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LEFT VENTRICULAR VOLUME ASSESSMENT BY GEOMETRICAL MODELS IN PATIENTS OPERATED ON FOR TETRALOGY OF FALLOT

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Abstract

Objectives: *MRI is proven to be an accurate method for noninvasive assessment of cardiac function in tetralogy of Fallot patients (TOF). Various geometrical models are used in healthy patients to quantify cardiac function. The purpose of this study is to assess the reproducibility and validity of these geometrical models in patients operated on for TOF by comparison with cMRI.* ***Methods:*** *This is a retrospective study of 59 patients with TOF (mean age 22.46±6.67). Left ventricular (LV) volumes and ejection fraction (EF) were quantified based on a 1.5 Tesla MRI. The LV volumes and EF were either assessed with modified Simpson rule (SR), hemisphere cylinder model (HC), single plane ellipsoid model (EM) and 4 chamber Simpson rule (4cSR).* ***Results:*** *Good correlations were found for all volumes and EF for SR mode compared with full volume data set (r^2 ranged between 0.63 and 0.82 with a p value <0.001 for all correlations). The HC, EM and 4cSR models proved to be less useful for the EF assessment ($r^2 >0.53$ for HC, $r^2 0.1$ and $r^2>0.41$ for 4cSR respectively).* ***Conclusion:*** *Only SR model has proven to be a valuable method for the assessment of LV volumes, stroke volume and EF in TOF patients.*

Key words*: magnetic resonance imaging, tetralogy of Fallot, left ventricular dysfunction, ventricular ejection fraction, stroke volume.*

INTRODUCTION

The incidence of congenital heart diseases (CHD) is approximately 7 to 1,000 new borns. Among them tetralogy of Fallot (TOF), is a complex CHD, with an incidence of 0.5/1,000 births (Zeng et al., 2016).

These defects are diagnosed through different techniques such as fetal echocardiography and postnatal referral to a specialized center. During the last two decades cardiovascular magnetic resonance (cMRI) has evolved as the reference imaging modality for anatomical and functional assessment in patients with repaired TOF. cMRI has emerged as an essential diagnostic tool in these patients because it overcomes many of the limitations of echocardiography, cardiac CT, and cardiac catheterization (Tal Geva, 2011).

Using cMRI, systolic function can be assessed by calculating the ejection fraction (EF). Still, this method requires, during the heart cycle, 20 to 25 frames at about 10 to 14 slices positions in order to cover the whole heart. This procedure can be quite time consuming, especially in studies requiring high spatial resolution. Likewise, the manual or semiautomatic analysis of these slices requires another time period (Young et al., 2009).

Additionally, long acquisition times can prolongs anesthesia time in patients who need this procedure, in particular in small children. Global left ventricular function represents an important parameter in all cardiologic patients.

Furthermore, it is advisable to rapidly assess cardiac function, without increasing scan time too much. In order to take up these challenges, several studies have implemented geometrical models to assess cardiac function in animals and patients. These geometrical models estimate left ventricular (LV) volumes based on maximum two or three slices in parallel or perpendicular planes (Dulce et al., 1993), thus allowing a more rapid assessment of the LV volumes and EF. Although these geometrical models were compared with echocardiogram and were validated in healthy humans (Bunck et al., 2009), none of the previous studies has determined whether or not any of these geometrical models is viable in determining cardiac function by comparison with *the gold standard* (cMRI) in patients operated on for tetralogy of Fallot.

Consequently, the purpose of this study is to assess the reproducibility and validity of these geometrical models in patients operated on for TOF by comparison with cMRI, which represents the gold standard.

MATERIALS AND METHODS

59 patients with a mean age of 22.46±6.67 years and a male: female ratio of 1.45:1, operated on for TOF, were examined. The cMRI assessment was performed between December 2004 and March 2012 and took into account their gender, the mean age at which they underwent MRI and the assessment of LV volumes and EF through the gold standard as well as by using various geometrical models, as described by Dulce et al., in 1993. The patients were selected from the database of the Division of Pediatric Radiology, Department of Radiology - University of Graz, Austria.

Image analysis: All images were assessed in DICOM Viewer version 3.5. The end-diastolic volumes (EDV) and the end-systolic volume (ESV) of the left ventricle were considered to be the largest and the smallest area of the LV area in each slice.

For the cMRI analysis, the window width and level were manually adjusted in order to recognize ventricular morphological characterristics. To measure LV volumes, the LV area was selected using the semiautomatic segmentation parameters in DICOM Viewer. The papillary muscle was excluded from the LV volume during the assessment.

The diameter (D) of the LV volume on the short-axis was measured as the longest distance between the septum and the ventricular wall. The length (L) of the LV was defined as the longest distance from the apex to the valves.

Data analysis: The end-diastolic volume (EDV), end-systolic volume (ESV), stroke-volume (SV=EDV-ESV) and EF (EF=SV/EDV) were calculated in all patients with TOF. The calculation was based either on cMRI images of the left ventricle (the gold standard) and on various geometrical models, as described by Dulce et al., in 1993 and van de Weijer Tet et al., in 2012 (Figure 1).

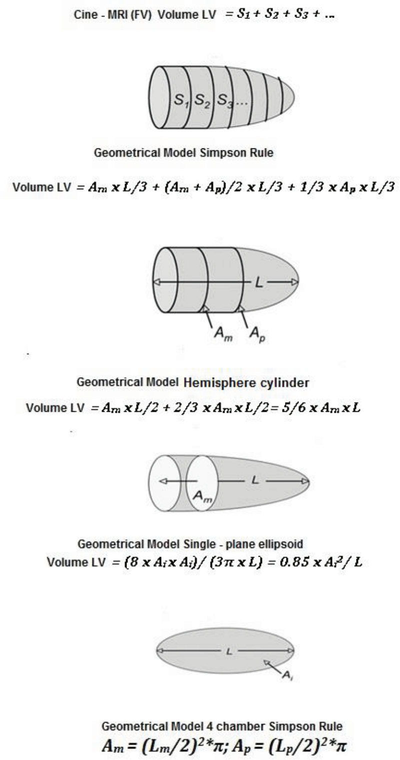

Figure 1. Algorithms and formula to calculate the LV volumes and EF by cine-MRI (full data set) and geometrical models based on a few MRI slices (After Dulce et al., 1993 and Weijer Tet et al., 2012)

The various geometrical models used to determine the LV volumes and the EF are presented: A_i - cross-sectional area of the LV cavity in the LA plane; A_m - cross-sectional area of the LV cavity in the short axis plane, 1-2 mm below the bicuspid valve; A_p - cross-sectional area of the LV cavity in the SA plane, approximately at the base of the papillary muscles; D - diameter of the LV cavity in the short axis plane, 1-2 mm below the bicuspid valve; L - the longest axis of the LV in the LA plane; S1, S2, S3 … 1 mm SA slices from the top to the bottom of the left ventricle.

Statistical analysis: The values of the LV volumes and the EF determined by cine-MRI were presented as mean values. The correlations between the LV volumes and the EF, determined through various geometrical models vs the LV data-set obtained through cine-MRI (the gold standard) were assessed by linear regression. R^2 and p values were reported for all regression analyses. The $p<0.05$ value was considered statistically significant. The difference between the geometrical models and the MRI data was assessed using the one-way ANOVA test.

RESULTS AND DISCUSSIONS

The values of the LV volumes and EF, calculated using the gold standard and various geometrical models, are listed in Table 1.

Table1. LV volumes and EF determined by cine MRI (FV) and various geometrical models

	EDV (µl)	ESV (µl)	SV (µl)	EF%
Cine-MRI (FV)	128.2±33.0	53.8±18.2	74.4±18.0	58.6±5.9
Simpson Rule (SR)	*123.6±33.9 (NS)*	*48.6±16.2 (NS)*	*75.2±21.2 (NS)*	*60.9±6.7 (NS)*
Single-plane ellipsoid (EM)	113.4±37.0*	45.9±23.0*	*73.0±18.6 (NS)*	*57.8±8.2 (NS)*
Hemisphere -cylinder (HC)	144.2±41.8*	*59.6±20.8 (NS)*	*74.4±18.0 (NS)*	*58.6±5.9 (NS)*
4 chamber Simpson Rule (4cSR)	100.4±35.7*	40.8±17.8*	59.6±26.9*	*59.2±11.8 (NS)*

The model relying on Simpson's rule was the only one to yield statistically indifferent values for the LV volumes and the EF by comparison with the gold standard. As far as the EF is concerned, no differences were noted by the single-plane ellipsoid model and the hemisphere cylinder model or by 4 chamber Simpson's rule (apical 4-chamber view). The EF was quantified by geometrical models vs cine-MRI. Pearson's correlation coefficient (r) and R^2 can also be identified in Figures 2-5.

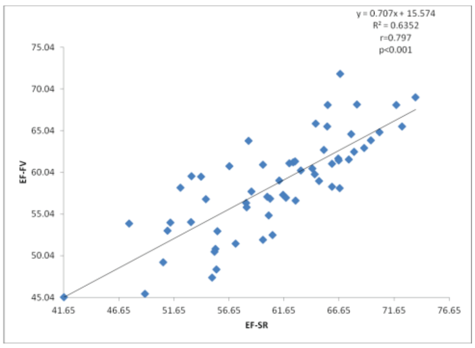

Figure 2. Scatter-plot showing the correlation between EF-FV and EF-SR

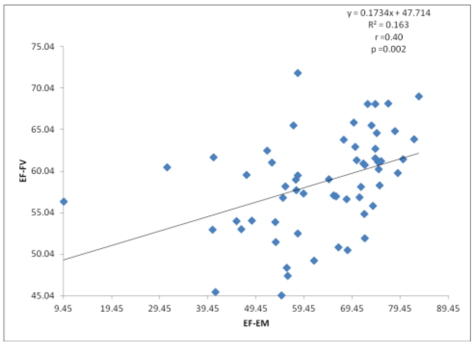

Figure 3. Scatter-plot showing correlation between EF- FV and EF-EM

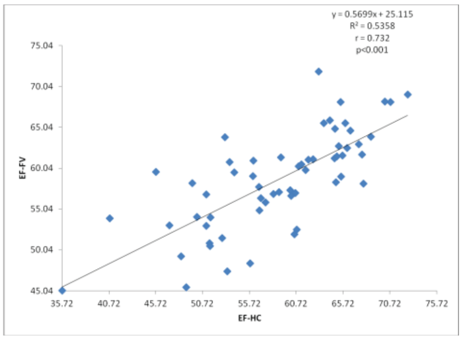

Figure 4. Scatter-plot showing correlation between EF-FV and EF-HC

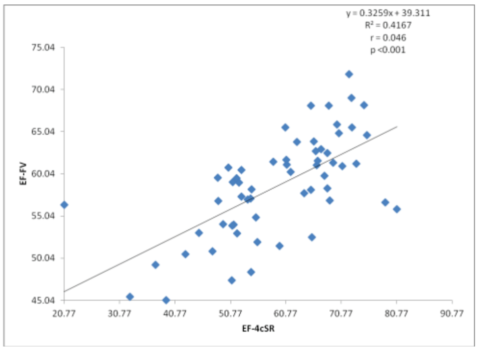

Figure 5. Scatter-plot showing weak correlation between EF-FV and EF-4cSR

The geometrical model based on Simpson's rule was the only one to provide perfectly accurate absolute values for the LV volumes and the EF. Despite the fact that these correlations were statistically significant, only the SR model showed a linear regression with a Pearson correlation coefficient >0.75. The other three models showed a poorer correlation, with correlation coefficients <0.75 and $R^2<$ 0.53. Since the geometrical model based on Simpson's rule presented the best correlations for the EF calculated, we performed the linear regression analysis of the EDV, ESV and SV of the LV by comparison with the gold standard. The recorded R^2 values ranged between 0.76 and 0.82, with $p<0.001$ for all assessed correlations. For EDV and ESV, the Pearson correlation coefficient obtained was of 0.909 and 0.908 respectively.

The number of patients with repaired TOF, many of them with considerable cardiac and non-cardiac disease burden, is growing rapidly (O'Rourke RA, 2000). Most of the studies concerning LV measurements by cMRI were based on healthy volunteers or patients with acquired heart disease (Hudsmith et al., 2005). Few studies have addressed reproducibility of volumetric measurements by cMRI in patients with repaired TOF (Heehan et al., 2010) and, to our knowledge, no studies were conducted in operated TOF patients concerning the LV assessment by geometrical models.

There are some particularities in pediatric patients characterized by higher heart rates, more significant variations in the breathing cycle and lower LV dimensions. Echocardiogram is currently the most common examination method. Nevertheless, the results for left ventricular volumetry are less accurate, especially in the case of surgically modified ventricles (Kai Thorsten Laser et al., 2010). Additional drawbacks include a bad assessment-reassessment correlation and weaker acoustic windows with weight gain. Cardiovascular magnetic resonance imaging (cMRI) is considered a first-line technique in the assessment of LV volumes, EF and myocardial mass, given its high accuracy and reproducibility (Pennell et al., 2004). It does not depend on irregular geometric shapes. Cardiac computed tomography (CT) provides very reproducible measurements of the LV volumes, with good spatial resolution and contrast, but it is not advised in pediatric patients, given the exposure to radiation and intravenous injection of iodine based contrast material. LV kinetics and its impact on long-term clinical evolution are more and more acknowledged in patients with TOF, after surgical repair (Geva et al., 2004). The differences in synchronicity characterizing the segmental contractions of the LV suggest the presence of ventricular mechanical dis-synchrony after TOF repair (Raedle-Hurst et al., 2009). The geometrical distortion of the LV subsequent to TOF repair develops due to septal changes and to the RV volume overload, which makes the assessment of the LV ever more complex.

In this study, we aimed to assess the viability of a series of geometrical models in quantifying the LV volumes and EF by comparison with the gold standard (cMRI). The comparison between these models and cMRI showed that Simpson's rule was the only model for which no significant statistical differences from the gold standard were recorded, for all calculated parameters. The values obtained using Simpson's rule for the LV volumes, SV and EF correlated well with the data obtained using the gold standard. Likewise, the EF calculated by the single-plane ellipsoid model and the hemisphere cylinder model showed good correlation coefficients with the full data set obtained by the standard method. Although these results are new for MRI applications, previous studies have already pointed out their importance. Still, different imaging methods were used (Bunck et al., 2009). All studies conducted on healthy animal models revealed statistically significant results for the Simpson model. The discrepancy in the absolute values obtained for all models - except for the Simpson's rule - by comparison with the gold standard, underlines the need to carefully interpret the results when the cardiac function is compared across studies, using different methodologies and applying to diseased patients.

The geometrical model based on Simpson's rule is the only model that divides the heart into three different compartments, based on three imaging planes. This may explain why it is more accurate in assessing LV volumes. Consequently, it may be a more sensitive method of quantification in the case of asymmetric pathologies (such as Tetralogy of Fallot, for instance). The other models are based on one (the single-plane ellipsoid model) or two (the hemisphere cylinder model) imaging planes. The more simplified models, which use a single imaging plane, have indeed shown the weakest correlations, whereas good correlations were obtained in the case of two-plane models. Despite the fact that the EF calculated by these two-plane models correlated well with the EF determined by cMRI, LV volumes were significantly over- or underestimated. Therefore, Simpson's rule alone may be used in the study of patients operated on for TOF. Even though cMRI is considered to be the gold standard in the assessment of the LV volumes and function, the measurement of EDV, ESV, SV and EF is not error-free and depends on the software used (Heijman et al., 2008). Despite advances in all cardiac imaging modalities, the accuracy and reproductibility of cMRI remains unrivalled. cMRI is being incorporated into clinical surveillance protocols once patients with repaired TOF reach adolescence (Kilner et al., 2010). The combination between low echocardiographic windows, examination without sedation, and the comprehensive nature of the cMRI data has contributed to its broad acceptance in this patient group. In addition to identifying anatomic and functional abnormalities, cMRI ability to quantify chamber size and function and measure blood flow is especially helpful in clinical decision-making.

CONCLUSIONS

Nevertheless, the study aimed to compare volume and EF values obtained by each geometrical model and their reproductibility, (goal that has been possible). The functional analysis based on Simpson's rule may represent a precious alternative – confirming the results obtained through cMRI, especially if a large number of patients is examined - in which the effectiveness-time relation is crucial.

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