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## ■ Original Article

# The relation between mitral annular calcification and dietary habits: Impact of desertification

## *Yaşlılarda diyet alışkanlıkları ile mitral anüler kalsifikasyon arasında ki ilişki: Çölleşmenin etkisi*

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### Abstract

**Aim:** This study is planned to find out the potential role of diet on the formation of mitral annular calcification initially thought to be age-related process.

**Material and Methods:** A total of 85 patients with mitral annular calcification and 91 patients with no- mitral annular calcification were enrolled in this cross- sectional study. A validated, self-administered, comprehensive 36 parameters-diet history questionnaire was applied to all patients on a voluntary basis. Univariate and multivariate analysis were done with possible risk factors.

**Results:** Mitral annular calcification was found significantly and independently higher in patients living in Kırıkkale, Kirsehir, Yozgat, Aksaray, Nevsehir and Mardin( OR= 1. 65, 95% CI= 1. 25 – 2. 89; p< 0, 001). These Central Anatolia cities' have soils with higher calcium, and higher salt, and lower humidity and soils have becoming more saltier and more calcified with desertification effects. Mitral annular calcification was found significantly and independently lower in patients living in Ordu and Sinop( OR= 1. 78, 95% CI= 1. 02 – 2. 89; p< 0. 01). These Black Sea Region cities' have the most humid soil types. Mitral annular calcifications were found significantly higher in aged( OR= 2. 55, 95% CI= 1. 05 – 3. 93; p=0.05),in women( OR= 1. 35, 95% CI= 1. 05 – 1. 89; p=0.04), in diabetes( OR= 1. 85, 95% CI= 1. 15 – 3. 21; p< 0. 001 )and in statin usage( OR=3. 01, 95% CI= 1. 59 – 5. 72; p= 0. 01). We didn't find any correlation between foods and with mitral annular calcification( p= 0. 23).

**Conclusion:** Our study couldn't demonstrate any association between mitral annular calcification and with a special food group but made to think for the first time in the literature a possible correlation between mitral annular calcification and with low humidity Cental Anatolia soil types.

**Keywords:** diet; climate; calcification; mitral annulus; ageing

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## Öz

**Amaç:** Bu çalışma önceleri yaşlanma ile alakalı bir olay olarak düşünülen mitral anüler kalsifikasyon oluşumunda diyetin olası rolünü araştırmak için planlandı.

**Gereç ve Yöntemler:** Mitral anüler kalsifikasyonu olan 85 adet ve olmayan 91 adet hasta bu çalışmaya dahil edildi. Tüm hastalara gönüllülük esasına bağlı olarak onaylı ve kapsamlı diyet hikayesini içeren, kendi kendilerine cevaplayabildikleri 36 parametrelilik anket uygulandı. Olası risk faktörlerinin tek yönlü ve çok yönlü analizleri yapıldı.

**Bulgular:** Mitral anüler kalsifikasyon Kırıkkale, Kırşehir, Yozgat, Aksaray, Nevşehir ve Mardin şehirlerinde yaşayan hastalarda belirgin ve bağımsız olarak fazla bulundu (OR= 1, 65, % 95 CI= 1, 25 - 2, 89; p< 0, 001). Bu şehirler İç Anadolu Bölgesinin en fazla kurak, tuzlu ve kalsifik topraklarına sahip şehirleridir ve çölleşme etkisi ile daha tuzlu ve kalsifik olmaktadır. Mitral anüler kalsifikasyon Ordu ve Sinop şehirlerinde yaşayanlarda anlamlı olarak düşüktü (OR= 1, 78, % 95 CI= 1, 02 - 2, 89; p< 0, 01). Bu şehirler Karadeniz Bölgesinin en fazla nem içeren topraklarının bulunduğu şehirlerdir. Mitral anüler kalsifikasyon yaşlıda (OR= 2, 55, % 95 CI= 1, 05 - 3, 93; p=0, 05), kadınlarda (OR= 1, 35, % 95 CI= 1, 05 - 1, 89; p= 0, 04), diyabeti olanlarda (OR= 1, 85, % 95 CI= 1, 15 - 3, 21; p< 0, 001) ve statin kullananlarda (OR=3, 01, % 95 CI= 1, 59 - 5, 72; p= 0, 01) belirgin olarak yüksek bulundu. Mitral anüler kalsifikasyonu olan ve olmayan hastaların beslenmelerinde anlamlı bir fark bulunmadı (p= 0, 23).

**Sonuç:** Çalışma sonuçları, mitral anüler kalsifikasyon ile beslenme arasında bir bağlantı gösteremedi ancak literatürde ilk kez mitral anüler kalsifikasyon ile Anadolu Bölgesi'nin kurak toprak yapısı arasında bir ilişki olabileceğini düşündürdü.

**Anahtar kelimeler:** diyet; iklim; kalsifikasyon; mitral anulus; yaşlanma

## Introduction

Mitral annular calcification (MAC) is a chronic progressive calcific degeneration of mitral annular support tissue is known to be as an age-related process that leading to valve insufficiency and other heart diseases [1]. It is usually detected incidentally on echocardiography. The Framingham database demonstrates a high correlation between MAC and coronary artery diseases, and a modest correlation with myocardial infarction, unstable angina pectoris, heart failure and non-haemorrhagic stroke [2]. The reported prevalence of MAC is 8%- 15% in the general population and 35% in patients with coronary heart disease patients and; the number of cases is increasing in the globally because of the growing number of aged individuals [3,6]. Although MAC was initially thought to be part of the ageing process, a growing body of evidence suggests the involvement of other mechanisms, like such as chronic kidney disease, atherosclerosis, calcium-phosphorus metabolism, vitamin K and D deficiencies [7,8]. Despite high incidence rate, the clinical relevance of MAC is grossly underappreciated. In particular, the association between MAC and dietary habits has never been examined. To test for correlations between dietary factors and MAC, we planned this study to assess the dietary intake with a validated questionnaire in patients with MAC and no - MAC patients.

## Material and Methods

### Study population

Following getting our trial permission from our hospital local ethics and trial committee, the trial number was 2018/ 2017, a total of 176 patients treated in our hospital outpatient clinics from January 2017 to December 2018 were included in this survey. All patients were voluntarily completed a 36-item self-administered, validated diet history questionnaire focusing on dietary intake of meat, meat products, egg, milk, dairy products, carbohydrate, vegetables, fruits, fish. Patients were divided on two groups as 85 patients with MAC and 91 patients with no-MAC echocardiographic examination. We excluded patients with chronic heart disease, heart failure, any systemic disease, chronic kidney disease and patients using vitamin and mineral supplements.

### Dietary assessment

Habitual food consumption and nutrient intake were assessed using self-administered The Short Diet Questionnaire (SDQ) is a 36-item screener developed diet history of questionnaire [9]. The questionnaire asks about the consumption foods to choose seven possible answers to indicate how often they had consumed foods ( never, >1 times a week, once per week, 2- 3 times per week, 4- 6 times per week, once per day, and more than 2 times per day). Combined with standard serving sizes,

the intake frequencies were converted into the average daily intake in grams for each food item.

### Other variables

Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters, and subjects were classified by BMI category (BMI < 20, 20- 24.9, 25- 29.9, > 30 kg/m<sup>2</sup>). Obesity was defined as BMI > 25 kg/m<sup>2</sup>. A self-reported questionnaire was used to assess current smoking (yes, no). Hypertensive status was defined as a systolic blood pressure recording 140 mm Hg or a diastolic blood pressure recording 90 mm Hg based on the mean of 2 measurements, a patient's self-reported history of hypertension, or antihypertensive treatment (yes, no). Diabetes mellitus was defined by a patient's self-report, insulin use, oral hypoglycemic use (yes, no). Hypercholesterolemia was defined as total serum cholesterol 240 mg/dl, a patient's self-report, or the presence of lipid-lowering treatment drug usage. Homeland and resident cities that classified by years (< 5 years, 6- 9 years, and > 10 years) were defined by patient's self report. Patients' with MAC and no- MAC demographic and clinical characteristics were listed in Table 1.

**Table 1.** Baseline demographic characteristics of the patients with or without mitral annular calcifications (MAC)

Variables	MAC Group (n=85)	No- MAC Group (n=91)	P value
Age, year	66.2±7.2	69.2±5.5	0.05
Female sex, n (%)	96 (54.5)	82 (45)	0.04
BM, kg/m <sup>2</sup>	26.1±4.4	25.9±4.8	0.023
Diabetes Mellitus, n (%)	37 (21.4)	22 (13.6)	<0.001
Hypertension, n (%)	65 (38.4)	66 (37.5)	0.34
Hyperlipidemia, n (%)	51 (29.3)	54 (31.5)	0.53
Cigarette smoking, n (%)	68 (39.2)	66 (38.3)	0.67
Medications			
ASA/ Clopidogrel, n (%)	14 (8.4)	11 (6.1)	0.56
Statin, n (%)	28 (16.3)	19 (11.3)	0.01
ACEI/ ARB, n (%)	29 (17.4)	31 (18.1)	0.56
BB, n (%)	22 (13.5)	28 (16.5)	0.23
CCB, n (%)	10 (6.3)	17 (7.2)	0.56
OAD/ insulin, n (%)	22 (13.9)	25 (15.8)	0.12
BMI (kg/m <sup>2</sup> )	27±5.6	26±4.5	0.67
Estimated GFR, mean (SD)	1.7±76	2.4±23	0.45

Data are expressed as means± standard deviation (SD) for continuous variables, and as percentages for dichotomous variables. P-values denote overall differences between groups.

### Echocardiography

Baseline two-dimensional and Doppler echocardiographic examination was performed by experienced echocardiographer. Studies were performed and measurements taken according to the recommendations of the American Society of Echocardiography. MAC was defined as an intense echocardiographic-producing structure with highly reflective characteristics that was located at the junction of the atrioventricular groove and the posterior or anterior mitral leaflet on the parasternal long-axis, apical 4- or 2-chamber, or parasternal short-axis view. The severity of MAC, expressed as maximal thickness in millimeters, was measured from the leading anterior to the trailing posterior edge at its greatest width. Calcification thickness 1 mm and 4 mm was considered mild to moderate, and 4 mm was considered severe. Severity of MAC is typically reported qualitatively, with calcification of less than one- third of the annulus graded as mild and greater than two- thirds graded as severe.

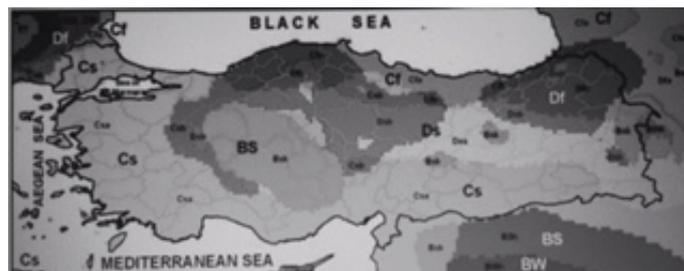
### Statistical analysis

SPSS software (Version 18.0, SPSS Inc. Chicago, IL, USA) was used for statistical analysis. Variables were analyzed using the Kolmogorov- Simirnov test. Categorical variables were presented as percentages and parametric variables were presented as mean ± standard deviation. Non-parametric variables were expressed as median (minimum- maximum). The normally distributed numeric variables were analyzed with the Student's t-test, and non-normally distributed variables were evaluated by the Mann-Whitney U test variance analysis. The categorical variables compared with Chi-square test. P value < 0.05 was accepted as statistically significant.

### Results

Among the 176 patients analyzed in this study, MAC was observed in 81 (46.02%). Median age was 66.2±7.2 in MAC group, and 69.2±5.5 in no- MAC group. Table 1 shows demographic and clinical characteristics of participant with MAC and no MAC. Participants in MAC group was significantly older (OR= 2.55, 95% CI= 1.05 – 3.93; p=0.05) Female ratio was significantly higher (OR= 1.35, 95% CI= 1.05 – 1.89; p=0.04) in MAC group. Diabetes was significantly higher (OR= 1.85, 95% CI= 1.15 – 3.21; p< 0.001) and statin usage was also significantly higher (OR=3.01, 95% CI= 1.59 – 5.72; p= 0.01) in MAC group. Body mass index, hypertension, hyperlipidemia, serum cholesterol, smoking, estimated glomerular filtration and drugs show no significant difference between in both groups. Food intake shown in Table 2 were not significantly different in patients with MAC and no- MAC (p= 0.023). Fish and corn consumption were significantly higher in patients

from Black Sea Region(  $p = 0.01$ ). Wheat consumption was significantly higher in patients from Middle Anatolia Region (  $p = 0.002$ ). Butter, cheese, spicy foods and organ meats consumption were significantly higher in patients from Eastern and Southeastern Anatolia Region(  $p = 0.002$ ). MAC was significantly and independently higher in patients living in Central Anatolia Region cities' as Kırıkkale, Kirsehir, Yozgat, Aksaray and Nevsehir and Mardin(  $OR = 1.65$ , 95%  $CI = 1,25 - 2.89$ ;  $p < 0.001$ ) shown in Table 3. These cities are in the region of Central Anatolia Region with cold snow forest climate and soils have been becoming more salty and calcified with climate changes as less rainy climate and desertification[10]. ( Figure 1) MAC was significantly lower in patients living in Ordu and Sinop cities(  $OR = 1.78$ , % 95  $CI = 1.02 - 2.89$ ;  $p < 0.01$ ). These cities have the most humid soils of Turkey. This study results showed for the first time a significant association between soils with high calcium, high salt and low water from Anatolia Region and with MAC.



**BS:** Steppe Climate **Cs:** Temperate rainy climate with dry summer or Mediterranean climate **Ds:** Cold snow forest climate with dry summer **Df:** Cold snow forest climate humid in all season.

### Discussion

MAC tends to be more prominent with ageing; however in our study, patients with MAC from cities located in the steppe were significantly younger. The prevalence of MAC increases with increasing age (mean ages, 70 and 76 years); in this age group, the prevalence of MAC was 42% [11]. Other underlying processes, such as atherosclerosis, altered mineral metabolism, or increased mechanical stress, also promote the development of MAC. As another pathophysiological factor, our study results showed that MAC was significantly and independently associated with low-humidity steppe soils. To the best of our knowledge, this is the first study to show a correlation between soil types and MAC formation. Previous studies showed a good correlation between MAC and chronic kidney disease [12]. Additionally, diets high in vitamin K have been shown to promote reverse aortic calcification, and vitamin K may play a role in vascular calcification in animal and in vitro studies, although the evidence is less clear [13]. Data on the pathophysiology of MAC are limited, but it is thought to be initiated by endothelial disruption at the junction between the mitral annulus and ventricular myocardium. Focal calcific deposits in regions of microinjury and lipoprotein accumulation may then coalesce over time into the dense, fibrotic bands that are macroscopically evident as MAC [14-15].

Echocardiography is the primary imaging modality for identification and characterisation of MAC, which is commonly found as an incidental finding on echocardiographic imaging. MAC is characteristically identified on parasternal and apical views of the heart with acoustic shadowing of structures indicative of calcification. Although mitral valve leaflets and chordae tendineae are generally not involved, calcification may progressively accumulate in the subvalvular region beneath the posterior leaflet, with encroachment on the leaflet and into the myocardial wall. Cohort studies have demonstrated an association of MAC with atherosclerotic disease and adverse cardiovascular events or arrhythmias, including atrial fibrillation, conduction system disease,

**Table 2.** Food intakes result from the questionnaire converted into grams/ per day

Food	MAC Group (n= 85)	No- MAC Group (n= 91)	P values
Fruits (g/ day)	85± 29	89± 31	0.45
Vegetables (g/ day)	120± 45	142± 62	0.91
Meat (g/ day)	82± 43	88± 53	0.23
Dairy (g/ day)	56± 34	49± 62	0.54
Eggs (g/ day)	23± 76	28± 31	0.08
Grain, (g/ day)	549± 43	557± 65	0.14
Bread (g/ day)	377± 55	423± 42	0.52
Rice (g/ day)	92± 17	86± 82	0.43
Corn (g/ day)	53± 29	56± 65	0.56
Legumes (g/ day)	223± 29	231± 32	0.34
Fish (g/ day)	65± 34	59± 87	0.45

Data are mean± SD.

**Table 3.** The incidence of MAC in different regions.

Regions, n (%)	MAC Group (n= 85)	No- MAC Group (91)	P values
Central Anatolia	68	60	0.001
Black Sea	7	17	<0.01
Marmara	0	0	0
Eastern Anatolia	6	9	0.1
Southeastern Anatolia	4	5	0,02
Mediterranean	0	0	0

P values < 0,05 considered significant.

obstruction of left ventricular inflow, symptomatic mitral stenosis, stroke and increased mortality [16- 17]. Significant cardiovascular morbidity has been associated with MAC, but limited data exist regarding its association. This is the first study to demonstrate that MAC was independently associated with the soil type and the humidity in which foods are grown. Previous studies reported an association between diet and cardiovascular disease [18, 19]. But the lack of definitive evidence has left clinicians, scientists and the public uncertain about the best foods to recommend and consume [20]. Our study has some limitations. First, our study shares the same limitations with all survey studies and was a small study without a follow-up period. We also used echocardiography as a diagnostic method; if computed tomography had been used, we could diagnose more calcifications in addition to coronary calcification and other calcifications. Genetic counselling may also be helpful for understanding MAC aetiology. The results of this study show that dietary habits themselves seem to be contributing factors of MAC formation.

According to the latest scientific assessment report of the Intergovernmental Panel on Climate Change (IPCC, 2007), the Earth's annual average surface temperature has increased by approximately 0.8°C over the past 100 years, with large regional variations. Evidence of global warming comes from the warming of the oceans, increasing sea levels, glaciers melting, sea ice retreating in the Arctic and diminished snow cover in the Northern Hemisphere [21]. Climate changes in Turkey from 1950 to 2010, included a decrease in humidity and ongoing desertification process in the Central Anatolia Region.

## Conclusion

Humidity changes make soils more calcific and salty, disarrange mineral components and the results of our study confirmed that foods that are grown in this region may be causing to increase the calcification in heart tissue. Besides the consequences of malnutrition and drought, desertification may create problems for human bodies directly.

## Declaration of conflict of interest

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