ORIGINAL ARTICLE

Role of Computed Tomographic Evaluation of Mitral Valve in Predicting the Outcomes of Balloon Mitral Valvuloplasty

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Abstract

Background: ***The prognosis for people who go untreated for mitral valve stenosis (MVS) is not good because the illness progresses over time. Congestive heart failure is still commonly caused by MVS, even though its occurrence has declined significantly over the last several decades. This is especially true in underdeveloped nations.***

Aim and objectives: ***To explore the role of computed tomography in predicting the success and safety of balloon mitral valvuloplasty in patients with significant rheumatic mitral stenosis.***

Subjects and methods: ***This prospective observational study was carried out on 50 patients which underwent transthoracic echocardiography, transosophageal echocardiography and contrast-enhanced cardiac computed tomographic scan in the echocardiography and cardiac CT labs of Al-Azhar University Hospitals, Cairo, from October 2022 till October 2024.***

Results: ***There was a strong association between the following CT variables and the success of PMC :MVA (cm2) was a strong predictor of success of PMC with a P value 0,calcification of mitral leaflets according to wilkins score : score 2 calcification (confined to margins) was significat predictor of successful PMC with a P value 0 and Subvalvular calcification was predictor of success of PMC with high significance (P value 0.002) .***

Conclusion: ***MDCT can predict the success and safety of PMC by various predictors.***

Keywords: Balloon mitral valvuloplasty; Computed tomography; Outcomes

1. Introduction

The prognosis for people who go untreated for mitral valve stenosis (MVS) is not good because the illness progresses over time. Despite a significant decline in MVS incidence over the last several decades, it is still a leading cause of congestive heart failure globally, especially in underdeveloped regions. Symptom presence and reduction of mitral valve area (MVA) are the main criteria for clinical assessment and therapy of individuals with mitral valve dysfunction (MVD).[1]

Clinical management relies heavily on mitral valve imaging. Presently, there are a number of methods that can be used to measure the MVA; however, each of these approaches has its own set of constraints. Quantification of the MVA using helical MDCT has also been proposed in a brief article that was published earlier.[1]

Additional information regarding the presence and severity of MVS may be obtained from a routine contrast-enhanced ECG-gated MDCT scan. Measurements of planimetric MVA using MDCT show a strong agreement with MVA computations using TTE and cardiac catheterization. Nevertheless, it is important to acknowledge that when employing planimetric MVA measurements from MDCT and indirect MVA estimates from TTE and cardiac catheterization for clinical care, there is a systematic overestimation.[2]

The purpose of this research was to assess the utility of computed tomography in determining whether or not balloon mitral valvuloplasty would be safe and effective for individuals suffering from severe rheumatic mitral valve stenosis.

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2. Patients and methods

This prospective observational study was carried out on 50-patients which underwent transthoracic echocardiography, transosophageal echocardiography and contrast-enhanced cardiac computed tomographic scan for anatomical assessment of the mitral valve before balloon mitral valvuloplasty in the echocardiography and cardiac CT labs of Al-Azhar University Hospitals, Cairo, from October 2022 till October 2024.

Ethical consideration:

The scientific and ethical committee at Al-Azhar University's Faculty of Medicine gave their stamp of approval. Each patient's informed consent was carefully sought.

Inclusion criteria:

Adult patients, patients with significant rheumatic mitral stenosis, and patients who were anatomically suitable for balloon mitral valvuloplasty by transthoracic echocardiography.

Exclusion criteria:

Consent refusal, pregnancy, extreme obesity, and anatomically unsuitable patients with mitral stenosis to balloon mitral valvuloplasty, and chronic kidney disease.

Methods:

All patients were subjected to: personal information: age(years) and gender; risk factors: general risk factors and history of RHD; prior surgical/balloon commissurotomy; symptoms: shortness of breath and its severity; medications, especially oral anticoagulation; and full routine clinical examinations.

Measurements:

Two-dimensional echocardiographic-Doppler assessment:

Planimetry was carefully performed in parasternal short-axis view (PSXV) (Mitral valve level) at the leaflet tips, adjusting the probe for optimal mitral valve orifice using the time gain compensation during the early diastolic phase at the onset of the p wave ECG gated loop, as the diastolic opening is maximal, setting to visualize the whole mitral orifice, including commissures when opened.[3]

Figure 1. Parasternal short axis at the tips of the mitral valve in early diastole in a patient with mitral stenosis.

Trans-mitral mean pressure gradient:

Examining the mitral valve from above allowed us to measure its mean pressure gradient. The highest velocity across the mitral valve was shown using continuous wave Doppler and a color-guided parallel alignment of the Doppler beam in an apical four-chamber image. Then, the Doppler envelope of the mitral diastolic inflow was traced.[4]

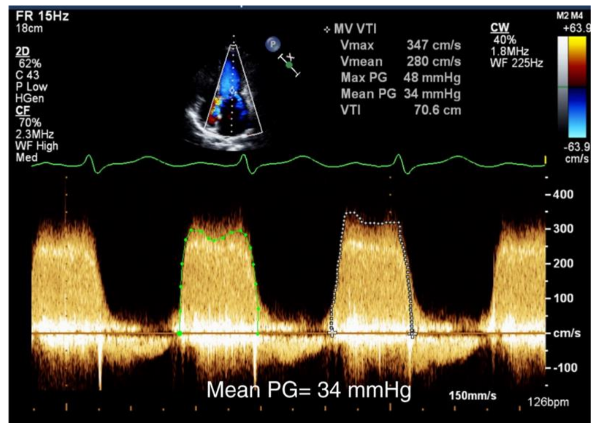

Figure 2. (Mean PG) across the mitral valve.

Pressure at halftime:

Just like the mean pressure gradient, PHT can be determined by following the E-wave's deceleration slope on the Doppler spectral display. To get an accurate estimate of MVA using the PHT approach, you need to wait at least three consecutive beats (or five in the event of atrial fibrillation) after percutaneous balloon mitral valvuloplasty.[5]

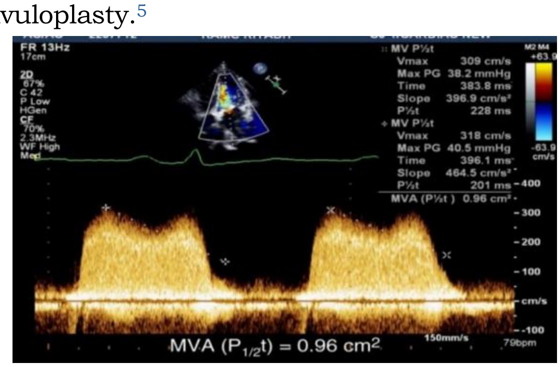

Figure 3. Calculation of(PHT). Quoted from.[5]

Wilkin's score calculation:

This morphologic score includes valvular calcification, subvalvular disease, leaflet thickness, and mobility of the leaflets. Based on these factors, an echocardiographic score was calculated, with values ranging from 0 (normal) to 4 (very abnormal), as shown in the table below. This resulted in a total score between 0 and 16.[6]

Complications of balloon mitral valvuloplasty:

More than grade-II mitral regurgitation. Cardiac tamponade due to perforation during septostomy, others, including thromboembolism, residual left-right shunt, or complete heart block.

Cardiac computed tomographic scan:

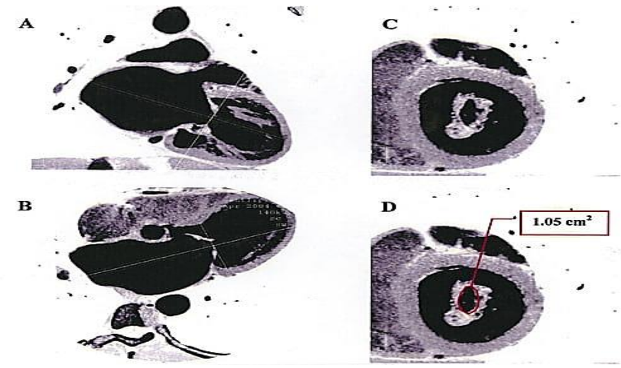

Figure 4. MVA tracing by MSCT

Figure 5. Rheumatic mitral valve leaflets. (A) Measurement of leaflet length. (B) Measurement of leaflet thickening degree.

Due to echocardiography's dominance in the field, cardiac computed tomography's (MDCT) use in MV evaluations has been restricted. Nevertheless, the MV's architecture and shape may now be examined in great detail thanks to recent advancements in cardiac CT.[7]

The Toshiba 160-slice scanner, which uses MDCT technology, was used. Detailed procedure for cardiac CT scanning of mitral valve disease.8 Among these methods is the collection of images taken at various points in the cardiac cycle as well as retrospective ECG-gated scanning of the heart. A 120kV tube voltage and clever mA-automated current optimization are scanning parameters. Procedure for contrast injection: triphasic double-cylinder double-flow. A 75-milliliter volume of a non-ionic low-osmolar contrast agent was administered at a rate of 4-5 milliliters per second.

The examination utilized the contrast tracer approach to identify the ROI at the level of the aortic root. Once the ROI reached 100 HU (Hounsfield units), the scan began automatically. Following this, the computer autonomously established the optimal systolic and diastolic times for picture post-processing in order to extract data about the coronary arteries. Reducing the reconstruction range around the valves to eliminate duplicate data allowed us to monitor the movements of the aortic and mitral valves using multiphase data reconstruction of the full cardiac cycle at 10% intervals.

In our study, we used cardiac CT with a protocol resembling a coronary protocol; a 64-slice scanner and detector element width < 0.625 mm. A check scan was done in mid diastole at HR < 70 bpm and mid diastole to end systole at HR 70-80 bpm. Contrast injection at a rate of 5-6 ml/second. Analysis was done at 70 % of the diastolic period.

Statistical analysis:

An analysis was conducted using SPSS v26, which was developed by IBM Inc. and is located in Chicago, IL, USA. The quantitative variables were shown using standard deviation (SD) and mean (M). The frequency and percentage (%) of qualitative characteristics were displayed. Logistic regression was employed to evaluate the association between a dependent variable and an independent variable. It was deemed statistically significant if the two-tailed P-value was less than 0.05.

3. Results

According to success and failure of PMC, the study population were divided in to two groups (success and failed groups). The success of PMC was defined as MVA post PMC is > 1.5 cm2 and increased by more than 50% of the baseline MVA pre PMC.

Table 1 . Comparison of demographic variables in predicting the outcome of balloon mitral valvuloplasty :

VARIABLES		FAILED = 5 CASES	SUCCESS = 45 CASE	P VALUE
		Mean ± SD / Frequency (Percent%)	Mean ± SD/ Frequency (Percent%)	
GENDER	Female	3 (11.1%)	27 (89.9%)	1
	Male	2 (10.0%)	18 (90.0%)	
AGE		40.83±5.52	40.5±6.09	0.908
WEIGHT		75.83±5.94	79.25±11.41	0.515
HIGHT		163±6.7	158.25±2.1	0.0007

(P value <0.05 is significant and < 0.001 is highly significant).

The distribution of females and males shows a higher failure rate among females (11.1%) compared to male patients (10%). The P-value of 1 indicates no statistical significance.

In terms of age, the mean age of patients with failed outcomes (40.83±5.52 years) is slightly higher compared to those with successful outcomes (40.5±6.09 years). However, the P-value of 0.9 suggests no statistically significant difference between the two groups in terms of age.

Table 2 . Comparison of echocardiographic variables in predicting the outcome of balloon mitral valvuloplasty :

VARIABLES		FAILED=5CASES Mean ± SD / Frequency (Percent%)	SUCCESS=45CASES Mean ± SD/ Frequency (Percent%)	P VALUE
MVA PLANIMETRY		1.15±0.16	1.15±0.17	1
MEAN PG		12.33±2.47	9.75±2.55	0.037
MOBILITY (WILKINS SCORE)	1	0 (00.0%)	25 (100.0%)	0.06
	2	2 (12.5%)	14 (87.5%)	
	3	3 (33.3%)	6 (66.6%)	
THICKNESS (WILKINS SCORE)	1	0 (0.0%)	21 (100.0%)	0.184
	2	1 (6.0%)	14 (94.0%)	
	3	4 (28.5%)	10 (71.5%)	
CALCIFICATION (WILKINS SCORE)	1	2 (6.0%)	31 (94.0%)	0.0195
	2	3 (17.0%)	14 (82.0%)	
SUBVALVULAR THICKNESS (WILKINS SCORE)	1	0 (00.0%)	20 (100.0%)	0.022
	2	2 (11.1%)	16 (88.8%)	
	3	3 (27.2%)	9 (81.8%)	
ANTEROLATERAL COMMISSURAL FUSION	0	3 (21.3%)	11 (78.6%)	0.08
	1	1 (9.0%)	10 (91.0%)	
	2	1 (4.0%)	24 (96.0%)	
ANTEROLATERAL COMMISSURE CALCIFICATION	No	2 (5.0%)	37 (95.0%)	0.03
	Yes	3 (27.3%)	8 (72.7%)	
POSTEROMEDIAL COMMISSURAL FUSION	0	3 (21.4%)	11 (78.6%)	0.014
	1	2 (20.0%)	8 (80.0%)	
	2	0 (00.0%)	26 (100.0%)	
POSTEROMEDIAL COMMISURE CALCIFICATION	No	1 (2.0%)	35 (98.0%)	0.006
	Yes	4 (28.5%)	10 (71.5%)	
MR GRADE (I-IV)	1	3 (10.0%)	25 (90.0%)	0.849
	2	2 (11.0%)	20 (89.0%)	
TR PG		40.75±2.65	37.33±4.97	0.138

(success means MVA > 1.5 cm2 and increased by more than 50% of the baseline MVA, P value <0.05 is significant and < 0.001 is highly significant, MVA: mitral valve area, MR: mitral regurgitation, TR : tricuspid regurgitation, PG: pressure gradient, commisure fusion scores: 0= completely unfused, 1= partially unfused, 2=fused).

For thickness, patients with thickness score 3 had a higher failure rate (28.5%) compared to those with scores 1 and 2 (0% and 6% respectively). The P-value of 0.1 suggests no significant difference based on thickness.

Regarding calcification, failure rate was higher (17%) in patients with score 2 calcification while patients with score 1 calcification had less failure rate 6 % .The P-value 0.01 which is statistically significant.

Subvalvular thickness showed a significant difference, with a higher failure rate in patients with score 3 (27.2%) and lower rates for scores 1 and 2. The P-value is 0.022 indicating a significant difference.

The analysis indicates that mean PG, subvalvular thickness, leaflet calcification, AL commisural calcification and PM commisural fusion and calcification may be significant predictors of the success or failure of balloon mitral valvuloplasty.

Table 3 . Comparison of computed tomographic variables of mitral stenosis in Predicting the outcome of balloon mitral valvuloplasty :

VARIABLES		FAILED=5 CASES Mean ± SD / Frequency (Percent%)	SUCCESS=45CASES Mean ± SD/ Frequency (Percent%)	P VALUE
CT MVA (CM^2)		1.46±0.16	1.56±0.05	0.0025
CT SHORTEST LENGHT OF CHORDAE (MM)		7.27±2.57	9.83±5.05	0.2724
CT THICKEST DIAMETER OF CHORDAE (MM)		4.85±1.21	4.41±1.14	0.419
CT MITRAL LEAFLETS CALCIFICATION	No	0 (00.0%)	32 (100.0%)	0.022
	Yes	5 (27.7%)	13 (72.3%)	
CT SUBVALVULAR CALCIFICATION	No	1 (2.0%)	37 (98.0%)	0.002
	Yes	4 (33.3%)	8 (66.6%)	
CT ANTEROLATERAL COMMISURE FUSION	Completely unfused (0)	4 (26.6%)	11 (73.4%)	0.007
	Partially unfused (1)	1 (8.0%)	11 (92.0%)	
	Completely fused (2)	0 (00.0%)	23 (100.0%)	
CT POSTEROMEDIAL COMMISURE FUSION	Completely unfused (0)	3 (25.0%)	9 (75.0%)	0.038
	Partially unfused (1)	1 (10.0%)	9 (90.0%)	
	Completely fused (2)	1 (3.0%)	27 (97.0%)	
CT ANTEROLATERAL COMMISURE CALCIFICATION	No	1 (2.7%)	36 (97.3%)	0.003
	Yes	4 (31.0%)	9 (69.0%)	
CT POSTEROMEDIAL COMMISURE CALCIFICATION	No	0 (00.0%)	35 (100.0%)	0.006
	Yes	5 (33.3%)	10 (66.6%)	
CT SUBVALVULAR THICKNESS (WILKINS SCORE)	1	0 (00.0%)	20 (100.0%)	0.003
	2	1 (5.0%)	16 (95.0%)	
	3	4 (30.0%)	9 (70.0%)	
CT LEAFLET THICKNESS (WILKINS SCORE)	1	0 (00.0%)	21 (100.0%)	0.03
	2	2 (13.3%)	13 (86.6%)	
	3	3 (21.4%)	11 (78.5%)	
CT CALCIFICATION (WILKINS SCORE)	1	1 (3.3%)	28 (96.6%)	0.000
	2	3 (15.0%)	17 (85.0%)	
	3	1 (100.0%)	0 (00.0%)	

(P value <0.05 is significant and < 0.001 is highly significant, CT: computed tomography, MVA: mitral valve area, commisure fusion scores: 0= completely unfused, 1= partially unfused, 2=fused).

CT anterolateral and posteromedial commisural calcification show a 31.0% and 33.3% failure rates respectively in patients with calcification whereas those without calcification have higher success rates. The P-values are 0.003 and 0.006 suggesting significant differences.

CT subvalvular thickness shows varied results, with higher failure rates in patients with higher score (score 3) and higher success rates in those with lower scores (1 and 2). The P-value is 0.003 indicating a significant difference.

CT leaflet thickness shows higher failure rates in patients with scores 3(21.4%) and score 2 (13.3%) compared to score 1 which has a higher success rate . The P-value is 0.03 suggesting a significant difference.

CT calcification shows that higher calcification scores (score 2 and 3) are associated with higher failure rates. The P-value of 0 indicates a highly significant difference.

Overall, the analysis indicates that CT MVA, CT mitral leaflets calcification, CT subvalvular calcification, CT anterolateral and posteromedial commisural fusion and calcification, CT subvalvular thickness, CT leaflet thickness and CT calcification could be significant predictors of the success or failure of balloon mitral valvuloplasty.

Table 4 . Comparison of computed tomographic variables in predicting the complication (MR) of balloon mitral valvuloplasty :

VARIABLES		COMPLICATED =6 CASES	NO COMPLICATION=44CASES	P VALUE
		Mean ± SD / Frequency (Percent%)	Mean ± SD/ Frequency (Percent%)	
CT MVA (CM²)		1.46±0.16	1.56±0.05	0.002
CT SHORTEST LENGHT OF CHORDAE (MM)		7.27±2.57	9.83±5.05	0.23
CT THICKEST DIAMETER OF CHORDAE (MM)		4.85±1.21	4.41±1.14	0.38
CT MITRAL LEAFLETS CALCIFICATION	No	1 (3.0%)	31 (97.0%)	0.01
	Yes	5 (27.7%)	13 (72.3%)	
CT SUBVALVULAR CALCIFICATION	No	1 (2.0%)	37 (98.0%)	0.000
	Yes	5 (41.6%)	7 (58.4%)	
CT ANTEROLATERAL COMMISURE FUSION	Completely unfused (0)	5 (33.3%)	10 (66.6%)	0.001
	Partially unfused (1)	1 (8.0%)	11 (92.0%)	
	Completely fused (2)	0 (00.0%)	23 (100.0%)	
CT POSTEROMEDIAL COMMISURE FUSION	Completely unfused (0)	4 (33.3%)	8 (66.6%)	0.008
	Partially unfused (1)	1 (10.0%)	9 (90.0%)	
	Completely fused (2)	1 (3.0%)	27 (97.0%)	
CT ANTEROLATERAL COMMISURE CALCIFICATION	No	1 (2.7%)	36 (97.3%)	0.001
	Yes	5 (38.4%)	8 (61.6%)	
CT POSTEROMEDIAL COMMISURE CALCIFICATION	No	1 (2.8%)	34 (97.2%)	0.002
	Yes	5 (33.3%)	10 (66.6%)	
CT SUBVALVULAR THICKNESS (WILKINS SCORE)	1	0 (00.0%)	20 (100.0%)	0.007
	2	2 (11.7%)	15 (88.2%)	
	3	4 (30.0%)	9 (70.0%)	
CT LEAFLET THICKNESS (WILKINS SCORE)	1	0 (00.0%)	21 (100.0%)	<0.01
	2	2 (13.3%)	13 (86.6%)	
	3	4 (28.5%)	10 (71.5%)	
CT CALCIFICATION (WILKINS SCORE)	1	1 (3.3%)	28 (96.6%)	0.001
	2	4 (20.0%)	16 (80.0%)	
	3	1 (100.0%)	0 (00.0%)	

(complication include grade III and grade IV MR, P value <0.05 is significant and < 0.001 is highly significant, MVA: mitral valve area, commisure fusion scores: 0= completely unfused, 1= partially unfused, 2=fused).

For anterolateral commisural fusion, patients with scores of 2(completely fused) had a lower complication rate (0.0%) compared to those with scores of 1 (8.0%) and 0 (33.0%). The P-value of 0.001 indicates a significant difference.

Posteromedial commissural fusion shows a significant difference with a 33.3% and 10% complication rate for scores of 0 and 1 respectively compared to a lower rate for score 2 (3.0%). The P-value is 0.008 indicating a significant difference.

Anterolateral and posteromedial commissural calcifications both show higher complication rates for patients with calcification (33.3% for posteromedial calcification and 38.4 % for anterolateral calcification). The P-values are 0.001 and 0.002 suggesting a highly significant differences.

Subvalvular thickness shows varied results, with higher complication rates for score 3 (30.0%) and score 2 (11.7%) and lower complication rate for score 1 (0.0%). The P-value is 0.007 indicating a significant difference.

Leaflet thickness shows higher complication rates for score 3 (28.5%) and score 2 (13.3), whereas no complication with score 1. The P-value is < 0.01 suggesting a significant difference.

Calcification shows higher complication rates for scores 3 and 2 (100% for score 3 and 20 % for score 2) compared to score 1 (3.3% compliation rate). The P-value is 0.001 indicating a significant difference.

Table 5 . Logistic regression analysis for predicting the outcome of PMC using CT parameters

MVA (CM²)	3.191 - 2.223	0.00
CALCIFICATION OF LEAFLETS	1.081 - 1.189	0.00
THICKEST DIAMETER OF CHORDAE	0.911 - 1.168	0.62
SUBVALVULAR CALCIFICATION	1.079 - 1.402	0.002
ANTEROLATERAL COMMISSURAL FUSION	0.576 - 7.334	0.02
POSTEROMEDIAL COMMISSURAL FUSION	0.614 - 3.417	0.03
ANTEROLATERAL COMMISSURAL CALCIFICATION	0.059 - 16.92	1.00
POSTEROMEDIAL COMMISSURAL CALCIFICATION	0.193 - 2.329	0.5

MVA measurement by cardiac CT can predict the success of PMC with significant P value (0.00) . detection of calcification of leaflets is a strong predictor of success of PMC with P value 0.00 . Subvalvular calcification can predict the success of PMC with significant P value 0.002 . commissural fusion can predict the success of PMC with significant P values . commissural calcification can predict the success of PMC with statistically significant P values .

Table 6 . logistic regression analysis for predicting MR as a complication using CT parameters :

SUBVALVULAR CALCIFICATION	0.984 - 1.297	0.08
ANTEROLATERAL COMMISSURAL FUSION	1.081 - 1.189	0.00
POSTEROMEDIAL COMMISSURAL FUSION	0.943 - 1.187	0.03
ANTEROLATERAL COMMISSURAL CALCIFICATION	0.417 - 0.732	0.00
POSTEROMEDIAL COMMISSURAL CALCIFICATION	0.994 - 0.998	0.00

By logistic regression of cardiac CT parameters, commissural fusion can predict the complication of PMC with significant P value 0.00 for AL commissural fusion and P value 0.03 for PM commissural fusion. AL and PM commissural calcifications are strong predictors for significant MR post PMC with statistically significant P values (P value 0.00 for both parameters) .

4. Discussion

In mitral stenosis, a valvular heart ailment, the mitral valve's aperture becomes narrowed. The cause is usually rheumatic valvular heart disease. During diastole, the mitral valve is normally about 5cm2. Mitral stenosis is caused by a decrease in the area of less than 2cm2.[9]

The distribution of females and males shows a higher failure rate among females (11.1%) compared to male patients (10%). The P-value of 1 indicates no statistical significance.

Regarding CT parameters of the studied patients, we compared CT parameters to the TTE parameters in terms of the significance of each parameter in the prediction of success and complication (MR) of PMC.

There was a strong association between the following CT variables and the success of PMC :

MVA (cm2) was a strong predictor of the success of PMC with a P value of 0.

Calcification of mitral leaflets according to Wilkins score: score two calcification (confined to margins) was a significant predictor of successful PMC with a P value of 0.

Subvalvular calcification was a predictor of the success of PMC with high significance (P value 0.002).

The following CT variables were significant predictors of the severity of MR as a complication of PMC :

Anteroposterior commissure fusion was a highly significant predictor with a P value of 0.

Posteromedial commisure fusion was a significant predictor with a P value of 0.03.

Anterolateral commisure calcification was highly statistically significant at a P value of 0, suggesting a strong association between PM commisural fusion and the occurrence of significant MR post PMC.

Posteromedial commisure calcification was highly statistically significant at a P value of 0.

High leaflet calcification score (score two or more) was highly statistically significant at P value of 0 suggesting a strong association between higher CT calcification scores and the occurrence of complications.

In agreement with our study, this study primarily compared different commissurotomy techniques, highlighting the importance of pre-procedural imaging in patient selection. The findings suggest that advanced imaging modalities, such as CT, can aid in assessing valve morphology and predicting procedural outcomes (10).

Parallel to our study, Helvacioglu et al. included thirty-one patients (mean age 50.4 ± 10.2, 90.3% women) with isolated MS who were in a normal sinus rhythm. The mean planimetric MVA by TTE was 1.50+0.53 cm2 (range 0.98 –2 cm2). Number of mitral regurgitations was 3 (9.7%) .[11]

We agreed with Kemaloğlu et al., who compared various imaging modalities, including CT, in evaluating patients with mitral stenosis for PMC. It concluded that CT provides detailed anatomical information, particularly regarding leaflet calcification and subvalvular apparatus, which are crucial for determining PMC suitability.[12]

In comparison to our study, Morris et al. concluded that echocardiography remains the gold standard for the diagnosis and grading the severity of MS. However, CT can confirm the presence of related features such as left atrial enlargement, as well as certain appearances, which point to specific causes of mitral stenosis, such as thickening of the mitral valve leaflets with commissural fusion and calcification, commonly seen in rheumatic mitral stenosis (so-called fish mouth appearance) .[13]

4. Conclusion

Cardiac CT can predict the success and safety of PMC by various parameters, including leaflet and subvalvular calcifications and commissural fusion and calcifications.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

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Conflicts of interest

There are no conflicts of interest.

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