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Relationship between coronary artery disease assessed by coronary computed tomography angiography and carotid artery disease assessed by ultrasound

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Abstract

Background: Atherosclerosis is a diffuse vascular disease, which may have a common mechanism of stenosis in both carotid and coronary arteries. Cardiovascular and cerebrovascular events happened due to the atherosclerosis are the causes of more than 50% of deaths in developed countries. Determination of IMT of large superficial arteries, especially the carotid, using B-mode ultrasonography has emerged as one of the methods of choice for determining early structural deterioration of arterial wall and assessing cardiovascular risk. Methods: This is a multicenter prospective study conducted at Kobry El-Kobba and El-Maadi Military Hospitals from 3-2021 to 12-2021. Included 300 cases subjected to both MSCT and carotid duplex. Results: The mean age of symptomatic patients (n=116) enrolled during the study was 66.6±11.8, while was 56±9.5 for asymptomatic patients (n=184). Subjects referred for screening were younger with less CAD on CT, hypertension, and diabetes compared with subjects with symptoms or known CAD. In our study, we observed high prevalence of carotid plaque (71%) as compared with other studies. There was a significant association between carotid plaque and IMT and CACs score and coronary artery disease by MSCT. Conclusion: Carotid IMT and plaque are associated with the presence and degree of coronary calcification and disease on CTA.

Keywords: Atherosclerosis, Carotid duplex, Coronary artery disease, IMT.

1. Introduction

Atherosclerosis is a diffuse vascular disease, which may have a common mechanism of stenosis in both carotid and coronary arteries. [1] Atherosclerosis-related cardiovascular and cerebrovascular events account for more than half of all deaths in developed countries. [2]

An association between carotid atherosclerosis and coronary artery disease (CAD) has been well established because atherosclerosis is considered to be a generalized disease.

It is estimated that these two conditions could be coexist ranging between 2-22% with the average of 8 %. These two conditions can be viewed as same disease process but different organs manifestation. [3]

Etiologically, cases of atherosclerosis occurring in different arterial vascular beds may have the same risk factors. Carotid and coronary atherosclerosis share common risk factors like diabetes mellitus, hypertension, older age, smoking and dyslipidemia. [4]

The involvement of arteries from different vascular areas indicates a significant burden of the atherosclerotic process, even if patients did not experience any clinical symptoms of atherosclerosis. Large international registries and postmortem studies have shown that atherosclerosis can co-exist in the coronary arteries, carotid arteries, and other vascular areas. [5]

Polyvascular atherosclerosis is linked to poor clinical outcomes in people with single or multifocal clinical symptoms. [6]

The use of B-mode ultrasonography to determine IMT of large superficial arteries, particularly the carotid, has emerged as one of the preferred approaches for detecting early structural alteration of the artery wall and predicting cardiovascular risk.[7]

Moreover, the intima medium thickness (IMT) of the carotid artery has been demonstrated to be as a practical tool for screening CAD. [8] Also, IMT is a well-described marker for cardiovascular disease, increased IMT is being linked to the development of CAD and stroke.[9]

Also, the occurrence of new carotid plaques is a strong indicator for the occurrence of all the cardiovascular events, including stroke, myocardial infarction and new angina. [10]

2. Aim of the study

To evaluate the relation between measurement of carotid IMT and the severity of coronary artery disease (CAD) by multislice CT (MSCT) among patients presenting by chest pain or dyspnea or asymptomatic with low to intermediate pre-test probability (PTP) for CAD.

3. Patients and methods:

3.1. Study design

It is a multicenter prospective study conducted at Kobry El-Kobba and El-Maadi Military Hospitals from 3-2021 to 12-2021.

3.2. Patients selection

The current study included 300 patients subjected to MSCT and carotid duplex.

3.3. Inclusion criteria

All patients presented by chest pain or dyspnea or asymptomatic with low to intermediate PTP of CAD by MSCT.

3.4. Exclusion criteria

1- Patients with renal insufficiency (S.creatinine >1.5 mg/dl).
2- Patients with bodyweight over 120kg.
3- Patients with previous history of PCI or previous CABG.
4- Patients with recent myocardial infarction.
5- Patients with dye allergy.
6- Patients with irregular heart rate like AF and frequent extrasystoles.

Measurement of mean IMT is performed on the right and left common carotid artery, excluding the bulb. Mean IMT is an average of readings at two or more points of measurement. Maximal IMT was the greatest near or far wall thickness, was manually measured. The presence of carotid plaque was based criteria that required at least 2 of the following: an IMT >1.5 mm, change in the carotid wall surface contour, or focal change in the carotid wall echogenicity.

A- Measurement of Coronary Artery Calcium Score (CACS):

The sum of calcified plaque scores in all coronary arteries categorized into 4 categories: Zero (CACS=0), mild (CACS=1-100), moderate (CACS =101- 400), high (CACS>400).

B- Evaluation of coronary artery stenosis:

The number of coronary arteries with any evidence of atherosclerosis was counted to a maximum of 4 vessels: right coronary artery (including the posterior descending artery branch), circumflex coronary artery (including the first and second obtuse marginal branches), left anterior descending artery (including the first and second diagonal branches and ramus if present), and left main coronary artery.

3.5. Statistical methods

Descriptive data are presented as frequency and mean±SD. Chi-square analyses were used to examine associations between categorical variables. The Mantel-Haenszel chi-square test for linear trend was used to determine whether there was a linear trend in the percentage of individuals with carotid plaque by calcium score and number of coronary vessels with stenosis. Spear-man's rho was used to examine correlations between continuous and categorical variables; Pearson correlation was used to examine linear associations between continuous variables. Means were compared using the Student t test or analysis of variance. Medians were compared using the Mann-Whitney U statistic. Logistic regression was used to model the probability of having a CAC score >0 or ≥1 diseased coronary vessels controlling for age, sex, and 2 categorical measures of IMT. Intraclass correlation coefficients (ICCs) were generated to determine interobserver and intraobserver variability for the maximal carotid IMT and CT calcium score. The kappa statistic was used to examine interexaminer and intraexaminer variability in the number of coronary vessels with disease. All analyses were performed using IBM SPSS software, version 18.0 (New York, New York). A p value <0.05 was used to indicate statistical significance.

4. Results

As shown in (*Table 1*), the mean age of symptomatic patients (n=116) enrolled during the study was 66.6±11.8, while was 56±9.5 for asymptomatic patients (n=184). Subjects referred for screening were younger with less CAD on CT, hypertension, and diabetes compared with subjects with symptoms or known CAD. 192 (64%) of patients were male and 108 (36%) were female. 92 patients (30.6%) were Diabetic, 150 patients (50%) were hypertensive, 127 patients (30.3%) were current smokers and only 29 patients (5%) were ex-smokers. 23.3% (n=70) of patients had history of coronary artery disease, while only 5.6% (n=17) of them had history of Peripheral vascular disease.

The mean values of total cholesterol were 185.5±41.9 mg/dl in asymptomatic patients vs. 192.7±40.5 mg/dl in symptomatic patients. Moreover, triglycerides values were 110.5±30.0 and 125±31.9 in asymptomatic and symptomatic patients respectively.

Regarding clinical presentation, of the 300 patients enrolled during the study, 8.3% of the patients presented with dyspnea, 14% of them presented with chest pain, 10% presented with dizziness and only 6.3% of them presented with palpitation. While 61.4% of the patients were asymptomatic *(Figure 1).*

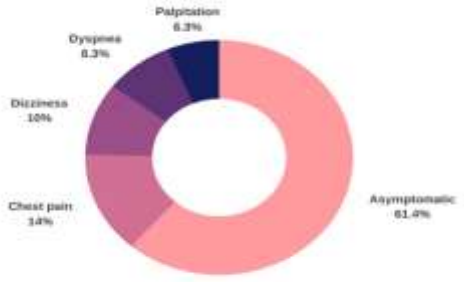

Fig. (1) Clinical Characteristics of the study Participants.

Table (1) Baseline Characteristics of the Study Participants.

Baseline Characteristics	Indication for Study	
	Asymptomatic (n= 184)	Symptomatic (n=116)
Age, yrs	56.0±9.5	66.6±11.8
Body mass index, kg/m^2	27.4±3.8	30.5±5.2
Fasting glucose, mg/dl	93.4±20.5	97.9±30.4
Total cholesterol, mg/dl	185.5±41.9	192.7±40.5
Triglycerides, mg/dl	110.5±30.0	125±31.9
High-density lipoprotein, mg/dl	50.6±15.9	45.8±23.0
Low-density lipoprotein, mg/dl	96.9±48.3	115.9±34.5
Male	100	92
Female	84	24
History of CAD	0.0	70
Diabetes	42	50
Hyperlipidemia	40	70
Hypertension	60	90
Family history of coronary disease	20	33
Peripheral vascular disease	0.0	17
Current smoker	30	97
Past smoker	5	24
Aspirin	20	35
Beta-blocker	35	45
ARB	20	30
ACE inhibitor	5	15
Statin	20	35

Values are mean ±SD, %, or median (interquartile range).
ACE = angiotensin-converting enzyme; ARB =angiotensin receptor blocker.

(*Table 2*) shows the maximal IMT, the averaged mean IMT and the percentage of subjects with carotid plaque by CAC category and by the number of vessels with CAD on CTA. Carotid findings for patients with 1- and 2-vessel disease were similar, and so the data for these patients were merged. For the carotid plaque variable, the chi-square test for trend demonstrates a significant increasing trend in the percentage of subjects with carotid plaque with increasing CAC score ($p < 0.0001$). Similarly, there was a significant increase in the percentage of subjects with carotid plaque as the number of vessels with CAD on CTA increased (chi-squaretest for trend, $p < 0.0001$).

After examining the data, we chose a cut point of 0.75 for the average mean IMT and 1.5, a criteria for plaque, for the maximal IMT. Logistic regression was then used to model the probability of having a CAC score >0 or at least 1 diseased coronary vessel after controlling for age, sex, and either the categorical mean IMT or categorical maximal IMT score.

Carotid plaque was present in 47.6% (60 of 126) of subjects with a CAC score of 0 and 88.5% (154 of 174) of subjects with a CAC score >0 ($p= 0.0001$). Similarly, carotid plaque was present in 52.4% (66 of 126) of subjects with no CTA evidence of atherosclerosis versus 85.7% (144 of 168) of subjects with any CTA evidence of atherosclerosis ($p < 0.0001$).

Table (2) Differences in Carotid IMT and Presence of Plaque by Categorical Coronary Artery Calcium Score and Number of Coronary Arteries With Any Evidence of Atherosclerosis on CT.

	Coronary Artery Calcium (Agatston Score)			
	0	**1-99**	**100-399**	**400+**
Maximal carotid IMT	1.61±0.78	2.08±0.88	2.48±0.91	2.64±1.06
Mean of 6 segment IMT mean	0.71±0.18	0.79±0.21	0.84±0.17	0.87±0.15
Plaque present	47.6%(60/126)	85.7%(60/70)	90%(36/40)	90.6%(58/64)
	No. of Coronary Arteries With Any Disease			
	0	**1-2**	**3**	**4**
Maximal carotid IMT	1.62±0.74	2.18±0.92	2.41±0.95	2.98±1.13
Mean of 6 segment IMT mean	0.72±0.18	0.80±0.19	0.86±0.17	0.90±0.14
Plaque present	52.4%(66/126)	82.6%(76/92)	88.0%(44/50)	92.3%(24/26)

Values are mean ±SD or % (n/N). Multiple pairwise comparisons were computed using the Bonferroni correction.

A maximal carotid IMT of ≥1.5 mm or the presence of carotid plaque was similarly predictive of CAD with a positive predictive value of 70% and 69%, respectively, for disease involving at least 1 vessel on CTA (Compared with 71% and 72% for a CAC score >0). The negative predictive value of IMT <1.5 mm or no carotid plaque for CAD was 67% and 71%, respectively, for no disease affecting any vessel on CTA (vs. for 67% and 77%, respectively, for a CAC score of 0). An averaged mean IMT of at least 0.75 mm or maximal IMT of at least 1.5 mm similarly distinguished patients with CAD by CAC score or by at least 1 vessel with disease on CTA. However, disease predictability and reassurance were imperfect; a given patient could have severe disease at 1 arterial site and little or no disease at the other.

5. Discussion

Atherosclerosis is a diffuse vascular disease, which may have a common mechanism of stenosis in both carotid

and coronary arteries.[1] The use of B-mode ultrasonography to determine IMT of large superficial arteries, particularly the carotid, has emerged as one of the preferred approaches for detecting early structural alteration of the artery wall and predicting cardiovascular risk.[7] Moreover, Carotid intima media thickness (IMT) has been shown to be as a strong predictor of incident myocardial infarction (MI) in the general population aged ≥55 years.[11]

In our study, we observed high prevalence of carotid plaque (71%) as compared with other studies. In a cross sectional study by **Coll et al., 2013 [12]** found that 25.1% of patients had carotid plaque.

There was significant statistical difference between symptomatic and asymptomatic patients regarding risk factors like gender (Figure 2), hypertension, DM and smoking.

CAD was present in most patients with carotid plaque or increased IMT (maximal IMT ≥1.5 mm or mean IMT >0.75 mm) and absent in most patients without carotid plaque or with lower IMT values. Our findings were consistent with those of previous studies that found an association between carotid artery disease and CAD.

In study by **Bytyçi et al., 2021 [13]** the carotid plaque presence was less common in non-significant CAD compared with significant CAD.

We compared carotid IMT measurements with the numbers of coronary arteries with any amount of disease and found a significant and similar relationship irrespective of how carotid artery disease and CAD was measured or defined (by maximal or mean IMT, the presence of carotid plaque, CAC score, and number of diseased arteries on CTA). We found modest correlations, comparable to other studies, between IMT and CAC, but greater for maximal than mean IMT. Carotid plaque, maximal IMT ≥1.5 mm and averaged mean IMT >0.75 mm predicted CAD independent of age and sex. This was similar to **Ohman EM et al., 2006 [14]** found that 4-year coronary risks were 23.2% and 19.3% in patients with and without carotid atherosclerosis, respectively.

In study by **Anand et al., 2018 [15]**, carotid plaque was independently associated with the cardiac event and the risk of a cardiac event at any time was 5 times higher for patients with carotid plaque compared with those without carotid plaque.

The relationship that we found between carotid IMT and CAD on CT supports the concept that atherosclerosis is a systemic process. However, modest correlations indicate that atherosclerosis may have a heterogeneous distribution. This relationship may be affected by risk factor profile. **Bauer et al., 2009 [16]** found that carotid IMT was more closely related to diabetes and CAC was more closely related to hypertension.

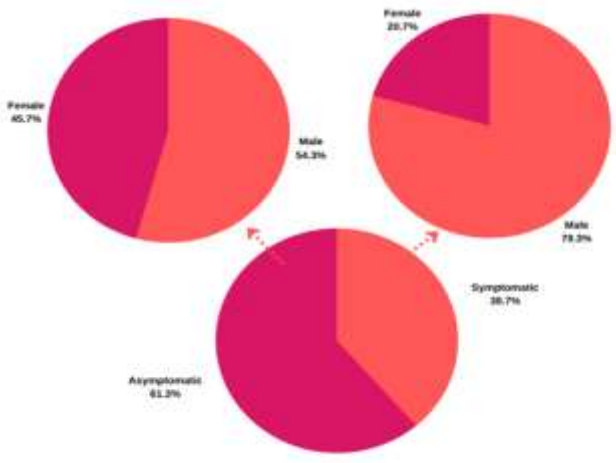

Fig. (2) Gender difference according to symptoms.

6. Conclusion

Carotid IMT and plaque are associated with the presence and degree of coronary calcification and disease on CTA. Because correlations between modalities are modest, the selection of an imaging modality should be guided by patient and methodological considerations and recognition of the heterogeneous distribution of atherosclerosis.

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