A Study of Some Echocardiographic Parameters in Patients with Aortic Valve Sclerosis

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Abstract

Background: Aortic valve sclerosis (AVS) is an important clinical disorder that often presented asymptomatically in many adult peoples.It carries an adverse outcome for cardiovascular system. It is an early stage of aortic valve stenosis as well as being a marker for cardiovascular disease.

Objectives: The study aims to determine relationships and its levels between AVS and some echocardiographic parameters that associated with this important acquired valvular disorder.

Materials & Methods: The study was carried out on 93 patients with aortic valve sclerosis (cases group) and 97 patients without AVS (control group) , patients were attended to Marjan Teaching Hospital from 1st of December 2010 to 30 of May 2011, echocardiographic study had been done for each one of them.

Results: The study results revealed that there was a high significant decrease ($p<0.01$) in ejection fraction(EF%) in patients of AVS compared with the non AVS group as well as very high significant increase ($p<0.001$) in each of pressure gradient (PG) and blood flow velocity across aortic valve in patients of AVS compared with the non AVS group.

In addition, the study showed that there was high significant increase ($p<0.01$) in left atrial dimension(LAD),significant increase ($p<0.05$) in interventricular septum thickness (IVS) and significant increase ($p<0.05$) in posterior wall thickness (PWT) of AVS group of patients compared with the non AVS group, besides to high significant difference ($p<0.01$)in aortic valve regurgitation, mitral annular ring calcification and aortic root calcification between the two groups.

Conclusion: In adult with aortic valve sclerosis (AVS) is associated with echocardiographic findings of preclinical CVD: increase in pressure gradient and blood flow velocity across aortic valve, decrease in ejection fraction% with abnormal left ventricular geometry (increase interventricular septum thickness, posterior wall thickness), increase left atrial size, aortic valve regurgitation, mitral annular ring calcification and aortic root calcification that may contribute to the adverse prognosis associated with aortic valve sclerosis.

الخلاصة

الخلفية: تصلّب الصمام الأبهر هو حالة مرضية مهمة، غالباً ما تحدث بدون أعراض في كثير من الاشخاص البالغين و يحمل آثار جانبية لجهاز الدوران فهو يعد مرحلة مبكرة من تضيّق الصمام الابهر بالاضافة الى كونه مؤشر لامراض جهاز الدوران.

الأهداف: تهدف هذه الدراسة الى قياس مدى العلاقة بين تصلب الصمام الابهر وبعض المتغيرات المقاسة بواسطة جهاز فحص القلب بالامواج فوق الصوتية(الايكو) المرتبطة بمرض صمّام القلب المكتسب هذا.

المواد والعمل: نُفذت هذه الدراسة على ٩٣ مريضاً مصاباً بتصلب في الصمام الابهر (مجموعة حالات) و ٩٧ مريضاً ليس لديهم تصلب في الصمام الابهر (مجموعة قياسية)، هؤلاء المرضى راجعوا مستشفى مرجان التعليمي منذ الاول من شهر كانون الاول ٢٠١٠ وحتى الثلاثين من شهر آيار ٢٠١١، أُجري فحص القلب بالامواج فوق الصوتية (الايكو) لكل مريض منهم.

النتائج: اظهرت نتائج الدراسة إنخفاضاً معنوياً ($p<0.01$) في نسبة الضخ الجزئي لدى مرضى تصلب الصمام الابهر مقارنةً بالمجموعة القياسية، بالاضافة الى زيادة معنوية عالية جداً ($p<0.001$) في كل من تيار الضغط على جانبي الصمام الابهر وسرعة جريان الدم في مرضى تصلب الصمام الابهر مقارنة بالمجموعة القياسية،بالاضافة الى ذلك، اظهرت الدراسة زيادة معنوية عالية($p<0.01$) في ابعاد الاذين الايسر وزيادة معنوية($p<0.05$) في سمك الحاجز بين البطينين وسمك الجدار الخلفي للبطين

الايسر لدى مرضى تصلب الصمام الابهر بالمقارنة بالمجموعة القياسية،إضافة الى فرقٍ معنوي عالٍ ($p<0.01$) في تهدل الصمام الابهر ،تصلب حلقة الصمام التاجي وجذر الصمام الابهر بين المجموعتين.

الاستنتاج: في البالغين المصابين بتصلب الصمام الابهر(AVS) انه يرتبط مع النتائج المقاسة بواسطة الايكو ،ما قبل السريرية لامراض القلب والاوعية الدموية ، كزيادة في انحدار ضغط الدم وسرعة تدفق الدم عبر الصمام الابهر وانخفاض في نسبة الضخ الجزئي و الابعاد غير الطبيعية للبطين الايسر (زيادة سمك جدران البطين الايسر) وزيادة حجم الاذين الايسر ،تهدل الصمام الابهر، تصلب حلقة الصمام التاجي وجذر الصمام الابهر مما قد يؤدي الى المآل السيئ المرتبط بتصلب الصمام الابهر.

Introduction

Calcific aortic valve disease ,which is a slowly progressive disorder with a disease continuum that ranges from mild valve thickening without obstruction of blood flow, termed 'aortic valve sclerosis' to severe calcification with impaired leaflet motion 'aortic stenosis '.It was previously considered a degenerative wear and tear process of the trileaflets valve, now known to be on the basis of research over the past two decades including (histopathologic, epidemiologic, and animal studies)**:** a complex biologically active process with many mechanistic similarities to atherosclerosis but also with some differences [1]. There is 21–29 % of adults aged > 65 years exhibit aortic valve sclerosis (AVS), which characterized by leaflet thickening and /or calcification without commissural fusion has an association with an increased cardiovascular risk [2].The histopathologic and clinical data suggested that mechanisms involved in the disease include active processes that are similar to those occurring in atherosclerosis, such as impairment of endothelium, inflammation, and lipid infiltration [3].

Despite multiple common risk factors, a discrepancy in coexisting prevalence exists between CAVD and coronary artery disease because many patients with significant CAD do not have aortic valve disease and vice versa, so understanding of both condition is of vital importance to see the sights for development of aortic valve sclerosis that associated with increased morbidity and mortality [4]

Aims of study

Aims of study are to show the relationship and it's level between the aortic valve sclerosis(AVS) and each of the following echocardiographic parameters:

1.Pressure gradient (PG) across aortic valve.
2.Blood flow velocity across aortic valve.
3.Ejection fraction (EF%).
4.Left atrial dimension (LAD).
5.Interventricular septum (IVS)thickness.
6.Left ventricular posterior wall thickness (PWTx).
7.Mitral annular calcification (MAC).
8.Aortic root calcification (ARC).
9.Aortic valve regurgitation (AR).

Materials and Methods

Patients:

The study conducted from 1st December 2010 to 31/May 2011, one hundred ninty patients of both genders (106 females and 84 males) were included to achieve the aim of study at Marjan teaching hospital in Babylon Province.

The patients had been referred to the echocardiographic unit at Marjan Teaching Hospital , they were of different heights and weights,the patients age were ranged from the mean age of patients in years was (58±12), they were subjected to echocardiographic study by the same senior, the patients were divided into

two groups: The first group involved 93 patients (45 males and 48 females) had aortic valve sclerosis (AVS). The second group involved 97 patients (58 males and 39females) didn't have (AVS). Patients with congenital heart diseases, valvular heart diseases and those with poor window on echocardiographic examination were excluded from study.

Characteristics of the ultrasound machine:

The operator machine of echocardiography in Marjan teaching hospital that used in the study is Phillips which provided with transducer for cardiac usage and had the capability of producing images in the following modes :

A- Two-Dimensional mode (2D).

B- Motion or M-mode .

C- Doppler; which has different types: Pulsed wave (PW),continuous wave (CW) and color flow Doppler [5].

Methods:

The chosen probe of echocardiographic machine placed on the anterior chest wall between the third to fifth intercostal space slightly to the left of the sternal border to find appropriate cardiac window from which the measurements had been taken [6].

1.Diagnosis of Aortic valve sclerosis:

A normal aortic valve and root are seen at M-Mode as two parallel signals, representing the anterior and posterior aortic walls, move in an anterior direction during systole, and in a posterior direction during diastole [7].

By using 2D technique via parasternal long axis view and short axis view, as in figure (1), the AV was analyzed, the AVS was defined as (focal increased echogenicity, thickening, or calcification of the leaflets with normal valve motion and a normal or only mildly increased antegrade velocity across the valve) definitions vary slightly but typically an outflow velocity less than 2.5m/s was used to separate sclerosis from mild aortic stenosis [7].

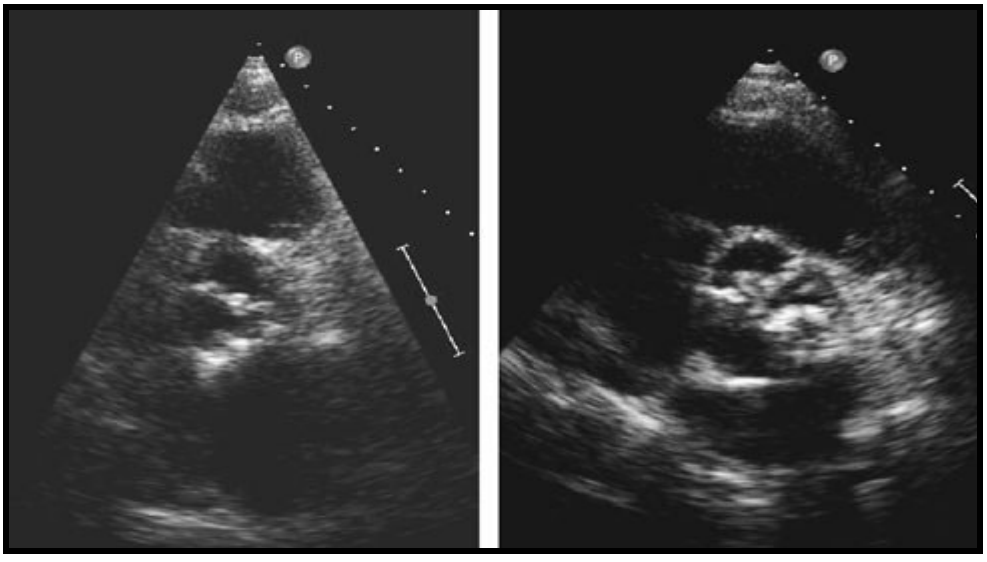

Figure 1 Examples of aortic valve sclerosis. Left panel: Patient with minimal aortic valve calcification;Right panel:Patient with massive aortic valve calcification.

2. LV Systolic Function (EF%):

EF% was estimated in values at difference of 5% , LV systolic function was assessed by M-mode ,2D techniques enhanced by visual assessment :

M-mode allowed measurements of LV dimensions and wall thickness, the

internal dimension measurements in end-systole (LVESD) and end-diastole (LVEDD) were made at the level of the MV leaflets tips in the parasternal long axis view, measurements were taken from the endocardium of the left surface of (IVS) to the endocardium of LV posterior wall (PW), the ultrasound beam were as perpendicular as possible to (IVS)[7].

2-D techniques were used to provide a visual assessment of LV systolic function both regional and global, LV systolic function could evaluated by multiple planes as parasternal long and short axis, apical 4-chamber and apical two-chamber view[5].

Visual estimation for EF% from the 2-D images with a reasonable correlation with EF% that measured quantitatively by echocardiography or other techniques by experienced observer is clinically useful [5].

3.Blood flow velocity & pressure gradient across aortic valve:

In all patients, continuous Doppler was used to record the peak flow velocity through the aortic valve. Peak systolic flow velocity was defined as the highest value recorded at one of the standard sites (as the apical) used for recording trans-aortic flow velocity [7]. So from the peak aortic systolic flow velocity the peak systolic pressure gradient of the aortic valve was calculated, the same was for the mean systolic pressure gradient that calculated by planimetry of the peak systolic flow velocity through the aortic valve [7,8].

4.Left Atrial Dimension(LAD) Measurement:

Because no single tomographic view conveys complete information about a three dimensional structure of left atrium (LA) so, the left atrium was visualized in a number of echocardiographic views including the parasternal long axis, short axis and the apical four and two-chamber views and combination of two or more imaging planes used for this purposes [9]. LA size was determined using M-mode echocardiography.From the parasternal window linear dimension approximating the anteroposterior plane was measured at end-systole just before mitral valve opening (when LA volume was maximum) to be standerd, this plane passed through the aortic valve [9].

5.Left ventricular wall thickness measurement:

Interventricular septum (IVS) and left ventricular posterior wall (PW) are seen at the base and midventricular level in the long-axis view with the 2D approach that allowed us to measure IVS and left ventricular PW thicknesses at the end of diastole [7].

6.Mitral annular calcification (MAC) detection:

MAC was defined by an echo-dense structure located at the junction of the atrioventricular groove and the posterior mitral leaflet on the parasternal long- axis, apical 4-chamber, or parasternal short-axis view[10].

7.Aortic root calcification (ARC) detection:

The aortic root calcification (ARC) was assessed visually by using 2Dtechnique through the parasternal long-axis PLAX view [10].

8.Aortic valve regurgitation (AVR) detection :

Aortic valve regurgitation (AVR) can be detected by either color flow imaging or continuous-wave Doppler ultrasound, while 2D imaging provides only a tiny indirect evidence for presence of AVR, with color flow imaging , detection of AVR based on identification of the flow disturbance downstream from the valve orifice, continuous-wave Doppler detection of AVR based on identification of the high-velocity jet through the regurgitant orifice [7]. Transthoracic

echocardiography is the most commonly used imaging tool ,it is indispensable in the diagnosis of the presence and degree of aortic insufficiency, its etiology,valve morphology and presence of vegetations and calcification, quantification of pulmonary hypertension, and determination of ventricular function [12].Two-dimensional (2D) echocardiography, along with Doppler color-flow mapping, has been used to diagnose and assess the severity of AR [12].

a.**Color Doppler imaging:** Evaluation of aortic valve regurgitation severity based on the size of flow disturbance in the chamber receiving the regurgitant jet in at least two views ,the AVR signal is diastolic [7]. The severity of AR can be defined by the ratio of the proximal jet width to left ventricular outlet tract width, with a ratio of less than 25% consistent with mild AR and a ratio of greater than 65% diagnostic of severe AR [12].

b.**Continuous-wave Doppler:** Signal intensity, antegrate flow velocity and shape of velocity curve are the types of information about the valve severity that could be obtained from Continuous-wave Doppler approach [7].

9.Statistical Analysis:

All continuous values were expressed as means ± standard deviation (SD), The Student *t* test was used to compare continuous variables. Chi-squar test; odd ratio,was used to examine the risk estimate in the categorical data between different groups.The data were analyzed by using computerized SPSS program version 17. P value < 0.05 is considered to be statistically significant [13].

Results

1.Systolic Function(EF%): Regarding the mean EF %was (53 ± 15 %) in the patients of AVS group and it was (59 ± 13%) in patients with non sclerosis AV group, so AVS independently associated with systolic dysfunction (low EF%) in significant relationship ($p<0.01$),See table 1.

2.Blood Flow Velocity: The results of this study showed that the mean flow velocity in AVS group of patients was (1.4±0.4 m/s) this result showed significant difference ($p <0.001$)as compared to the non AVS group of patients (1.2±0.26 m/s) See table 1.

3.Pressure Gradient (PG): The result of our study revealed that the mean PG across AV of AVS group was (9 ± 6 mmHg) which was significantly ($p<0.001$) higher than the mean PG of the non sclerosis group of patients (6.3 ± 3.5 mmHg).See table 1.

4.Left Atrial Dimension(LAD):

This study revealed that the mean LAD in patients with AVS was (38 ± 5 mm) compared with the non sclerosis group which was (35 ± 4.5 mm), there was significant difference($p<0.01$) between the two groups of patients.

Moreover , after indexed the LAD values of the AVS and the non sclerosis group of patients to body surface area ,they were (2.14 ± 0.3 cm/m^2) ; (1.9 ± 0.2cm/m^2)respectively, which revealed a highly significant difference ($p<0.001$) See table 1.

5.Left Ventricular wall thicknesses: The mean interventricular septum thickness (**IVS**) of AVS group was (10.7 ± 2.5 mm) when compared to that of the non AVS one (10 ±1.6mm) , a significant difference ($p<0.01$) was found.

The mean posterior left ventricle wall thickness **(PWTx)**in patients with AVS group was (10.6 ± 2mm) when compared with (10 ±1.8mm) in patients of non AVS group, there was statistically significant difference ($p<0.05$). between AVS and non AVS group of patients.See table 1.

Table 1 Shows continuous echocardiographic variables distribution in aortic valve sclerosis (AVS) and non (AVS) groups of patients.

Echocardiographic variables vs* AVS			
Variable	**AVS patients Mean±SD**	**Non AVS patients Mean±SD**	**P value**
EF%	**53 ± 15**	**59 ± 13**	**<0.01**
Velocity(m/s)	**1.4 ± 0.4**	**1.2 ± 0.26**	**<0.001**
PG(mmHg)	**9 ± 6**	**6.3 ± 2.5**	**<0.001**
LAD(mm)	**38 ± 5**	**35 ± 4.5**	**<0.01**
IVSTx (mm)	**10.7 ± 2.5**	**10 ± 1.6**	**<0.05**
PWTx(mm)	**10.6 ± 2**	**10 ± 1.8**	**<0.05**

AVS:aortic valve sclerosis, **EF%:**ejection fraction, **PG**:pressure gradient, **LAD**:left atrial dimension, **IVSTx**: interventricular septum thickness, **PWTx**: left ventricular posterior wall thickness.

6.Aortic Regurgitation and AVS: Table (2) revealed that out of 93 patients with AVS ,14 patients (15.1%) had aortic valve regurgitation(AR) while only one patient out of the 97 non sclerosis AV patients (1.04%) had AR. It was significant relationship (p<0.001) that patients with AVS were 17.01 times as likely as patient with normal AV to have AVR (OR: 17.01 , 9 5 % C I : 2 . 1 9 - 1 3 2 . 2) .

Table 2 Shows Aortic Regurgitation (AR) distribution in aortic valve sclerosis (AVS) group and non (AVS) group of patients.

Aortic Regurgitation (AR) vs* AVS			
	AVS patients	**Non AVS patients**	**Total**
AR(positive)	**14 15.1%***	**1 1.04%**	**15 7.9%**
AR(negative)	**79 84.9%***	**96 98.96%**	**175 100%**
Total	**93 100%**	**97 100%**	**190 100%**

***P** value:<0.001,**AR**:aortic regurgitation,**AVS**:Aortic Valve Sclerosis

7.Mitral Annular Calcification (MAC) and AVS:

Table (4) revealed that out of 93 patints with AVS we found 19 patients (20.4%) had Mitral Annular ring Calcification (MAC) compared with 3 patients (3.1%) with non sclerosis AV who had MAC, the statistical results showed that the relationship between the AVS and MAC was significant (p<0.001), (OR=7.48; 95%CI: 2.13-26.25).

Table 3 Shows Mitral Annular Calcification (MAC) distribution in AVS group and non AVS group of patients.

Mitral Annular Calcification (MAC) vs* AVS			
	AVS patients	**Non AVS patients**	**Total**
(MAC)positive	**19 20.4%***	**3 3.1%**	**22 11.6%**
(MAC)negative	**74 79.6%***	**94 96.9%**	**168 88.4%**
Total	**93 100%**	**97 100%**	**190 100%**

***P** value:<0.001, **AVS:**Aortic Valve Sclerosis

8.Aortic root Calcification and AVS:

The results of aortic root calcification (ARC) table (5) illustrated that; from all patients with AVS, 12 patients (13%) had aortic root calcification compared with 2 patients (2.1%) of non sclerosis group of patients who had ARC.So the prevelance of ARC was higher among patients with AVS than with non sclerosis group, which was significant relationship (p<0.001),(OR: 6.57, 95% CI: 1.43-30.22 ;p<0.001).

Table 4 Shows Aortic Root Calcification distribution in AVS group and non AVS group of patients.

Aortic Root Calcification(ARC) vs* AVS			
	AVSpatients	**NonAVS patients**	**Total**
(ARC)positive	**12 13%***	**2 2.1%**	**14 7.4%**
(ARC)negative	**81 87%***	**95 97.9%**	**176 92.6%**
Total	**93 100%**	**97 100%**	**190 100%**

*P value:<0.05, **ARC**: Aortic Root Calcification , **AVS**:Aortic Valve Sclerosis**.**

Discussion

1.Systolic Function (EF%):

For ejection fraction (EF%)values ,we had found a significant decrease (p<0.01) among aortic sclerosis patients as shows in table [1], this result agrees with this result agrees with **Palmiero**,**e*t al***., [2] whom also had found a higher prevalence of systolic dysfunction and left ventricular hypertrophyin such patients.These findings suggest that aortic sclerosis represents a marker of additional cardiac injury in vulnerable patients [2] and may be related to high prevelance of IHD patients in AVS group who had lower ejection fraction.

2.Blood flow velocity and pressure gradient:

Regarding blood flow velocity and pressure gradient across aortic valve there were a highly significant differences (p<0.001) between patients with AVS and the patients of non AVS group as shows in table (1) and this data was concurrent with **Stritzke, *et al.,***[14] who demonstrated that even mild aortic valve sclerosis is associated with a functionally detectable decrease in aortic valve area ,a higher peak transvalvular flow (Vmax) and a consecutive increase of the transvalvular pressure gradient, afterload increment could lead to left ventricular remodeling [14].

3.Left Atrial Dimension (LAD):

The results illustrated in table (1) revealed that there was significant difference($p<0.01$) between AVS group and non AVS group of patients that AVS patients had higher LAD than the non AVS group, this result agrees with **Agno**,***et al.,***[15].Increased LA size is associated with the occurrence and chronicity of atrial fibrillation [16]. In our study, LA size remained significantly higher in the AVS group even after indexed to body surface area for both males and females, the left atrial enlargement and mitral annular calcification shares with aortic sclerosis risk factors such as hypertension, coronary artery disease and the power of an index of cardiovascular risk [16].

In particular, left atrial enlargement is a marker of diastolic dysfunction in the general population , when used together with Doppler echocardiography can identify elderly patients with worse diastolic dysfunction who are at an increased risk of developing atrial fibrillation [17].

4.Left Ventricular wall thickness:

Our finding of significant increase ($p<0.05$) in LV thicknesses with AVS is consistent with findings of other researchers [2,15,18].When patients with electrocardiographic evidence of left ventricular hypertrophy (LVH) are considered, the prevalence of aortic sclerosis increases to 40%, as demonstrated by Oslen,*et al*.[19]

The incidence of left ventricular hypertrophy was found to be significantly higher in the AVS patients , independent of the presence of hypertension, on the other hand, various neurohumoral factors, including the rennin angiotensin system, have been shown to play a pivotal role in the causation of AVS and left ventricular hypertrophy [2,15]. In a population-based sample that includes mostly clinically healthy individuals, Stritzike,*et al.,* demonstrated that even mild aortic valve degeneration was associated with a functionally detectable decrease in aortic valve area and a consecutive increase of the transvalvular pressure gradient,as expected this increase in afterload is translated to concentric hypertrophy of left ventricular wall [14].

5.Aortic valve regurgitation (AVR):

Resulted data illustrated in table (2) revealed that there was significant difference ($p<0.001$) in aortic valve regurgitation (AVR) between AVS group and non AVS group of patients. AVR is the failure of leaflets to coapt versus stiffness of fibrotic or calcified leaflets,so the more the calcification process,the more likely to aortic valve insufficiency to occur [12].

6.Mitral Annular Calcification:

The results in table (3) showed that there was significant difference ($p<0.001$) in MAC between the AVS and non AVS patients groups ,it was more prevalent in patients with AVS group.This result agrees with the result of Cosmi et al.,[20] who demonstrated that there is strong association of AVS with MAC and this may reflect the effect of underlying atherosclerosis[21].This association may reflect parallel hemodynamic 'wear and tear' on the aortic and mitral valves due to old age and hypertension,thus both valves undergo extra stress specially in elderly and hypertensive patients .The presence and the severity of MAC has been found to be a predictor of morbidity and mortality as demonstrated by the CHS and Framingham Heart Study [22]. Individuals with MAC have been shown to have a higher prevalence and risk of severe CAD and total cardiac death, also an association with increased risk of incident atrial fibrillation [23]. Morover, the data of

Agno,*et al*.,[15] suggests that certain mechanisms capable of inducing changes in myocardial properties, resulting in increased filling pressures, and changes in the structure of mitral annulus, are strictly related to change in the aortic valve that probably represent a more generalized sclerotic process of the vascular tree.Although the primary initiator of the disease process is probably the same, the mechanism activated locally in each structure is different and remains difficult to clarify [16].

7.Aortic Root Calcification (ARC):

This study revealed that there was a highly significant difference ($p<0.001$) in ARC in patients with AVS than the AVS group of patients,as showed in table (4), this result goes together with data obtained by [24].

The focal lesions of sclerosis process on the aortic side of the leaflets can extend deep into the aortic annulus [12].A widespread extension of the calcification appears to portend a higher cardiovascular risk [24].The prevalence of AVS, mitral annulus calcification (MAC) or ARC by echocardiography is common and their presence is highly associated with aortic atheromatous disease and coronary, carotid and peripheral artery disease [25].

MAC,AVS and ARC frequently coexisted and are associated with coronary risk factors and CAD in the elderly ,that when coronary risk factors are taken into consideration , the presence of multiple calcium deposits in the mitral annulus, aortic valve or aortic root appears to be a marker of CAD in men less than 55 years old and women [25].

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