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Relationship between mitral annular calcification and first degree atrioventricular block in elderly

Suzan Sahan[a,*], Murat Karamanlioglu[b], Ekrem Sahan[c]

[a] *Çubuk Halil Şivgın Hospital, Department of Cardiology, Ankara, Türkiye*
[b] *Atatürk Sanatoryum Training and Research Hospital, Department of Cardiology, Ankara, Türkiye*
[c] *Ankara Bilkent City Hospital, Department of Cardiology, Ankara, Türkiye*

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Abstract

Aim: In this study, we aimed to reveal the relationship between these two degenerative processes, mitral annular calcification, and first-degree AV block.

Materials and Methods: The data of 2,347 patients over the age of 65 who were examined in the cardiology outpatient clinic. A total of 389 patients with echocardiography results and 12-lead ECGs obtained at the same visit were included in their electronic records. The patient population was divided into two groups as those with or without first-degree AV block, and those with or without mitral annular calcification.

Results: Considering the relationship between mitral annular calcification and first-degree AV block, first-degree AV block was observed more frequently in patients with mitral annular calcification, and this was statistically significant. [(Odds ratio: 6.881; 3.107 – 15.236 (95% CI), p<0.001)].

Conclusion: In our study, it was observed that first-degree AV block was more common in patients with mitral annular calcification. When these conditions are encountered in clinical follow-ups, the association should be kept in mind, and it should be remembered that a conduction defect may develop in patients with mitral annular calcification or valve pathology may occur in patients with a conduction defect.

Introduction

The mitral annulus is the intact fibrous formation that anatomically surrounds the mitral valve and is between the left atrium and the left ventricle. Mitral annular calcification is a degenerative and calcific process that frequently affects the posterior part of the mitral annulus and progresses to the anterior part over time [1, 2]. It may also restrict posterior mitral valve movement over time. Generally considered to be a result of chronic, age-related tissue degeneration leading to progressive calcium accumulation, mitral annular calcification (MAC) is now regarded as an active and regulated molecular process of injury, inflammation and calcium deposition. Although it is mostly asymptomatic, it is discovered incidentally when echocardiography is performed. Mitral annular calcification is more common with increasing age, and may be associated with other cardiovascular system diseases, especially coronary artery disease, stroke and rhythm disorders [3-5]. First-degree (I. Degree) atrioventricular (AV) block is defined as a PR interval longer than 200 ms on the ECG. Slowing of conduction in the AV node is mostly responsible for first-degree AV block. Although its incidence increases with age, it can also occur as a result of cardiovascular system diseases or medical treatment. In this study, we aimed to reveal the relationship between these two degenerative processes, mitral annular calcification, and first-degree AV block.

Materials and Methods

The data of 2,347 patients over the age of 65 who were examined in the cardiology outpatient clinic between January 1,2020 and June 1, 2021 were scanned. Revascularized or indicated for revascularization coronary artery disease, moderate to severe heart valve disease, heart failure, history of heart surgery (coronary, valve or congenital), chronic kidney failure, chronic liver disease, autoimmune or rheumatologic disease, thyroid disease Patients who received radiotherapy and/or chemotherapy to the mediastinum and thoracic regions were excluded from the study. In addition, patients with heart rate <40 bpm or >120 bpm, using antiarrhythmic drugs, especially beta blockers or nondihydropyridine calcium channel blockers,

*Corresponding author:
Email address: suzan-polat@hotmail.de (Suzan Sahan)

and those using digoxin, ivabradine or ranolazine were excluded from the study. Patients with bicuspid aortic valve, prosthetic heart valve, left ventricular ejection fraction <50%, and right and left atrial dilatation reported on echocardiography were not included in the study. Patients with atrial fibrillation, atrial flutter, and paced rhythm in their ECG recordings were also excluded from the study. A total of 389 patients with echocardiography results and 12-lead ECGs obtained at the same visit were included in their electronic records.

ECG findings of all patients were obtained from the Nihon Kohden ECG 1250 device, all ECGs were recorded at a speed of 25 mm/s and amplitude of 10 mV. The data reported automatically by the device was also verified manually by the cardiologist. Recordings with a PR interval longer than 200 ms were accepted as first-degree atrioventricular block. Mitral annular calcification was defined for patients with tricuspid valve with calcification, which was observed in the mitral annulus on echocardiographic images and was compatible with calcification in terms of echogenicity. The patient population was divided into two groups as those with or without first-degree AV block, and those with or without mitral annular calcification.

This retrospective study was conducted in compliance with the principles outlined in the Declaration of Helsinki and the use of data for this retrospective study was allowed by the institutional ethical committee. This retrospective study was approved by the Ankara Atatürk Sanatorium Training and Research Hospital Ethical Committee on February 08, 2023 (no: 2012-KAEK-15/2654).

Statistical analysis

Continuous variables were expressed as mean±SD and categorical variables were defined as percentages (%). A chi-square test was used for categorical variables. The data were tested for normal distribution using the Kolmogorov-Smirnov test. Continuous variables that were normally distributed were analyzed with an independent t-test, and continuous variables with non-normal distribution were analyzed with the Mann-Whitney U test. Multiple logistic regression analysis was used with all of the prespecified factors with a p <0.25 in the univariate analysis. Statistical significance in the multivariate analysis was accepted at p <0.05. IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA) was used for all of the statistical calculations. Statistical significance was defined as a p value less than 0.05.

Results

The mean age of participants was 70.68±5.51 years, 217 (55.8%) were women. Considering the patient groups with and without a diagnosis of first-degree AV block, there was a statistically significant difference in terms of age, creatinine, glomerular filtration rate, calcium, hemoglobin and hematocrit values (p<0.05) (Table 1). Patients with first-degree AV block had higher age (p=0.007) and worse renal function findings (p<0.001). There was no statistically significant difference between the patient groups with and without 1 degree AV block in terms of gender, hypertension, diabetes mellitus, left ventricular systolic function, uric acid, sodium and potassium values. Considering the patients with and without mitral annular calcification in echocardiography, there was a statistically significant difference in terms of age, female gender, hemoglobin and hematocrit values (p<0.05). Although there was a statistically significant difference in glomerular filtration rate, the absence of a significant difference in creatinine values suggested that this situation was related to the age-related calculation method. According to mitral annular calcification status, no significant difference was observed between the two groups in terms of atherosclerotic heart disease, diabetes mellitus, glucose, creatinine, electrolyte parameters and left ventricular ejection fraction (p>0.05) (Table 1).

Considering the relationship between mitral annular calcification and first-degree AV block, first-degree AV block was observed more frequently in patients with mitral annular calcification, and this was statistically significant. [(Odds ratio: 6.881; 3.107 – 15.236 (95% CI), p<0.001)] (Table 2).

When regression analysis was performed in the study population, age, female gender, presence of hypertension, low GFR and low hemoglobin-hematocrit values were found to be associated with the presence of mitral annular calcification in univariate regression analysis. In multivariate regression analysis, only age and gender were associated with the presence of mitral annular calcification (Table 3). In addition, age, high creatinine, low GFR, Calcium, low hemoglobin - hematocrit values were found to be associated with First Degree AV block in univariate regression analysis. In other multivariate regression analysis, low GFR, calcium and potassium values were associated with First Degree AV block (Table 4).

Discussion

With age, a degenerative process occurs in the heart's conduction system and valve structures. Disturbance in the structure of the heart valves and regression in their functions, as well as conduction system defects at different levels are observed. Mitral annular calcification (MAC) is usually detected asymptomatically, as a result of echocardiography or radiodiagnostic imaging studies performed for other indications. Although it has no significant hemodynamic effect, it can cause stenosis in the mitral valve or mitral insufficiency by affecting the valve movements in cases where calcification progresses. Although mitral annular calcification, initially described as a chronic, age-related, degenerative and non-inflammatory process in the fibrous support structure of the mitral valve, mitral annular calcification (MAC) is now regarded as an active and regulated molecular process of injury, inflammation and calcium deposition. Unfortunately, there is no treatment available to slow down or cure this chronic, degenerative and progressive condition. In mitral annular calcification, the degenerative process often begins in the vicinity of the posterior mitral valve and the annulus. Over time, it may spread along the annulus and affect the anterior mitral valve. In addition, mass accumulation at the junction of the posterior mitral valve and mitral annulus can lead to a formation called "caseoma" [6]. Previous studies have found a relationship between mitral annular calcification and cardiovascular events and death. In the study by Fox

Table 1. Demographic and basic biochemical laboratory characteristics of the study group.

Variables	Mitral Annular Calcification (MAC)			Atrioventricular (AV) Block		
	MAC (-) n = 332	MAC (+) n = 57	P value	AV block (-) n = 360	AV block (+) n = 29	P value
Age	70.14±5.25	73.82±5.96	**<0.001**	70.47±5.41	73.31±6.09	**0.007**
Gender						
Female	171 (51.5%)	46 (80.7%)	**<0.001**	203 (56.4%)	14 (48.3%)	0.397
Male	161 (48.5%)	11 (48.5%)		157 (43.6%)	15 (51.7%)	
Hypertension	200 (60.2%)	44 (77.2%)	**0.014**	225 (62.5%)	19 (65.5%)	0.746
Diabetes	72 (21.7%)	17 (29.8%)	0.177	82 (22.8%)	7 (24.1%)	0.867
ASCD	36 (10.8%)	5 (8.8%)	0.638	36 (10.0%)	5 (17.2 %)	0.222
Glucose	110.38±11.15	108.23±4.11	0.728	110.15±40.45	109.20±27.02	0.908
Creatinin	0.94±0.42	0.96±0.52	0.676	0.92±0.40	1.16±0.69	**0.005**
Uric Acid	5.73±1.45	5.82±2.15	0.747	5.72±1.53	5.99±2.01	0.439
GFR	75.48±16.56	68.74±18.89	**0.009**	75.44±16.54	63.44±19.41	**<0.001**
Ca^{+2}	9.54±0.57	9.42±0.72	0.288	9.55±0.57	9.15±0.76	**0.011**
Na^{+}	140.11±0.41	140.10+3.96	0.993	140.12±7.45	139.96±3.11	0.913
K^{+}	4.41±0.41	4.39±0.96	0.713	4.42±0.41	4.31±0.31	0.200
Hgb	13.52±1.91	12.65±1.65	**0.030**	13.46±1.86	12.60±2.19	**0.023**
Htc	41.06±4.62	38.58±4.49	**<0.001**	40.9±4.49	38.39±6.19	**0.007**
LVEF	59.83±3.82	59.16±3.96	0.221	59.80±3.81	59.97±4.28	0.264

ASCD: Atherosclerotic Cardiovascular Disease, AV: Atriovnetricular, GFR: Glomerular Filtration Rate, Hgb: Hemoglobin, Htc:Hematocrite, LVEF: Left Ventricular Ejection Fraction, MAC: Mitral Annular Calcification.

Table 2. Relation between mitral annuler calcification and First Degree Atrioventricular Block.

		First Degree AV Block (AVB)		
		AVB (-) n= 360	AVB (+) n= 29	P value
Mitral Annular Calcification (MAC)	MAC (-) n= 332	317 (95.5%)	15 (4.5%)	<0.001
	MAC (+) n= 57	43 (75.4%)	14 (24.6%)	

Table 3. Univariate and multivariate regression analysis of the study group for mitral annular calcification.

	Mitral Annular Calcification (MAC)					
	Univariate Regression Analysis			Multivariate Regression Analysis		
Variables	Odds Ratio	CI 95%	P value	Odds Ratio	CI 95%	P value
Age	1.107	1.058 – 1.158	**<0.001**	1.105	1.046 – 1.167	**<0.001**
Gender	3.937	1.971 – 7.867	**<0.001**	3.022	1.386 – 6.591	**0.005**
Hypertension	2.234	1.159 – 4.307	**0.016**	2.269	.979 – 5.261	0.056
Diabetes	1.535	.822 – 2.866	0.179	1.733	.849 – 3.535	0.131
ASCD	.791	.297 – 2.108	0.639			
Glucose	.999	.990 – 1.007	0.727			
Creatinin	1.139	.618 – 2.099	0.677			
Uric Acid	1.036	.836 – 1.283	0.746			
GFR	.979	.963 – .995	0.011	1.001	.982 – 1.021	0.888
Ca^{+2}	.717	.388 – 1.323	0.287			
Na^{+}	1.000	.959 – 1.042	0.993			
K^{+}	.868	.410 – 1.840	0.712			
Hgb	.821	.713 – .945	**0.006**	.954	.743 – 1.226	0.714
Htc	.901	.848 – .958	**0.001**	.938	.848 – 1.037	0.210
LVEF	.956	.889 – 1.027	0.221	.691	.983 – 1.071	0.691

ASCD: Atherosclerotic Cardiovascular Disease, AV: Atriovnetricular, GFR: Glomerular Filtration Rate, Hgb: Hemoglobin, Htc:Hematocrite, LVEF: Left Ventricular Ejection Fraction, MAC: Mitral Annular Calcification.

Table 4. Univariate and multivariate regression analysis of the study group for First-Degree Atrioventricular Block

	Atrioventricular (AV) Block			Atrioventricular (AV) Block		
Variables	Odds Ratio	CI 95%	P value	Odds Ratio	CI 95%	P value
Age	1.079	1.019 – 1.142	**0.009**	.950	.855 – 1.055	0.334
Gender	.722	.338 – 1.540	0.399			
Hypertension	1.140	.515 – 2.524	0.747			
Diabetes	1.079	.445 – 2.615	0.867			
ASCD	1.875	.674 – 5.216	0.229	.839	.127 – 5.561	0.856
Glucose	.999	.989 – 1.010	0.908			
Creatinin	1.933	1.103 – 3.389	**0.021**	.417	.106 – 1.642	0.211
Uric Acid	1.112	.851 – 1.453	0.438			
GFR	.965	.946 – .985	**0.001**	.926	.880 – .976	**0.004**
Ca^{+2}	.359	.159 – .814	**0.014**	.339	.128 – .901	**0.030**
Na^{+}	.997	.950 – 1.047	0.913			
K^{+}	.514	.187 – 1.411	0.197	.075	.012 – .461	**0.005**
Hgb	.841	.718 – .985	**0.031**	1.135	.418 – 3.076	0.804
Htc	.906	.842 – .976	**0.009**	.983	.670 – 1.444	0.983
LVEF	.947	.860 – 1.042	0.263			

ASCD: Atherosclerotic Cardiovascular Disease, AV: Atriovnetricular, GFR: Glomerular Filtration Rate, Hgb: Hemoglobin, Htc:Hematocrite, LVEF: Left Ventricular Ejection Fraction, MAC: Mitral Annular Calcification.

et al., the frequency of mitral annular calcification was found to be 14%, and cardiovascular events, cardiovascular death and all-cause death were more common in this patient group [7]. In addition to these studies, Ramaraj et al. showed mitral annular calcification as an independent risk factor for all-cause death in a study involving 2835 patients [8]. In the study of Völzke et al., mitral annular calcification was observed as an independent risk factor for cardiovascular death and death from all causes [9]. In another study, a relationship was found between the presence of mitral annular calcification and the presence of severe obstructive coronary artery disease [3]. In another study, it was shown that the risk of stroke is twice as high in elderly patients with the presence of mitral annular calcification [4]. In another study, atherosclerotic vascular risk was found. It has been stated that hypertension, diabetes, dyslipidemia, obesity and smoking, which are the factors of hypertension, may be risk factors for MAC [10]. In a previous study, it was observed that conduction defects at different levels were observed more frequently in patients with mitral annular calcification, regardless of age and gender [5].

With age, the degenerative process alone can also affect the cardiac conduction system, and Lev's disease defines this condition. Conditions such as sarcoidosis, amyloidosis, hemochromatosis, infective endocarditis, tuberculosis, ischemic heart disease or surgical trauma may affect the cardiac conduction system [11-13]. Degenerative processes in the heart's conduction system and anatomical structure can be expected to accompany each other. Considering that the mitral and tricuspid annular structure forms the hard skeletal structure of the heart and the cardiac conduction system continues on its way through this structure, the degenerative process in the annular structure may affect the cardiac conduction system.

Considering the patient group included in the study, the mean age of patients with first-degree atrioventricular block and patients with mitral annular calcification was statistically significantly higher. The increase in the degenerative process with age may be a reason for the emergence of both conditions. It is shown in Table 2 that these two conditions can often accompany each other. It can be said that in elderly patients, when first-degree AV block is observed on the ECG, it may be necessary to examine and follow up in terms of valve pathology, and to follow up in terms of the possibility of cardiac conduction defect in patients with MAC detected by echocardiography or radiodiagnostic imaging methods. Although there was no significant difference in creatinine in patients with mitral annular calcification, a lower glomerular filtration rate was observed. This is likely to be related to the age factor in the calculation method. In addition, since the study was retrospective, possible disorders in parathormone, phosphorus and calcium metabolism could not be evaluated clearly. Although no significant anemia was observed in patients with both mitral annular calcification and first-degree AV block, hemoglobin and hematocrit values were lower in these groups. Although it is thought that the effect of this process on the degenerative process is not clear, it was thought that it would be appropriate to specify it.

Conclusion

Considering the intracardiac route of the mitral annular structure and cardiac conduction system, it can be predicted that the degenerative process in mitral annular calcification may have an effect on the cardiac conduction system or may be observed together with conduction system defects. In the group we included in our study, it was observed that first-degree AV block was more common in patients with mitral annular calcification. When these conditions are encountered in clinical follow-ups, the association should be kept in mind, and it should be remembered that a conduction defect may develop in patients with mitral annular calcification or valve pathology may occur in patients with a conduction defect.

Ethical approval

This retrospective study was approved by the Ankara Atatürk Sanatorium Training and Research Hospital Ethical Committee on February 08, 2023 (no: 2012-KAEK-15/2654).

References

1. Xu B, Kocyigit D, Wang TKM, Tan CD, Rodriguez ER, Pettersson GB, et al. Mitral annular calcification and valvular dysfunction: multimodality imaging evaluation, grading, and management. Eur Heart J Cardiovasc Imaging. 2022;23(3):e111-e22.
2. Abramowitz Y, Jilaihawi H, Chakravarty T, Mack MJ, Makkar RR. Mitral Annulus Calcification. J Am Coll Cardiol. 2015;66(17):1934-41.
3. Atar S, Jeon DS, Luo H, Siegel RJ. Mitral annular calcification: a marker of severe coronary artery disease in patients under 65 years old. Heart. 2003;89(2):161-4.
4. Benjamin EJ, Plehn JF, D'Agostino RB, Belanger AJ, Comai K, Fuller DL, et al. Mitral annular calcification and the risk of stroke in an elderly cohort. N Engl J Med. 1992;327(6):374-9.
5. Nair CK, Runco V, Everson GT, Boghairi A, Mooss AN, Mohiuddin SM, et al. Conduction defects and mitral annulus calcification. Br Heart J. 1980;44(2):162-7.
6. Deluca G, Correale M, Ieva R, Del Salvatore B, Gramenzi S, Di Biase M. The incidence and clinical course of caseous calcification of the mitral annulus: a prospective echocardiographic study. J Am Soc Echocardiogr. 2008;21(7):828-33.
7. Fox CS, Vasan RS, Parise H, Levy D, O'Donnell CJ, D'Agostino RB, et al. Mitral annular calcification predicts cardiovascular morbidity and mortality: the Framingham Heart Study. Circulation. 2003;107(11):1492-6.
8. Ramaraj R, Manrique C, Hashemzadeh M, Movahed MR. Mitral annulus calcification is independently associated with all-cause mortality. Exp Clin Cardiol. 2013;18(1):e5-7.
9. Volzke H, Haring R, Lorbeer R, Wallaschofski H, Reffelmann T, Empen K, et al. Heart valve sclerosis predicts all-cause and cardiovascular mortality. Atherosclerosis. 2010;209(2):606-10.
10. Elmariah S, Budoff MJ, Delaney JA, Hamirani Y, Eng J, Fuster V, et al. Risk factors associated with the incidence and progression of mitral annulus calcification: the multi-ethnic study of atherosclerosis. Am Heart J. 2013;166(5):904-12.
11. Baruteau AE, Probst V, Abriel H. Inherited progressive cardiac conduction disorders. Curr Opin Cardiol. 2015;30(1):33-9.
12. Birnie DH, Sauer WH, Bogun F, Cooper JM, Culver DA, Duvernoy CS, et al. HRS expert consensus statement on the diagnosis and management of arrhythmias associated with cardiac sarcoidosis. Heart Rhythm. 2014;11(7):1305-23.
13. Ayyildiz P, Kasar T, Ozturk E, Ozyilmaz I, Tanidir IC, Guzeltas A, et al. Evaluation of Permanent or Transient Complete Heart Block after Open Heart Surgery for Congenital Heart Disease. Pacing Clin Electrophysiol. 2016;39(2):160-5.