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QUANTITATIVE EVALUATION OF THE MITRAL VALVE BY MULTI-SLICE COMPUTED TOMOGRAPHY FOR PLANNING MINIMAL INVASIVE OR PERCUTANEOUS INTERVENTIONS

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24 healthy patients vs22 patients with functional mitral regurgitation (grade II/III) who had undergone ECG-gated computed tomography angiography were retrospectively evaluated. Mean age was 47±11 vs 63±7 years ($p<0.05$), male gender 75 % vs 68 % (ns), BMI 26±2.8 kg/m² versus 26±3.5 kg/m² (ns), left ventricular ejection fraction 72±6 % vs 31±9 % $p<0.05$). The mean mitral saddle-shaped annular area averaged 12±2 cm² in the control group, 14.6±0.52 cm² in patients with functional mitral regurgitation, the D-shaped annular area 10.3±1.6 cm² vs. 12.7±0.5 cm², respectively, being significantly different between two groups and both approaches. This study showed that there are significant differences in the mitral annular morphology between the two groups, as well as several changes between sizing approaches of the mitral annulus throughout the cardiac cycle. Our study showed that with good optimization of procedure protocol and postprocessing process, computed tomography is a feasible method for precise preprocedural evaluation of mitral valve dimensions.

Key words: mitral valve, mitral annulus, functional mitral regurgitation, computed tomography, transcatheter mitral valve replacement.

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КІЛЬКІСНА ОЦІНКА МІТРАЛЬНОГО КЛАПАНУ ЗА ДОПОМОГОЮ БАГАТОЗРІЗОВОЇ КОМП'ЮТЕРНОЇ ТОМОГРАФІЇ ДЛЯ ПЛАНУВАННЯ МІНІМАЛЬНО ІНВАЗИВНИХ АБО ЧЕРЕЗШКІРНИХ ВТРУЧАНЬ

Було проведено ретроспективне обстеження 24 здорових пацієнтів порівняно з 22 пацієнтами з функціональною мітральною регургітацією II/III ступеня, яким було проведено комп'ютерну томографію серця. Середній вік становив 47±11 проти 63±7 років ($p<0,05$), чоловіча стать – 75 % проти 68 % (ns), ІМТ – 26±2,8 кг/м^2 проти 26±3.5 кг/м^2 (ns), фракція викиду лівого шлуночка 72±6 % проти 31±9 % ($p<0,05$). Середня площа сідлоподібного мітрального кільця склала в середньому 12±2см^2 у контрольній групі, 14,6±0,52 см^2 у пацієнтів з функціональною мітральною регургітацією, площа D-подібного кільця 10,3±1,6 см^2 проти 12,7±0,5 см^2 відповідно, що значно відрізнялося у двох групах та за обох підходів. Це дослідження показало, що існують значні відмінності у морфології мітрального кільця між двома групами, а також відмінності у розмірах мітрального кільця сідлоподібної та D-подібної форми протягом усього серцевого циклу. Наше дослідження показало, що при достатній оптимізації протоколу процедури та процесу постобробки комп'ютерна томографія є ефективним методом точної передпроцедурної оцінки розмірів мітрального клапана.

Ключові слова: мітральний клапан, мітральне кільце, функціональна мітральна регургітація, комп'ютерна томографія, транскатетерне протезування мітрального клапана.

Mitral valve (MV) disease is one of the most prevalent valvular heart diseases causing significant mortality and morbidity. The mitral valve consists of the three-dimensional, non-circular, saddle-shaped, highly dynamic mitral annulus, anterior and posterior mitral valve leaflets, highly individualized subvalvular apparatus (fibrous tendinous chords and the papillary muscles), left ventricle (LV) and left atrium (LA) [3]. Reduction or elimination of the normal systolic coaptation between mitral leaflets due to any abnormality in any of these components is the cause of mitral regurgitation (MR) in all cases [5]. Mitral regurgitation affects almost every 10 of 100 individuals over 75 years of age [6].

MR can be generally classified by underlying pathology as ischemic and non-ischemic, and by mechanism, MR is generally divided into two types: primary (organic) MR and secondary functional MR (FMR). The number of patients with ischemic heart disease or cardiomyopathies which lead to FMR is increasing with advancing age, thus FMR is more frequent than organic MV disorders and chronic functional/ischemic mitral regurgitation is associated with poor long-term survival [2]. Patients with unacceptably high surgical risk (e.g. those with significant comorbidities), open the door for several innovative transcatheter concepts and minimally invasive procedures can be a viable option for them [7]. In the last few years, transcatheter mitral valve implantation (TMVI) has evolved as a new therapy concept [8]. Detailed preprocedural analysis is imperative for patient selection and preoperative procedural planning.

For an appropriate patient selection, precise parameters of MV annulus, subvalvular apparatus and LV volumetric data must be obtained [3, 8].

The purpose of the study was to perform a comprehensive assessment of the geometric and anatomical changes of the mitral valve and subvalvular apparatus, spatial relationships and mobility of the mitral valve in multiple cardiac phases by Multi-Slice Computed Tomography in healthy people and patients with functional mitral regurgitation, finding basic differences between groups and sizing strategies in regards of optimization of the planning of transcatheter mitral valve procedures.

Material and methods. This retrospective data analysis was approved by the local ethics committee in Berlin (EA4/095/18). A total of 46 patients, referred to CTA in the German heart centre in Berlin, were retrospectively studied. The study population was divided into two groups; the first control group consisted of healthy subjects and the second FMR group of patients with FMR. CTA excluded the coronary artery disease in all healthy subjects, also they have had no previous history of any cardiac disease, cardiac surgery or intervention. All collected data was retrospectively analyzed.

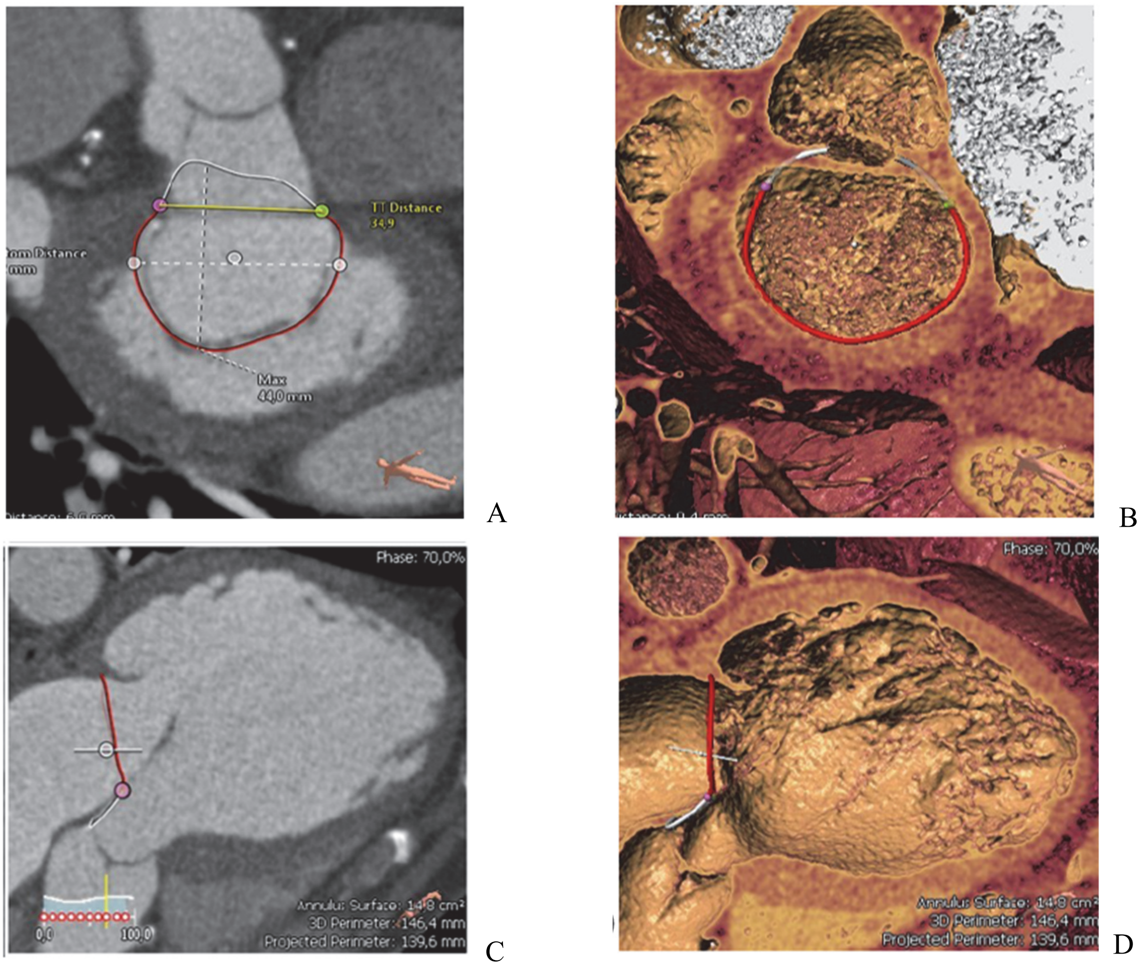


Fig. 1. Saddle-shaped MV annular 3D segmentation and parameters; (A, C) MPR reconstructions and (B, D) volume-rendered 3D images; red line represents posterior 3D perimeter; white line represents anterior 3D perimeter; pink and green dots are trigons'; yellow line between them represents TT distance. Short-axis view of MA region and 2-chamber view reformatted, and volume rendered images.

LV volumetric analysis was made using dedicated CT evaluation software (syngo.via Circulation, Siemens AG) and applying a 3D threshold segmentation algorithm. LV end-diastolic volume (LVEDV) and end-systolic volume (LVESV) were obtained; left ventricular ejection fraction (LVEF) was calculated by the difference between LVESV and LVEDV divided by LVEDV. The left ventricle measurements were performed in a long-axis MPR 2-chamber view. LV long-axis length was defined as the distance between the mitral annulus geometrical center and the LV apex and was measured in systole and diastole. All parameters obtained were indexed to body surface area (BSA).

Post-processing analysis of the MV complex was made with a 3mensio structural heart software package (8.0 module; Pie Medical Imaging, The Netherlands) offering a dedicated mitral analysis workflow. After initial segmentation of the saddle-shaped annulus, the annulus annotation was checked on the short-axis views. The lateral and medial fibrous trigones were manually identified as lateral and medial points of the attachment of the anterior leaflet. The saddle-shaped annulus includes the aortomitral continuity, whereas the D-shaped annulus is defined by being limited anteriorly by the trigone-to-trigone distance, excluding the aortomitral continuity.

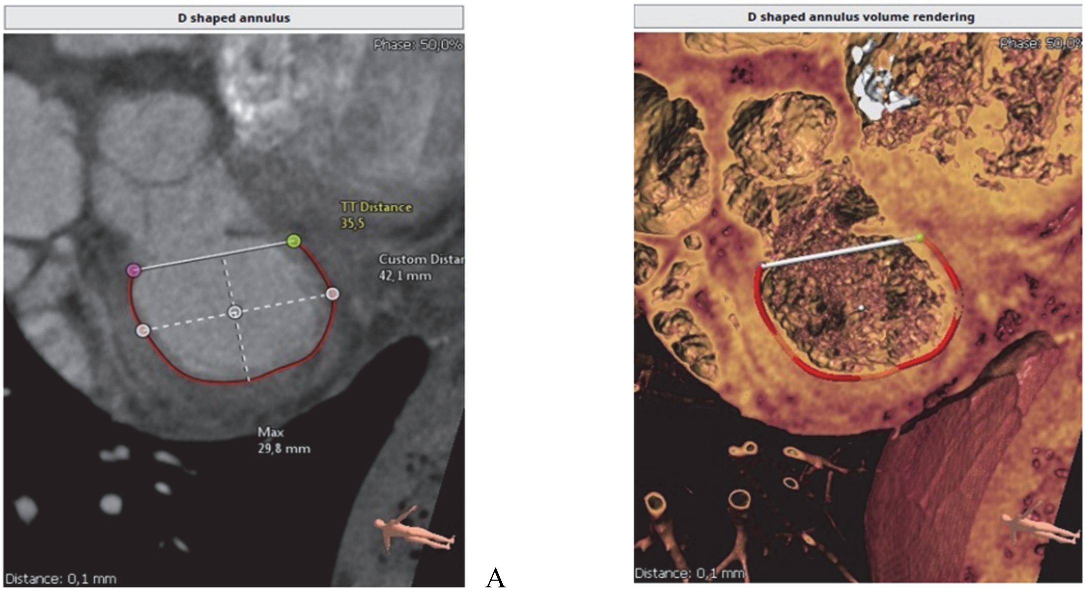
The annulus surface of a saddle-shaped annulus (As) is the area calculated when an annulus is projected to a plane perpendicular through the mathematical center of the annulus. 3D Perimeter of saddle shaped annulus (3D-Ps) is the entire circumference of the annulus as exist in a 3D space. 2D Perimeter of saddle shaped annulus (2D-Ps) is the length of the annulus as it exists when projected to a plane perpendicular to the mathematical center. A virtual line connecting both trigones, referred to as trigone-to trigone (TT) distance. The septal-lateral (SL) distance for Saddle-shaped MV was defined as the projected distance from aortic peak to the posterior peak.

Anterior and posterior 3D and 2D perimeters of saddle-shaped annulus represent the length of anterior and posterior aspects of the mitral annulus as exist in a 3D and 2D spaces respectively (Figure 1).

The annular height of saddle-shaped annulus (Hs) was assessed as the perpendicular distance between highest peak and lowest nadir of the 3D contour to the least squares plane.

There is an automatic technique to unsaddle the anatomical mitral annulus. The anterior margin of the annulus for a D-shaped MV annulus was defined by TT distance. An example of a D-shaped MA is shown in Figure 2.

Despite the use of radiation dose reduction CT protocol, obtaining MV parameters and segmentation of mitral annulus were successful in all subjects.



A B

Fig. 2. A representative example of D-shaped mitral annulus assessment. Short-axis view of MA region -reformatted (A), and volume rendered image (B).

All data were analyzed using the statistical software IBM SPSS Statistics, Version 22 (Armonk, NY, IBM Corp.). Continuous variables were expressed as means±SD (standard deviations) and categorical variables as frequencies and percentages. The Kolmogorov-Smirnoff test was employed to test the normal distribution of continuous variables. The Shapiro-Wilk Test was used to test normal distribution. T-test was used to compare means for normally distributed variables. The Wilcoxon test was used to assess variables that were not normally distributed between two groups (i.e., the control group and FMR). A P-value <0.05 was considered statistically significant.

Results of the study and their discussion. All parameters were analyzed for a total of 46 subjects, divided into a control group (healthy subjects n=24) and an FMR group (n=22) as mentioned above in the study population section.

The BMI mean value for the first group is 26±2.8 kg/m². LVEF mean value is 72±6 %. Second group consisted of 22 patients with FMR (15 males, 7 females; 63±7 years; range, 50–75 years, BMI 26±5 kg/m², LVEF 31±9 %). Patients in the control group had significantly smaller left ventricles than patients in the FMR group ($LVEDD_{control}$ vs. $LVEDD_{FMR}$: 55.2±5.6 mm vs. 81±11.2 mm, $p<0.0001$; The form of the ventricles was more oval in the control group (systolic sphericity $intex_{control}$ vs. systolic sphericity $index_{FMR}$ 0.16±0.08 vs. 0.44±0.1, $p<0.0001$, diastolic sphericity $intex_{control}$ vs. diastolic sphericity $index_{FMR}$ 0.3±0.07 vs. 0.5±0.09, $p<0.0001$).

The mean area of the mitral valve annulus for the saddle shaped model was smaller than in the control group (Mitral annulus area $(saddle)_{FMR}$ vs. Mitral annulus $area(saddle)_{control}$: 14.6±0.52 cm² vs. 12.1±2.2 cm², $p<0.001$). The same is true for the D-shaped models (Mitral annulus area $(D\text{-}shape)_{FMR}$ vs. Mitral annulus(D-shape) $area_{control}$: 12.7±0.49 cm² vs. 10.3±1.6 cm²)

The average mean 3D perimeter (the entire circumference of the annulus as it exists in a 3D space) of the saddle-shaped annulus (3D-Ps) was 130.8±10.8 mm vs. 143.1±2.7 mm ($p<0.001$) in the control group and the FMR group, respectively. The 2D perimeter of the saddle-shaped annulus (2D-Ps) was also significantly larger in the FMR group compared to the control group (Mitral annulus area $(D\text{-}shape)_{FMR}$ vs. Mitral annulus (D-shape) $area_{control}$: 136.7±2.4 mm vs. 124.8±10.3 mm, $p<0.001$).

The 3D and 2D perimeters of the D-shaped mitral annulus measurements were without a significant difference between both groups and with minor differences between the 3D and 2D values in the FMR group (121.5±8.1 mm vs. 132.5±2.7 mm for 3D-Pd, and 119.9±9.1 mm vs. 131.2±2.5 mm for 2D-Pd, ($p<0,05$). The difference between the trigone-to-trigone (TT) distance was 33.7±1.9 mm in the control group and 34.6±1.4 mm in the FMR group ($p<0,05$).

The septal-lateral (SL) distance for the saddle-shaped MV (measured from the aortic peak to the posterior peak) was found to be 36.64±5.7 mm for the control group and 43±1.3 mm for the FMR group ($p<0.001$). The septal-lateral (SL) distance for the D-shaped MV was measured at 29.3±5.7 mm for the control group and 34.7±1.4 ($p<0.001$) mm for Group 2. Mean values of MA dimensions for saddle-shaped and D-shaped approaches in systole and diastole are shown in Fig. 3.

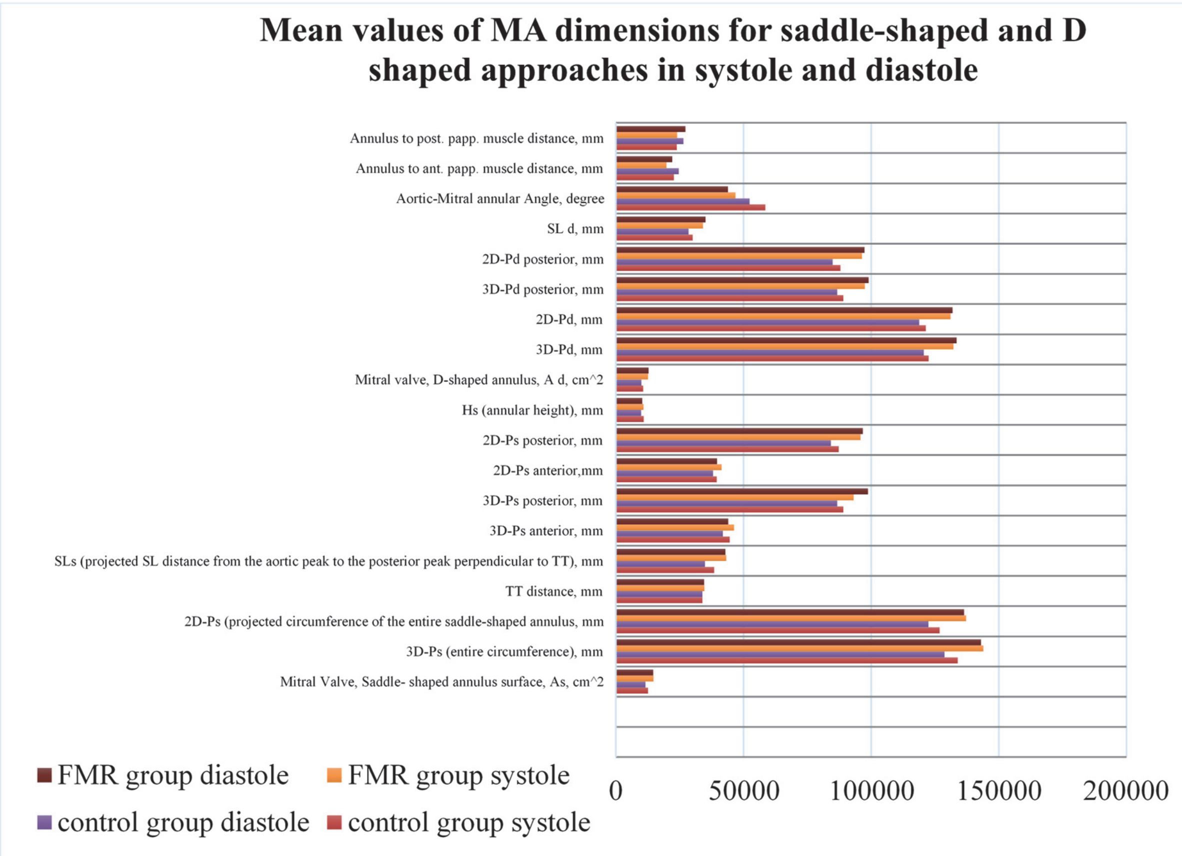


Fig.3. Mean values of MA dimensions for saddle-shaped and D shaped approaches in systole and diastole.

Mitral valve annular mobility was defined as the difference of maximum and minimum of each parameter measured at every time point during the cardiac cycle. The mean and standard deviation was calculated for every parameter. The mitral valve annulus was significantly more mobile in the control group compared to the FMR group.

Considering a lack of consensus in how to size mitral valve in terms of planning to minimal invasive procedures, we have comprehensively analyzed mitral apparatus, its anatomy, geometry, mobility and spatial relationships between its components and surrounding structures, such as the atrioventricular conduction axis and the aortic valve.

The major findings of this study are that:

1. There are significant differences in the mitral annular morphology between healthy subjects and patients with FMR.

2. When comparing the two approaches of the mitral annulus, the vast majority of parameters were found to be higher for the saddle-shaped approach compared to the D-shaped one.

3. 2D and 3D assessments of the mitral annular morphology throughout the cardiac cycle show differences between MA circumferential values.

4. The more pronounced discrepancy between MA to anterior papillary muscle mean distance compared to MA to posterior PM mean distance was observed between the two groups.

5. The mobility of the mitral annulus is higher in healthy subjects than in patients with FMR.

The results of the analysis presented here demonstrate that with good optimization of procedure protocol and postprocessing process, MSCT is a feasible method for precise evaluation of MV dimensions and mobility.

In this study, we investigated the anatomy, morphology and mobility of the mitral valve annulus based on CT imaging in patients with functional mitral valve regurgitation (FMR) in regards to the optimization of preprocedural analysis. Several studies already described the importance of computed tomography assessment of the anatomy of the mitral valve apparatus. In this regard, Blanke and colleagues first defined the "D-shaped Mitral annulus" [1]. It is characterized by defining the anterior border of the MA as a virtual line connecting both trigons instead of integrating the whole anterior, saddle-shaped annulus into the measurements. They hypothesize that this is the ideal approach for pre-procedural device sizing before transcatheter mitral valve implantation to prevent obstruction of the left ventricular outflow tract. The dimensions of the D-shaped modelled annulus were closely comparable to those of this study and our study. In contrast to our study, the latter only measured the mitral annular dimensions during diastole and not throughout the cardiac cycle. This might explain why they found on average, smaller dimensions of the saddle shaped mitral annulus. Nevertheless, the results of the studies are very similar due to the use of the same software tools.

In agreement with the previous study of the Mak group, we showed approximately similar results for SL and TT distances and slightly different results for the annular area of D-shaped mitral annulus mean dimensions for the FMR group in mid-diastole [4].

Natarajan and colleagues reported that the area of MA was significantly higher in heart failure patients compared with controls, which indicated annular dilatation [6]. The present study reported similar results. Compared to our study, Theriault-Lauzier et al. provided MA data only for diastolic phase and only half of the cohort was also evaluated in systole [9]. There is also not a big gap in MA area, aorto-mitral angle, and annulus to papillary muscles distance values for FMR patients between our study and the results reported by Theriault-Lauzier et al. [9]. Using the same methodology and the same software, there is no marked difference in the results in comparison to Blanke et al. and Theriault-Lauzier studies [1, 9].

Considering all the findings detailed above, we assume good reproducibility of assessing most of the MV parameters in studies conducted with similar techniques.

Our data highlight the importance of taking into account not only the mitral valvular apparatus when considering the relevant anatomy but also the relationship between its components and the surrounding structures, like the atrioventricular conduction axis, the aortic valve, etc. In comparison with echocardiography and CMR, CTA can provide such information with accurate 3D datasets of the cardiac morphology, excellent image quality, a higher spatial resolution and lower signal-to-noise ratio, and a higher contrast between the cardiac chamber wall and blood flow. Furthermore, CTA provides direct visualization and quantification of mitral calcifications. Other advantages of pre-procedural cardiac CTA are the possibility of finding an ideal access point to guide echocardiography by identifying the intended intraprocedural epicardial access point and predicting LVOT obstruction by preprocedural device simulation. Although CTA is associated with many advantages, we cannot ignore the fact that it involves radiation exposure and iodinated contrast injection in MSCT compared to echocardiography and CMR. Despite these disadvantages, when used appropriately, patients would most likely benefit from CT, especially elderly patients who are potential candidates for percutaneous minimally invasive procedures.

First, the current study was limited by its retrospective nature, with all the disadvantages coming along with this study design. Second, only relatively few patients were included in each group. Another limitation is that our study concentrated on establishing the pre-procedural post-processing technique without a correlation to the clinical outcome. However, to the extent of our knowledge, this is the first study that assesses and compares mitral valve dimensions and mobility, the subvalvular apparatus, LV hemodynamic, LA volume, aortal-mitral and LA-to-LV angles by MSCT in healthy subjects as controls and in patients with FMR, with detailed relation to all phases of the cardiac cycle.

Conclusion

In this study, the significant differences in the mitral annular morphology between healthy patients and patients with FMR were presented, as well as several changes between different sizing approaches of mitral annulus throughout the entire cardiac cycle. Our study showed that with the proper optimization of procedure protocol and postprocessing process, MSCT is a feasible method for the precise evaluation of MV dimensions and could play an important role in preprocedural evaluation.

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