ORIGINAL PAPER

doi: 10.5455/medarh.2018.72.9-12
MED ARCH. 2018 FEB; 72(1): 9-12
RECEIVED: NOV 20, 2017 | ACCEPTED: JAN 08, 2018

Clinic for Heart, Blood Vessel and Rheumatic Diseases. University Clinical Center Sarajevo, Sarajevo, Bosnia and Herzegovina

Corresponding author: Enisa Hodzic, MD, PhD. Clinic for Heart, Blood Vessel and Rheumatic Diseases. University Clinical Center Sarajevo, Sarajevo, Bosnia and Herzegovina. ORCID ID: http://www.orcid.org: 0000-0002-7436-7708.

Assesment of Rhythm Disorders in Classical and Nonclassical Mitral Valve Prolapse

Enisa Hodzic

ABSTRACT

Introduction: Mitral Valve Prolapse (MVP) is the most common cardiac valve pathology of to day. Aim of article was to identify the types and frequency of potentially malignant arrhythmia and atrial brillation in patients with MVP, to determine the differences in these arrhythmias between classical and non-classical MVP, to evaluate the correlation of potentially malignant arrhythmia and atrial fibrillation with MVP with possible clinical complications of arrhythmogenic sudden cardiac death and potential risk of thromboembolic vascular incident. **Patients and methods:** Article has retrospective-prospective analytical character and present observational study on 239 patients (120 with MVP (66 with classical and 54 with non-classical MVP), who had a subjective feeling of palpitations and/or pain in the chest, and/or episode of syncope, and did not have ischemic heart disease or another valve pathology) and 119 healthy patients in the control group. All patients were analyzed by 24-hour ECG Holter. **Results:** Signifficant difference in all analyzed arrhythmias between classical MVP and control group ($p < 0.001$) between non-classical and control group in the presence of preexcitation signs ($p = 0.047$), and between classical and non-classical in presence of QT prolongation and AV block of II and III degree ($p = 0.023$), ventricular arrhythmias of the 3rd, 4th and 5th grade at scales according to Lown ($p = 0.002$) and atrial brillation in favor of classical MVP ($p = 0.016$). **Conclusion:** The potential risk of cardiac death and vascular incidence is signi cantly higher in classical MVP than in non-classical MVP, implying the need for routine ECG-Holter monitoring in their diagnosis for timely prevention of clinical arrhythmogenic complications.

Keywords: mitral valve prolapse, arrhythmia, ECG Holter monitoring.

1. INTRODUCTION

Mitral valve prolapse is the most common cardiac valve pathology of today, in modern industrial countries. It is most often diagnosed by echocardiography, both in symptomatic and asymptomatic patients, as an accidental finding (1). Estimation of incidence and prevalence of MVP was changed according to diagnostic echocardiographic criteria. Echocardiographic criteria determine the so-called primary prolapse in the narrow sense that is hereditary and degenerative disease, and secondary prolapse resulting from previous cardiac pathology, primarily ischemic heart disease with papillary dysfunction and dilatation of mitral valve anulus (1-3).

Primary prolapse occur in two forms such as: a) Classical prolapse with a redundant prolapsed valve of either anterior, posterior, or both chondroses, which prolapse at the left atrium >2 mm during the ventricular systole, above the anulus attachment line, with a chrondroses thickness > 5 mm; b) Non-classical prolapse of mitral valve that is prolapsing >2 mm into the left ventricle during ventricular systole but has a thickness of <5 mm (1,3).

Although the prolapse of the mitral valve is a primary valve disease, the term "mitral valve prolapse syndrome" implies neuroendocrinological and autonomic dysfunction, registered in patients with this syndrome. Complex symptoms that present mitral valve prolapse syndrome such as chest pain, palpitations, cardiac arrhythmia, chronic fatigue, presynaptic and syncope, orthostatic phenomena, lack of air sensation and neuropsychiatric symptoms originate from neuroendocrine and autonomic dysfunction. This neurophysiological association of the heart in case of MVP, renal and adrenal function with the autonomic nervous system is described in the literature as a "neuro-endocrine cardiovascular process", which may explain many symptoms, including heart rhythm disorders. A direct link between the occurrence of ventricular arrhythmias and the concentration of catecholamine in the urine

has been demonstrated, and the connection between worsening of cardiac arrhythmia with worsening of mitral insufficiency as well as the connection between mitral valve prolapse syndrome and magnesium deficiency, as demonstrated in 85% of patients with MVP with latent tetanus present (4-6).

2. GOALS

* Determine the types and frequency of potentially malignant arrhythmia and atrial fibrillation in patients with primary MVP.

* Identify differences in the type and frequency of these arrhythmias between patients with classical and non-classical MVP.

* Estimate the risk for classical and non-cloned MVP from possible arrhythmogenic complications of sudden cardiac death and/or vascular incident.

3. PATIENTS AND METHODS

A retrospective-prospective, analytical, observational study was performed, which included 239 subjects, 120 subjects with primary MVP in the experimental group (Group A), and 119 subjects in the control group (B group) from a general, healthy population. Experimental group respondents are divided into two subgroups according to the ECHI criterion of the existence of classical MVP (A1) or non-classical MVP (A2). All subjects were tested and analyzed by 24-hour ECG Holter on the Quinton Trilium 3000 machine. Potentially malignant cardiac rhythm disorders that could directly or indirectly lead to arrhythmogenic sudden cardiac death (SCD) were: prophylaxis, prolongation and shortening of the QT interval and ventricular cardiac rhythm disorders of III, IV and V grade on the Lown scale, and the appearance of AV II stage-Moebitz 2 and AV block III stage, as well as the occurrence and frequency of atrial fibrillation with potential risk of thromboembolic vascular incident. The criterion for inclusion in the experimental group was echocardiographically verified MVP, accompanied by a subjective feeling of palpitations and/or chest pain, and/or syncope episodes. Exclusion criteria in the study: associated pathology of coronary ischemic heart disease, prior valve surgery or another valve pathology and hypertrophic obstructive cardiomyopathy.

Prior to the study, the approval of the Ethics Committee of the Clinical Center of Sarajevo University was obtained.

Statistical analysis

To prove the hypothesis, a chi-square test (X2-test) was used. This test was used because in the work there were frequencies of two or more independent groups of subjects, and the intention was to determine whether samples differed in the observed properties. Used is the exact probability test by Fisher (for two independent samples). If there was only one degree of freedom, a continuity correction was carried out by Yates correction. If the differences between the observed and the expected frequencies were small, no correction was made. The test of two independent samples of the Mann Whitney test uses the ranges divided into two categories, and tested whether two samples belong to populations with the same medians. The model "t" test (Student) for two samples shows how many standard errors the sample mean value differ from the hypothetical mean value of the basic set. The significance level is set at $p<0.05$.

4. RESULTS

No significant difference was found in the age structure of the respondents, between the experimental and control group ($p = 0.076$), nor between the respondents with the classical and the non-classical MVP ($p = 0.078$), as shown in Table 1.

Table 2 shows statistically significant difference in all of the examined rhythm disorders in subjects with classical MVP in relation to the control group and in relation to the non-classical MVP, except in the presence of signs of preexcitation where there was no statistically significant difference between classical and non-classical MVP.

Table 3 shows that there is a statistically significant difference in the potential risk of sudden arrhythmogenic cardiac death–"SCD", in all groups or in favor of experimental in relation to the control group, and within the experimental groups in favor of the respondents with classical MVP compared to these with non-classical MVP. There is a significant difference in the risk of a potential vascular incident, as a result of atrial fibrillation and thromboembolic complications, in subjects with classical MVP versus control group, as well as within experimental groups in favor of subjects with classical MVP versus non-classical MVP. There was no statistically significant difference between subjects with non-classical MVP and control group.

	Classic MVP (A1)		Total
	Male	Female	
Interval years	17-69	9-70	9-70
n	36	30	66
X	33.333	36.000	34.545
S	15.941	15.308	15.594
SX	2.657	2.795	1.919
Median	26	33	29.5
Mann-Whitney Rank Sum Test	p = 0.207		
	Non-classic MVP		Total
	Male	Female	
Interval years	17-54	26-51	17-54
n	30	24	54
X	30.633	35.708	32.889
S	10.529	7.799	9.671
SX	1.922	1.592	1.316
Median	29.5	36	34
Mann-Whitney Rank Sum Test	p = 0.034		

Table 1. Basic demographic data of respondents with MVP

	Classic MVP (A1) n = 66	Non-classic MVP (A2) n = 54	Control group (B) n = 119	
Ventricular disorders of the rhythm of 3., 4. and 5. degree by Lown scale	17 (25.7%)	2 (3.7%)	1 (0.8%)	A1 Vs B p<0.001 A2 Vs B p=0.479
Preexcitation signs (WPW and LGL syndrome)	12 (18.1%)	6 (11.1%)	3	A1 Vs B (2.5%) p<0.001 A2 Vs B p=0.047
QT Prolongation	8 (12.1%)	0	0	A1 Vs B p<0.001
AV block of II (Mobitz II) and III degree	8 (12,1%)	0	0	A1VsB p<0.001
Atrial fibrillation	10 (15,2%)	1 (0,8%)	0	A1 Vs B p<0.001 A2 Vs B p=0.684

Rhythm disorders by subgroups A1 and A2 with classical and non-classical MVP

	Classical MVP (A1) n = 66	Non-classical MVP (A2) n = 54	
Ventricular disorders of the rhythm of 3., 4. and 5. degree by Lown scale	17 (25.7%)	2 (3.7%)	X2 = 9.248; p = 0.002
Preexcitation signs (WPW and LGL syndrome)	12 (18.1%)	6 (11.1%)	X2 = 0.676; p = 0.411
QT Prolongation	8 (12.1%)	0	X2 = 5.200; p = 0.023
AV block of II (Mobitz II) and III degree	8 (12.1%)	0	X2 = 5.200; p = 0.023
Atrial fibrillation	6 (9.1%)	1 (0.9%)	X2 = 5.834 p = 0.016
Intermittent atrial fibrillation	4 (6.1%)	0	X2= 4.785 p = 0.029

Table 2. Rhythm disorders by groups

	Classical MVP (A1) n = 66		Non-classical MVP (A2) n = 54		Control group (B) n = 119	
	Yes	No	Yes	No	Yes	No
n	49	17	7	47	9	110
	74.2%	25.8%	12.9%	87.1%	7.5%	92.5%
(A1) Vs (A2)	X2 = 42.382; p < 0.001					
(A2) Vs (B)			X2 = 10.816; p = 0.001			
(A1) Vs (B)	X2 = 84.632; p < 0.001					

Table 3. Potential risk of arrhythmogenic sudden cardiac death ("SCD")

5. DISCUSSION

The subject of the study was the arrhythmia in patients with primary MVP with possible clinical outcome of sudden cardiac death and/or thromboembolic vascular incident, according to the criterion of classical or non-classical mitral valve prolapse. Other echocardiographic criteria as systolic function of the left ventricle, the presence and severity of the accompanying mitral insufficiency were not considered in this study. No static significance has been demonstrated in this study between groups in relation to the age of respondents, nor in relation to gender between the patients with classical and non-classical MVP. Ventricular stage 3 hearth rhythm disorder at scale by Lown (polymorphic VES), 4 A degree (VES linked) and 4 degree B (VES in spikes) and 5 degree (VES type R/T) at scale by Lown; the occurrence of prolongation of the QT interval as a possible trigger of ventricular tachycardia of Torsades de pointes type, signs of preexcitation, the appearance of AV blocks II and III and the appearance of atrial fibrillation. In our work we observed a shortened QT interval (QT interval duration = or < than 300 msec.) As a possible cause of arrhythmogenic sudden cardiac death and the appearance of ECG signs of Brugada syndrome. The aforementioned disorder was not recorded in neither of analyzed cases.

	Classical MVP (A1) n = 66		Non-classical MVP (A2) n = 54		Control group (B) n = 119	
	Yes	No	Yes	No	Yes	No
N	10	56	1	53	0	119
	15.15%	84.85%	0.02%	98.98%	0.00%	100.0%
(1) Vs (2)	X2 = 6.3265; p = 0.0118					
(2) Vs (3)			X2 = 2.2449; p = 0.1175			
(1) Vs (3)	X2 = 14.0426; p < 0.0002					

Table 4. Potential risk of vascular incident

Statistical significance has been demonstrated for patients with MVP in the following arrhythmias: VES 3 and 4 at Lown scale (WPW and LG syndrome), AV block II (Mobitz 2) and stage III, as well as prolongation of QT interval. Namely, the subjects of the MVP experimental group had statistically significantly more frequent occurrence in all of the above-mentioned cardiac rhythm disorders compared to the control group of healthy subjects (p <0.001). Within the group of subjects with classical and non-classical MVP, statistical significance was observed in all observed arrhythmias (p <0.001) in the patients of the classical MVP, except for preexcitation signs found in non-classical MVP patients (p = 0.0411).

Using the chi-square test (X2-test), there was a statistically significant difference in the risk of potential sudden arrhythmogenic heart death–"SCD", as well as between the classical MVP group compared to the control group of healthy subjects (X2 = 42,382; p <0.001), as well as those with non-classical MVP versus healthy group of respondents (X2 = 10.816, p = 0.001).

Within the experimental group, this risk was statistically significantly higher in favor of the classical MVP compared to non-classical MVP (X2 = 42.382; p <0.001).

In the study of the Polish authors (Kitlinski and Piwowarska) in 59% of cases, ventricular extrasistolysis was demonstrated without a degree of insight into the Lown scale, and it was not possible to estimate the relationship between the more severe forms of ventricular extrasisturia and the possible sudden cardiac death.

Zouridakis demonstrated a statistically significant incidence in the primary prolapse of the redundant frontal mitral valve (p <0.005) prolapse with a higher incidence of complex ventricular arrhythmias and an increased risk

of life-threatening malignant arrhythmias, with a proven increase in QT prolongation and ventricular arrhythmia with echocardiographic evidence of a more severe degree of prolapse of the mitral valve (8). Abdullaev in his work of monitoring the rhythm disturbance and prolongation of the QT interval indicates the incidence of as much as 29.2% of the prolapse of the mitral valve (6).

Corrado and colleagues in their study of monitoring sudden cardiac deaths in young people with prolapse of the mitral valve indicate the occurrence of ventricular electrical instability and sudden cardiac death in relation to the weight of accompanying mitral regurgitation, left ventricular dysfunction and autonomic dysfunction (9). In 10% cases (17 of the total number of 163) sudden cardiac death postmortem is a patoanatomically proven primary classical prolapse of mitral valve with an average life expectancy of 24 years and without other cardiac pathology, of which two cases were reported in pregnancy. Out of this number, 47% of them had ventricular prolapses verified during life, and 35% of them were symptomatic during their lifetime with palpitation and/or syncope.

In Circulation 2002, a study entitled "Natural History of Asymptomatic Mitral Valve Prolapses in the Community" was published on 883 subjects with prolapse of the mitral valve, classified according to the existence of primary risk factors (moderate to severe mitral regurgitation with EF <50%) and secondary risk factors (mild mitral regurgitation with a left atrial diameter less than 4 cm, fluttering mitral valve, atrial fibrillation and over 50 years of age) (10). Ten years mortality and cardiovascular morbidity were assessed according to the criteria for the existence of these risk factors. It has been shown that with 2 or more secondary risk factors there was a high cardiovascular morbidity of 6.2% ($p < 0.01$), with no significant difference in mortality. Patients with primary risk factors had mortality of 45±9% as expected, and 8% had atrial fibrillation. According to some earlier studies, the incidence of atrial fibrillation and cerebrovascular incidence in patients with MVP syndrome is not greater than in the general population, and the incidence of sudden cardiac death is controversial and is estimated at 1%, which is consistent with that in the general population (11-13).

In our study patients with classical MVP who were symptomatic, atrial fibrillation was observed in 10 cases and high statistical significance in relation to the control group ($p < 0.001$) was demonstrated. No significant difference was found in the leading rhythm of atrial fibrillation, nor the occurrence of intermittent atrial fibrillation between the non-classical MVP and the control group of the subjects. Thus, potential risk of cardio-source thromboembolic complications due to atrial fibrillation exists in subjects with a classic prolapse of the mitral valve, while it is not proven in subjects with a non-classical prolapse of the mitral valve.

6. CONCLUSION

Patients with primary MVP, regardless of age and gender, have multiple rhythm disorders. The occurrence and frequency of heart rhythm disturbances, including ventricular cardiac rhythm disturbances (grade 3, 4 and 5 classified by the Lown scale), preexcitation syndrome, QT prolongation, imply greater risk of sudden arrhythmogenic cardiac death, the statistically significant more frequent occurrence of atrial fibrillation and the risk of vascular incidence in relation to the general population. The risk of a potential vascular incident has not been proven in non-classical MVP. The classical MVP was followed by more frequent and varied and potentially malignant cardiac rhythm disorders compared to the non-classical primary prolapse of the mitral valve. The findings of the study indicate the need for routine ECG-Holter monitoring in the diagnosis of echocardiographically verified primary MVP for timely prevention of arrhythmic sudden cardiac death and/or vascular incidence. Patients with MVP need regular and continuous cardiological follow-up for the prevention of clinical arrhythmogenic complications.

- **Author Contribution:** E.H. performed each step of research and gave final approval for article publishing (last revised version):
- **Conflict of interest:** The author has no conflict of interest.

REFERENCES

1. Bonow RO, Braunwald E. Valvular Heart Disease.in: Zipes DP, Liby P, Bonow RO, Braunwald E. Braunwald's heart disease: a textbook of cardiovascular medicine. 7tn ed.Philadelphia: Elsevier Saunders, 2005: 1553-32.
2. Pellerin D, Brecker S, Veyrat C. Degenerative mitral valve prolapse with emphasis on mitral valve prolapse.Heart. 2002; 88: iv20-iv28.
3. Bonow RO, Braunwald E. Echocardiography.in: Zipes DP, Liby P, Bonow RO, Braunwald E. Braunwald's heart disease: a textbook of cardiovascular medicine. 7tn ed.Philadelphia: Elsevier Saunders, 2005: 187-260.
4. Bobkowski W, Siwinska A, Zachwieja J, Mrozinski B, Paluszak W, Macijewski J. Electrolyte abnormalites and ventricular arrhythmias in children with mitral valve prolapse. Pol Merkuriusz Lek. 2001 Aug; 11(62): 125-8.
5. Curtis AB. Fighting sudden cardiac death: Aworldwide challange N Eng J Med. 2001 Sep; 345: 927.
6. Abdullaev RF, Gelfgat EB, Babaev ZM, Akhmedov TM, Tarivardieva GA. Disorders of cardiac rhythm and the changes in QT interval in mitral valve prolapse syndrome. Kardiologiia. 1991 Dec; ;31(12): 74-6.
7. Kitlinski M, Piwowarska W. Arrhythmias in patients with mitral valve prolapse. Folia Med Cracov. 1994; 35(1-4): 61-7.
8. Zouridakis EG, Parthenakis FI, Kochiadakis GE, et al. QT dispersion in patients with mitral valve prolapse is related to the echocardiographic degree of the prolapse and mitral leaflet thickness. Europace. 2001; 3(4) :292-8.
9. Corrado D, Basso C, Rossi L, Thiene G. Sudden death in young people with apparently isolated mitral valve prlapse. G Ital cardiol. 1997Nov; (27)11: 1097-105.
10. Avierinos JF, Gersh BJ, Melton LJ. et al. Natural history of asymptomatic mitral valve prolapse in the community. Circulation. 2002; 106: 1355.
11. Schaal SF. Mitral valve prolapse: cardiac arrhythmias and electrophysiological correlates. In: Boudoulas H, Wooley CF (eds). Mitral Valve: Floppy Mitral valve, Mitral Valvular Regurgitation, 2nd ed. Armonk, NY, Futura, 2000: 409-30.
12. Begic Z, Begic E, Mesihovic-Dinarevic S, et al. The Use of Continuous Electrocardiographic Holter Monitoring in Pediatric Cardiology. Acta Inform Med. 2016; 24(4): 253-6. doi:10.5455/aim.2016.24.253-256.
13. Masic I, Dilic M, Raljevic E, Vulic D, Mott D. Trends in Cardiovascular diseases in Bosnia and Herzegovina and Perspectives with HeartScore Programme. Med Arh. 2010; 64(4): 260-3.