

# CORONARY ATHEROSCLEROSIS: RISK FACTORS AND EARLY PREDICTION BY NON-INVASIVE TECHNIQUES

*By*

Mohamed S. El-Deen Hammada\* MD., Nihal S. Shihab\*\* MD & Abd Elaziz F. El-Deib\*\* MD.

*From*

*Departments of Cardiology\* and Public health\*\*,  
Faculty of Medicine, Tanta University*

## ABSTRACT

**Background:** Coronary heart disease commonly affects adults in most of the developed region of the globe. It is responsible for an extremely large fraction of hospital admissions among middle aged and elderly, contributing greatly to disability and death(1).

**Aim:** to study the cardiovascular risk factors for coronary artery disease and their association with atherosclerosis in the aortic, carotid and femoral arteries. Also, it aimed to study the use of extra-coronary atherosclerosis for early prediction of coronary artery disease (CAD).

**Methods:** The study was conducted during the year 2000 in the Cardiology Department at Tanta University Hospital. It included 103 cases complaining of chest pain and other symptoms related to coronary heart dis-

ease and were divided into two groups according to examination by coronary angiography. Group I (58 cases with CAD) and group II (45 control free of CAD). All patients underwent transesophageal echocardiography for assessment of aortic atherosclerosis and B-mode ultrasound for evaluation of the carotid and femoral atherosclerosis. Intima media thickness of more than 1 mm was considered a criterion for atherosclerosis.

**Results:** There were significant association between CAD and the atherosclerosis in the three extra-coronary vessels (carotid, aortic & femoral). Some of the cardiovascular risk factors were significantly recorded in subjects with atherosclerosis in the three extra-coronary sites including, old age, male gender, HDL, obesity, DM and triglycerides. A significant as-

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sociation between atherosclerosis in the carotid, aortic and femoral arteries was present with the number of coronary vessels involved. The atherosclerotic plaques in the aorta was a good sensitive and highly predictor for CAD than the carotid or the femoral arteries, while the use of the three extra-coronary sites together was the most sensitive and a better predictor. This study recommended the use of non-invasive techniques by screening the carotid, aortic and femoral atherosclerosis for prediction of CAD.

## INTRODUCTION

Coronary heart disease commonly affects adults in most of the developed region of the globe. It is responsible for an extremely large fraction of hospital admissions among middle aged and elderly, contributing greatly to disability and death(1). Early signs of atherosclerosis are readily apparent in adults in the United States. This reservoir of asymptomatic persons with subclinical atherosclerotic cardiovascular disease ensure that myocardial infarction will remain a public health problem for decades (2).

Dyslipidemia, hypertension, smoking and other risk factors known to predict coronary heart disease have

recently been shown to be strongly associated with the atherosclerotic changes represented by the increase in the intima-media thickening (IMT) of the arterial walls(3&4). Many other studies have demonstrated an association between intima-media thickness especially of the carotid and aortic walls and the risk for coronary diseases and stroke (5 &6 &7).

There is a growing belief that carotid intima-media thickness as well as aortic atherosclerotic changes can be regarded as indicators of generalized atherosclerosis that may be used as markers for the presence of coronary artery disease (CAD). These atherosclerotic changes may be used also as an intermediate end point in observational studies or as a suitable alternative for cardiovascular morbidity and mortality (8 &9).

### *Aim of the work*

1- Assessing the risk factors for coronary artery disease (CAD) and comparing their pattern with that for the carotid, aortic and femoral atherosclerosis.

2- The use of extra coronary atherosclerosis as predictors for CAD in asymptomatic individuals instead of

the use of other invasive techniques.

### *Subjects and Methods*

The study population:

This study was conducted during the year 2000 in the Cardiology Department of Tanta University Hospitals. It included 103 subjects complaining of chest pain or other symptoms related to coronary heart disease.

All the studied sample were subjected to:

1- A designed questionnaire sheet filled by the researchers, which included the followings:

\* Personal data: - age, sex and level of education .

\* Habits: - smoking habit was divided into (non smokers) and (current or ex smokers since six months).

\* Family history: it was coded as positive if a first-degree relative had a significant coronary event.

\* Body mass index BMI (W (kg) / H<sup>2</sup> (m)): according to Garrow (1981) the BMI was subdivided into: grade 0 (<25), grade I (25 -29.9), grade II(30-40) and grade III (> 40). In this study, the sample was divided into two groups; obese, when BMI was > 29.9 (by summing grades II & III obesity)

and less obese- or non obese when BMI was < or= 29.9 (by summing grades 0 & I) (10).

\* Blood pressure: hypertension was recorded +ve when the measured blood pressure exceeded 140/90 mm Hg (1).

\* Clinical examination of the heart and ECG (twelve leads resting electrocardiogram) is performed for the entire sample.

\*- Laboratory investigations: - blood was analyzed for;

\* Fasting plasma glucose level (FPG): diabetes mellitus was defined +ve if the FPG level exceeded 126 mg/dL.

\* Total plasma cholesterol (TPC): average cholesterol reached up to 220 mg/dL and a higher level was considered risky.

\* High density lipoprotein (HDL): levels < or= 35 mg/dL were risky for CAD..

\* Low density lipoprotein (LDL): levels >Or = 160 mg/dL were considered risky.

\* Triglycerides: levels above the average (75-170 mg/dl) were risky.

*II- Coronary angiography to evaluate coronary artery lesions:*

Coronary angiography was considered a gold standard test used for



definite diagnosis of CAD. According to angiography results the sample was divided into two groups; Group I (58 cases): including cases with significant coronary artery lesions  $>$  or  $=$  50% reduction of the luminal diameter of one or more coronary arteries. Group II (45 control): including those with normal coronary arteries "or insignificant lesions such as non-obstructive CAD or less than 50% diameter stenosis".

### *III- Assessment of the carotid and femoral atherosclerosis:*

All the studied sample was screened by duplex B-mode ultrasound for both of the carotid and femoral arteries.

\* For the carotid arteries, to assess atherosclerosis, a careful search was performed for all interfaces of up to twelve different sites (for both right and left sides in the near and far walls at the distal common bifurcation and proximal internal carotid artery). For each individual, the carotid intima-media thickness (IMT) was calculated as the overall mean of the maximum IMT in mm in all the sites (named by carotid score).

\* For the femoral arteries, the atherosclerosis was evaluated using the femoral plaque score which is the

sum of the maximal intima-media thickness at 3 sites high, mid and low common femoral artery at the near & far walls. Carotid and femoral arteries were considered normal when their IMT score was 1mm.

IV- Assessment of aortic atherosclerosis by transesophageal echocardiography: the aortic intimal changes were defined using the modified classification of Fazio et al (11). Grade I: - The aortic wall was considered normal when the intima thickness measured  $<$  or  $=$  1 mm, the intimal surface was continuous and smooth without lumen irregularity or increased density. Grade II: - was defined as a smooth focal or linear increased echo density or the intima protruding less than or equal to 3 mm into the aortic lumen. Grade III: - plaque presented as a smooth increased echo density of the intima protruding more than 3mm into the aortic lumen. Grade IV: - was defined as irregular plaque protruding more than 3mm into the aortic lumen with ulceration. The sum of the maximal plaque thickness of the lower, mid and upper third of the descending aorta (2mm at each level) at the near and far walls was considered as a measure of the extent of aortic atherosclerosis (aortic plaque score  $>$  or  $=$  1mm).

**Statistical analysis:** - all the studied sample was divided into two major groups according to the coronary angiographic results; group I including the cases with CAD (N =58) and group II including the control (N =45). The control group was subdivided into 3 groups according to the extra-coronary vessel affected (carotid, aortic & femoral) and each vessel was divided whether it was atherosclerotic or not by ultrasonography, in order to study the association of risk factors with the atherosclerotic changes without including the cases. Results were tabulated and analyzed by Chi square, Fisher Exact and Student t-test. Test performance characteristics including, sensitivity, specificity and predictive values of the diagnostic tests for the carotid, aortic and femoral atherosclerosis were performed.

## RESULTS

According to the coronary angiography, the studied sample was divided into two groups; group I (n=58) with evident coronary artery disease (CAD) and group II (n=45) with no coronary heart disease (CAD).

The B-mode Ultrasonography revealed the followings: - 63 of the total sample showed carotid atherosclerosis

(IMT >1mm), where as 39 were in group one and 24 in group two. Subjects with femoral atherosclerosis were 59 (37 in group one & 22 in group two).

Transesophageal Echo showed 64 individuals with aortic atherosclerosis where as 42 were in group I and 22 in group II. According to Fazio et al classification of aortic atherosclerosis(11); there were 30 subjects(46.9%) in grade II [15 in group I & 15 in group II] & 24 subjects (37.5%) in grade III [18 in group I & 6 in group II] & 10 in grade IV [ 9 in group I & 1 in group II ], while there was no one in grade I .

Table (1) represents the different risk factors for coronary artery disease. The mean ages of both groups were 53.72 versus 56.58 respectively with a non significant statistical difference between group I and group II (t =1.42, P>0.05). As regards sex, males were more affected than females with a significant statistical difference between both groups (67.2% male cases versus 35.6% male control,  $\chi^2 = 10.22$ , P <0.05). About half of the cases had a significant family history of CAD compared to 27.3% of the control ( $\chi^2 = 4.98$ , P<0.05). A high percentage of cases with CAD suf-

ferred from diabetes mellitus compared to the control group, with a significant statistical difference (36.2% versus 4.4%,  $X^2 = 14.74$ ,  $P < 0.05$ ), also obesity with a body mass index  $> 29.9$  was recorded more among the cases than the control, but the difference was not statistically significant (27.6% versus 13.3%,  $P > 0.05$ ). Hypertension was significantly recorded among the control (group II), [ 60% among cases versus 82.2% among control,  $P < 0.05$ ]. The table also reveals that there were non significant statistical differences between cases and control regarding the total cholesterol, low density lipoprotein (LDL) and high density lipoprotein (HDL) [ $P > 0.05$ ]. There were higher levels of triglycerides among cases more than the control with a non significant difference ( $189.34 \pm 114.39$  vs  $157.82 \pm 88.34$ ,  $p > 0.05$ ). Concerning the means of carotid intima-media thickness score, aortic IMT score and femoral thickness scores; they were significantly higher among the CAD cases more than the control ( $t = 4.55$ ,  $t = 7.25$ ,  $t = 4.38$  &  $P < 0.05$ ) respectively.

Table (2) represents the different risk factors and their association with the atherosclerosis in the aortic, ca-

rotid and femoral arteries among the control group (with no evidence of CAD).

#### *\*Aortic atherosclerosis:*

There were significant statistical differences between subjects with aortic atherosclerosis and those free of aortic atherosclerosis regarding, obesity (27.3% versus 0.0%), HDL (177.36 versus 139.13), associated carotid atherosclerosis (6.09 versus 2.0) and femoral atherosclerosis (5.18 versus 1.91) respectively. Male sex, current smoking, hypertension and diabetes mellitus were more recorded among subjects with aortic atherosclerosis compared to those without atherosclerosis (45.5% versus 26.1%; 36.4% versus 17.4%; 90.9% versus 73.9% and 18.2% versus 8.7% &  $P > 0.05$  respectively). Neither total cholesterol, low density lipoprotein (LDL) nor triglycerides were significantly associated with aortic atherosclerosis in this study.

#### *\*Carotid atherosclerosis:*

old ages, family history of CAD, diabetes mellitus and associated aortic atherosclerosis were significantly associated with carotid atherosclerosis (59.42 mean age versus 53.33; 41.7% versus 9.5 %; 25.0% versus



0.0 %; and 7.33 mean IMT versus 5.51 &  $P < 0.05$ ) respectively. Carotid atherosclerosis were more prevalent among males and obese but with non statistical significant differences between those with and without carotid atherosclerosis.

*\*Femoral atherosclerosis:-*

There were significant associations between subjects with femoral atherosclerosis and male sex, HDL, triglycerides, carotid atherosclerosis and aortic atherosclerosis (54.5% versus 17.4%; 32.55 versus 49.09, 5.63 versus 2.43 and 7.45 versus 2.61,  $P < 0.05$ ) respectively. There were non significant differences between subjects with and without femoral atherosclerosis concerning the other risk factors.

Table (3) portrays the relationship between the severity of coronary artery disease among the cases (by the number of arteries involved) and the atherosclerosis in the three extracoronary sites. It shows that there was a significant increase in the percentage of the associated aortic atherosclerosis by the increase in numbers of coronary arteries affected among cases as compared to those without aortic atherosclerosis, a difference which

was statistically significant ( $X^2 = 19.92$ ,  $P < 0.05$ ), the same results were found with both of the associated carotid and femoral atherosclerosis ( $X^2 = 14.23$  &  $x^2 = 10.97$ ,  $P < 0.05$ ). Also the table reveals that the more the numbers of coronary arteries affected, the more extra coronary sites of atherosclerosis involved and vice versa, which was statistically significant ( $X^2 = 29.70$ ,  $P < 0.05$ ).

Table (4) represents tests performance characteristics as regards sensitivity, specificity and predictive values of the extra coronary atherosclerosis detected by ultrasonography as screening tests. It shows that aortic atherosclerosis screening had a higher sensitivity (72.4%) and predictive value positive (65.6%) than either of the carotid and femoral atherosclerosis (67.2% & 61.9% and 63.8% & 62.7%, respectively). This means that aortic atherosclerosis screening was more predictive for the subjects truly diseased with CAD followed by the carotid and femoral atherosclerosis screening tests. The femoral and aortic tests had higher specificity values than the carotid test, 51.1 % for each of the aortic and femoral and 46.7% for the carotid. The table shows also that the ability of all

the screening tests to predict the truly positive (diseased) were more valuable than their ability to predict subjects which were truly negative (disease-free). That was evident by the lower values for predictive value negative (PVN). Regarding the combi-

nations between more than one screening tests, the table showed that screening of the three extra coronary sites for atherosclerosis had the highest sensitivity value (86.7%) and acceptable predictive values (PVP = 65% & PVN = 66.7%).

Table (1) Risk factors for coronary artery disease among groups I and II

Risk factors	Group I N= 58	Group II N= 45	Tests of significance
	% or mean $\pm$ SD	% or mean $\pm$ SD	
Age	53.72 $\pm$ 10.73	56.58 $\pm$ 9.19	t = 1.42
Gender (males )	67.2	35.6	X <sup>2</sup> = 10.22 *
Level of education (high)	32.8	42.2	X <sup>2</sup> = 0.98
family history +ve	48.3	26.7	X <sup>2</sup> = 4.98 *
Current smokers	25.9	26.7	X <sup>2</sup> = 0.01
Obese with BMI > 29.9	27.6	13.3	X <sup>2</sup> = 3.06
Hypertension +ve	60.0	82.2	X <sup>2</sup> = 5.76 *
DM ( +ve)	36.2	4.4	X <sup>2</sup> = 14.74 *
Total cholesterol	238.74 $\pm$ 74.95	256.04 $\pm$ 95.27	t = 1.03
LDL	113.98 $\pm$ 46.65	122.27 $\pm$ 49.42	t = 0.87
HDL	40.29 $\pm$ 13.35	41.0 $\pm$ 17.99	t = 0.23
Triglycerides	189.34 $\pm$ 114.39	157.82 $\pm$ 88.34	t = 1.53
Carotid atheros. (I M T score)	9.71 $\pm$ 7.52	4 $\pm$ 4.25	t = 4.55 *
Aortic atheros. ( aortic score)	23.1 $\pm$ 16.09	4.98 $\pm$ 5.35	t = 7.25 *
Femoral atherosclerosis	8.97 $\pm$ 7.61	3.51 $\pm$ 3.89	t = 4.38 *

\* significant at 5% level of significance. DM= diabetes mellitus. LDL= low density lipoprotein. Atheros.= atherosclerosis. HDL= high density lipoprotein



Table (2) Distribution of group II (control gp.) with and without atherosclerosis in the three extracoronary sites according to the different risk factors

Risk factors	Aortic Artery			Carotid Artery			Femoral Artery		
	With Atheros. N = 22	Without Atheros. N = 23	Test of Signifi-cance	With Atheros. N = 24	Without Atheros. N = 21	Test of Signifi-cance	With Atheros. N = 22	Without Atheros. N = 23	Test of Signifi-cance
	% or mean $\pm$ SD	% or mean $\pm$ SD		% or mean $\pm$ SD	% or mean $\pm$ SD		% or mean $\pm$ SD	% or mean $\pm$ SD	
Age	9 $\pm$ 10.8	54.4 $\pm$ 6.9	t=1.70	59.4 $\pm$ 9.2	53.3 $\pm$ 8.3	t=2.32 *	57.2 $\pm$ 11.2	56.0 $\pm$ 7.0	t=0.43
Gender -M	45.5	26.1	X <sup>2</sup> =1.84	41.7	28.6	X <sup>2</sup> =0.84	54.5	17.4	X <sup>2</sup> =6.27*
HI. educ	40.9	43.5	X <sup>2</sup> =0.03	37.5	47.6	X <sup>2</sup> =0.47	45.5	39.1	X <sup>2</sup> =0.18
Family his.+ve	18.2	34.8	X <sup>2</sup> =1.59	41.7	9.5	X <sup>2</sup> =5.91 *	27.3	26.1	X <sup>2</sup> =0.01
Curr sm..	36.4	17.4	X <sup>2</sup> =2.07	25.0	28.6	X <sup>2</sup> =0.07	36.4	17.4	X <sup>2</sup> =2.07
Obese with BMI >29.9	27.3	0.0	F.E= 0.01*	16.7	9.5	F.E=0.67	9.1	17.4	F.E=0.67
Hypertension (+ve)	90.9	73.9	F.E=0.24	91.7	71.4	F.E=0.12	72.7	91.3	F.E=0.14
D.M (+ve)	18.2	8.7	F.E=0.41	25.0	0.0	F.E=0.2 *	18.2	8.7	F.E=0.41

\* significant at the 5% level . Family his.=family history .

HI .educ.= higher level of education. Current sm.= current smokers. BMI=body mass index. F.E= fisher exact test.

Continue table (2)

Risk factors	Aortic Artery			Carotid Artery			Femoral Artery		
	With Atheros. N=22	Without Atheros. N=23	Test of significance	With Atheros. N=24	Without Atheros. N=21	Test of Significance	With Atheros. N=22	Without Atheros. N=23	Test of Significance
	% or mean $\pm$ SD	% or mean $\pm$ SD		% or mean $\pm$ SD	% or mean $\pm$ SD		% or mean $\pm$ SD	% or mean $\pm$ SD	
Total chol.	237.2 $\pm$ 90.3	274.1 $\pm$ 98.3	t=1.31	240.1 $\pm$ 87.8	274.3 $\pm$ 102.2	t=1.21	238.7 $\pm$ 92.2	272.6 $\pm$ 97.2	t=1.20
LDL	118.7 $\pm$ 57.1	125.7 $\pm$ 41.9	t=0.47	132.8 $\pm$ 46.9	110.2 $\pm$ 50.5	t=1.56	130.6 $\pm$ 55.1	114.4 $\pm$ 43.1	t=1.10
HDL	35.3 $\pm$ 12.7	46.5 $\pm$ 20.7	t=2.18 *	38.3 $\pm$ 19.6	44.1 $\pm$ 15.9	t=1.09	32.6 $\pm$ 11.7	49.1 $\pm$ 19.4	t=3.44 *
triglyceride	177.4 $\pm$ 112.7	139.1 $\pm$ 52.3	t=1.47	161.3 $\pm$ 86.9	153.9 $\pm$ 92	t=0.28	184.8 $\pm$ 108.9	132 $\pm$ 53.6	t=2.08 *
C A	6.1 $\pm$ 4.4	2.0 $\pm$ 3.0	t=3.65 *	7.5 $\pm$ 2.7	0.0	t=1.0	5.6 $\pm$ 3.9	2.4 $\pm$ 4.6	t=2.69 *
A A	10.2 $\pm$ 2.1	0.0	T=1.0	7.3 $\pm$ 5.5	2.3 $\pm$ 3.7	t=3.55 *	7.5 $\pm$ 5.0	2.6 $\pm$ 4.6	t=3.38 *
F A	5.2 $\pm$ 3.7	1.9 $\pm$ 3.4	t=3.07 *	4.3 $\pm$ 3.5	2.6 $\pm$ 4.2	t=1.54	7.2 $\pm$ 2.0	0.0	t=1.0

C A= carotid atherosclerosis (mean IMT)

A A=aortic atherosclerosis ( mean IMT )

F A=femoral atherosclerosis (mean IMT )

LDL= low density lipoprotein.

HDL= high density lipoprotein.

**TABLE (3)** Distribution of cases in group I according to the number of coronary arteries affected and the associated atherosclerosis in the three extra-coronary vessels.

No. of Coronary Arteries affected	Aortic Artery		Carotid Artery		Femoral Artery		All cases in group I	
	With athero sclero -sis	Without Athero sclero- sis	With athero sclero -sis	Without athero- sclero- sis	With athero sclero -sis	Without athero sclero- sis	With ** atherosc -lerosis	With no atherosc -lerosis
1 No	6	12	6	12	6	12	4	13
%	14.3	75.0	15.4	63.2	16.2	57.1	9.52	81.25
2 No	18	4	17	5	16	6	19	3
%	42.9	25.0	43.6	26.3	43.2	28.6	45.24	18.75
3 No	18	0	16	2	15	3	19	0
%	42.9	0.0	41.0	10.5	40.5	14.3	45.24	0.0
Total No	42	16	39	19	37	21	42	16
%	100	100	100	100	100	100	100	100
Test of significa nce	*X <sup>2</sup> = 19.92		*X <sup>2</sup> = 14.23		*X <sup>2</sup> = 10.97		*X <sup>2</sup> = 29.70	

\* significant at 0.05 level of significance . \*\* with more than one vessel with atherosclerosis.

**Table (4)** sensitivity, specificity and predictive values (positive & negative) of aortic, carotid and femoral atherosclerosis as screening tests for CAD.

Screening tests	Sensitivity %	Specificity %	PVP %	PVN %
Aortic Atherosclerosis	72.4	51.1	65.6	59.0
Carotid atherosclerosis	67.2	46.7	61.9	52.5
Femoral atherosclerosis	63.8	51.1	62.7	52.3
The three extra- coronary vessels	86.7	36.4	65.0	66.7



## DISCUSSION

Epidemiological studies have documented that individuals with clinical cardiovascular disease related to one specific peripheral vascular bed are at a higher risk of clinical disease caused by atherosclerosis at another site such as, the heart or brain (12). An atherosclerotic ascending aorta detected by Multiplan transesophageal echocardiography, represent a marker for presence of coronary artery disease (13). Carotid and aortic atherosclerosis are both associated with coronary artery disease and thromboembolism (14). The total studied cases (N=103) were subjects admitted with anginal pain or symptoms related to CAD to Cardiology Department at Tanta University Hospitals during the year 2000.

In the present study, there was no significant difference in the mean age for both groups I & II. Males represented 53.4% of the study sample while females were 46.6%. Males were more frequent with positive angiography compared to patients with negative angiography (67.2% & 35.6% respectively) with a significant difference. The sex differential for atherosclerosis and cardiovascular disease events is not adequately explained on

the basis of any known effects of hormones on the level of risk factors, but it may be related in part to women and greater to HDL cholesterol blood fraction (15).

As regards educational level, 32.8% of group I were highly educated compared to 42.2% of group II persons which may indicate more awareness of highly educated non-coronary about preventive measures for coronary heart disease. Current smokers were about 26% for both groups, but it doesn't exclude smoking as a risk factor because the duration and amount of smoking may be more in cases than group I persons, also sample size may be a limiting factor. However, Levy D & Wilson PWF (1998) reported that cigarette smoking has been significantly linked to the occurrence of coronary artery disease and its cessation reverses this increased risk within few years (1) >. A mild increase in risk is present among persons passively exposed to smoke from another persons burning cigarettes (16).

In this work, there was a significant positive family history of ischemic heart disease among cases with positive coronary angiography than

non-coronary persons. Also obesity and diabetes mellitus were more frequent among cases with coronary than those without. This was in agreement with Levy et al (1998) who mentioned that, diabetes mellitus double the risk for coronary artery disease in men and triple the risk in women during middle age but this tendency may diminish in the elderly (1). Obesity as measured by body mass index or central adiposity (waist-hip ratio) is associated with increased risk of coronary heart disease. Obesity is highly associated with abnormal levels of other risk factors with greater tendency toward hypertension, abnormal lipids, impaired glucose tolerance and physical inactivity (1). The mean serum triglycerides was non-significantly higher among cases with coronary heart disease than non-coronary group ( $189.34 \pm 114.39$  &  $157.82 \pm 88.34$  respectively). This finding was similar to that reported by Sharrett et al (1999) who noticed that elevated triglycerides & reduced HDL cholesterol were associated more with coronary heart disease than with a direct measure of arterial thickness. He also added that these factors might affect the progression from arterial disease to myocardial infarction (3). However Chambless et al (1997)

found that the prevalence of hyperlipidemia was statistically higher for incident cases than for the control (17). Other elements of lipid profile were more or less similar for both groups, as they were considered both at high risk for CAD. Hypertension was more frequent among group II persons compared to group I cases, this may be due to older age of non-coronary compared to the other group as hypertension incidence increase with aging. Also both groups were at high risk for coronary artery disease, besides, in group I they may have had longer duration of hypertension compared to group II. The differences in socioeconomic, dietary or life style factors may have a role.

Mean score of carotid atherosclerosis among patients with positive coronary angiography was  $9.71 \pm 7.52$  while it was  $4 \pm 5.20$  for those with negative angiography and the difference was significant. Regarding the mean aortic and femoral atherosclerosis measured by IMT, it was significantly higher among cases with coronary heart disease compared to patients with negative coronary heart disease. This was in agreement with Davis et al (1995), who concluded that an association was present between increased carotid atherosclerosis

sis as measured by IMT and coronary artery calcification. Presence of calcification in the coronary arteries has been correlated with atherosclerotic changes in the coronary arteries found on postmortem or coronary angiography (18). Chambless et al (1997) showed that the mean carotid IMT is a non invasive predictor of future CHD incidence (17). Kallikazaros et al (2000), reported high prevalence of combined aortic and carotid atherosclerosis in cardiac patients without clinical evidence of atherosclerotic cardiovascular disease (14). Kuller et al (1995) mentioned that, the presence of subclinical markers of atherosclerosis in subjects without evidence of clinical cardiovascular disease is associated with significant increased risk of incident coronary heart disease for both men and women (19).

As regards the well-defined cardiovascular risk factors and their association with atherosclerosis among the control group, it was found that; obesity, low HDL, femoral and carotid atherosclerosis were significantly associated with aortic atherosclerosis. Same findings were reported by sunk et al (2000) who demonstrated that aortic atherosclerosis measured by

maximal aortic wall thickness had a negative correlation with high-density lipoprotein -cholesterol (20). In consistence with our study, Kallikazaros et al (2000) reported that, the prevalence of aortic plaque increased as the degree of carotid atherosclerosis increased suggesting that in cardiac patients, the ascending aorta was the part most exposed to early asymptotic atherosclerosis (14).

In the present study, carotid atherosclerosis was associated with advanced age, positive family history of CAD, diabetes mellitus and aortic atherosclerosis. In agreement with these findings, Kallikazaros et al (2000), in their study reported that patients with carotid atherosclerosis suffered from diabetes mellitus and were all of advanced age (14). Both studies of Sharrett et al (1999) and Bonithon-Kopp et al (1991) reported that; age, smoking, plasma low HDL, high LDL, cholesterol and hypertension were related to the severity of carotid atherosclerosis (3& 21).

In our study, femoral atherosclerosis was associated with increased triglycerides, low HDL cholesterol, male sex and aortic & carotid atherosclerosis. Kristenson et al (2000) found that



smoking, systolic blood pressure and LDL cholesterol were significantly contributed to increase IMT for femoral and carotid arteries (22). The differences between this study and our study may be because this study was done on males only.

Regarding the severity of coronary heart disease as measured by the number of diseased coronary blood vessels; the study revealed that, with only one coronary blood vessel affected, the least percentages of associated extracardiac atherosclerosis were found (14.3% with aortic atherosclerosis, 15.4% with carotid atherosclerosis and 16.2% with femoral atherosclerosis). While in cases with 3 coronary blood vessels affected, a significant higher percentages of associated extracardiac atherosclerosis were detected (42.9% with aortic atherosclerosis, 41% with carotid atherosclerosis and 40.5% with femoral atherosclerosis.) and the differences were statistically significant. Also the less the number of coronary blood vessels affected, the more the percentage of cases free from extracardiac atherosclerosis and vice versa with a significant statistical difference ( $X^2=29.70$ ). These findings were in agreement with those of Geroulakos et al

(1994) who found a significant linear trend between increasing IMT of the great vessels and the number of coronary arteries involved (23).

In the present study, Aortic atherosclerosis screening had an acceptable sensitivity (72.4%) followed by the carotid atherosclerosis (67.2), while the femoral atherosclerosis was the least sensitive predictor of coronary atherosclerosis and coronary heart disease. The sensitivity of the carotid in our study was near to that reported by Kallikazaros et al (2000), [75%] while the specificity of the carotid in this study was much less than that of Kallikazaros et al (46.7% & 74% respectively) (14). The sensitivity of predicting CHD reached 86.7% when using the three extracoronary sites. This was similar to that concluded by Chambless et al (1997) (17). Amarenco et al (1994) reported that, atherosclerotic ascending aorta is a marker for the presence of coronary heart disease (13). Another study showed that the presence of carotid plaques had an acceptable sensitivity (75%) and specificity (74%) for the presence of aortic plaques (22).

As regard predictive value of extra coronary sites for detection of coro-

nary heart disease, the positive predictive value was 59% for aortic atherosclerosis compared to 52% for the femoral or carotid atherosclerosis. The negative predictive value for femoral or carotid atherosclerosis was higher (85.3%) than that for aortic atherosclerosis (63.1%).

In conclusion, the present study revealed that the cardiovascular risk factors strongly associated with coronary heart disease were; diabetes, male gender, positive family history of CAD together with significant increase in the IMT of the carotid, aortic and femoral arteries. Atherosclerosis in the carotid, aortic and femoral arteries were significantly associated with old age, positive family history of CAD, diabetes mellitus, obesity, HDL and triglycerides.

Thus the association of the increase IMT of the large central and peripheral vessels with major cardiovascular risk factors suggests that they may be used as markers of the general atherosclerotic process.

There were significant associations between the carotid, aortic and femoral atherosclerosis with the number of coronary arteries affected, reflecting the severity of the disease. The presence of atherosclerotic

plaques in the extra-coronary vessels can be used as a reliable positive predictive factor for CAD in asymptomatic individuals.

### *Recommendations*

1- A population-wide approach to risk factors intervention is recommended for the reduction of atherosclerotic cardiovascular diseases.

2-Aortic atherosclerosis measured as IMT by transesophageal echocardiography can be used as a good non-invasive technique for prediction of coronary heart disease even in asymptomatic persons.

3-The use of the three extracardiac sites together; the aortic, carotid and femoral atherosclerosis for screening of CHD are more sensitive predictor than the use of only one vessel. They may be used for prediction, assessment of the case severity and follow up of at risk individuals.

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