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ORIGINAL ARTICLE

Assessment of Mitral Annular Disjunction by Echocardiography in patients with Mitral Valve Prolapse and its Arrhythmogenic effects as assessed by Holter 24 hours

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Abstract

Background: ***The cause of ventricular arrhythmias and sudden cardiac mortality in patients with MVP is not completely known.***

Aim: ***To investigate the significance of assessing mitral annular disjunction using echocardiography in patients with mitral valve prolapse (MVP) and its impact on arrhythmias as evaluated by Holter monitoring. Additionally, to determine specific clinical and echocardiographic parameters that can predict the development of arrhythmias in MVP patients.***

Methods: ***Seventy consecutive individuals with an MVP diagnosis were enrolled in our cross-sectional investigation. Using 2D echocardiography, patients were categorized into the following groups based on whether they met the MAD criteria: There were 50 mitral annular disjunction (MAD) patients in Group A and 20 non-MAD patients in Group B.***

Results: ***A strong positive correlation between the degree of disjunction and the presence of arrhythmia, and the burden of PVCs. The AUC of 0.765±0.073, statistically significant P value of 0.001, sensitivity of 81%, specificity of 65%, and PLAX view cut-off disjunction distance of 9.8 mm. With an AUC of 0.655±0.079, a statistically insignificant P value of 0.056, and a sensitivity and specificity of 69% and 76%, respectively, a 10.1 mm cut-off disjunction distance in the AP4 presentation. AUC of 0.755±0.078 and statistical significance are achieved with a 10.2 mm cut-off overall disjunction distance, which yields 76% sensitivity and 70% specificity.***

Conclusions: ***When considering the degree of disjunction, there was a statistically significant positive association between the PVC burden and disjunction degree.***

Keywords: Echocardiography; Mitral Valve Prolapse; Mitral Annular Disjunction

1. Introduction

About 2-3% of people in general suffer from MVP, a common heart valvular anomaly. As long as one or both mitral valve leaflets are displaced symbolically beyond the long axis of the mitral annular plane into the left atrium, it is considered to be present, regardless of leaflet thickening. (Highest Ranking).[1,2,3] Regarding possible AMVP traits, there is still uncertainty. Bi-leaflet MVP may be essential to the AMVP phenotype, according to certain research. It is still debatable, nonetheless, whether bi-leaflet MVP would indicate higher mortality and arrhythmia because this claim was based on scant data[4,5,6], in light of epidemiological research' positive findings and high prevalence. There has been talk of a connection between ventricular arrhythmia, and MVP and another morphological anomaly called MAD [7]; however, other research has shown that MAD may exist independently of concurrent MVP or arrhythmias.[8,9]

Particularly when hemodynamically substantial mitral regurgitation is absent, the mechanism underlying ventricular arrhythmias and sudden cardiac death in patients with MVP remains incompletely understood. Though most of them are still theoretical, a number of theories have been proposed to explain the mechanism of severe ventricular arrhythmias in MVP patients.[10]

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These include factors associated with MVP, such as prolapsing leaflets' excessive traction on the papillary muscles (PMs); the elongated chordae's mechanical stimulation of the endocardium, which results in depolarization-induced triggered activity; the diastolic depolarization of muscle fibers in redundant leaflets, which triggers repetitive automaticity; and the endocardial friction lesions that extend into the myocardium.[11]

There has been attention to the myocardial substrate of the electrical instability in patients with MVP, and histopathology has revealed the presence of LV fibrosis at the PMs and LV inferno-basal wall levels.[12]

This study's primary goals were to show the utility of echocardiography in assessing mitral annular disjunction in patients with MVP and its effects on arrhythmias as measured by a 24-hour Holter. It also sought to determine whether there were any particular clinical and echocardiographic parameters that could be used to predict the development of arrhythmias in patients with mitral valve prolapse.

2. Patients and methods

Our work was a cross-sectional study that enrolled 70 consecutive patients who presented to echocardiographic labs at Al-Azhar University and (NHI) hospitals and were diagnosed with MVP. Patients were categorized using 2D echocardiography into the following groups based on whether they met the MAD criteria: Fifty patients with MAD were in Group A, while twenty patients without MAD were in Group B.

Transthoracic Echocardiography:

Vivid S5, Siemens Acuson, and Philips HD5 devices equipped with an M3S matrix array probe operating in the frequency range of 1.7 to 3.2 MHz were utilized for the 2-D transthoracic echocardiographic exams. Machine-integrated ECG recording was linked to every echocardiography examination. The LV dimensions (LVEDD, LVESD), EF, IVD, PW, LA size, and LA volume were measured in accordance with the most recent ASE guideline for the assessment of cardiac chambers.[13] The PLAX and AP4 images were used to assess the mitral annular disjunction distance. In the echocardiographic parasternal long-axis view, the length of the annular disjunction was measured from the left atrial wall-mitral valve posterior leaflet junction to the top of the LV posterior wall during end-systole. If the measurement is less than 2 mm, MAD is suspected. Speckle tracking echocardiography(STE) was used to measure the strain pattern of the left ventricle function. Using the biplane area length approach, the LA volume will be evaluated. Echocardiographic examination was used to exclude other significant structural heart disease-causing arrhythmias, such as valvular, myocardial, and pericardial heart diseases. The mitral valve regurgitation severity was assessed by measured vena contracta and regurgitation volume.

Holter monitoring was done for 24 hours:

A digital Holter device was used to perform round-the-clock cardiac Holter monitoring. Every patient received the normal 24-hour, three-channel Holter monitoring system, during which all medications- such as beta blockers- that may influence the occurrence of arrhythmias were stopped prior to the 48-hour mark. Based on a 24-hour digitally recorded ECG signal with a 100 Hz sampling rate, heart rate variability analysis was performed.

Statistical analysis:

The Shapiro-Wilk test was used to assess the data distribution's normality. We used IBM Corp.'s Armonk, New York SPSS Version 22.0 to determine frequencies and percentages for qualitative variables and the means and standard deviations for quantitative data. For numerical variables, the independent sample t-test was employed, and for categorical data, the Chi-square test was utilized to compare the treatment groups. The correlation between category and numerical variables was evaluated using the Spearman test, while the correlation between the two types of variables was determined using the Pearson test. To assess mitral annular disjunction's predictive value for arrhythmia, a receiver operating characteristic (ROC) analysis was conducted. A statistically significant P value was defined as one that was smaller than 05.

3. Results

The mean age of the study was 32.5±9.9 years (Range, 14-52) and 29 (41.4%) patients were males, while 41 (58.6%) were females. The mean weight was 72.9±14.6 kg (range, 51-100), while the mean height was 165.45±7.2 cm (range, 151-177). The mean BMI was 26.8±5.7 kg/m2, ranging from 18.1 to 43.3 kg/m2. Regarding comorbidities, 3 (4.3%) had diabetes mellitus, 9 (12.9%) had hypertension. Smoking was present in 10 (14.3%) patients. lastly, 50 (71.4%) patients had MAD, while 20 (28.6%) hadn't MAD, Table 1.

Table 1. Baseline Demographic Data (N=70)

VARIABLES	NO.	%
AGE, YEARS	32.5±9.9 (Range,14-52)	
GENDER		
MALE	29	41.4
FEMALE	41	58.6
WEIGHT, KG	72.9±14.6 (Range,51-100)	
HEIGHT, CM	165.5±7.2 (Range,151-177)	
BMI, KG/M^2	26.8±5.7 (Range,18.1-43.3)	
COMORBIDITIES		
DIABETES MELLITUS	3	4.3
HYPERTENSION	9	12.9
SMOKING	10	14.3

MITRAL ANNULAR DISJUNCTION		
YES	50	71.4
NO	20	28.6

Within group A, ages ranging from 14 to 52 years old, the mean age was 33.1±9.7 years. The age distribution of group B was 17-49 years old, with a mean age of 30.9±10.7 years. P=0.424 indicates that there wasn't not a statistically significant distinction in the age distribution between the groups,table 2.

In group A, there were twenty-two (44%) male and twenty-eight (56%) female patients. In contrast, group B consisted of 13 (65%) females and 7 (35%) males, Figure 2. The gender distribution did not differ statistically significantly between the groups (P=0.595).

Group A had a mean BMI of 26.6±5.6 kg/m2, with a range of 18.1 to 43.3 kg/m2. The BMI ranged from 18.1 to 40.4 kg/m2, with group B having a mean of 27.2±7.5 kg/m2. There was not a statistically significant distinction (P=0.704) in the BMI comparison between the study groups, Table 2.

Of the patients in group A, six (12%) smoked, and 44 (88%) did not smoke. Of the patients in group B, 16 (80%) did not smoke, and four (20%) did. Comparatively, there was no statistically significant variation in the prevalence of smoking between the groups (P=0.456), Table 2.

Of the patients in group A, two (4%) had diabetes, and seven (14%), hypertension. Two patients (10%) and one patient (5%) in group B had hypertension and diabetes, respectively. As demonstrated in figure 5. In contrast, there was no statistically significant variance in the prevalence of diabetes or hypertension was observed between the groups (P>0.05),Table 2.

Table 2. Demographic data of the study population

AGE DISTRIBUTION (N=70)			
	Group A (N=50)	Group B (N=20)	P value*
AGE, YEARS			0.424
MEAN±SD	33.1±9.7	30.9±10.7	
RANGE	14-52	17-49	
GENDER DISTRIBUTION (N=70)			
GENDER			0.595
MALE	22(44%)	7(35%)	
FEMALE	28(56%)	13(65%)	
WEIGHT, HEIGHT, AND BMI DISTRIBUTION (N=70)			
WEIGHT, KG	72.5±14.1	73.8±15.9	0.756
HEIGHT, CM	165.4±7.3	165.8±7.1	0.856
BMI, KG/M^2	26.6±5.6	27.2±7.5	0.704
PREVALENCE OF SMOKING (N=70)			
SMOKING			0.456
YES	6(12%)	4(20%)	
NO	44(88%)	16(80%)	
MEDICAL COMORBIDITIES (N=70)			
COMORBIDITIES			
DM	2(4%)	1(5%)	0.852
HTN	4(14%)	2(10%)	0.652

Comparison of 2D echocardiography data between two study groups:

The mean EF of group A was 64.6±5.4%, ranging from 55 to 74%. In group B, the mean EF was 67.5±4.7%, ranging from 59 to 73%. The MAD group (group B) had significantly lower EF in contrast to the non-MAD group (P=0.036). Also, the MAD group had significantly larger LA volume than the non-MAD group (29.9±7.5 mL Vs 24.5±7.3 mL, P=0.008),(Table 3,figures 1-2). However, for LVEDD, LVES, IVSd, IVSs, PWd, and PWs, no statistically significant distinction was seen between the groups (P>0.05),(Table 3, Figure 3).

In relation to the degree of regurgitation, group A's mean vena contracta measured 3.2±2.6, while group B's mean was 1.8±3.4. In group A, it was 29.5±22.4 ml, while in group B, it was 15.2±25.4 ml. In comparison to the non-MAD group, the MAD group had noticeably more severe regurgitation (Independent sample t test, P=0.024),(Table 1,Figure 4).

Table 3. Echocardiography data of study groups(N=70)

	GROUP A (N=50)		GROUP B (N=20)		P VALUE*
	Mean	SD	Mean	SD	
EJECTION FRACTION,%	64.6	5.4	67.5	4.7	0.036
LV DIMENSIONS					
LVEDD, MM	49.3	8.9	46.7	8.7	0.267
LVESD, MM	32.4	8.1	30.4	6.8	0.329
IVSD, MM	19.5	14.3	15.3	14.5	0.270
IVSS, MM	11.7	3.9	10.5	2.3	0.204
PWD, MM	8.8	1.7	8.5	1.5	0.570
PWS, MM	11.8	3.7	11.8	3.3	0.985
LA SIZE					
LA DIMENSION, MM	34.8	7.6	33.1	7.9	0.402
LA VOLUME, ML	29.9	7.5	24.5	7.3	0.008
MITRAL REGURGITATION					
VENA CONTRACTA	3.2	2.6	1.8	3.4	0.057
VOLUME, ML	29.5	22.4	15.2	25.4	0.024

* INDEPENDENT SAMPLE T TEST.

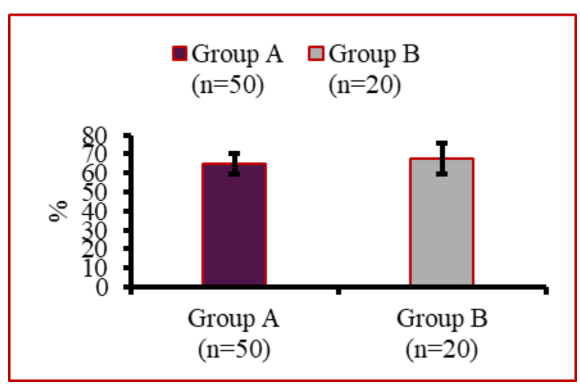

Figure 1. Comparison of ejection fraction among study groups.

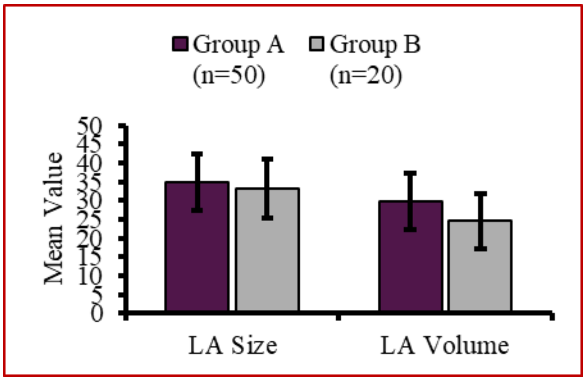

Figure 2. Comparison of LA size among study groups.

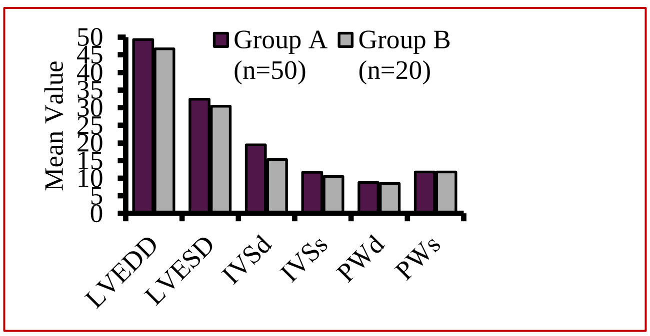

Figure 3. Comparisons of LV Dimensions among study groups.

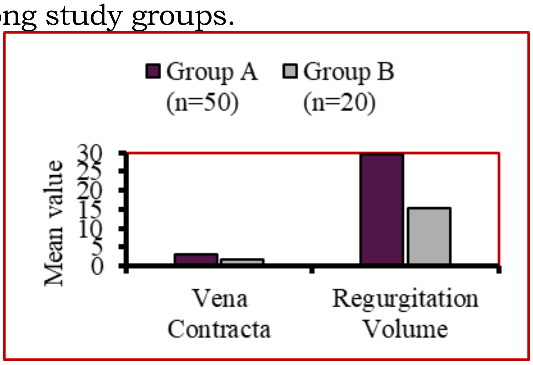

Figure 4. comparison of seveirty of mitral regurgitation among groups.

Speckle tracing echocardiography was used to compare the left ventricular strain between study groups:

Groups A and B did not differ statistically significantly in terms of AP4, AP3, AP2, or global longitudinal strain (Independent sample t test. P>0.05). In groups A and B, the mean AP4 strain was -22.1±5.7% and -20.1±5.8%, respectively. The average AP3 strain in groups A and B was -19.6±3.1% and -20.3±3.1%, respectively. -19±4.3% was the mean AP2 strain in group A and -17.9±4.2% in group B. The GLS mean for group A was -20.3±3.1%, whereas group B's mean was -19.4±3.1%,(Table 4, Figure 5).

Table 4. Speckle Tracking Echocardiographic data (N=70)

	GROUP A (N=50)		GROUP B (N=20)		P VALUE*
	Mean	SD	Mean	SD	
AP4 STRAIN	-22.1	5.7	-20.1	5.8	0.195
AP3 STRAIN	-19.6	3.1	-20.3	3.1	0.446
AP2 STRAIN	-19.0	4.3	-17.9	4.2	0.330
GLOBAL STRAIN	-20.3	3.1	-19.4	3.1	0.317

* INDEPENDENT SAMPLE T TEST.

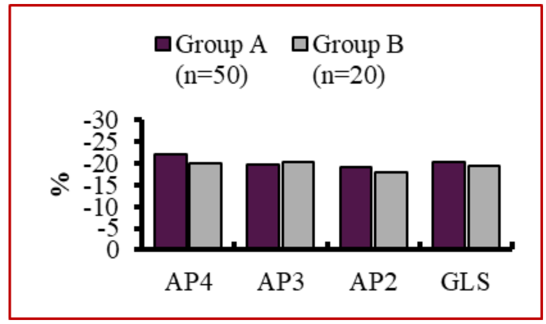

Figure 5. Speckle Echocardiography data among study groups.

Comparison of the findings of 24-hour Holter ECG monitoring data between the two study groups:

The mean heart rate for groups A and B was 75.6±9.2 bpm and 74.5±10.8 bpm, respectively, according to data from a 24-hour Holter ECG monitoring. Regarding average heart rate, there was no statistically significant difference between the groups (P=0.664). 53 (75.7%) patients in all reported having arrhythmia, of which 44 (88%) were in the MAD group and 9 (45%) were in the non-MAD group. There was a statistically significant distinction between the two groups (P=0.000),(Table 5, Figure 6).

While the mean PACs were 0.2±0.4% and 0.5±0.9% in groups A and B, respectively, the mean PVCs were 4.6±5.9% in group A and 0.4±0.7% in group B. Compared to the non-MAD group, the MAD group experienced considerably higher PVCS (P=0.003),(Table 5, Figure 7).

In terms of ST elevation, group A's mean value was 21.4±22.5 segments, while group B's mean value was 25.2±20.6 segments. For groups A and B, the average maximum elevation was 0.1±0.08 mV/min and 0.1±0.07 mV/min, respectively. Regarding ST elevation, there was not a statistically significant distinction between the groups (P>0.05),(Table 5).

Table 5. 24-hour Holter Monitoring data among study groups (N=70)

	GROUP A (N=50)	GROUP B (N=20)	P VALUE
AHR, BPM	75.6±9.2	74.5±10.8	0.664*
ARRHYTHMIA	44(88%)	9(45%)	0.000**
PVCS,%	4.6±5.9	0.4±0.7	0.003*
PACS,%	0.5±0.9	0.2±0.4	0.187*
ST ELEVATION MAX (SEG)	21.4±22.5	25.2±20.6	0.512*
ST ELEVATION MAX (MV/MIN)	0.1±0.08	0.1±0.07	0.977*

* INDEPENDENT SAMPLE T TEST. ** CHI-SQUARE TEST.

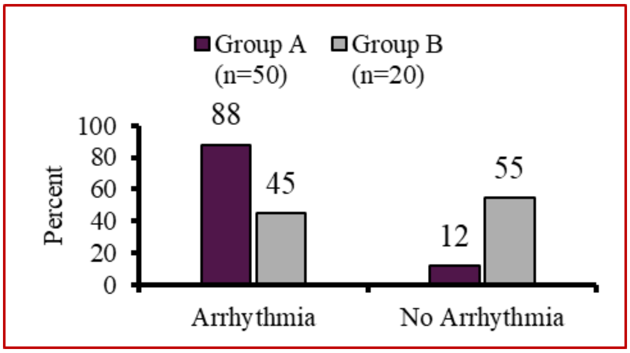

Figure 6. Arrhythmia

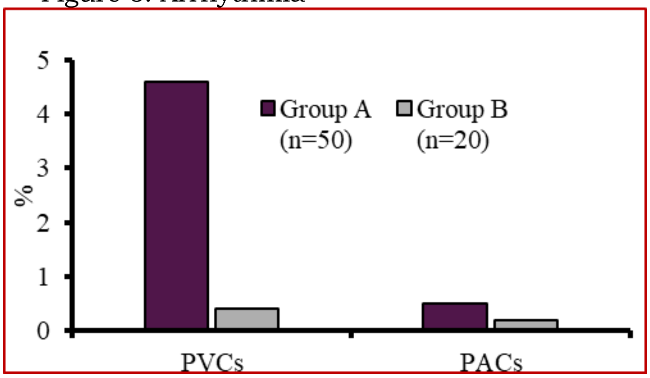

Figure 7. PVCs and PACs

Correlation between degree of MAD and ventricular arrhythmia

The burden of PVCs (r=0.252, P=0.036) and the degree of disjunction and the existence of arrhythmia (r=0.379, P=0.001) show an independently significant positive connection,(Table 6, Figure 8).

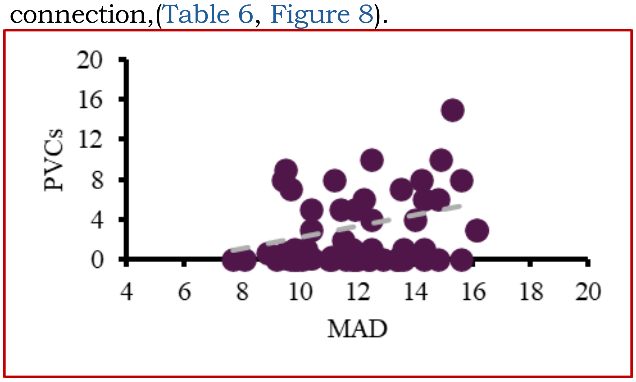

Figure 8. Correlation Between MAD and PVCs.

Correlation between degree of MAD and EF

The EF measurement of ventricular function showed a negative correlation (r=-0.252, P=0.030) with the degree of disjunction, (Table 6)

Correlation between degree of MAD and GLS

As determined by GLS, there was a negative correlation (r=-0.089, P=0.465) between the degree of disjunction and ventricular function, (Table 6, Figure 9).

Table 6. Correlation Analysis between arrhythmias and LV function (N=70 patients)

VARIABLES	MAD	
	Correlation Coefficient	*P* value
ARRHYTHMIA	0.379	0.001*
PVCS	0.252	0.036**
EF	-0.259	0.030**
GLS	-0.089	0.465**

* SPEARMAN TEST ** PEARSON TEST

Cut off points of MAD related to occurrence of PVCS:

The predictive usefulness of disjunction distance (PLAX, AP4A, overall) for arrhythmia, a (ROC) study was performed. In the PLAX perspective, a cut-off disjunction distance of 9.8 mm yields an AUC of 0.765±0.073, a statistically significant P value of 0.001, sensitivity of 81%, and specificity of 65%, Figure 9.

AUC of 0.655±0.079, statistically insignificant P value of 0.056, and sensitivity and specificity of 69% and 76%, respectively, are associated with a 10.1 mm cut-off disjunction distance in the AP4 view. AUC of 0.755±0.078, statistically significant P value of 0.002, and sensitivity and specificity of 76% and 70%, respectively, are achieved using an overall disjunction distance cut-off of 10.2 mm.

Thus, in patients with MVP, overall MAD and PLAX-view MAD exhibited a good prognostic value for arrhythmia.

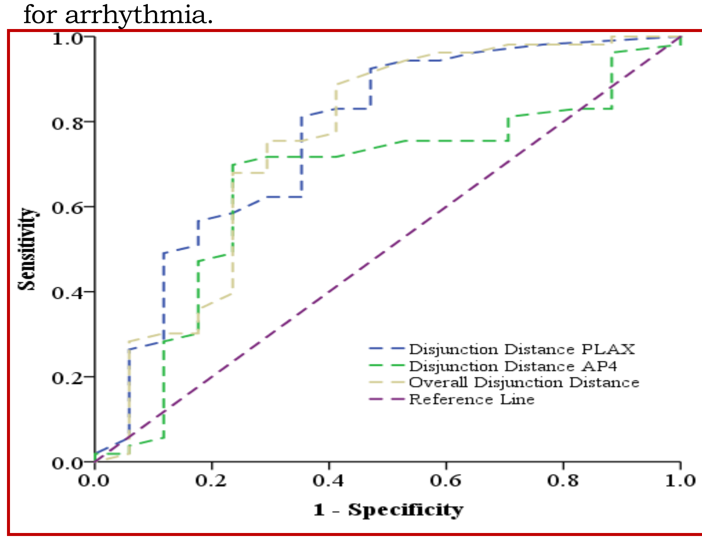

Figure 9. ROC Analysis for cut-off points of disjunction distances.

Table 7. ROC Analysis of MAD data (N=70 patients)

VARIABLES	ARRHYTHMIA					
	Cut-off	Sensitivity	Specificity	AUC	SE	*P* value
MAD PLAX	9.8	81%	65%	0.765	0.073	0.001
MAD AP4	10.1	69%	76%	0.655	0.079	0.056
MAD OVERALL	10.2	76%	70%	0.755	0.078	0.002

AUC, AREA UNDER THE CURVE; SE, STANDARD ERROR

4. Discussion

The results of our investigation revealed that group A's mean age ranged from 14 to 52 years old, at 33.1±9.7 years. The age distribution of group B was 17-49 years old, with a mean age of 30.9±10.7 years. Furthermore, we discovered that the age differences between the groups were not statistically significant. According to our findings, there were 28 (56%) female patients and 22 (44%) male patients in group A. Group B, on the other hand, included 13 (65%) females and 7 (35%)

males. They stated that the gender distribution did not show a statistically significant difference between the groups (P=0.595)

We found that group A's mean BMI in the current study was 26.6±5.4 kg/m2, with a range of 18.1 to 43.3 kg/m2. The average BMI in group B was 27.2±7.5 kg/m2, with a range of 18.1 to 40.4 kg/m2. Regarding the distribution of BMI, they discovered that there was no statistically significant difference between the groups (P=0.704). According to our analysis, 44 (88%) of group A's patients did not smoke, while six (12%) did. Out of the 16 patients in group B, 16 (80%) did not smoke, and four (20%) did. We discovered that there was no statistically significant difference in the prevalence of smoking between the groups (P=0.456). Based on our findings, two patients (4%) in group A had diabetes, and seven patients (14%) had hypertension. Within group B, two patients (10%) had hypertension and one patient (5%) had diabetes. There was no statistically significant difference between the groups when it came to the prevalence of diabetes or hypertension.

Group A's mean EF, according to the current study, ranged from 55 to 74%, with a mean of 64.6±5.4%. With a range of 59 to 73%, group B's mean EF was 67.5±4.7%. As compared to the non-MAD group, the MAD group (group A) exhibited a significantly lower EF (P=0.036).

The LA volume was observed to be substantially bigger in the MAD group (29.9±7.5 mL Vs. 24.5±7.3 mL, P=0.008) than in the non-MAD group based on echocardiographic data. Nonetheless, no statistically significant difference was discovered between the groups for PWd, PWs, IVSd, IVSs, LVEDD, or LVES (P>0.05).

We discovered that the mean vena contracta in group A was 3.2±2.6 and in group B it was 1.8±3.4, indicating the severity of regurgitation. In group A, it was 29.5±22.4 ml, while in group B, it was 15.2±25.4 ml. In comparison to the non-MAD group, the MAD group had noticeably more severe regurgitation (Independent sample t test, P=0.024).

The current study's findings on Speckle Tracking Echocardiography revealed that there was no statistically significant variation between the groups in terms of global longitudinal strain (ICT), AP4, AP3, and AP2. P is greater than 0.05.

With respect to the 24-hour Holter ECG monitoring, our findings indicated that the average heart rate in groups A and B was 75.6±9.2 bpm and 74.5±10.8 bpm, respectively. It was observed that there was no statistically significant variation in the average heart rate across the groups (P=0.664). Our study's results on the Holter ECG monitoring revealed that, for groups A and B, the mean PVCs were 4.6±5.9% and 0.4±0.7%, respectively, whereas the mean PACs were 0.5±0.9% and 0.2±0.4%.

It was discovered that there were considerably more PVCS in the MAD group than in the non-MAD group (P=0.003). The mean value of ST elevation was found to be 21.4±22.5 segments in group A and 25.2±20.6 segments in group B. The mean maximum elevation was found to be 0.1±0.08 mV/min for group A and 0.1±0.07 mV/min for group B. There was no statistically significant variation in ST elevation between the groups (P>0.05).

According to the current investigation, the degree of disjunction and the burden of PVCs had a statistically significant positive association (r=0.252, P=0.043). However, as determined by EF (r=-0.431, P=0.001) and GLS (r=-0.264, P=0.034), the degree of disjunction interacted negatively with ventricular function.

AUC of 0.765±0.073 and a statistically significant P value of 0.001 were found for a 9.8 mm cut-off disjunction distance in the PLAX view, which indicated arrhythmia with a sensitivity of 81% and specificity of 65%. In the AP4 view, a 10.1 mm cut-off disjunction distance statistically insignificantly predicted arrhythmia with a sensitivity of 69% and specificity of 76%, with an AUC of 0.655±0.079.

With an AUC of 0.755±0.078, a statistically significant P value of 0.002, and a sensitivity of 76% and specificity of 70%, an arrhythmia was predicted using an overall disjunction distance cut-off of 10.2 mm. Thus, in patients with MVP, overall MAD and PLAX-view MAD exhibited a good prognostic value for arrhythmia.

4. Conclusion

The MAD group had significantly more frequent PVCS than the non-MAD group. The burden of PVCs and degree of disjunction showed a statistically significant positive link, but the degree of disjunction showed a negative correlation with ventricular function as determined by EF and GLS. Overall, MAD and PLAX-view MAD had a good predictive value for arrhythmia in patients with MVP.

Disclosure

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Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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