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Correlation between the incidence and severity of Aortic Valve Calcific Stenosis and Carotid Atherosclerosis

Samir Rafla[1]*, Sahar Hamdy[2], Mohamed Loutfy[3] and Mohamed Elneklawy[4]

[1-4]Alexandria Faculty of Medicine, Cardiology Dept. Alexandria, Egypt

Email: dr.samirrafla@yahoo.com

ABSTRACT

Background: Aortic valvular calcification (AVC) and carotid arterial disease (CaAD) have a high prevalence in elderly patients (pts). Aim of the work: To study the severity and relation of carotid plaques and coronary atherosclerotic lesions (CAD) in pts with calcific aortic sclerosis/stenosis.

Methods: The study included 70 patients, 50 who had Aortic valve calcification (AVC) or stenosis, which was detected in TTE (systolic gradient more than 10 mmHg). The 20 other patients had Aortic valve thickening only or mild calcification (systolic gradient less than 10 mmHg). Risk factors were recorded.

Results: Compared with pts with aortic valve thickening only, AVC was associated with significantly higher incidence of carotid plaques. . In the presence of aortic valve calcification/stenosis, there was 86% (43/50) incidence of carotid plaques or stenosis (0.002) and 75% incidence of coronary heart disease or LV hypertrophy p=0.037. IMT was abnormal in 80% and 40% in the two groups (P=0.01). Those with as systolic gradient > 35 mmHg (total 15), 12 patients, had carotid stenosis > 30% in (80%). Those with less AS (55 patients) had carotid stenosis > 30% in 2 only; p=0.0001.

Conclusions: We found that aortic valve calcific stenosis with systolic gradient above 35 mmHg is associated with incidence of carotid stenosis in most patients (80%). This is new parameter to our knowledge. Thus carotid study is recommended in this level of stenosis.

Key words: Carotid plaques, aortic calcific stenosis, intima media thickness, coronary heart disease.

INTRODUCTION

Obstructive coronary disease (OCAD) and aortic valve calcium: Aortic valve sclerosis as detected with echocardiography is associated with a 50% increase in cardiovascular mortality[(1)]. Furthermore, older subjects with aortic valve sclerosis have a 1.8-times higher chance of a new coronary event developing than subjects without valvular aortic sclerosis [(2).] This increase in cardiovascular events and mortality may be related to sub clinical CAD.

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Study showed that the presence of AVC was an independent predictor of advanced OCAD, thus possibly reflecting the atherosclerotic burden rather than just a degenerative change. Furthermore, patients with a high AVC score (> 110) had the highest prevalence of severe aortic stenosis (50%) [(3-10).]

Common carotid artery and coronary artery:

Atherosclerosis of the CCA and its role in the estimation of the atherosclerotic burden of the entire vasculature has been most frequently examined, as the CCA is the most easily accessible artery.[(11-14)] The prognostic value of CCA IMT was also confirmed.[(15)] The cardiovascular health study (almost 6000 subjects) found that a thicker CCA IMT is associated with higher risk of myocardial infarction and stroke in adults without history of cardiovascular disease[(16)].

Relation of carotid intima-media thickness and aortic valve sclerosis:

The association between an early forms of atherosclerotic disease, increased carotid intima-media thickness (IMT), and an early stage of calcific aortic valve disease, aortic valve sclerosis (AVS), could be of great significance in risk stratification. Also, the presence and

extent of aortic valve calcification has been demonstrated to be directly correlated with atherosclerotic risk factors and atherosclerotic disease, suggesting that it could represent a marker of atherosclerosis. The perspective of atherosclerotic process and AVS having common pathologic mechanisms has been emphasized in previous research. [17] Also, several studies have demonstrated an association between AVS and classic atherosclerotic risk factors (age, male gender, hypertension, smoking, diabetes, and hypercholesterolemia). [17-19]

The associated between carotid IMT and aortic valve calcification has been demonstrated in different populations: patient with end-stage renal disease,.[20] elderly subjects,[21] and even healthy subjects.[22, 23]

Aim of the work

To study the correlation between severity of carotid plaques and coronary atherosclerotic lesions in patients with calcific aortic sclerosis/stenosis.

PATIENTS AND METHODS

The study included 70 patients who had Aortic valve calcification (AVC) or atherosclerotic stenosis or just thickening. Findings were detected in TTE as local areas of increased echogenicity and thickening of the aortic valve leaflets. The 70 patients were divided into 2 groups: 50 patients had Aortic valve calcification or stenosis with systolic gradient > 10 mmHg, and 20 patients who had aortic valve thickened /calcification with systolic gradient < 10 mmHg (taken as controls). In spite of the low number of the two groups, statistical analysis can be applied. Study was conducted in the Cardiology department in 2012

The apparatus used was Philips Envisor 7 with 7 MH probe for carotid study.

Inclusion criteria:

Patients with echocardiographic finding of aortic valve thickening or calcification or atherosclerotic stenosis were included. We picked these cases even before doing the echo by auscultation of the aortic area and suprasternal area and finding systolic murmur.

Exclusion criteria:

Patients with rheumatic heart disease were excluded. Consent was taken from all patients, echo for the heart and carotids were done free of charge, they were informed of the value of this study. The ethical committee of the Alexandria Faculty of Medicine accepted the protocol.

Baseline evaluation: All patients were subjected to the following:

History taking and clinical examination, emphasizing on:

Cardiovascular risk factors (smoking, diabetes, hypertension, dyslipidemia, and positive family history); angina class and drug history.

Laboratory investigation:

Fasting and post- prandial blood glucose level; blood urea and serum creatinine. Lipid profile: including; Serum cholesterol, Triglycerides level, HDL cholesterol, LDL cholesterol level and high sensitivity CRP.

Electrocardiography; X- ray chest: Echocardiography was done with Philips Envisor for diagnosis, assessment of left ventricular dimensions, systolic function, and aortic valve assessment including valve morphology, presence of calcification, leaflets mobility and severity of aortic stenosis. The morphology of the aortic valve was assessed during TEE by high-frequency, high resolution imaging of the valve in multiple (short-and long-axis) echocardiographic views.

"Aortic valve sclerosis" was defined as abnormal irregular thickening of the aortic valve leaflets (at least one abnormal leaflet per valve). Continuous- wave Doppler recordings for determining the prevalence and severity of aortic stenosis. Peak flow velocity across the aortic valve ≤ 1.5 m/s was defined as normal (no gradient) peak flow velocity 1.6 to 2.5 m/s (peak gradient 10 to 25 mmHg) was defined as mild aortic stenosis. Peak flow velocity 2.6 to 3.5 m/s (peak gradient 26 to 49 mmHg) was defined as moderate aortic stenosis. Peak aortic flow velocity ≥ 3.6 m/s (peak gradient ≥ 50 mmHg) was defined as severe aortic stenosis. We did not measure aortic valve area, only peak systolic gradient.

Echo was done also for: Mitral valve assessment and wall motion abnormalities (hypokinesia, akinesia or dyskinesia).

The structure of the aortic valve was tricuspid in 45 patients could not be defined because of calcification in 5.

Coronary angiography:

Coronary angiography was done for various indications in 24 patients. Significant obstructive coronary artery disease was defined as either a ≥70% reduction of the internal diameter of the left anterior descending, right coronary, or left circumflex artery distribution or a ≥50% reduction of the internal diameter of the left main coronary artery.

The indications for coronary angio were persistent angina of effort in spite full medical therapy or highly positive exercise ECG.

Multi Detector Computed Tomography (MDCT) was done in 14 patients who refused coronary angio and were having same indications for angio. Thallium study was done in 6 patients. There was no indication to do coronary angiography for the other patients.

Carotid Duplex was done in 21 patients with transducer 7.5 mega Hertz. The carotid study was done in the cardiology department, Alexandria Main University Hospital. Twenty nine other patients were studied with Esaote Mylab Gold 30 with transducer 3.5 MH but with specific vascular program. Fig-1.

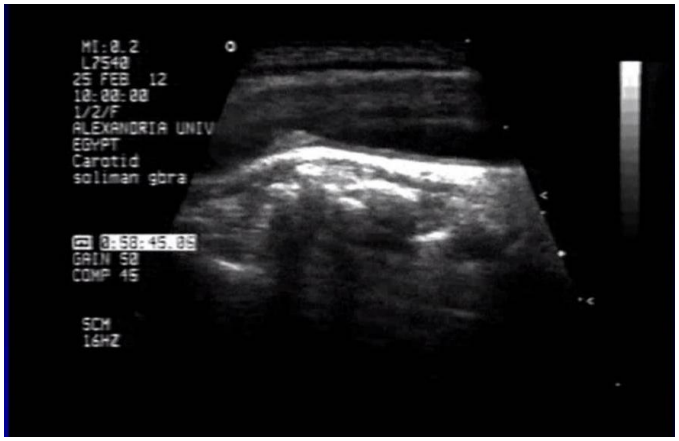
Measurement of carotid plaque area using ultrasound: Each plaque (a local thickening exceeding 1.2 mm and protruding into the lumen) seen (from the clavicle to the angle of the jaw on both sides) is measured in the longitudinal view. The thickening seen on the near wall would be measured separately, in its own view. The cross-sectional area of the plaque is measured by tracing around

the plaque with a cursor. The total of all plaque areas represents atherosclerosis burden.

Whenever a plaque was present, defined as a focal lesion > 1.2 mm thick, measurements were performed before or after the plaque. An upper limit of normality for IMT was set at 0.80 mm.

Body mass Index: Body mass index was calculated = weight / square height in meters. Normal BMI is below 27, overweight below 30, obese = or more than 30.

Figure-1. Increased intima media thickness and obstructive plaque



The analysis of the aortic valve:

Patients were divided into two groups according to aortic valve gradient: those with gradient > 10 mmHg and those less than 10 mmHg. This division was our choice.

The analysis of LV echocardiography:

Study of LV concentrated on degree of LV hypertrophy, wall motion abnormality, diameters of LV cavity and ejection fraction.

Statistical analysis of the data:

Data were fed to the computer and analyzed using IBM ***SPSS software package version 20.0.*** Qualitative data were described using number and percent. Quantitative data were described using mean and standard deviation. Comparison between different groups regarding categorical variables was tested using Chi-square test. When more than 20% of the cells have expected count less than 5, correction for chi-square was conducted using Fisher's Exact test. Correlations between two quantitative variables were assessed using Pearson coefficient. Significance of the obtained results was judged at the 5% level.

RESULTS

Age and gender:

In our study 25 were males (36 %) and 45 were females, their ages ranged between 50-96 years with mean of 69.5 years.

Risk factors:

Hypertension:

Fifty seven patients in our study were hypertensive 81%.

Dyslipidemia:

All our patients were under statin therapy, although LDL cholesterol ≥ 150 in 56 patients 80%.

Smoking:

Nine patients were smoker (12.8 %).

Diabetes:

12 patients were diabetics.

There was positive correlation between presence of calcific aortic valve disease and carotid plaques

Table-1. Results according to metabolic syndrome

	Group I (non metabolic syndrome) (n= 23)	Group II (metabolic syndrome) (n= 27)	χ^2 (p)
M/F	21/2	21/6	1.691 (0.193)
Diabetes (–ve / +ve "1+2")	14/9	6/21	7.729* (0.005)
HT (–ve / +ve)	17/6	9/18	8.194* (0.004)
Smoking = 38 pts (non smoker / ex smoker + smoker)	3/20	9/18	2.803 (0.094)
Family history + = 37 pts	16	21	NS
BMI ≥30 = 19 pts	5	14	4.78 0.028
Waist ≥ 102, 88 = 25 pts	7	18	6.52 0.010

χ^2: Chi square test
*: Statistically significant at p ≤ 0.05

(P=0.002) and with presence of LV hypertrophy or coronary disease (P=0.033). Also there was positive correlation between presence of calcific aortic valve and increased intima media thickness (P=0.011) tables 1, 2.

Table-2. Results according to risk factors

	Total =50	%
Age	55± 11	
Males	42	84
Non diabetic	20	40
Type 1 diabetes mellitus	1	2
Type 2 diabetes mellitus	29	58
No hypertension	26	52
Hypertensive	24	48
Smoking history		
None or ex smoker	12 +10	44
Current smoker	28	56
Degree of obesity		
None obese	8	16
Over weight	23	46
Obese	12	24
Severe obese	7	14
Waist circumference		
Normal	29	58
Abnormal	21	42
Precipitating factors		
No	12	24
Physical stress	20	40
Emotional stress	13	26
Heavy meal	5	10
HDL		
Normal	11	22.0
High risk	39	78.0
TRIGLYCERIDES		
Normal	18	36.0
High	32	64.0
LVH	6	12
Normal	44	88

Table-3. Comparison with Egyptian prevalence

Total 50 pts	Our study	Prevalence in Egypt in age > 15 y	Chi (P)
Diabetes	30 (60%)	10 %	0.0000
HT	24 (48%)	26 %	7.2 (0.0071)
Smoking	38 (76%)	40 % in males 4 % in females	17.3 (0.0000)
Metabolic S.	27 (54%)	24 -25 %	13.3 0.0003

Comparison of Aortic sclerosis to age, sex, smoking, family history and HTN were statistically not significant, but there is statistical significance between AS and diabetes mellitus.

As regard to dyslipidemia and renal insufficiency no statistically significant difference was found between patients with and without Aortic valve stenosis.

Dorsalis pedis was occluded in 3 patients only. TIA and CVS (3 cases only) were not significantly related to aortic sclerosis and stenosis.

Coronary heart disease or LV hypertrophy (combined together) was positively correlated with increased IMT Table-1 or presence of carotid plaques table 1.

The severity of aortic stenosis:

Aortic systolic gradient was less than 35 mmHg in 55 patients and >35 mmHg in 15 patients.

Carotid Duplex:

Revealed carotid plaques in 29 patients in right side and in 45 patients in left side (total 45). Significant stenosis (defined as lumen narrowing > 30%) was present in 13 patients in right side and in 22 patients in left side (total 22). There was highly significant correlation between degree of AS and carotid stenosis. Those with AS systolic gradient > 35 mmHg, 15 patients, had carotid stenosis > 30% in 12 (80%). Those with less AS (55 patients) had carotid stenosis > 30% in 3 only (6%); p=0.0006 (Table-2).

DISCUSSION

Atherosclerotic Risk Factors in Carotid Plaques (CP) and Calcified Aortic Valve Stenosis (AS) are similar. Aortic valve "sclerosis" was defined as a focal area of increased echogenicity and thickening of the aortic valve leaflets without restriction of leaflet motion and a transaortic flow velocity of less than 2.5 m/s, measured by transthoracic echocardiography using the criteria of Otto et al.[1]

Mazzone et al. [24] studied 2 groups of cases: 47 were affected by hemodynamic atherosclerotic carotid plaque (group1) and 35 by severe calcified aortic valve stenosis (group2). They compared the groups for atherosclerosis risk factors, morphologic features, and immunohistochemical phenotypes. They demonstrated that these 2 different clinical cardiovascular diseases have common atherosclerotic risk factors and have confirmed that more advanced age is associated with more clinically diffuse and advanced atherosclerotic disease. They found the CP cases in their study had coronary artery disease (32%) and peripheral artery disease (26%). In the AS cases, they found a high incidence (89%) of non-hemodynamic CP and a 43% incidence of coronary artery disease associated with peripheral artery disease (14%).

Belhassan et al. [27] 2002 studied 55 patients in pilot study then added 152 patients. They reached conclusion that CIMT <0.55 mm were excellent predictors of the absence of CAD.

We found significant correlation between aortic valve calcification/stenosis with carotid plaques p= 0.002. Also there was significant correlation between aortic valve calcification/stenosis and coronary heart disease (or LVH) p=0.037

Our results were comparable to the findings of Mazzone (24) and Adler (26).

We tried to analyze the patients with aortic valve affection by two methods. We divided them into those with systolic gradient less than and > 10 mmHg. Also we divided them into those with just cusp thickening and those with cusp calcification or stenosis. The patients with only cusp thickening (10 patients) were put as control. As regards coronary disease, patients were divided into those with coronary disease or ECG evidence of LV hypertrophy (34 patients) and those free of any (16 patients).

Yamaura et al. [22] in 2004 studied 252 healthy adults by echocardiography and carotid ultrasonographic to determine the relation between early subclinical aortic valve sclerosis (AVS) and carotid intima-media thickness (IMT). Carotid IMT was significantly greater in subjects with AVS than in those without AVS. There was a significant correlation between the grade of AVS and carotid IMT (24-25).

Anvari et al. [28] in 2009 reported on Aortic and mitral valve atherosclerosis. They studied 68 patients who had atherosclerotic valves during histopathological evaluations (after surgery). Risk factors for valvular atherosclerosis were identified via a comparison between the 68 cases and 115 controls that had valvular surgery without valvular atherosclerotic changes. They found that stages of coronary artery atherosclerosis using Gensini score were significantly higher in patients with valvular atherosclerosis.

Estari Mamidala et al [29], Rajendra Prasad Gujjeti et al [30] Soylu et al. [31] in 2003 demonstrated the strong correlation between AVC and carotid atheromas. They also found that the plaques in patients with AVC are more unstable in morphology than in those without AVC, and this may explain the higher stroke incidence in these patients.

CONCLUSIONS

The clear finding of this work is that in presence of aortic valve calcification and stenosis there is association with higher incidence of carotid plaques. The new statement from this work is that aortic calcific stenosis with systolic gradient more than 35 mmHg is associated with very significant higher incidence of carotid stenosis.

Recommendations:

We found that aortic valve calcific stenosis with systolic gradient above 35 mmHg is associated with incidence of carotid stenosis in most patients (82%). Thus carotid study is recommended in this level of stenosis.

Limitations of the study:

The small number of the study population and the control are the main limitations of the study**.** Assessment of coronary disease was done by more than one method; we could not do coronary angiography to all patients.

Conflict of Interests

Authors declare that there is no conflict of interests regarding the publication of this paper.

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