

STUDY ON CHARACTERISTIC ARRHYTHMIAS BY 24 - HOUR ELECTROCARDIOGRAPHIC HOLTER IN PATIENTS WITH CHRONIC MITRAL REGURGITATION

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ABSTRACT

Objectives: To investigate arrhythmias in patients with primary chronic mitral regurgitation by using a 24 - hour ECG Holter and to evaluate the association between arrhythmias and the degree of mitral valve regurgitation, left atrial diameter, degree of NYHA, left ventricular ejection fraction (LVEF%).

Methods: A cross - sectional descriptive study of 48 patients diagnosed with chronic mitral regurgitation with valvular involvement lesions such as rheumatism or prolapse valve at the Department of Internal Cardiology of Hue Central Hospital from 4/2021 - 4/2022.

Results: The mean age of sample was 58.19 ± 16.46 years, women accounted for 64.58%. Among patients who had arrhythmias with 24 - hour Holter ECG monitoring, the majority were atrial fibrillation (58.30%), followed by premature ventricular complex (54.20%) and premature supraventricular complex (16.70%). The incidence of atrial fibrillation increased when the degree of mitral regurgitation was heavier, and the group had a left atrial diameter of > 45 mm ($p < 0.05$). The incidence of atrial fibrillation varies between levels of heart failure according to the NYHA ($p < 0.05$). Meanwhile, there was no difference in the incidence of atrial fibrillation between the two groups, $EF < 50\%$ and $EF \geq 50\%$. When analyzing multivariate logistic regression, age (OR = 1.062, 95% CI: 1.005 - 1.121) and left atrial diameter (OR = 1.181, 95% CI: 1.033 - 1.349) are prognostic factors for atrial fibrillation in patients with chronic mitral regurgitation.

Conclusions: Cardiac arrhythmias are a common complication in patients with chronic mitral regurgitation. Atrial fibrillation remains the most common arrhythmia. Age factors and left atrial diameter are 2 factors that increase the likelihood of atrial fibrillation in these patients.

Key words: Arrhythmias, chronic mitral regurgitation.

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I. INTRODUCTION

Mitral regurgitation is a common valvular heart disease in cardiovascular clinics. According to data from the United States, mitral valve disease is the second most common valvular heart disease, second only to aortic valve stenosis. The results of severe asymptomatic chronic mitral regurgitation are as follows: Mortality rates range from 50 - 73% at

5 years. Mortality in patients with preserved left ventricular function ranges from 27 - 45%. Sudden death can be common about 1 - 8% per year in patients with a rupture of the mitral valve ligament [1]. Research showing arrhythmias in patients with valvular heart disease published in the journal Clinical Research in 2018 showed that 30.2% of patients with mitral regurgitation had arrhythmias,

up to 85% of cases were atrial fibrillation, the remaining 15% were ventricular arrhythmias alone. In 52.3% of patients with combined mitral valve stenosis and regurgitation have arrhythmias, up to 97% are atrial fibrillation, the rest are ventricular arrhythmias [2]. In Vietnam, in recent years, up to 50% of all patients hospitalized due to cardiovascular diseases are rheumatic heart valve diseases and account for more than 90% of acquired heart diseases, mainly mitral valve disease. From a study by the Institute of Cardiology in 2017 about ventricular arrhythmias in patients with rheumatic mitral valves, up to 80% of cases have premature ventricular complex frequently and complicatedly (Lown III, IV, V) accounting for 63.3%. Of these, 6.7% of patients developed transient ventricular tachycardia and 26.7% had R/T premature ventricular complex [3]. Mild mitral regurgitation usually causes no problems. However, if it is more severe, the disease can lead to complications such as: heart failure, arrhythmias, thromboembolism, infectious endocarditis, and increased pulmonary arterial pressure. When these complications appear, it means that heart disease will become more and more severe, which can be life - threatening, so early detection and treatment of these complications is very important and necessary, in which arrhythmias are one of the complications of mitral regurgitation. To monitor and detect complications of the arrhythmia rate in patients with valvular heart disease such as mitral regurgitation, the use of 24 - hour electrocardiogram Holter is very useful. Holter 24 - hour electrocardiography is a non - invasive technique, continuous electrocardiogram monitoring, allowing to observe the progress of electrocardiography continuously for 24 hours, thus helping to see arrhythmias and conduction disorders that are difficult for conventional electrocardiograms to detect fully. The detection of arrhythmias by 24 - hour electrocardiographic Holter will help guide treatment and especially prevent possible accidents from improving the quality of life for patients. For the above reasons, we chose to carry out the project “Study on characteristics of arrhythmias by 24 - hour electrocardiogram in patients with primary chronic mitral regurgitation “ with these objectives: To

investigate characteristic arrhythmias in patients with primary chronic mitral regurgitation by using a 24 - hour Holter ECG and to evaluate the association between arrhythmias with mitral regurgitation, left atrial diameter, degree of NYHA, left ventricular ejection fraction (LVEF%).

II. MATERIALS AND METHODS

2.1. Subjects of study

A study of 48 patients diagnosed with mitral regurgitation with valvular lesions such as rheumatoid or valvular prolapse were monitored and treated at the Department of Internal Cardiology, Hue Central Hospital, from April 2021 to April 2022.

Criteria for disease selection: patients aged from 15 years and older admitted to the hospital are diagnosed with mitral regurgitation with valvular lesions without cardiomyopathy or ischemic heart disease. And have not used antiarrhythmic drugs before. Diagnosis is clinically based, and definitive diagnosis is based on echocardiography. The patient agreed to participate in the study.

Exclusion criteria: Severe patients are undergoing emergency treatment such as: severe heart failure, ventricular tachycardia, ventricular fibrillation, circulatory arrest, etc. Patients with congenital heart disease, hypertrophic cardiomyopathy. Mitral regurgitation do not have damage to the heart valves, such as ischemia or intrinsic cardiomyopathy that causes secondary mitral regurgitation. Patients with mitral valve injury along with moderate and severe aortic valve and tricuspid valve injury. Patients with mitral valve lesions but comorbidities that also cause arrhythmias such as: hyperthyroidism, thyroiditis, etc. Patients with electrolyte disorders, taking drugs that affect arrhythmias such as: Atropine, beta - receptor blocker I, etc. The patient did not volunteer to participate in the study.

2.2. Research methodology

Cross - sectional descriptive research methods. Choose a convenient template.

Research steps: Personal information, history, and medical history through the set of questions on the study sheet. Basic tests according to the convention of Hue Central Hospital. The patient will then undergo an echocardiogram and 24 - hour ECG Holter monitoring to assess the arrhythmia.

NYHA heart failure assessment [4]:

Table 1: Heart failure classification according to NYHA

Grade I	No restrictions - normal physical activity does not cause fatigue, shortness of breath or nervousness
Grade II	Mild restriction of physical activity. The Patient is well at rest. Normal physical activity leads to fatigue, nervousness, shortness of breath or chest pain
Grade III	Limit a lot of physical activity. Although patient is well at rest, only mild exercise has symptoms
Grade IV	Do no physical activity without discomfort. Symptoms of heart failure occur immediately upon rest. Only one physical activity, increased the symptoms

Mitral regurgitation grading [5]

- Slight regurgitation (1/4): Backward flow to 1/4 along the longitudinal axis of the left atrium
- Medium regurgitation (2/4): Backward flow > 1/4 - 1/2 along the longitudinal axis of the left atrium.
- Severe regurgitation (3/4): Backward flow > 1/2 - 3/4 along the longitudinal axis of the left atrium.
- Very severe regurgitation (4/4): Backward flow > 3/4 along the longitudinal axis to near the left atrial base.

atrial base.

EF is measured by 2D ultrasound using the Simpson method: The left ventricle is cut into several slides from the bottom to the apex on 2 - chamber or 4 - chamber sections (including the sternal cross - section). In fact, just look at the ventricular contour and ventricular length (both systolic and diastolic) and the machine will automatically calculate the systolic and diastolic volume parameters, thereby calculating EF. As recommended by the American Echocardiographic Association, EF is considered normal when $\geq 55\%$. For the convenience of comparison with other studies, we divided EF into 2 groups: normal ($EF \geq 55\%$) and decreased ($EF < 55\%$) [6].

Data processing: data is processed using SPSS 20.0 software.

III. RESULTS

The mean age of the study sample was 58.19 ± 16.46 years. There were more female patients than male (64.58% and 35.42%) (**table 2**). In the left atrial diameter, the pulmonary artery pressure of patients with mitral regurgitation both increased compared to the average. Patients with severe mitral regurgitation (3/4 to 4/4) accounted for 77.10% of the patients studied (**table 3**).

Table 2: Distribution of patients by age and gender

Age	Male		Female		Sum	
	n	%	n	%	n	%
< 60 years old	7	41.20%	18	58.10%	25	52.10%
60 - 69 years old	6	35.30%	5	16.10%	11	22.90%
≥ 70 years old	4	23.50%	8	25.80%	12	25.00%
X $\pm$ SD	58.19 $\pm$ 16.46					
Sum					48	100

Table 3: Features of echocardiography of the studied patient

Parameter (n = 48)	X $\pm$ SD
Left atrial diameter (mm)	47.83 $\pm$ 12.66
Systolic pulmonary artery pressure	43.12 $\pm$ 12.18
LVEF %	54.6 $\pm$ 9.37

Parameter (n = 48)	X ± SD	
Mitral regurgitation degree	n	%
Medium	11	22.90
Severe	34	70.80
Very severe	3	6.30

Table 4: Characteristics of arrhythmias by 24 - hour electrocardiographic Holter in the study group

Holter ECG 24h	Number of patients (n = 48)	%
Atrial fibrillation	28	58.30%
Premature supraventricular complex	8	16.70%
Supraventricular tachycardia	2	4.20%
Premature ventricular complex	26	54.20%

Among patients with arrhythmias with 24 - hour Holter ECG monitoring, the majority were atrial fibrillation (58.30%), followed by premature ventricular complex (54.20%) and premature supraventricular complex (16.70%). Only 4.16% of patients had supraventricular tachycardia (**table 4**).

Table 5: Association between arrhythmias and mitral regurgitation

Parameter	Medium regurgitation (n = 11) (%)	Severe and very severe (n = 37) (%)	P
Premature supraventricular complex ratio	3 (37.50)	5 (62.50)	> 0.05
Supraventricular tachycardia	1 (50)	1 (50)	> 0.05
Atrial fibrillation	3 (10.70)	25 (89.30)	< 0.05
Premature ventricular complex ratio	8 (30.80)	18 (69.20)	> 0.05
Lown 0	3 (13.60)	19 (86.40)	> 0.05
Lown 1 - 2	6 (40)	9 (60)	> 0.05
Lown 3 - 5	2 (18.20)	9 (81.80)	> 0.05

The incidence of atrial fibrillation increased with the degree of mitral regurgitation ($p < 0.05$), a statistically significant difference. Ventricular and supraventricular arrhythmias tended to be more present in the medium mitral regurgitation group, but the difference was not statistically significant (**table 5**). In the 48 cases in which the study found elevated atrial fibrillation in the group with a left atrial diameter $\geq 45\text{mm}$ ($p < 0.05$), the difference was statistically significant. Ventricular arrhythmias, supraventricular arrhythmias have no difference (**table 6**). The proportion of patients with elevated atrial fibrillation varies with the NYHA degree ($p < 0.05$). Ventricular and supraventricular arrhythmias also tended to be more present in the NYHA II group or higher, but the difference was not statistically significant ($p > 0.05$) (**table 7**). Statistical results showed that the proportion of patients with atrial fibrillation present in patients with $\text{EF}\% < 55\%$ tended to be higher than the $\text{EF}\%$ group $\geq 55\%$ (75% vs 56.80%), however the difference was not statistically significant ($p > 0.05$) (**table 8**). Multivariate logistic regression analysis showed that age and left atrial diameter were independent prognostic factors for atrial fibrillation (**table 9**).

Table 6: Association between arrhythmias and left atrial diameter

Parameter	Left atrial diameter < 45mm (n = 19) (%)	Left atrial diameter ≥ 45mm (n = 29) (%)	p
Premature supraventricular complex ratio	5 (62.50)	3 (37.50)	> 0.05
supraventricular tachycardia	1 (50)	1 (50)	> 0.05
Atrial fibrillation	7 (25)	21 (75)	< 0.05
Premature ventricular complex ratio	11 (42.30)	15 (57.70)	> 0.05
Grading by Lown			
Lown 0	8 (36.40)	14 (63.60)	> 0.05
Lown 1 - 2	6 (40)	9 (60)	> 0.05
Lown 3 - 5	5 (45.50)	6 (54.50)	> 0.05

Table 7: The association of arrhythmias with the degree of heart failure according to the NYHA

Parameter	NYHA I (n = 2) (%)	NYHA II (n = 14) (%)	NYHA III (n = 31) (%)	NYHA IV (n = 1) (%)	p
Premature supraventricular complex ratio	0	4 (50)	4 (50)	0	> 0.05
supraventricular tachycardia	0 (0)	1 (50)	1 (50)	0 (0)	> 0.05
Atrial fibrillation	1 (3.60)	4 (14.20)	22 (78.60)	1 (3.60)	< 0.05
Premature ventricular complex ratio	1 (3.80)	8 (30.80)	17 (65.40)	0 (0)	> 0.05
Lown 0	1 (4.50)	6 (27.30)	14 (63.60)	1 (4.50)	> 0.05
Lown 1 - 2	0 (0)	5 (33.30)	10 (66.70)	0 (0)	> 0.05
Lown 3 - 5	1 (9.10)	3 (27.30)	7 (63.60)	0 (0)	> 0.05

Table 8: Association of arrhythmias with systolic ejection fraction LVEF%

Parameter	EF < 55% (n = 4) (%)	EF ≥ 55% (n = 44) (%)	p
Premature supraventricular complex ratio	1 (12.50)	7 (87.50)	> 0.05
Supraventricular tachycardia	0 (0)	2 (100)	> 0.05
Atrial fibrillation	3 (10.70)	25 (89.30)	> 0.05
Premature ventricular complex ratio	1 (3.80)	25 (96.20)	> 0.05
Grading by Lown			
Lown 0	3 (13.60)	19 (86.40)	> 0.05
Lown 1 - 2	1 (6.7)	14 (93.30)	> 0.05
Lown 3 - 5	0 (0)	11 (100)	> 0.05

Table 9: Multivariate logistic regression model in evaluating factors associated with the incidence of atrial fibrillation in patients with mitral regurgitation.

Factors	B	OR	95% CI	p
Age	0.048	1.049	1.006 - 1.094	< 0.05
Gender	-1.243	0.288	0.077 - 1.084	> 0.05
Left atrial diameter (OG)	0.102	1.108	1.014 - 1.210	< 0.05
Systolic pulmonary artery pressure (Paps)	0.029	1.030	0.979 - 1.083	> 0.05
Left ventricular ejection fraction (LVEF %)	-0.042	0.959	0.894 - 1.027	> 0.05

IV. DISCUSSION

Among patients with arrhythmias with 24 - hour Holter ECG monitoring, the majority were atrial fibrillation (58.3%), followed by premature ventricular complex (54.2%) and premature supraventricular complex (16.7%). Only 4.16% of patients had supraventricular tachycardia. This study is similar to the study of Nirufer Eksi Duran et al., which found that 50.8% of atrial fibrillation in a group of patients with severe mitral regurgitation [7]. The results showed that the incidence of atrial fibrillation increased as the degree of mitral regurgitation increased ($p < 0.05$), a statistically significant difference. In the 48 cases which atrial fibrillation was elevated in the group with left atrial diameter ≥ 45 mm ($p < 0.05$), the difference was statistically significant. Ventricular arrhythmias, supraventricular arrhythmias had no statistically significant difference. This study is like the results of Francesco Grigioni et al. in patients with mitral regurgitation due to degeneration: The annual rates of AF with LA ≥ 50 mm and < 50 mm were $8.4 \pm 1.6\%$ and $2.9 \pm 0.7\%$, respectively ($p < 0.0001$). The incidence of atrial fibrillation in those with left atrial diameter ≥ 50 mm ($67 \pm 8\%$ vs $37 \pm 9\%$, $p = 0.001$) [8]. The proportion of patients with elevated atrial fibrillation differed by the degree of heart failure according to the NYHA ($p < 0.05$), a statistically significant difference. Ventricular and supraventricular arrhythmias also tended to be more apparent in the NYHA II heart failure group or higher, but the difference was not statistically significant ($p > 0.05$). The results of the study show that the frequency of atrial fibrillation tends to increase with the degree of heart failure, according to the NYHA. Because the mechanism of atrial fibrillation in patients with mitral regurgitation worsens as the degree of heart failure

increases, the frequency of atrial fibrillation in the group of patients with more severe heart failure will be higher than in the group with lower levels of heart failure. This can be clearly seen in studies on heart failure patients, such as author Nguyen Duy Toan's study on the association of atrial fibrillation in patients with chronic heart failure, showing that patients with chronic heart failure have atrial fibrillation, the NYHA III - IV group is dominant (72.31%) [9]. The study results showed that atrial fibrillation tended to be elevated in the LVEF group $< 55\%$ compared to the LVEF group $\geq 55\%$, however the difference was not statistically significant. This result differed from K M Krishnamoorthy's study of atrial fibrillation in patients with mitral regurgitation due to rheumatism, which found a lower left ventricular ejection fraction in the group with atrial fibrillation than in the group without atrial fibrillation ($58.8 \pm 8.0\%$ vs $72.4 \pm 7.4\%$, $p = 0.0003$) [10]. Studies on chronic heart failure have also shown an increased frequency of atrial fibrillation in the group with a lower left ventricular ejection fraction. Specifically, Nguyen Duy Toan's study analyzed the left ventricular ejection fraction in the group with atrial fibrillation was lower than the group without atrial fibrillation (45.60 ± 16.52 compared to 51.47 ± 14.06) [9]. The results of my study only indicate that atrial fibrillation tends to be higher in the group with a left ventricular ejection fraction $< 55\%$, but not statistically significant. This is because the number of patients in my sample is somewhat limited, so the results do not show that association.

Advanced age is known as one of the prognostic factors of atrial fibrillation, especially on the base of cardiovascular diseases, the higher the incidence of atrial fibrillation the older the age. The mechanism by which aging affects the occurrence

of atrial fibrillation remains unclear, but it may have something to do with the structural or functional characteristics of the atrial tissue. However, atrial fibrillation also often occurs in young people with mitral regurgitation at sinus rhythm initially. In another study on the frequency and predictors of atrial fibrillation in patients with mitral regurgitation by Nilufer Eksi Duran, the analysis of multivariate logistic regression of advanced age ($p < 0.014$), and left atrial diameter ($p < 0.001$) were predictors of atrial fibrillation in patients with mitral regurgitation, left atrium size is a strong independent predictor for atrial fibrillation [7]. This result is similar to KM Krishnamoorthy's study of atrial fibrillation in patients with severe mitral regurgitation due to rheumatism: logistic regression analysis of factors predicting the presence of atrial fibrillation are age ($p < 0.03$) and left atrial diameter ($p < 0.01$) [10]. One predictor of atrial fibrillation considered stronger than that age is left atrial diameter. Large atrial size has long been noted with chronic atrial fibrillation. In Francesco Grigioni's study on atrial fibrillation in patients with mitral regurgitation due to degeneration, in patients with mitral regurgitation with sinus rhythm at diagnosis, the expansion of the left atrial diameter led to a tendency to develop atrial fibrillation. Specifically in the logistic multivariate regression analysis, this study showed that age and left atrial diameter are 2 independent predictors for atrial fibrillation [8]. The mechanism of atrial fibrillation with left atrial dilation: the anatomical and electrical properties of the left atrium contribute to arrhythmias. Left atrial expansion prior to atrial fibrillation may be associated with a larger transvalve regurgitation current volume or alterations of the atrial heart muscle, or both, but in all cases, left atrial dilation disturbs impulse propagation, resulting in atrial fibrillation. The results of my research are like the above studies. Univariate regression analyses have shown that age and left atrial diameter are 2 independent predictors of the incidence of atrial fibrillation in patients with chronic mitral regurgitation. Other factors in the model such as

gender, systolic pulmonary artery pressure, or left ventricular ejection fraction were not significant in the logistic multivariate regression model.

V. CONCLUSION

Cardiac arrhythmias are a common complication in patients with chronic mitral regurgitation. Atrial fibrillation remains the most common arrhythmia. Age factors and left atrial diameter are 2 factors that increase the likelihood of atrial fibrillation in these patients.

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