ES)]/end diastolic area (Area RVED).

degree of PS/PR. Normal reference of TAPSE in pediatric population was according to a previous publication[9]. FAC <35% was defined as an abnormal value[10]. The right ventricular myocardial performance index (RVMPI) from TDI assessment between 0.24 and 0.55 was defined as the normal value[8]. Mild PR was defined as an insufficient jet less than one-third of the RVOT, and traceable PR cranially to the pulmonary valve on pulse wave (PW) Doppler ECHO. Moderate PR was defined as an insufficient jet between one- and two-thirds of the RVOT, and traceable PR up to the middle of the main pulmonary artery on PW Doppler ECHO. Severe PR was defined as an insufficient jet more than two-thirds of RVOT and traceable PR over the bifurcation of the main pulmonary artery on PW Doppler ECHO. All parameters were measured 3 times. The mean of these 3 measurements were used in the final record. Patients who had severe RVOT obstruction, significant pulmonary artery branch stenosis, and incomplete information or requested to terminate the study were excluded. This study has been officially approved by the Queen Sirikit National Institute of Child Health ethical committee.

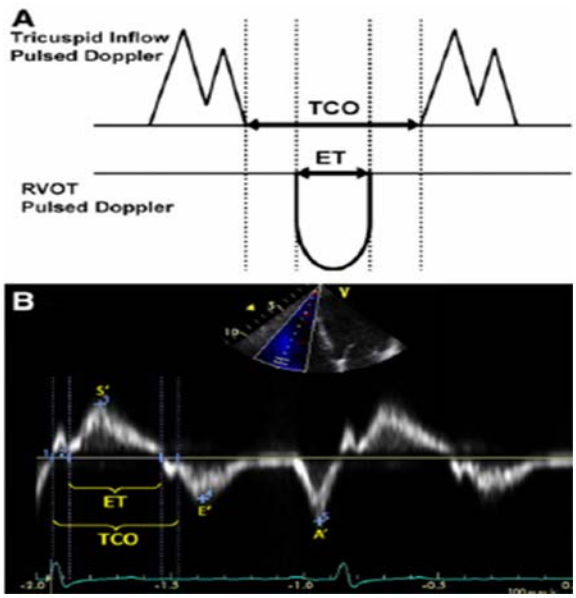

Fig. 3 Measurement of myocardial performance index (MPI) using tissue doppler imaging (TDI) modality at tricuspid valve annulus in apical four-chamber view.
MPI = (TCO-ET)/ET

Statistical analysis

Comparative analysis was assessed by Pearson's sample correlation coefficient, Crosstab Kappa, and sensitivity and specificity of area RVEDi was calculated from ROC curve analysis.

Results

Twenty patients were enrolled into the study (Table 1). Seventy percent of them were male. The mean age of the patients was 14 years and 1 month, while the mean age at surgery was 8 years and 9 months. The mean duration after surgery was 9 years. The mean duration of ECHO after CMR was 32 days. Eighty percent of the cases were in NYHA functional class 1. Sixty percent had CT-ratio from chest x-ray above 0.5 and 75% had QRS duration from ECG above 90 msec.

CMR showed 25% of the patients had RVEDVi

Table 1. Demographic data (n = 20)

Sex (male/female)	14/6
Age (year) (Mean ± SD)	14±2
Age at Total correction (year) (Mean ± SD)	8±3
Duration from surgery to ECHO (year) (Mean ± SD)	9±3
Duration from CMR to ECHO (day) (Mean ± SD)	32±19
BSA range (m^2)	0.78-2.25
NYHA	
Functional class I (%)	80
Functional class II (%)	20
Chest x-ray CT-ratio	
≤0.5 (%)	40
>0.5 (%)	60
ECG	
QRS duration (msec) (Mean ± SD)	124±35
≤90 (%)	25
>90 (%)	75

above 160 mL/m^2 (Table 2 and 3). Thirty-five percent had RVEF less than 45%. Pulmonary valve insufficiency was in the moderate degree in 45% of the patients, and severe degree in 45% of the patients. None of the patients had significant pulmonary valve or pulmonary branch stenosis.

Echocardiographic information of the patients showed abnormal TAPSE (Table 2 and 3). Based on the normal reference in pediatric population[9], 70% of the cases had abnormal TAPSE. Ten percent of the patients had FAC less than 35%, which is defined as abnormal RV systolic function. The minimum area RVEDi was 9 and the maximum was 29, with the mean value of 17±4 cm^2/m^2. RVMPI demonstrated an abnormality in 35% of the study group. Fifty percent of the cases had moderate PR and 45% had severe PR.

There were significant correlations between RVEDVi and area RVEDi (R = 0.768, p<0.01), RVEF with FAC (R = 0.759, p<0.01), and RVEF with TAPSE (R = 0.688, p<0.01) (Fig. 4-6). One hundred percent correlation was found in moderate to severe PR, through assessment by ECHO and CMR (Kappa = 0.912). Abnormal RVMPI was not correlated with NYHA functional class, chest X-ray, and ECG (Kappa -0.10, 0.15 and -0.04 respectively). The area RVEDi ≥20.43 cm□/m□ had a significant correlation with RVEDVi ≥160 mL/m□ (sensitivity 64%, specificity 83 %), with the area under the curve of 0.857 from the ROC curve analysis.

Discussion

CMR is the gold standard for RV volume and function assessment after surgical RVOT, pulmonary valve and pulmonary artery reconstruction of TOF patients. It provides adequate standardization and high reproducibility with a low inter-observer variability[11,12]. However, performing routine CMR on pediatric patients is not completely feasible. Therefore, ECHO, a less invasive and less time-consuming method, is the main modality for daily basis evaluation. Since the complex geometry of the RV is age dependent[11], there are still some limitations of ECHO in the investigation of RV performance for post-repaired TOF. As result, assessment of RV function remains a challenge in the clinical practice. It is usually limited to subjective qualitative evaluation by using at least one of the following ECHO parameters in order to assess RV function. The parameters include FAC, TAPSE, or RVMPI[13].

Table 2. CMR and ECHO parameters in each patient

Case No.	CMR			ECHO				
	RVEDVi (ml/m^2)	RVEF (%)	Degree of PR	TAPSE (mm)	Area RVEDi (cm^2/m^2)	FAC (%)	MPI	Degree of PR
1	87.81	52.30	Mild	15.0	8.92	45.00	0.50	Moderate
2	142.07	52.90	Severe	17.3	21.21	46.75	0.49	Severe
3	160.25	49.10	Severe	16.7	16.31	41.43	1.04	Severe
4	130.20	49.60	Moderate	13.3	20.20	40.30	0.36	Moderate
5	147.28	45.30	Moderate	17.0	13.77	37.32	0.29	Moderate
6	153.57	41.30	Severe	13.7	16.73	34.95	0.56	Severe
7	95.63	46.10	Mild	14.7	12.18	43.34	0.55	Mild
8	157.53	48.62	Severe	16.0	18.59	43.29	0.37	Severe
9	167.82	45.70	Severe	15.5	15.46	40.71	0.54	Severe
10	138.36	50.40	Moderate	16.0	16.53	36.63	0.61	Moderate
11	184.30	43.30	Severe	17.3	21.22	35.25	0.51	Severe
12	117.90	60.20	Moderate	18.9	12.76	47.19	0.28	Moderate
13	83.38	57.50	Moderate	17.4	11.53	45.71	0.32	Moderate
14	161.78	32.10	Moderate	13.3	18.59	33.19	0.58	Moderate
15	153.64	44.80	Moderate	15.1	15.18	42.75	0.44	Moderate
16	138.39	45.20	Moderate	16.0	13.82	41.79	0.49	Moderate
17	122.93	32.20	Severe	13.1	13.26	38.44	0.59	Severe
18	247.86	35.80	Moderate	14.1	28.37	39.90	0.55	Moderate
19	116.57	43.70	Severe	18.4	21.57	39.34	0.58	Severe
20	132.52	56.35	Severe	19.0	14.39	50.05	0.66	Severe

Table 3. Cardiac magnetic resonance imaging (CMR) and echocardiographic (ECHO) parameters (n = 20)

Modality	Parameter	n
CMR	RVEDVi (mL/m^2) (Mean ± SD)	142±36
	≥160 (%)	25 (5)
	<160 (%)	75 (15)
	RVEF (%) (Mean ± SD)	47±83
	<45 (%)	5 (7)
	≥45 (%)	65 (13)
	Degree of PR	
	Mild (%)	10 (2)
	Moderate (%)	45 (9)
	Severe (%)	45 (9)
ECHO	TAPSE (mm) (Mean ± SD)	16±2
	Normal (%)	30 (6)
	Abnormal (%)	70 (14)
	FAC (%) (Mean ± SD)	41±4
	<35 (%)	10 (2)
	≥35 (%)	90 (18)
	Area RVEDi (cm^2/m^2) (Mean ± SD)	17±4
	MPI	
	Normal (%)	60 (13)
	Abnormal (%)	40 (7)
	Degree of PR	
	Mild (%)	5 (1)
	Moderate (%)	50 (10)
	Severe (%)	45 (9)

The present study demonstrated significant correlations among ECHO and CMR parameters for RV assessment in post-op TOF patients. Results from this study demonstrated correlations between ECHO parameters of TAPSE, FAC and RVMPI with CMR parameters. FAC and TAPSE from ECHO correlated well with RVEF from CMR, while area RVEDi from ECHO was significantly associated with RVEDVi from CMR. Moreover, the degree of PR from ECHO also showed a significant correlation with PR severity from CMR. With these strong correlations among the two modalities, ECHO could be an effective tool for RV assessment after TOF repair.

The most challenging issue for following-up post-surgical TOF patients with severe PR is to define the appropriate time for PVR. Surgical PVR at an appropriate age may restore RV function and improve the symptoms; however, cardiopulmonary bypass and ventriculotomy required for such operations may further impair RV functions[14]. In addition, RV recovery following PVR for chronic, significant PR, after repair of TOF, may be compromised in the adult population[15].

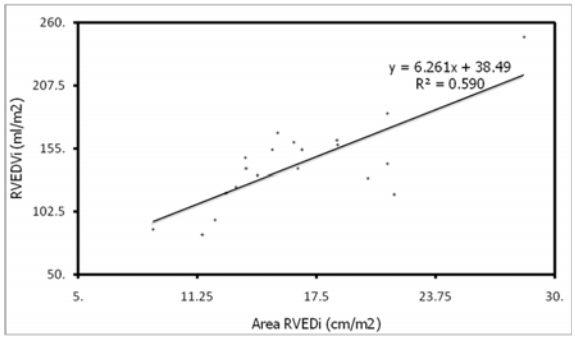

Fig. 4 Correlation of RVEDVi from CMR and Area RVEDi from ECHO.

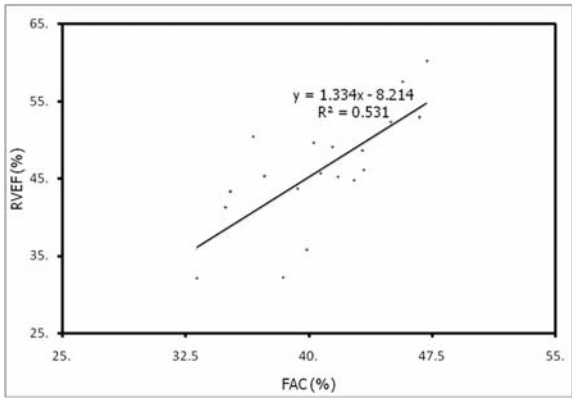

Fig. 5 Correlation between RVEF from CMR and FAC from ECHO.

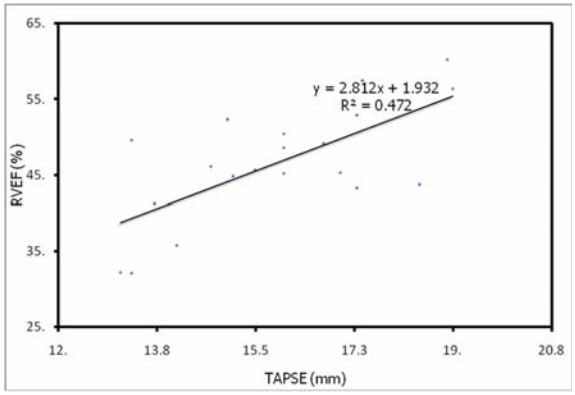

Fig. 6 Correlation between RVEF from CMR and TAPSE from ECHO.

Although indications and timing of PVR is still controversial; the trend for the treatment nowadays is to replace the valve as early as possible to prevent irreversible damage[14,15]. RVEDVi >160 mL/m^2 from CMR has been an indication for PVR[3]. The present

study showed the area RVEDi ≥20.43 cm^2/m^2, from ECHO, significantly correlated with RVEDVi ≥160 mL/m^2, from CMR, with the sensitivity and specificity of 64 and 83%, respectively. The area RVEDi >20.43 cm^2/m^2 is indicated for consideration for PVR.

Conclusion

In conclusion, ECHO is an effective tool for RV evaluation in TOF with PR. Results showed that FAC, TAPSE and the degree of PR from ECHO correlated well with CMR parameters. Measurement of area RVEDi from ECHO is the best parameter to predict RVEDVi from CMR.

Potential conflicts of interest

None.

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การศึกษาเปรียบเทียบ: การประเมินหัวใจห้องล่างขวาในผู้ป่วยหลังผ่าตัดรักษาโรค Tetralogy of Fallot โดยเครื่องตรวจคลื่นเสียงสะท้อนหัวใจกับเครื่องเอ็มอาร์เอหัวใจ

วรการ พรหมพันธุ์, ธีระ วงศ์ลิขิตปัญญา, ภูมิพร กตัญญูวงศ์, สุวิภาภรณ์ ศิริพรพิทักษ์

ภูมิหลัง: *ผู้ป่วยโรค Tetralogy of Fallot (TOF) หลังการผ่าตัดรักษายังคงต้องมีการติดตามการทำงานของหัวใจอย่างต่อเนื่อง โดยเฉพาะอย่างยิ่งเวนตริเคิล ซึ่งพบว่าการทำงานมักจะเสื่อมลงจากการที่มีลิ้นหัวใจพัลโมนารีรั่วเรื้อรัง ปัจจุบันการตรวจคลื่นแม่เหล็กไฟฟ้าหัวใจถือเป็นมาตรฐานสำหรับประเมินการทำงานของหัวใจของเวนตริเคิลขวาแต่มีข้อจำกัดในการส่งตรวจ ในขณะที่การตรวจโดยคลื่นเสียงสะท้อนหัวใจ มีการพัฒนาเทคนิคการตรวจเพิ่มขึ้นถึงขั้นที่อาจจะสามารถนำมาใช้ทดแทนกันได้ ผู้ศึกษาจึงได้วิจัยการเปรียบเทียบเครื่องมือทั้งสองในการประเมินหัวใจเวนตริเคิลขวา*

วัตถุประสงค์: *เพื่อประเมินความสัมพันธ์ระหว่างการตรวจคลื่นเสียงสะท้อนหัวใจและการตรวจคลื่นแม่เหล็กไฟฟ้าหัวใจ ในการประเมินขนาดตลอดจนการทำงานของเวนตริเคิลขวา และเพื่อหาตัวแปรจากการตรวจคลื่นเสียงสะท้อนหัวใจที่สามารถคาดเดาค่า RVEDVi จากการตรวจคลื่นแม่เหล็กไฟฟ้าหัวใจได้*

วัสดุและวิธีการ: *โดยทำการศึกษาแบบเปรียบเทียบผู้ป่วย TOF หลังได้รับการผ่าตัดรักษาในสถาบันสุขภาพเด็กแห่งชาติมหาราชินีจำนวน 20 รายในช่วง เดือนมิถุนายน พ.ศ. 2554 ถึง เดือนมีนาคม พ.ศ. 2555 โดยนำค่าผลการตรวจการทำงาน (RVEF) ปริมาตรของหัวใจห้องล่างขวา (RVEDVi) และระดับการรั่วของลิ้นหัวใจพัลโมนารี (degree of PR) ที่ได้จากการตรวจคลื่นแม่เหล็กไฟฟ้าหัวใจ เปรียบเทียบกับค่าผลการตรวจการทำงาน (TAPSE, FAC, MPI) พื้นที่ของหัวใจห้องเวนตริเคิลขวา (Area RVEDi) และระดับการรั่วของลิ้นหัวใจพัลโมนารี (degree of PR) ที่ได้จากการตรวจคลื่นเสียงสะท้อนหัวใจ โดยใช้สถิติเพื่อหาค่าความสัมพันธ์ โดยวัดค่าสัมประสิทธิ์สหสัมพันธ์ รวมทั้งการหาค่าความไวและค่าความจำเพาะ ระหว่างการตรวจสองวิธีนี้*

ผลการศึกษา: *ผู้ป่วย 20 คน อายุเฉลี่ย 14 ปี 1 เดือน และระยะเวลาหลังผ่าตัดเฉลี่ย 8 ปี 9 เดือน พบว่ามีความสัมพันธ์ปานกลาง ในการวัดการทำงานของหัวใจห้องล่างขวาทั้งโดยการวัด Area RVEDi เทียบกับ RVEDVi ($R = 0.768$, $p<0.01$), TAPSE เทียบกับ RVEF ($R = 0.688$, $p<0.01$) และ FAC เทียบกับ RVEF ($R = 0.759$, $p<0.01$) รวมถึงมีความสอดคล้องกันของค่า degree of PR ตั้งแต่ระดับปานกลางถึงรุนแรง ($R = 0.912$) ของวิธีการตรวจทั้งสองและเลือกใช้ค่า Area RVEDi ที่มากกว่าหรือเท่ากับ 20.43 cm^2/m^2 ในการส่งต่อผู้ป่วยเพื่อตรวจ CMR โดยมีค่าความไวร้อยละ 64 และค่าความจำเพาะร้อยละ 83*

สรุป: *การตรวจโดยเครื่องคลื่นเสียงสะท้อนหัวใจในผู้ป่วยหลังผ่าตัด TOF สามารถใช้ประเมินเวนตริเคิลขวาได้ดี เมื่อเทียบกับการตรวจคลื่นแม่เหล็กไฟฟ้าหัวใจโดยการวัดค่า Area RVEDi จากการตรวจคลื่นเสียงสะท้อนหัวใจ สามารถคาดเดาค่า RVEDVi จากการตรวจคลื่นแม่เหล็กไฟฟ้าหัวใจได้ดีที่สุด*