CLINICAL STUDY

The optimal timing for magnetic resonance imaging in long-term follow-up of patients after a complete correction of the Tetralogy of Fallot

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Abstract: *Objectives:* Long-term pulmonary regurgitation (PR) leads to right ventricular (RV) dilatation and dysfunction. In patients after a complete correction of the tetralogy of Fallot (TOF) it represents the most frequent and high risk late complication. Magnetic resonance imaging (MRI) is an objective possibility for RV measurements; on the other hand MRI is complicated and not always accessible method.
Background: We analyzed echocardiography (ECHO) and MRI parameters regarding RV dilatation and function and the correlation between these two methods with the aim to define optimal ECHO parameters indicating a necessity for further investigations.
Patients and methods: In 50 patients with TOF > 10 years, after a complete surgical correction, ECHO and MRI were performed.
Results: ECHO finding of end-diastolic diameter (EDD) of RV > 30mm was detected in 13 patients (26 %) and in 30 patients (60 %) RV EDD above 4 standard deviations (SD) their normal values was present. MRI finding of end-diastolic volume (EDV) > 160 ml/m^2 was present in 14 patients (28 %) and end-systolic volume (ESV) > 85 ml/m^2 in 17 patients (34 %). Significant correlations between ECHO and MRI RV diastolic measurements were found (p=0.0001, r=0.34, resp. p=0.001, r=0.39). PR was significantly affecting diastolic RV dilatation (p=0.0001), on the other hand. RV dysfunction resulted in systolic RV dilatation (p=0.007). PR did not correlate with RV function (p=0.56).
Conclusions: MRI is a golden standard for exact RV measurements and for the indication of pulmonary valve replacement, but ECHO still can be used during long-term follow-up, defining the point for further and more exact RV measurements *(Tab. 2, Fig. 11, Ref. 17).* Full Text in free PDF *www.bmj.sk.*
Key words: tetralogy of Fallot, pulmonary regurgitation, cardiovascular magnetic resonance imaging, right ventricle, end-diastolic volume, end-systolic volume.

Abbreviations: BSA – body surface area, ECHO – echocardiography, EDD – end-diastolic diameter, EDV – end-diastolic volume, EF – ejection fraction, ESV – end-systolic volume, LV – left ventricle, MRI – magnetic resonance imaging, PR – pulmonary regurgitation, PRF – pulmonary regurgitation fraction, PW – pulsed-wave Doppler, RV – right ventricle, SD – standard deviation, TAP – trans-annular patch, TOF – tetralogy of Fallot.

The presence of severe pulmonary regurgitation (PR) is an inevitable surgical result of a complete correction of the tetralogy of Fallot (TOF). PR has been often reported to be the causative factor for right ventricular (RV) volume overload leading to the enlargement of RV. Long-term PR may with time lead to severe progressive RV dilatation and dysfunction and also to an increased risk for life-threatening arrhythmias and/or sudden death.

Pulmonary valve replacement (PVR) represents so far the only possibility the management of this late complication. The optimal timing for PVR is though a hot subject of discussion. After PVR a considerable improvement of RV functional and metric parameters in many studies was seen (1–6). On the other hand, in patients with RV end-diastolic volume (EDV) > 170 ml/m^2 measured by magnetic resonance imaging (MRI) before intervention, no RV volume "normalization" after PVR could be achieved (2, 7).

MRI is an objective and exact possibility for evaluating RV volume and at present represents the golden standard for indicating the intervention (1, 3). On the other hand, MRI is a relatively complicated, time-consuming and not always accessible method; so to estimate the reasonable timing for MRI may be very helpful.

The aim of our study was to find during routine echocardiographic (ECHO) measurements the optimal criteria and timing when to perform MRI examination. Despite the excellent possibilities of the exact ECHO measurement of volume and

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function of the left ventricle (LV), the ECHO measurement of RV is due to its irregular shape very problematic (8–11) and usually has just an approximate value. On the other hand, ECHO is an easy, save, always accessible (even bedside) and well reproducible method. We analyzed the correlation between various ECHO and MRI measurements in evaluating the RV, with the aim to define possible ECHO parameters that would indicate the necessity for further MRI investigations.

Patients and methods

We examined by ECHO and MRI 50 selected patients with secondary post-operative RV dilatation, 22 females (44 %) and 28 males (56 %) (Tab. 1).

All patients in the study underwent a complete surgical correction at our institution and were examined in routine follow-up during regular outpatient visits. The median age of the patients at the time of surgical repair was 27.5 months (7 days – 10 years). A prior palliative shunt procedure had been performed in 12 patients (24 %). In 31 patients (62 %), surgery had been performed using a trans-annular patch (TAP) for enlargement of the right ventricular outflow tract, whereas in 14 patients (28 %) a different method had been used and the trans-annular ring was conserved. Five patients (10 %) had a primary correction with a homograft (Tab.1).

The median age of the patients at the time of the MRI study was 15 years (range 8.6–27.1 years). The MRI was performed at the median time of 12.6 years (range 10–22.1 years) after the complete correction of the congenital heart defect (Tab. 1). ECHO assessment was performed within a period of 5 days before MRI examination.

In all 50 patients, a trans-thoracic ECHO was performed by an experienced paediatric cardiologist using the GE Vivid 7 system with digital storage system. On ECHO, the degree of pulmonary regurgitation (PR), RV end-diastolic diameter (EDD) with the severity of RV dilatation, as well as the RV ejection fraction (EF) was measured and calculated. PR was semi-quantitatively classified into three degrees (mild – grade I, moderate – grade II, severe – grade III) according to the length and width of the regurgitant flow in colour Doppler mode and localisation on pulsed-wave (PW) Doppler ECHO (Tab. 2). RV EDD (mm) was measured in parasternal long axis view, both by 2D and by M mode; and the severity of RV dilatation was calculated according to the standard deviation (SD) above normal values ac-

Tab. 1 Clinical data.

Number of patients	50
Male/female	22/28
Diagnosis	
– Tetralogy of Fallot (TOF)	41 (82 %)
– Pulmonary atresia (PA)	5 (10 %)
–TOF + absent pulmonary valve	4 (8 %)
Age at definitive surgical repair	median 27.5 months (7 days–10 years)
Palliative shunt prior definitive correction	12 (24 %)
Definitive surgical repair method	
–With trans-annular patch (TAP)	31 (62 %)
– Correction without TAP	14 (28 %)
– Homograft implantation	5 (10 %)
Age at MRI examination (years)	median 15 years (8.6–27.1 years)
MRI after surgery (years)	median 12.6 years (10–22.1 years)

MRI – magnetic resonance imaging

Tab. 2. Echocardiographic classification of pulmonary valve regurgitation.

Grade I	Insufficiency jet less than one-third of the right ventricular outflow tract, PR traceable cranial to the pulmonary valve on PW Doppler ECHO.
Grade II	Insufficiency jet between one- and two-thirds of the right ventricular outflow track, PR traceable up to the middle of the main pulmonary artery on PW Doppler ECHO.
Grade III	Insufficiency jet more than two-thirds of the right ventricular outflow tract, PR traceable over the bifurcation of the main pulmonary artery on PW Doppler ECHO.

PR – pulmonary regurgitation, PW – pulsed-wave Doppler, ECHO – echocardiography

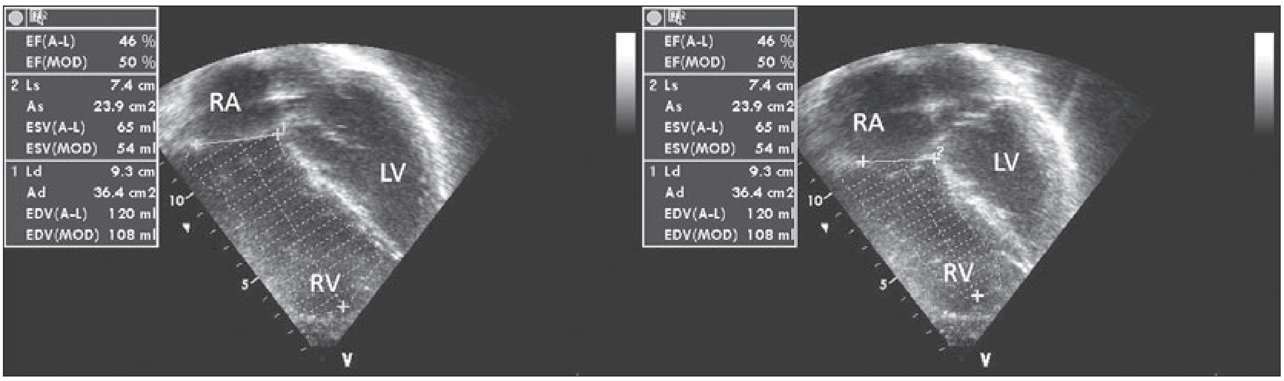

Fig. 1. Measurement of the right ventricular ejection fraction by Simpson method (the difference of the end-diastolic and end-systolic volume). RA – right atrium, RV – right ventricle, LV – left ventricle.

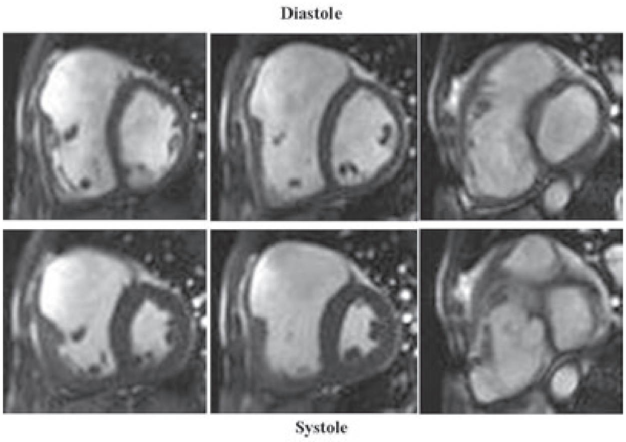

Fig. 2. Measurements of end-diastolic and end-systolic volume of right ventricle by MRI. MRI – magnetic resonance imaging.

cording to patient´s weight and height. RV EF was established by the Simpson method from the difference between the end-diastolic and end-systolic RV volume measured from the apical 4 chamber view (Fig. 1).

All MRI examinations were performed on the 1.5 T Siemens Avanto. RV EDV and RV ESV, pulmonary regurgitation fraction (PRF) and RV EF was measured (Fig. 2). For the assessment of RV EDV and RV ESV, the cine-MRI sequence in a short-axis view was used. The RV EF was calculated as the difference between RV EDV and RV ESV. For the assessment of PRF, the phase shift velocity mapping with flow-sensitive gradient-echo sequence was performed.

Statistical analysis

Data were analyzed using the statistical program (JMP 5.0.1a, Statistical Analysis, Cary, NC). The data are presented as the median and range. P value < 0.05 was considered significant and comparison was made using the Pearson´s, Wilcoxon and Fisher exact test. Subgroups were compared using the log-rank test. The standard values used at our institution were considered as the normal ECHO RV diameters (12).

Results

1.Echocardiography

- *End-diastolic diameter of the right ventricle*

Median of RV EDD was 25.8 mm (12 mm – 46.7 mm). Patients were divided into the two groups according to the RV EDD measured by ECHO. The cut-off diameter for severe RV dilatation was EDD > 30 mm (13 patients, 26 %) or EDD > 4 SD of its normal values according to patient´s weight and height (30 patients, 60 %).

- *Ejection fraction of the right ventricle*

Median of RV EF in or patients was 52 % (26–69 %), and four patients (8 %) had a decreased RV EF < 40 % measured on ECHO.

- *Pulmonary regurgitation*

Semi-quantitative estimation of PR showed 41 patients (82 %) with severe PR, 5 patients (10 %) with moderate and 4 patients (8 %) with mild PR. Patients with TAP had a significantly higher PR (p=0.01).

2.Magnetic resonance imaging

- *End-diastolic and end-systolic volumes of the right ventricle*

Median of RV EDV was 133 ml/m² of patient´s body surface area (BSA) (59.5 – 233.3 ml/m²) and of RV ESV was 71.8 ml/m² of patient´s BSA (20.1–155 ml/m²). On MRI, 14 patients (28 %) had RV EDV > 160 ml/m² a 17 patients (34 %) had RV ESV > 85 ml/m² (which are considered as indication criteria for PVR at out institution).

- *Ejection fraction of the right ventricle*

Median of RV EF measured by MRI was 44 % (28–75 %). In 12 patients (24 %), a reduced RV EF (< 40 %) was found.

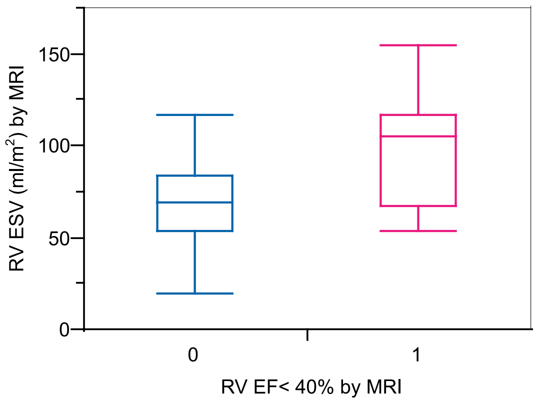

Fig. 3. Right ventricular end-systolic volume (RV ESV) measured by ECHO in correlation with right ventricular ejection fraction (RV EF) < 40 % measured by MRI. RV ESV – right ventricular end-systolic volume, RV EF – right ventricular ejection fraction, MRI – magnetic resonance imaging, ECHO – echocardiography.

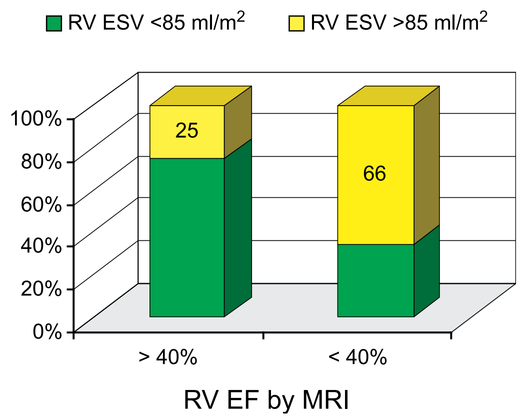

Fig. 4. Right ventricular end-systolic volume (RV ESV) < 85 ml/m² measured by MRI in correlation with right ventricular ejection fraction (RV EF) < 40 % measured by MRI. RV ESV – right ventricular end-systolic volume, RV EF – right ventricular ejection fraction, MRI – magnetic resonance imaging.

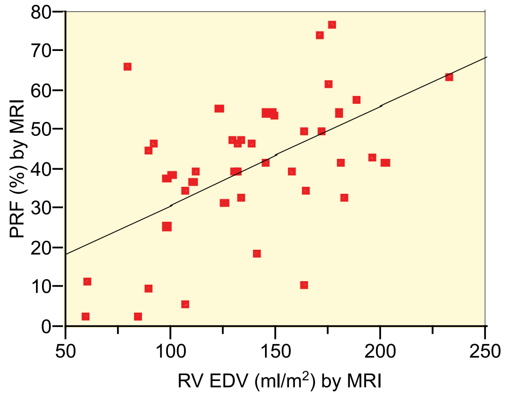

Fig. 5. Pulmonary regurgitation fraction (PRF) measured by MRI in correlation with right ventricular end-diastolic volume (RV EDV) measured by MRI. PRF – pulmonary regurgitation fraction, RV EDV – right ventricular end-diastolic volume, MRI – magnetic resonance imaging.

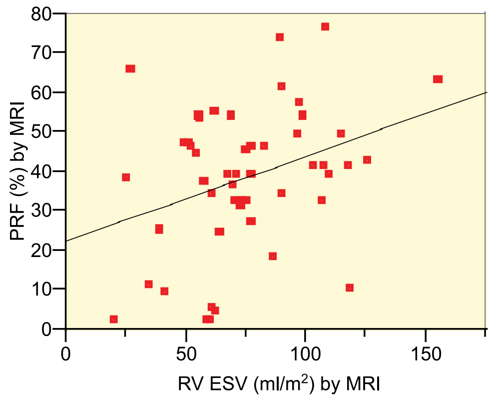

Fig. 6. Pulmonary regurgitation fraction (PRF) measured by MRI in correlation with right ventricular end-systolic volume (RV ESV) measured by MRI. PRF – pulmonary regurgitation fraction, RV ESV – right ventricular end-systolic volume, MRI – magnetic resonance imaging.

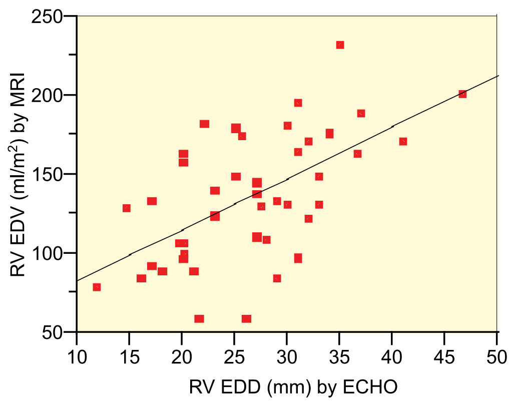

Fig. 7. Right ventricular end-diastolic volume (RV EDV) in correlation with right ventricular end-diastolic diameter (RV EDD) measured by ECHO measured by MRI. RV EDV – right ventricle end-diastolic volume, RV EDD – right ventricular end-diastolic diameter, MRI – magnetic resonance imaging, ECHO – echocardiography.

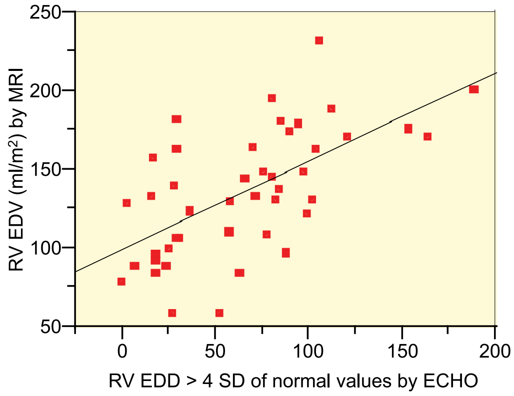

Fig. 8. Right ventricular end-diastolic volume (RV EDV) measured by MRI in correlation with right ventricular end-diastolic diameter (RV EDD) > 4 SD of normal values measured by ECHO. RV EDV – right ventricular end-diastolic volume, RV EDD – right ventricular end-diastolic diameter, ECHO – echocardiography.

In patients with a decreased RV function (RV EF < 40 %), there was a significant correlation to RV systolic dilatation – both to RV ESV (p 0.007) (Fig. 3) and to RV ESV > 85 ml/m^2 (p=0.006) (Fig. 4), although no correlation to diastolic RV volumes was present – RV EDV (p=0.28) and RV EDV > 160 ml/m^2 (p=0.39).

There was also no correlation between MRI measurements of RV EF (p=0.72, r=0.001) and PRF.

• *Pulmonary regurgitation and pulmonary regurgitation fraction*

The median of PRF determined by MRI was 40 % (3–77 %). The PRF varied depending on the surgical method. Patients with TAP had significantly higher PRF than patients with valve sparing procedure: 43.2 % (11–74.5 %) versus 34 % (5–66.5 %) (p=0.04).

Figures 5 and 6 show a significant, although low degree of correlation between PRF and RV EDV (p= 0.0001, r=0.48) (Fig. 5) as well as between PRF and RV ESV (p=0.0195, r=0.40) (Fig. 6). There were also a significant correlation between MRI measurements of PRF (%) and RV EDV > 160 ml/m^2 (p=0.01), but on the other hand a low degree of correlation to RV ESV > 85 ml/m^2 (p=0.06).

3. Echocardiography and MRI correlations

• Right ventricular dimensions

Patients with RV EDD > 30 mm measured by ECHO had a significantly higher incidence of severe RV dilatation estimated by MRI – both diastolic (RV EDV > 160 ml/m^2 (p=0.0012)) and systolic (RV ESV > 85 ml/m^2 (p=0.007)). Also in patients with RV EDD > 4 SD of normal values measured by ECHO there was a significantly higher incidence of RV EDV > 160 ml/m^2 (p=0.0025) found on MRI, but on the other hand, no correlation with RV ESV > 85 ml/m^2 (p=0.21) was found.

There was a significant, although low degree of correlation between RV EDD (mm) measured by ECHO and RV EDV (ml) measured by MRI (p=0.0001, r=0.34) (Fig. 7), and similarly be-

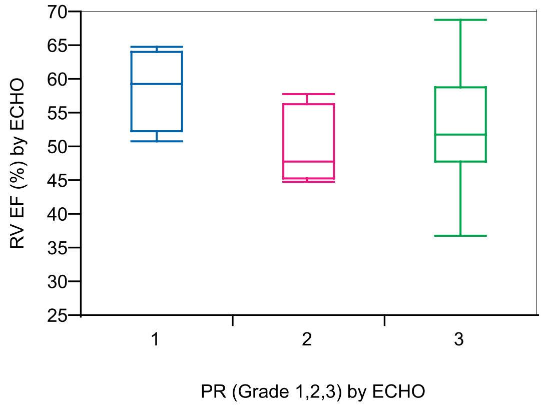

Fig. 9. Right ventricular ejection fraction (RV EF) measured by ECHO in correlation with pulmonary regurgitation (PR) measured by ECHO. RV EF – right ventricular ejection fraction, PR – pulmonary regurgitation, ECHO – echocardiography.

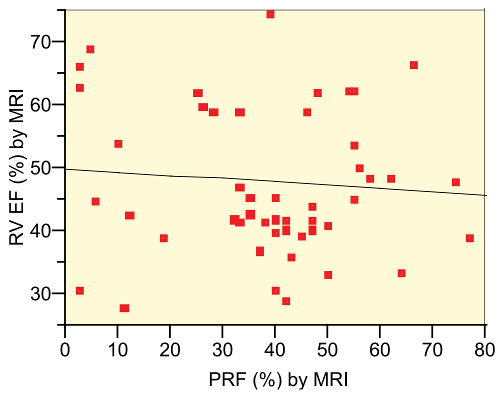

Fig. 10. Right ventricular ejection fraction (RV EF) measured by MRI in correlation with pulmonary regurgitation fraction (PRF) measured by MRI. RV EF – right ventricular ejection fraction, PRF – pulmonary regurgitation fraction, MRI – magnetic resonance imaging.

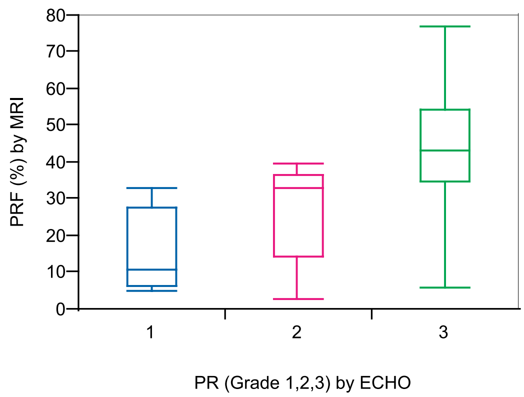

Fig. 11. Pulmonary regurgitation fraction (PRF) measured by MRI in correlation with pulmonary regurgitation measured by ECHO. PRF – pulmonary regurgitation fraction, MRI – magnetic resonance imaging, ECHO – echocardiography.

tween RV EDD (SD of normal values) measured by ECHO and RV EDV (ml) measured by MRI (p=0.001, r=0.39) (Fig. 8).

• *Right ventricular function*

There was no correlation between RV EF (%) measured by ECHO a MRI (p=0.50, r=0.01). There was also no correlation between RV EF (%) and PR (mild / moderate / severe) measured by ECHO (p=0.22) (Fig. 9), nor between RV EF (%) to PRF (%) established by MRI (p=0.56) (Fig. 10).

• *Pulmonary regurgitation*

In our study, there was a significant correlation between PR measured by ECHO (mild / moderate / severe) and PRF (%) measured by MRI (p=0.005) (Fig. 11). Also, a significant correlation was found between PR measured by ECHO and RV EDV (ml/m^2) established by MRI (p=0.04), on the other hand no correlation to RV ESV (ml/m^2) was present (p=0.1).

Discussion

PR is very common consequence after a definitive correction in patients with TOF, especially when TAP is used. PR may lead to a progressive RV enlargement due to chronic volume overload, which may finally result in RV dysfunction and failure. This also may lead to significantly higher incidence of severe ventricular arrhythmias and higher risk of sudden death (13).

Pulmonary valve replacement represents so far the only possibility for contributing to the management of these complications. Optimal timing for replacement is though still a topic of discussion. Reliable estimation of PR as well as RV dilatation and function is therefore one of the central points of follow-up examinations after TOF correction.

Several studies concerning the criteria for PVR were presented. The RV EDV and RV ESV and the RV EF obtained by MRI are at present time the most reliable criteria.

The up-to-date criteria for pulmonary valve replacement obtained by MRI are (1, 2):

• *RV EDV > 150–160 ml/m^2*

• *RV ESV > 85 ml/m^2*

• *RV EF < 40 %.*

On the other hand, there are some limitations for MRI studies. MRI is relatively complicated, expensive, time consuming and not always accessible method; so to estimate the reasonable timing for MRI may be very helpful. MRI is still at most diagnostic institutions contraindicated in patients with implanted pacemaker, cardioverter/defibrilator or other metallic implants.

At the same time, RV evaluation by ECHO because of its irregular shape represents a serious problem and RV dimension and volume estimation are therefore only approximative. Also, a Doppler ECHO estimation of PR, another very important late finding in patients after TOF correction, is only semi-quantitative.

On the other hand, ECHO is a very useful, easy, save, always accessible (even bedside) and well reproducible method. ECHO can be used on a regular base during the long-term follow-up of patients and is optimal for screening and selecting high risk patients and as well in determining the time-progression of RV dilatation in every single patient.

The advantages and disadvantages of both diagnostic methods were the reason for our study:
1. to find a correlation between routinely measured ECHO and MRI parameters regarding RV dilatation;
2. to define the correlation between RV function (EF) measured by ECHO and MRI, as well as to find possible anatomic and/or functional parameters correlating to decreased RV function;
3. to define the correlation between pulmonary regurgitation measured by ECHO and MRI and its correlation to the degree of RV dilatation.

1. Correlation between RV dilatation measured by ECHO and MRI

There was a significant, although a low degree of correlation between RV EDD (mm) measured by ECHO and RV EDV measured by MRI (p=0.0001, r=0.34) and similarly between RV dilatation (SD of normal values) measured by ECHO and RV EDV measured by MRI (p=0.001, r=0.39). It was reported previously, that **echocardiographically assessed diastolic RV dimensions correlated with RV EDV obtained by MRI** (14).

In our study, we established the cut-off diameter of RV EDD > 30 mm and/or > 4SD measured by ECHO as a definition for severe RV dilatation. Similarly, MRI measurements of RV EDV > 160 ml/m^2 and RV ESV > 85 ml/m^2 (indication criteria for PVR at our institution) were taken as severe RV dilatation. There was a strong correlation found between RV EDD > 30 mm measured by ECHO and the cut-off indication values established by MRI (p=0.0012 and p=0.007 respectively). The same correlation was present in ECHO finding of RV EDD > 4 SD of normal values and MRI RV EDV > 160 ml/m^2 (p=0.0025), although there was no correlation to RV ESV > 85 ml/m^2 (p=0.21). According to our findings, we believe that the above mentioned ECHO parameters are suitable for defining severe RV dilatation, especially a diastolic dilatation.

2. Correlation between RV function measured by ECHO and MRI and other anatomic and functional parameters

In our study, there was **no correlation found between RV EF measured by ECHO and by MRI** (p=0.50, r=0.01). This may be caused by the inaccuracy of the ECHO measurement of right ventricle, due to RV irregular shape and only 2D tracing, and also because only a part of RV is included into the measurement (completely leaving out the RV outflow tract). On the contrary, MRI is a 3-dimensional measurement, and is also taking into account all three parts of the RV, so estimating RV EF should be more reliable.

There was no correlation between RV function (EF) and pulmonary regurgitation, measured either by ECHO (p=0.22), or by MRI (p=0.56). This confirms that **the right ventricle is able to tolerate pulmonary regurgitation for a long time** (2, 6). Other factors (besides volume overload) may play an important role as well, which contribute to the decrease of RV function.

There was no correlation between RV EF and diastolic RV dilatation. On the other hand, in patients with decreased RV function (RV EF < 40 %) established by MRI there was a significant correlation to systolic RV dilatation (both to RV ESV (p=0.007) and to RV ESV 85 > ml/m^2 (p=0.006)). **RV dysfunction resulting in systolic RV dilatation may represent a risk factor for further intervention.** This would though need a more detailed study.

3. Correlation between pulmonary regurgitation measured by ECHO and MRI and other anatomic and functional parameters

Patients with TAP have a significantly higher degree of pulmonary regurgitation and right ventricular impairment than patients, in whom a different method of correction had been used (15–17). This was also confirmed in our study, considered both by ECHO (p=0.01), as well as by MRI (p=0.04).

In our study, there was a correlation between pulmonary regurgitation severity established by ECHO and MRI (p=0.05). **Although defining PR by ECHO may be semi-quantitative, both methods (MRI and ECHO) proved to be able to determine and classify pulmonary regurgitation well.** In a previously published study (15) also the significance of Doppler ECHO in the assessment of PR in patients after TOF correction was demonstrated.

There was a correlation between pulmonary regurgitation and diastolic RV dilatation (established by MRI), and this was present both in ECHO quantification of PR (p=0.04) and also in MRI estimation of PRF (p=0.0001). On the other hand, the correlation of pulmonary regurgitation to systolic RV dilatation was more questionable: there was also a significant, although a low degree of correlation between PRF (%) measured by MRI and RV ESV (ml/m^2) (p=0.0195, r=0.40), but this was not true in the group of patients with a severe RV dilatation (RV ESV > 85 ml/m^2) (p=0.06) and also no correlation of PR measured by ECHO to RV ESV (ml/m^2) (p=0.1) was found. This means that **pulmonary regurgitation has an impact on diastolic RV dilatation.** As long as RV systolic function is preserved, thanks to Frank-Starling mechanism, systolic RV dimensions are not significantly affected.

Conclusions

MRI is a golden standard for indicating pulmonary valve implantation in TOF patients after the correction. MRI though cannot always be carried out. We found a correlation between ECHO and MRI parameters. Although ECHO is not optimal for establishing the exact RV volume, RV EDD > 30 mm or > 4 SD of RV normal values meet most probably the MRI criteria for reintervention (pulmonary valve replacement); and so reaching these ECHO values may be the optimal timing for further examinations and exact RV volume estimation by MRI.

The exact measurement of RV function may be a problem in ECHO due to a difficult assessment of the whole 3-dimensional irregularly shaped RV. In TOF patients after a complete correction, the RV seems to tolerate long-term volume overload well; on the other hand RV dysfunction resulting in systolic RV dilatation may mean a risk factor for further intervention.

Patients with TAP have a significantly higher degree of pulmonary regurgitation. Pulmonary regurgitation affects more significantly diastolic RV dilatation; systolic RV dimensions are preserved for longer time. Although defining PR by ECHO may be semi-quantitative, both methods (MRI and ECHO) proved to be able to determine and classify pulmonary regurgitation well.

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