Journal of the Medical Research Institute
JMRI, 2020; Vol. 41 No. 1: (1--5)

Journal of the Medical Research Institute

CORRELATION BETWEEN CLINICAL AND ECHOCARDIOGRAPHIC FINDINGS WITH THE OCCURRENCE OF VENTRICULAR ARRHYTHMIAS IN PATIENTS WITH MITRAL VALVE PROLAPSE

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ABSTRAct

Background: Chronic Mitral valve prolapse (MVP) has been linked to the occurrence of serious ventricular arrhythmias and sudden cardiac death. However, their mechanism is not fully understood particularly in the absence of haemodynamically significant mitral regurgitation (MR).

Objectives: The aim of the study is to identify if there are specific clinical and echocardiographic criteria that can predict the occurrence of ventricular arrhythmias in patients with mitral valve prolapse.

Methods:We prospectively enrolled 30 consecutive patients with MVP. Clinical examination, echocardiography (standard and speckle tracking) and 24 hours Holter monitoring were performed in all patients. The patients were further divided into 2 groups: arrhythmic MVP (7 patients) and non- arrhythmic MVP (23 patients) based on the presence of complex ventricular arrhythmias on Holter monitoring.

Results: Patients with arrhythmic MVP experienced syncope more frequently compared to the non- arrhythmia group (57 vs 4%, p=0.006). They also had larger left ventricular (LV) end systolic volume (45 ± 8.8 vs 36 ± 8 ml, p=0.023) despite similar LV ejection fraction (EF) and global longitudinal strain (GLS). The arrhythmic MVP patients had wider mitral annular disjunction (7.7 ± 3.8 vs 3.9 ± 3.9 mm, p=0.033).There were no significant difference between the 2 groups regarding the degree of mitral regurgitation, leaflet affection (single or bileaflet) or mitral annular diameters.

Conclusion:Increased left ventricular end systolic volume and the degree of annular disjunction by echocardiography may contribute to the arrhythmic risk in patients with MVP irrespective of the presence and severity of mitral regurgitation.

Keywords: *Mitral valve prolapse; ventricular arrhythmias; mitral annular disjunction*

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INTRODUCTION

Mitral valve prolapse (MVP) is a common cardiac valvular abnormality affecting about 2-3% of the general population.[1-4] It is defined as systolic displacement of one or both mitral valve leaflets >2 mm into the left atrium, with or without leaflet thickening, beyond the long axis of mitral annulur plane.[4,5]

MVP is not a completely understood clinical entity, despite being known for more than a century. Although it is generally considered as a benign condition, [1,3] it has been associated with various clinical complications including significant mitral regurgitation, congestive heart failure, infective endocarditis and stroke; even ventricular arrhythmias and sudden cardiac death have been reported. [8-10]

The mechanism of ventricular arrhythmias and sudden cardiac death in patients with MVP is not fully understood particularly in the absence of hemodynamically significant mitral regurgitation. Several theories were suggested to explain the mechanism of significant ventricular arrhythmias in MVP patients but most of them are still speculative. These include MVP-related factors such as the excessive traction on the papillary muscles (PMs) by the prolapsing leaflets;[12] the mechanical stimulation of the endocardium by the elongated chordae, with after depolarization induced triggered activity; the diastolic depolarization of muscle fibers in redundant leaflets with triggered repetitive automaticity; [13] and the endocardial friction lesions with the extension into the myocardium.[14] Myocardial substrate of the electrical instability in patients with MVP has been addressed and LV fibrosis was detected in histology at the level of PMs as well as in the LV infero-basal wall.[15]

Till now, there are no definite criteria that can predict the incidence of life threatening ventricular arrhythmias in patients with MVP. We thought that by combining clinical, electro-cardiographic and echocardiographic findings in patients with MVP, we may be able to provide more specific criteria to identify patients with MVP

liable to suffer from serious ventricular arrhythmias.

METHODS:

Study population:

In this prospective cross-sectional study, 30 MVP patients were consecutively recruited from our adult echocardiography lab after approval of the Institutional Ethics Committee. MVP was defined as systolic displacement of one or both mitral valve leaflets >2 mm into the left atrium beyond the plane of the mitral annulus in the parasternal long axis view on transthoracic echocardiography.[(4)] Exclusion criteria were Patients with possible alternative cause for arrhythmia (e.g: coronary artery disease, long or short QT syndromes, Brugada syndrome, arrhythmogenic cardiomyopathy, hypertrophic cardiomyopathy and electrolyte disturbances) and patients with left bundle branch block (LBBB), conduction delay or paced rhythm.

All patients underwent history taking, clinical examination, echocardiography and 24 h Holter monitoring,

Study cases were further divided into arrhythmic MVP (A-MVP) and non arrhythmic MVP (NA-MVP) groups based on the presence of complex ventricular arrhythmias on 24 hours Holter monitoring. Complex ventricular arrhythmia was defined as the presence of couplets, sustained or non-sustained ventricular tachycardia (VT) and R on T pattern ventricular ectopy.

All participants gave written informed consent.

Echocardiography:
The echocardiographic studies were performed iE 33 machine (Philips Medical Systems, Andover, MA, USA). Mitral valve morphology and function were assessed including annular diameters, leaflet thickness, degree of displacement, presence and degree of annular disjunction and severity of mitral regurgitation. Ejection fraction (EF) was calculated by modified Simpson's biplane method.(16) Atrial diameter was determined by M-mode or 2D echocardiography in the parasternal long-axis plane and left atrial volume was calculated using the area length method corrected for body surface area [left atrial volume index (LAVI)]. [(16)]

Speckle tracking echocardiography (STE):
Longitudinal strain was obtained from three apical views at frame rate >50/s. Segments that failed to track were manually adjusted. Region of interest (ROI) was adjusted to fit the average of the myocardial thickness. LV GLS was defined as the average of peak longitudinal strains from a17 LV segments model.[(17)]

Holter monitoring:
All patients underwent 24 hours three channel Holter monitoring to detect the presence and frequency of ventricular premature contractions (VPCs).

STATISTICAL ANALYSIS:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative data were described using number and percent Quantitative data were described using range (minimum and maximum), mean and standard deviation. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Significance of the obtained results was judged at the 5% level. The used tests were: Chi-square test, Fisher's Exact or Monte Carlo correction as correction for chi-square; and Student t-test.

RESULTS:

Comparison between the A-MVP and NA- MVP patients:

Basic clinical characteristics:
A-MVP patients experienced syncope more frequently than the NA-MVP group. They also had greater utilization of beta- blockers (BB). No other significant differences between the 2 groups regarding baseline characters or resting ECG findings.
Basic clinical characteristics of the 2 groups are summarized in table (1).

Echocardiographic findings:
The A-MVP cases had larger LV end systolic volume (ESV) compared to the NA-MVP group (p=0.023) despite similar LVEF and GLS and similar grades of MR. They also had wider mitral annular disjunction (p=0.033, figures 1). There was no significant difference in other echocardiographic parameters between the 2 groups. Echocardiographic characteristics of the 2 groups are summarized in table [(2)]

Holter monitoring:
Seven patients had complex ventricular arrhythmias (figure 2). Non sustained ventricular tachycardia (NSVT) was the most frequent form (3 patients, 43%) followed by couplets (2 patients, 28.6%). One patient had NSVT and ventricular premature contraction (VPC) burden of 18%/day and one patient had Ron T pattern ventricular ectopy and VPC burden of 17%/day

Table (1): Clinical characteristics of mitral valve prolapse patients with and without ventricular arrhythmia:

Clinical characteristics	A-MVP (N=7)	NA-MVP (n=23)	P value
Age, years mean (SD)	39 (15)	29 (11)	0.068
Female sex, n(%)	4 (57)	22(95.7)	0.031
BSA,m2 mean(SD)	1.8 (0.2)	1.7 (0.1)	0.080
HR, bpm mean (SD)	70 (11)	80 (12)	0.087
Systolic BP, mmHg mean(SD)	115.8 (12)	112.6 (10)	0.507
Diastolic BP, mmHg mean (SD)	77.50 (10.55)	73.42 (7.45)	0.535
HTN, n(%)	1 (14.3)	1(4.3)	0.418
DM, n (%)	0	0	
CAD, n (%)	0	0	
Tobacco use, n (%)	0	1 (4.3)	1.000
Palpitations, n (%)	7 (100)	19 (82.6)	0.548
Chest pain, n (%)	3 (43)	13 (56.5)	0.325
Syncope, n (%)	4 (57)	1 (4.3)	0.006*
Beta-blockers, n (%)	3 (43)	1 (4.3)	0.031*

BSA, body surface area; CAD, coronary artery disease; DM, diabetes mellitus; HR, heart rate; HTN, hypertension.

*: Statistically significant at $p \leq 0.05$

Table (2): Echocardiographic characteristics of mitral valve prolapse patients with and without ventricular arrhythmia

Echocardiographic characteristics	A-MVP (n=7)	NA-MVP (n=23)	P value
LAVI, ml/m2 mean(SD)	29 (6)	31.76 (13.55)	0.169
Annular disjunction, n (%)	6 (85.7%)	13 (56.5%)	0.215
Annular disjunction, mm mean (SD)	7.7 (3.8)	3.9 (3.9)	0.033*
LVEDV, ml mean (SD)	110.1 (27)	97.4 (20.5)	0.191
LVESV, ml mean(SD)	45 (8.8)	36.3 (8.2)	0.023*
LVEF, % mean (SD)	59 (3.2)	62.3 (4.2)	0.064
GLS, % mean (SD)	-21.6 (-1.7)	-22.5 (-2.4)	0.358
A-P annular diameter, mm mean (SD)	34.9 (4.6)	34 (4.9)	0.680
Bicommissural annular diameter, mm mean (SD)	36.9 (6.2)	36.3 (5.9)	0.832
Bileaflet prolapse, n (%)	6 (85.7%)	18 (78.3%)	1.000
No significant MR, n (%)	3 (42.9%)	10 (43.5%)	0.132
Mild MR, n (%)	4 (57.1%)	4 (17.4%)	
Moderate MR, n (%)	0	5 (21.7%)	
Severe MR, n (%)	0	4 (17.4%)	

GLS: global longitudinal strain; LAVI, left atrial volume index; LV, left ventricle; LVEDV, left ventricular end diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end systolic volume; MR, mitral regurgitation.

*: Statistically significant at $p \leq 0.05$

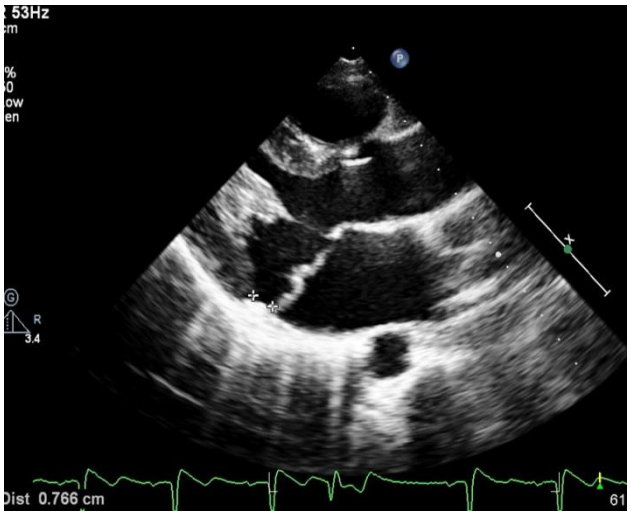

Figure (1): Mitral annular disjunction in patient with bileaflet prolapse

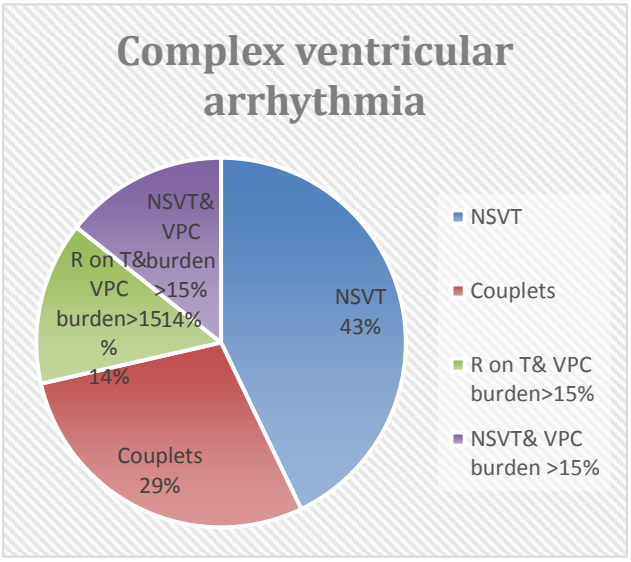

Figure (2): Distribution of ventricular arrhythmias in the arrhythmic MVP group

DISCUSSION:

In our study, complex ventricular arrhythmias was found in 23% of the study population. Although more than 40% of the patients in the arrhythmia group was maintained on BBs, this failed to control the ventricular arrhythmia and one patient on BB therapy had VPC burden of 17%/day. This finding is disappointing but not surprising. In a study done by Basso et al on sudden cardiac death (SCD) and MVP, [15] 21% of young adult SCD victims and two living patients had aborted SCD despite beta-blocker therapy.The ability of BB to control ventricular arrhythmias in the setting of MVP is questionable and its role is less established than in many other diseases.

There was no significant difference in the number of patients having annular disjunction in both groups, but the degree of annular disjunction was significantly larger in the arrhythmia group in agreement with several previous studies.[18-20] There is an increasing interest in the association between mitral annular disjunction (MAD) and ventricular arrhythmias and a recent study had reported that MAD itself is arrhythmogenic even in the absence of MVP.[19] Unlike previous studies, bileaflet prolapse was not a predictor of ventricular arrhythmia in our study. [10,15,20] Although a previous study [21] found that the presence of moderate to severe mitral regurgitation is the only independent predictor for occurrence of arrhythmia in MVP, several subsequent studies showed that ventricular arrhythmia can occur in MVP in the absence of significant MR.[15,20] In our study population, all patients in the arrhythmia group had no or mild MR asserting the belief that MVP itself is arrhythmogenic even in the absence of hemodynamically significant MR. The increased LVESV in the arrhythmia group supports the theory of myocardial substrate being a possible mechanism of ventricular arrhythmia in MVP.[15] No significant difference in EF and GLS was found between the 2 groups and the same observation was reported in a recent study on arrhythmic MVP.[20]

Although female sex was significantly higher among the NA- MVP patients, this is most probably a selection bias as 87% of the total study population were females.

STUDY LIMITATIONS:

Small number of patients included in the study.

CONCLUSIONS:

Increased left ventricular end systolic volume and the degree of annular disjunction by echocardiography may contribute to the arrhythmic risk in patients with MVP irrespective of the presence and severity of mitral regurgitation.

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