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MITRAL ANNULAR CALCIFICATION: A MARKER OF SEVERE CORONARY ARTERY DISEASE IN PATIENTS UNDER 60 YEARS OLD

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Background: Mitral Annular calculation (MAC) is a fibrous, degenerative calcification of the mitral valve support ring. Mitral Annular calcification is a common condition. In other population-based study, the prevalence of MAC was reported as 13%. It is more common in women and people over 70 years old. Most previous pathological and clinical studies have proposed that MAC may be a form of atherosclerosis and suggested that coronary atherosclerosis and MAC have similar etiology. **Methods:** A Cross Sectional Study was conducted at Sir Salimullah Medical College & Mitford, Dhaka, Bangladesh. Patients of coronary artery disease with or without MAC who were selected for coronary angiography. Group–1: Patients with mitral annular calcification. Group–2: Patients without mitral annular calcification. **Results:** Total 79 patients was selected, mean age was 48.94±8.1 years. In MAC group male patients were 41(85.4%) & female 7(14.6%). In no MAC group male patients were 19(61.2%) & female 12(38.8%). Significant sex difference was observed among MAC & no-MAC group (p=0.005). In this study, 66% of patients with MAC and 33% of patient without MAC had single vessel disease, 68% patients with MAC and 32 % without MAC had double vessel disease, 83% of patient with MAC and 17% patient without MAC had triple vessel disease, and 100% of patient with MAC had left mean coronary artery disease, and 12% of MAC and 88% of patient without MAC had no significant coronary artery disease. Among 2 left main patients, 100% had severe MAC. Among 15 patients of TVD none was mild,

2(20%) moderate and 13(54.1%) had severe MAC. Among 15 patient of DVD 2(13.3%) were mild, 5 (33.4%) moderate and 8(53.3%) had severe MAC. Among 14 patients of SVD 10(71.4%) were mild, 3(30%) moderate and 1(4.2%) had severe MAC. Among 2 patient of non-significant coronary artery disease, 2(14.3%) without CAD had mild MAC and none had moderate and severe MAC. Multivariate analysis shows MAC (p=0.007) as an independent predictor for coronary artery disease. **Conclusions:** This study finding suggest that in patient aged less than 60 years, mitral annular calcification associated with an increased prevalence of severe and extensive obstructive coronary artery disease. Mitral annular calcification may be an easily detected echocardiographic marker of the presence of obstructive coronary artery disease, especially when associated with angina symptoms.

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INTRODUCTION

Mitral annular calcification has been associated with various systemic and cardiac disease with a higher prevalence in women and patients over 70. A possible association between mitral annular calcification and coronary artery disease has recently been suggested. A sub group the Framingham Heart Study, which consisted of 1197 patients, revealed that MAC was represent in 14% of these patients [1,2,3]. The association between MAC and mean risk factors for coronary artery diseases hypertension, diabetes and hyperlipidemia was suggested. Mitral annular calcification a marker of severe coronary artery disease [4,5,6]. Mitral annular calcification may result in mitral stenosis, mitral regurgitation, infective endocarditis, atrial arrhythmias, and heart block [7-11]. It is one of the known independent risk factors for systemic embolism and stroke and its severity as measured by the thickness off the valve in M mode is linearly correlated with the risk of stroke. An increased prevalence of mitral annular calcification has also been found in patient with systemic hypertension, increased mitral valve stress mitral valve prolapse, raised left ventricular systolic pressure, aortic valve stenosis, chronic renal failure secondary hyperparathyroidism, and atrial fibrillation. Along with other calcific valuvar processes mitral annular calcification is associated with a high prevalence of risk factors for the development of coronary atherosclerosis. S Atar and colleagues screened 17,735 patients found that. 6207 (35%) had mitral annular calcification and 885 (5%) were also <65 years old; coronary angiography was done in 100 of the latter (64 men; 36 women), mainly for anginal symptoms or a positive stress test [12]. A control group (n=121; 88 men, 33 women) was identified from 2840 consecutive patients screened. There was no significant difference between the groups in patient characteristics, Indication for angiography, or atherosclerotic risk factors. As such, it may also be a manifestation of generalized atherosclerosis in the elderly population. However, age is more closely related to this condition and to other forms of valuvar calcification than any other factors, and this may strengthen its association with coronary artery disease in a younger population [13]. Finally, Acarturk and colleagues found that the presence of mitral annular calcification and aortic valve calcification on transthoracic echocardiography may help in predicting coronary artery diseases and should be added to conventional risk factors [8]. Absence of mitral annular calcification and aortic valve calcification is a stronger predictor for absence of coronary artery diseases than all conventional risk

factors, except diabetes mellitus, patients with mitral annular calcification and aortic valve calcification should be taken into consideration for the presence of significant coronary artery diseases and thereby for diagnostic and therapeutic interventions in order to improve the Prognosis [14]. Recently, Adler and colleagues found that mitral annular calcification was a marker of a high prevalence and severity of coronary artery disease in patients with a mean age of 70 years undergoing coronary angiography [4]. The clinical significance of mitral annular calcification in a selected population of younger patients has not yet been defined. Our aim in this study was to determine whether there is a correlation between the presence of mitral annular calcification on echocardiography and the finding of significant obstructive coronary artery disease on cardiac catheterization in patients aged less than 65 years. In such a relatively young group of patients, mitral annular calcification may serve as an important and specific marker of severe coronary artery disease.

MATERIALS AND METHODS

In the department of cardiology, Sir Salimullah medical college & Mitford Hospital, Dhaka, this cross-sectional observational study was conducted & by purposive sampling technique total 100 patients were selected & divided into two groups based on the presence or absence of mitral annular calcification.

Group-1: (Presence of MAC)

Group -2: (Without MAC)

Patients with aged >60 years, Valvular heart disease, Valvular prosthesis, Post PTCA or Post CABG were excluded from the study. After having matched inclusion and exclusion criteria the patients were selected for this study.

Echocardiographic technique:

Complete 2 dimensional & M-mode echocardiography was performed in all patients with the 2.5 MHz transducer of phased-array sector scanner. The 2-dimensional echocardiographic criteria for MAC included an intense echo-producing structure located at the junction of the atrioventricular groove and posterior mitral valve leaflet on the parasternal long axis, apical 4 chambers, or parasternal short axis views. Cardiac valve calcification was defined as the presence of bright echoes of more than one mm on one or more cusps of the mitral valve or mitral annulus. The degree of valvular calcification was graded as mild (spot like calcification <2mm thickness and more than 5mm in length), or severe (shadowing or extensive calcification of the valvular annulus, the semi-lunar cusps, or both). All patients were evaluated independently by two cardiologists' experts in echocardiography. In case of disagreement, a third examiner was consulted. The observer who made the diagnosis of MAC were blinded to the presence or absence of CAD.

Coronary Angiography:

Coronary angiography was done to all patients. Number of coronary arteries affected & degree of stenosis was recorded for the studying of severity of coronary artery disease. Cardiac Catheterization and angiography were performed by the Judkins technique. Angiographic films were interpreted by the angiographer who had no knowledge of the echocardiographic result. Obstructive CAD was defined as either ≥50% of reduction of the internal diameter of the left main coronary artery or ≥70% reduction of the at least one major epicardial coronary artery.

RESULTS

This is a cross sectional study a total of 79 patients were enrolled in this study. Patients were divided into two groups on echocardiographic findings and subsequently coronary angiography was done. The findings obtained from data analysis are presented below:

Table-I: Age distribution among study groups (N=79)

Age (yrs.)	Group		Mean
	MAC (n=48)	**No MAC (n=31)**	
20-29	1(50%)	1(50%)	48.94±8.17
30-39	2(40%)	3(60%)	
40-49	15(60%)	10(40%)	
50-59	29(61.7%)	18(38.3%)	
Total	48(58.5%)	31(41.5%)	

P value reached from Pearson Chi-square test.

Table-I shows in MAC group 20-29 were 1(50%), 30-39 were 2(40%), 40-49 were 15(60%) and 50-59 were 29(61.7%). In no MAC group 20-29 were 1(50%), 30-39 were 3(60%),40-49 were 10(40%) and 50-59 were 18(38.3%).(p=0.453).

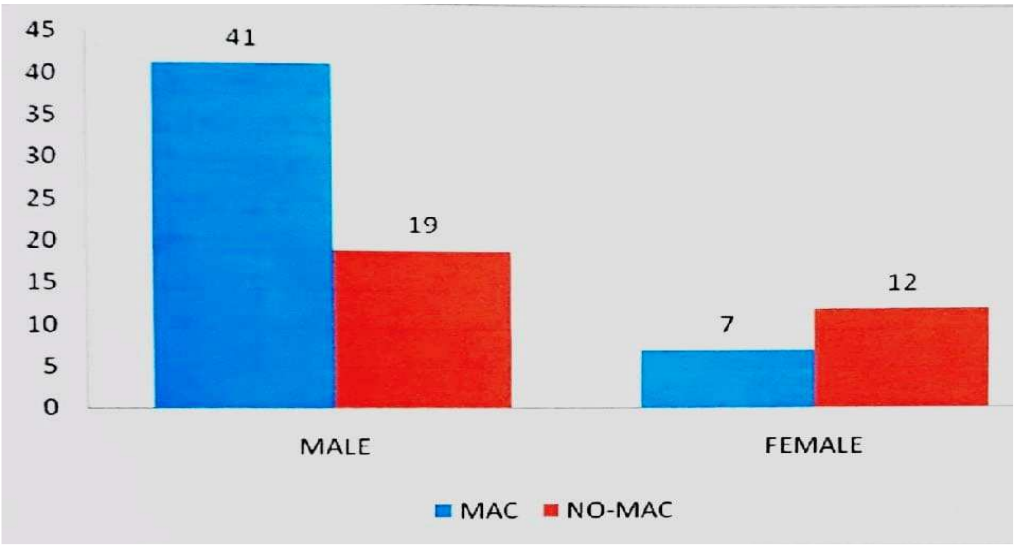

Figure-1: Sex distribution among study group.

Fig-1 Shows in MAC group male was 41(68.3%) & Female 7(31.7%). In no MAC group male were 19(61.3%) & Female 12(38.7%). Significant sex difference was observed among MAC & NO MAC group (p=0,005)

Table-II: Comparison of cardiovascular risk factors between Mac & no Mac groups (N=79)

Risk Factor	MAC Present		MAC Absent	Total	P - Value
Smoking	No-Smoker	8(28.6%)	20(71.4%)	28	0.001
	Smoker	39(76.5%)	12(23.5%)	51	
HTN	Absent	36(65.5%)	19(34.5%)	55	0.136
	Present	11(45.8%)	13(54.2%)	24	
DM	Absent	38(61.3%)	24(38.7%)	62	0.584
	Present	9(52.9%)	8(47.1%)	17	
Dyslipidemia	Absent	11(47.8%)	12(52.2%)	23	0.212
	Present	36(64.3%)	20(35.7%)	56	

P value reached from Pearson Chi-square test

Table-II Shows in MAC group smoker was 39(76.5%) & in no MAC group 12(23.5%). Hypertension was present in MAC group 11(45.8%) & in no MAC group 13(54.2%). Diabetes was present in MAC group 9(52.9%) & in no MAC group 8(47.1%). Dyslipidemia was present in MAC group 36(64.3%) & in no MAC group 20(35.7%). Smoking is significantly higher in MAC group (p=0.001).

Table-III: Distribution of patient according to severity MAC (n=48)

Severity	Frequency	Percent
Mild	14	29.2
Moderate	10	20.8
Severe	24	50.0
Total	48	100.0

Table-III showed among 48 cases 14(29.2%) had mild MAC, 10(20.8%) moderate and 23(50.0%) had severe MAC.

Table-IV: Distribution of CAD in patients with MAC (N=48)

CAD	**MAC (n=48)**			**Total**
	Mild	**Moderate**	**Severe**	
LM	0(0%)	0(0%)	2(8.4%)	2
TVD	0(0%)	2(20%)	13(54.1%)	15
DVD	2(14.3%)	5(50%)	8(33.3%)	15
SVD	10(71.4%)	3(30%)	1(4.2%)	14
Normal	2(14.3%)	0(0%)	0(0%)	2
Total	14(100%)	10(100%)	24	48

Table-IV Showed among 2 left main patients, 100% had severe MAC. Among 15 patients of TVD none was mild, 2(20%) moderate and 13(54.1%) had severe MAC. Among 15 patients of DVD 2(14.3%) were mild, 5(33.4%) moderate and 8(53.3%) had severe MAC. Among 14 patients of SVD 10(71.4%) were mild, 3(30%) moderate and 1(4.2%) had severe MAC. Among 2 patients of non-significant CAD, 2(14.3%) without CAD had mild MAC and none had moderate and severe MAC

Table-V: Distribution of severity of CAD by MAC (N=48)

CAD	**MAC (n=48)**			**p - value**
	Severe	No Severe	Total	
Severe	15(62.5%)	2(8.3%)	17(35.4%)	<0.001
Not Severe	9(37.5%)	22(91.7%)	31(64.6%)	
Total	24(100%)	24(100%)	48(100%)	

P value reached from Pearson chi-square test

Table-V showed the correlation between the severity of MAC group and severity of coronary artery disease as done by Pearson chi-square test. Correlation revels the severity of MAC is significantly related to severity of coronary artery disease.

Table-VI: Angiographic finding in patients with& without MAC on the basis of number of vessels involved (N=79)

Stenosis in coronary arteries	MAC(n=48)	No MAC(n=31)	p-value
LM Stenosis	2(100%)	0(0)	0.001
TVD	15(83.3%)	3(16.7%)	0.001
DVD	15(68.2%)	7(31.8%)	0.001
SVD	14(66.7%)	7(33.3%)	0.001
No Significant CAD	2(12.5%)	14(87.5%)	0.001

P value reached from Pearson Chi-square test

Table-VI Shows in MAC group Left main 2(100%), triple vessel disease 15(83.3%), Double vessel disease 15(68.2%), Single vessel disease 14(66.7%), No significant coronary artery disease 2(12.5%). In no MAC group Left main 0(0%), Triple vessel disease 3(16.7%), Double vessel disease 7(31.8%), Single vessel disease 7(33.3%), No significant coronary artery disease 14(87.5%). In MAC group LM, TVD, DVD, SVD & no significant CAD are significantly higher in MAC group than no MAC group (p=0.001).

Table-VII: Angiographic findings among MAC & no MAC group according to coronary vessels involved.

Stenosis in coronary	Angiographic findings		P Value
	MAC (n=48)	No MAC (n=31)	
LAD	47(59.5%)	32(40.5%)	0.001
LCX	22(66.7%)	11(33.3%)	0.193
RCA	47(59.5%)	32(40.5%)	0.004
LM	2(100%)	0(0%)	0.345

P value reached from Pearson Chi-square test

Table-VII showed in MAC group Left anterior descending 47(59.5%), Left circumflex 22(66.7%), Right coronary artery 47(59.5%) & left main 2(100%). In no MAC group Left anterior descending 32(40.5%), Left circumflex 11(33.3%), Right coronary artery 32(40.5%) & left main 0(0%). LAD & RCA lesion are statistically significant in MAC group.

Table-VIII: Logistic regression analysis of the factors associated with the presence of significant coronary artery disease.

Factor	P Value	OR	95%CI
MAC	0.007	10.618	1.902 to 59.260
Dyslipidemia	0.035	4.999	1.123 to 22.251
Smoking	0.723	1.441	0.191 to 10.852
Male Sex	0.198	3.587	0.513 to 41.793
DM	0.128	5.106	0.624 to 41.793

P value reached from Pearson Chi-square test

Table-VIII Showed Mitral annular calcification (p=0.007), Dyslipidemia (p=0.035) are independent risk factor of the presence of significant coronary artery disease. Patient who had mitral annular calcification are 11 times higher risk for developing coronary

artery disease. Patients those are dislipidaemic and diabetic are 5 times higher risk for developing coronary artery disease. Male sex and smoking have 3.5 times and 1.4 times higher risk for developing CAD respectively.

DISCUSSION

The main finding of my study is that mitral annular calcification is an independent predictor of the presence of severe stenosis (> 70% diameter stenosis) in at least one major epicardial coronary artery on angiography in patients presenting with chest pain under the age of 60. Moreover, mitral annular calcification is an indicator of a higher prevalence of triple vessel disease. In women under 60 years of age, the absence of mitral annular calcification was an indicator of the absence of obstructive coronary artery disease. These finding are consistent with the finding of Atar et al [12]. Angiographic findings of this study on the extent and severity of obstructive coronary artery disease are similar to those reported by Adler et al [4]. Both studies show that mitral annular calcification is a marker and independent predictor of the presence of extensive coronary artery disease. However, the mean age of the patients in Adler's study was 70 and Atar's was 57 years, whereas the mean age of our patients was 49 years [4,12]. The strong association of mitral annular calcification with obstructive coronary artery disease in this relatively young group of patients significantly increases the specificity of this condition as a marker of coronary artery disease. In contrast to my results, Nair and colleagues et al [15], did not find a correlation between mitral annular calcification and coronary heart disease in patients younger than 60 years. However, the patients in Nair's study did not undergo coronary angiography, and the diagnosis of coronary artery disease was based solely on clinical data. Benjamin and colleagues et al [16], first reported an increased incidence of coronary artery disease from the Framingham database. They found that patients with mitral annular calcification had a higher prevalence of coronary artery disease than a control group (28.8% v 17.4%, p=0.006). These finding also similar to my study are finding. In this study I found significantly more coronary artery disease in mitral annular calcification (MAC) group than no MAC group (96% vs 56%, p=0.001) & triple vessel disease are significantly higher in MAC group than no MAC group (78% vs 22%, p=0.001). These results are similar to the finding of Atar et al [12], where they found significantly more obstructive coronary artery disease in patients in the index group than in the control group (88% v 68%, p= 0.0004) and, patients in the index group had a higher prevalence of significant left main coronary artery stenosis (14% v 4%, p=0.009) and a higher prevalence of triple vessel coronary artery disease (54%Vs 33%, p=0.002). The prevalence of double and single vessel disease was not different between the two groups. Moreover, I also found significant double vessel disease & single vessel disease which may be due to small sample size, race and geographical variation. Mitral annular calcification and dyslipidemia are strongly associated with the development of coronary artery disease. Patient who had mitral annular calcification are 11 times higher risk for developing coronary artery disease. Patients those are dyslipidemic and diabetic are 5 times higher risk for developing coronary artery disease. Male sex and smoking have 3.5 times and 1.4 times higher risk for developing CAD respectively. Boon and colleagues found an association with mitral annular calcification and coronary artery disease [17]. Age, female sex, hypertension, diabetes mellitus, and hypercholesterolemia were strongly associated with mitral annular calcification, with odd ratios varying between 2.2 and 2.8. Thus, a significant association of mitral annular calcification with known major risk factors for coronary disease may partly explain the association of mitral annular calcification with significant obstructive coronary artery disease on angiography. Nonetheless, whether mitral annular calcification is only a marker for the presence of significant coronary artery disease

or is involved in the atherosclerotic process remains to be elucidated [18]. It is, however, likely that calcific processes are part of the spectrum of arteriosclerosis. The strong association between mitral annular calcification and extensive coronary artery disease in my study and Adler et al [3] suggests hathis mitral valve pathology becomes more common when atherosclerosis is extensive and involves all three major epicardial coronary arteries.

CONCLUSIONS

This study finding suggest that in patients aged less than 60 years, mitral annular calcification is associated with an increased prevalence of severe and extensive obstructive coronary artery disease. Mitral annular calcification may be an easily detected echocardiographic marker of the presence of obstructive coronary artery disease, especially when associated with angina symptoms.

Limitations

My study was done in patients who had both echocardiography and coronary angiography for various indications. This may have caused a bias in selecting patients with a high pretest likelihood of having coronary artery disease. However, both groups were selected in the same way and were similarly affected by the selection bias, yet showed a highly significant difference in their angiographic findings. Nonetheless, our results are only preliminary and should be confirmed in population-based studies.

Conflict of interest: None

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