

## Carotid Artery Doppler Ultrasound and Coronary Calcium Score in Assessment of Atherosclerosis in Patients with Suspected Coronary Artery Disease

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### Abstract

**Background:** Cardiovascular Disease (CVD) is the leading cause of morbidity and mortality in both industrialized and low income to middle-income countries. As atherosclerosis is the underlying cause for most of CAD, so identification of subclinical disease in the asymptomatic phase has emerged as a public health and economic imperative.

**Aim of Study:** The aim of the study was to evaluate the ability of carotid artery Doppler ultrasound and coronary artery calcium score as screening tools for atherosclerosis in patients who underwent CT coronary angiography for suspected coronary artery disease.

**Patients and Methods:** This study was conducted on 30 patients (17 males and 13 females) with mean age of 58 years with atypical chest pain underwent Cardiac CT (CCT) and carotid Ultrasound (US) on the same day. Carotid artery atherosclerosis was evaluated by detection of Carotid Intimal Thickness (CIMT) & Carotid Plaque Score (CPS) then coronary arteries were evaluated by CCT. Coronary artery calcium score was obtained from axial non contrast cardiac CT and finally Coronary Artery Disease (CAD) was evaluated by Gensini score. The relation between both carotid artery Doppler findings & CACS and severity of coronary artery disease were detected.

**Results:** There were significant association between carotid artery disease that was estimated by CIMT, CPS and Gensini score ( $p=0.045$  &  $0.004$ ). There was also a significant association between CACS and Gensini score ( $p=0.039$ ).

**Conclusion:** Subclinical atherosclerosis as defined by CIMT, CPS and CACs can be simple, non-invasive yet sensitive risk-prediction tools to promptly identify those individuals at risk of CVD.

**Key Words:** Carotid intima media complex thickness – Carotid plaque score – Gensini score – Cardiovascular disease.

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### Introduction

IT has been established that people with Cardiovascular Disease (CVD) or who are at high risk for CVD, benefit significantly from early detection and management using counseling and medicines, as appropriate [1]. Subclinical atherosclerosis is an early indicator of atherosclerotic burden and its timely recognition can slow or prevent progression to CVD. Thus, individuals with subclinical atherosclerosis are a priority for primary prevention [2].

Because atherosclerosis is a systemic process, it is intuitive that assessing disease at multiple, rather than single, vascular sites may provide greater insight on the overall burden and risk associated with subclinical atherosclerosis [3]. The process of early detection of heart disease begins with risk assessment. Yet, any early detection and subsequent prevention relies heavily on the ability to accurately, identify the individuals who are at high risk of developing CVD. Thus, there is a pressing need to diagnose subclinical atherosclerosis to facilitate optimum CVD risk stratification in asymptomatic individuals [4].

Cardiac risk assessment involves determining the probability of a severe cardiac event such as MI or death associated with the presence of risk factors such as advancing age, male gender, family history of premature CAD, smoking, hypertension, hyperlipidemia, and diabetes. Risk assessment classification is then used as a means to guide treatment recommendations for prevention of severe cardiac events. For example, those classified as high risk are typically started on statin therapy; those classified as intermediate risk typically undergo additional screening for further risk stratification to determine need for preventative treatment

with aspirin and statin therapy, and those classified as low risk are typically managed with lifestyle modifications [5].

Within this context, cardiac risk stratification begins with calculating the probability of an incident event using conventional algorithms, such as the Framingham equation. However, most initial cardiac events do not occur among those considered "high risk," highlighting the need to improve risk stratification over existing approaches [3]. Although multiple studies have examined such associations, many combined direct (i.e., coronary artery calcium [CAC]) and indirect markers of atherosclerosis (i.e., Carotid Intima-Media Thickness (cIMT) & carotid plaque score) [4].

### Patients and Methods

This prospective study included 30 patients, 17 male (56.7%) and 13 female (43.3%) with age ranging from 40 to 72 years with mean age of 58 years complained of symptoms suggestive of ischemic heart disease referred to Radiodiagnosis Department at Tanta University from Cardiology Department and private clinics with symptoms suggestive of ischemic heart disease for evaluation by multislice CT angiography of coronary arteries during the period between February 2018 and February 2019. Ethics Committee approval and informed consent were obtained.

#### *Inclusion criteria:*

Patient who has any type of chest pain suggestive of ischemic heart disease referred for evaluation by MDCT.

#### *Exclusion criteria:*

- 1- Patients with history of Coronary Artery Disease (CAD) (myocardial infarction, previous percutaneous or surgical revascularization).
- 2- Pregnancy/lactation.
- 3- Patient who is clinically unstable to withstand the duration of CT examination.
- 4- Patient who has impaired renal function (creatinine level >1.5mg/dl).
- 5- Patient who can't tolerate the required breath holding time for examination.
- 6- Patients with bad general condition needing life support.

*All the patients were dealt with in the following manner:*

- 1- Full history taking.

- 2- Clinical examination including measuring patient's height and weight to calculate Body Mass Index (BMI) and measuring vital signs as heart rate and blood pressure before and after CT examination.

- 3- Laboratory investigations: We reviewed the results of renal function tests to ensure that the patient was fit for contrast material injection. We did not proceed if serum creatinine was above ( $\geq 1.5$ mg/dl).

- 4- Radiological and imaging assessment:

#### *I- Carotid artery Doppler ultrasound:*

- Carotid artery Doppler ultrasound scanning was performed in all the patients, using a Toshiba Aplio 500 scanner with 7-15MHz linear transducer.

- The optimal patient head position was tilted about 45° away from the artery being examined. The neck of the patients should be relaxed.

- The carotid artery was imaged from both the anterior approach, medial to the sternocleidomastoid muscle, and the lateral approach, through the jugular vein.

- Spectral and colour Doppler evaluation is performed with the longitudinal images at a slight angle with respect to the vertical plane. The sample volume is kept center stream and marched carefully through the CCA and ICA in order to detect the discrete areas of flow abnormality suggestive of stenosis.

- Intima-media thickness measurements were obtained from a gray-scale image. The measurements were made from the intima lumen interface (echogenic layer) to the media adventitia border (echo-poor layer) at far wall of the CCA, bulb, and ICA.

- Carotid Plaque Score (CPS) was calculated by summing each single plaque with its maximum thickness in the ipsilateral carotid artery without considering the length of each plaque so as to obtain the plaque score of this side. Adding bilateral carotid plaque scores to obtain a total PS was then performed. We stratified participants according to CPS into no (0 points), low (1.2-4.9 points), and high ( $> 5.0$  points) CPS groups [6].

#### *II- Multislice CT angiography for evaluation of the coronary arteries.*

- I- Instructions:* Fasting 4-6 hours before scan, encourage water intake till one hour before scan, avoid caffeine products like tea or coffee, smoking exercising and strenuous physical activity the day before and on the day of CT exam. Stop taking

phosphodiesterase inhibitors used to treat pulmonary hypertension for 48 hours before scan as they may cross react with sublingual nitrates that will be given during scan and precipitate severe hypotension.

## II- Patient preparation:

- A- Detailed explanation of the procedure to all patients with reassurance was done to relief any anxiety.
- B- Heart rate and blood pressure were recorded on arrival to set a baseline for monitoring. Patients with heart rate below 65bpm not given any heart rate control medications they were 9 patients. Patients with higher heart rate were given oral  $\beta$ -blockers provided that there was no contraindication to their use.
- C- IV cannula (18G) was inserted after heart rate control at patient preparation room.
- D- *At scanner room:* Patients were given gown to put on and then instructed to lie supine on scanner table with arms raised above their heads. The patient was positioned on table to ensure that the heart was in the isocenter of the gantry for optimal spatial resolution. ECG electrodes were applied to chest wall after skin preparation with alcohol and ECG trace was monitored to ensure good amplitude of R wave that was used for scan trigger. The IV line was connected and test injection with saline was done to ensure good IV access with no extravasation. Breath holding instructions was given to the patients to avoid respiratory motion artifacts. 5.0mg sublingual Isosorbide Dinitrate was given. Finally, non-ionic contrast media (Ultravist 370 mgI/ml) was injected through the peripherally inserted IV cannula using dual-head powered automatic injector followed by 50cc saline flushing. The amount of contrast material was adapted according to patient body habitus (1.0ml/kg).

III- *CT scan protocol:* 320-row multidetector CT scanner (Aquilion One, Toshiba Medical Systems, Otawara, Japan) installed at Tanta University Educational Hospital was used for scanning through these steps:

- Initial scanogram was obtained in AP and lateral projection for automatic radiation dose calculation and for planning scan range. The scan started from carina down to the apex of the heart.
- Automatic bolus tracking technique was used to detect the arrival of contrast material at descending aorta. In patients with coronary stents, the ROI

was placed at descending aorta at mid heart level with trigger threshold set at 230 repetitive low-dose monitoring examinations (120kV, 50mAs, 0.5 second scanning time) were performed 10 seconds after contrast medium injection began. When the trigger threshold was reached, the scan started immediately after breath holding command.

IV- *Image acquisition:* Acquisition parameters: 0.35sec gantry rotation time, variable mA (range: 250-580mA), variable kv (range: 100-135kv). Single heart beat acquisition was routinely performed in those with heart rate below 65bpm they were 21 patients and the scan window was set at 70-80% of R-R interval while two heart beats acquisition was performed in patients with heart rate above 70bpm they were 2 cases. In those with heart rate ranged from 65 to 70bpm they were 7 cases, the scanning window was set to 30-80% of R-R interval to include end systolic phase.

VII- *Image reconstruction:* Images were reconstructed at 0.5mm slice thickness and 0.5mm interval with smooth and sharp reconstruction kernels at 75% of R-R interval and at the best diastolic phase. The best systolic phase was also reconstructed in those whom scan window was set to include 30-80% of R-R interval.

VIII- *Post processing:* The reconstructed images were transferred to workstation (Vitrea Fx, Vital Images, USA) to obtain multiplanar reformatted images in axial, sagittal and coronal planes. Also maximum intensity projection, 3D volume rendered images, semitransparent 3D volume rendered images and curved planar reformations were obtained for demonstration of coronary artery pathology.

IX- *Image analysis for evaluation of coronary arteries:*

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

The sum of calcified plaque scores in all coronary arteries which were separately calculated quantitatively according to the Agatston method. The presence of CAC was defined as CACS >0, and the risk level of CHD was defined by CACS according to the 4 commonly used thresholds in clinical practice (0, 10, 100, and 400 Agatston units). Due to the relative small number of subjects in the group of the 0-10, we merged it with the 10-100, and finally categorized into 4 categories: Low (CACS=0), moderate (0<CACS<100), high (100<CACS<400), very high (CACS>400) [7].

B- *Evaluation of coronary artery stenosis:*

Calculation of the Gensini score was initiated by giving a severity score to each coronary stenosis

as follows: 1 point for  $\leq 25\%$  narrowing, 2 points for 26 to 50% narrowing, 4 points for 51 to 75% narrowing, 8 points for 76 to 90% narrowing, 16 points for 91 to 99% narrowing, and 32 points for total occlusion. Thereafter, each lesion score is multiplied by a factor that takes into account the importance of the lesion's position in the coronary circulation (5 for the left main coronary artery, 2.5 for the proximal segment of the left anterior descending coronary artery, 2.5 for the proximal segment of the circumflex artery, 1.5 for the mid-segment of the left anterior descending coronary artery, 1.0 for the right coronary artery, the distal segment of the left anterior descending coronary artery, the posterolateral artery, and the obtuse marginal artery, and 0.5 for other segments). Finally, the Gensini score was calculated by summation of the individual coronary segment scores [8].

#### Statistical methodology:

Data were fed to the computer and analyzed using IBM SPSS software package Version 20.0. (Armonk, NY: IBM Corp) qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level. The used tests were: Chi-square test for categorical variables, to compare between different groups, Monte Carlo correction used when more than 20% of the cells have expected count less than 5.

## Results

The mean value of CIMT was  $1.28 \pm 0.32$ , only 6 patients had normal CIMT (20%) and 24 patients had CIMT  $> 9$  (80%). 8 patient (20%) had coronary plaque score=0, 6 patients had low CPS (1-5) & 16 patients had high CPS  $> 5$  (Table 1).

Table (1): Distribution of the studied cases according to carotid artery Doppler.

Carotid artery Doppler	No.	%
<i>Intimal thickness (CIMT):</i>		
Normal ( $\leq 0.9$ )	6	20
Abnormal ( $> 0.9$ )	24	80
Min.-max	0.50-2.0	
Mean $\pm$ SD	1.22 $\pm$ 0.364	
Median	1.30	
<i>Carotid plaque score:</i>		
No plaque (0)	8	26.7
Low (1-5)	6	20
High ( $\geq 5$ )	16	53.3
Min.-max	0.0-1 0.90	
Mean $\pm$ SD	4.95 $\pm$ 3.24	
Median	5.45	

According to CACS we found that 5 patients out of 30 had low CACS representing 16.7%, 10 patients had moderate CACS representing 33.3%, 7 patients had high CACS representing 23.3% and 8 cases had very high CACS representing 26.7% with mean 279 (ranging from 0 to 1186) (Table 2).

Table (2): Distribution of the studied cases according to CACS.

Coronary artery calcium score (CACS)	No.	%
Low	5	16.7
Moderate ( $0 < \text{CACS} \leq 100$ )	10	33.3
High ( $100 < \text{CACS} \leq 400$ )	7	23.3
Very high ( $\text{CACS} > 400$ )	8	26.7
Min.-max	0.0-1186.0	
Mean $\pm$ SD	279.0 $\pm$ 349.7	
Median	125.0	

According to Gensini score, 6 patients out of 30 had Gensini score=0 representing 20%, 11 patients had low Gensini score representing 36.7%, 13 patients had high Gensini score representing 43.3% (Table 3).

Table (3): Distribution of the studied cases according to Gensini score.

Gensini score	No.	%
Normal (0)	6	20
Low ( $< 20$ )	11	36.7
High ( $\geq 20$ )	13	43.3
Min.-max	0.0-112.0	
Mean $\pm$ SD	21.03 $\pm$ 25.33	
Median	14.50	

#### Relation between carotid artery Doppler and Gensini score shown at (Table 4) as follow:

1- The relation between carotid intimal thickness and Gensini score:

- Sex patients had normal CIMT, 4 of them had normal Gensini score, one case had low Gensini score & one case had high Gensini score.

- Twenty four patients had abnormal CIMT, 2 cases had normal Gensini score, 10 cases had low Gensini score & 12 cases had high Gensini score.

\*\* There was significant association between carotid intimal thickness and Gensini score ( $p$  value=0.045).

2- The relation between Gensini score and carotid plaque score:

- Eight patients had normal (CPS=0), 5 of them had normal Gensini score, 2 had mild Gensini score & 1 had sever Gensini score.

- Six patients had low CPS, 4 of them had low Gensini score & 2 had high Gensini score.

- Sixteen patients had high CPS, one of them had normal Gensini score, 5 cases had low Gensini score & 10 cases had high Gensini score.

\*\* There was significant association between carotid plaque score and Gensini score ( $p$ -value=0.004).

Table (4): Relation between carotid artery Doppler and Gensini score.

Carotid artery Doppler	Gensini score						$\chi^2$	MC <sub>p</sub>
	Normal (n=6)		Low (n=11)		High (n=13)			
	No.	%	No.	%	No.	%		
<b>CIMT:</b>								
Normal ( $\leq 0.9$ )	4	66.7	1	18.2	1	7.7	5.250*	0.045*
Abnormal ( $> 0.9$ )	2	33.3	10	81.8	12	92.3		
<b>CPS:</b>								
No plaque (0)	5	66.7	2	37.5	1	7.7	7.569*	0.004*
Low (1.2-4.9)	0.0	0.0	4	25.8	2	15.3		
High ( $\geq 5$ )	1	16.7	5	37.5	10	77		

Relation between coronary artery calcium score (CACS) and Gensini score as shown in (Table 5):

- Patients with Gensini score=0 (no atherosclerosis) were 6 patients, 4 of them had CACS=0 & 2 of them had moderate CACS.
- Patients with Gensini score less than 20 (mild atherosclerosis) were 11, 7 of them had moderate CACS, 2 of them had high CACS and 2 of them had very high CACS.
- Patients with Gensini score more than 20 (severe atherosclerosis) were 13 patients, 1 of them had CACS=0, 1 of them had moderate CACS, 5 of them had high CACS and 6 of them had very high CACS.

\*\* There was significant association between Gensini score and coronary artery calcium score ( $p$ -value=0.045).

Table (5): Relation between Coronary Artery Calcium Score (CACS) and Gensini score.

Coronary artery calcium score (CACS)	Gensini score						$\chi^2$	FE <sub>p</sub>
	Normal (n=6)		Mild (n=11)		Sever (n=13)			
	No.	%	No.	%	No.	%		
• Low (CACS=0) (n=5)	4	66.7	0.0	0.0	1	7.7	3.61	0.039*
• Moderate (0<CACS $\leq 100$ ) (n=10)	2	33.3	7	63.6	1	7.7		
• High (100<CACS $\leq 400$ ) (n=7)	0.0	0.0	2	18.2	5	38.5		
• Very high (CACS $> 400$ ) (n=8)	0.0	0.0	2	18.2	6	46.1		

Coronary plaques presented a calcified pattern in 43.3% (n=13), soft pattern in 30% (n=11), and

mixed in 53.3% (n=16), while carotid plaques were calcified in 30% (n=9), soft in 40% (n=12), and mixed in 43.3% (n=13), there was significant association between types of coronary and carotid arteries plaques ( $p$ -value=0.013, 0.045 & 0.025) (Table 6) & Fig. (1).

Table (6): Comparison between carotid Doppler and coronary according to type of plaque.

Type of plaques	Carotid artery		Coronary artery		$p$
	No.	%	No.	%	
Calcified	9	30	13	43.3	0.013
Soft	12	40	11	30	0.045
Mixed	13	43.3	16	53.3	0.025

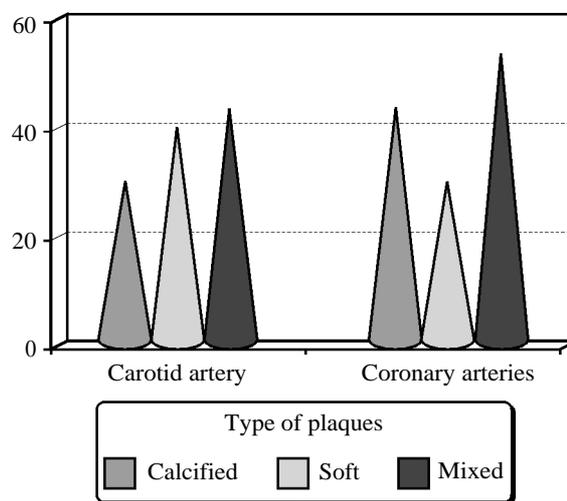


Fig. (1): Comparison between carotid Doppler and coronary according to type of plaque.

Relation between coronary artery calcium score (CACS) and Carotid Doppler shown in (Table 7) as follow:

A- The relationship between Coronary Calcium Score (CACS) and carotid intimal thickness as follow:

- Patients with CACS=0 were 5 patients 2 of them had normal carotid intimal thickness and 3 of them had increased intimal thickness  $> 9$ mm.
- Patients with moderate CACS were 11 patients 4 of them with normal carotid intimal thickness and 7 of them with increased intimal thickness  $> 9$  mm.
- Patients with high CACS were 5 all of them with increased intimal thickness  $> 9$ mm.
- Patients with very high CACS were 9 all of them showed increased intimal thickness  $> 9$ mm.

\*\* There was significant association between coronary artery calcium score and carotid intimal thickness ( $p$ -value=0.048).

Table (7): Relation between Coronary Artery Calcium Score (CACS) and Carotid Doppler.

Carotid artery Doppler	CACS								$\chi^2$	MC <sub>p</sub>
	Low (n=5)		Moderate (n=10)		High (n=8)		Very high (n=8)			
	No.	%	No.	%	No.	%	No.	%		
<b>CIMT:</b>										
• Normal (<0.9)	2	40	4	36.4	0	0.0	0	0.0	3.565	0.048
• Abnormal (>0.9)	3	60	6	63.6	7	100	8	100		
<b>Carotid plaque score:</b>										
• No plaque (0)	3	60	4	36.4	1	20	0	0.0	2.439	0.025
• Low (1-5)	1	20	4	36.4	0	0	1	11.1		
• High (≥5)	1	20	3	27.2	4	80	8	88.9		

**B- The relationship between Coronary Calcium Score (CACS) and carotid plaque score as follow:**

- Patients with CACS=0 were 5 patients 3 of them had carotid plaque score=0, 1 of them had carotid plaque score <5 and 1 of them had carotid plaque score >5.
- Patients with moderate CACS were 11 patients 4 of them had carotid plaque score=0, 4 of them had carotid plaque score <5 and 3 of them had carotid plaque score >5.
- Patients with high CACS were 5 patients 1 of them had carotid plaque score=0, 0 of them had carotid plaque score <5 and 4 of them had carotid plaque score >5.

• Patients with very high CACS were 9 patients 0 of them had carotid plaque score=0, 1 of them had carotid plaque score <5 and 8 of them had carotid plaque score >5.

\*\* There was significant association between coronary artery calcium score and carotid plaque score (p-value=0.025).

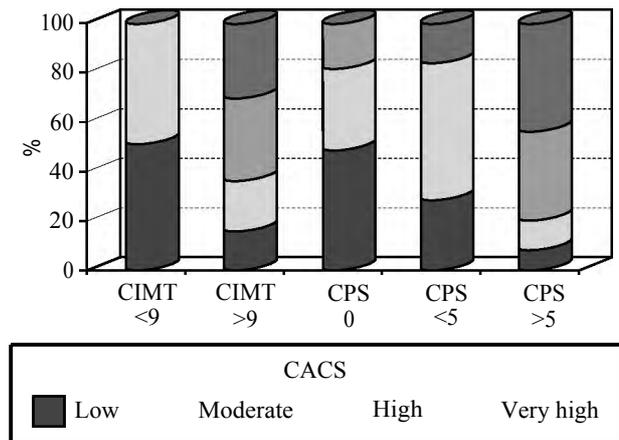


Fig. (2): Relation between CACS and carotid artery Doppler examination (n=30).

**Illustrated cases:**

**Fig. No. (3):** Diabetic hypertensive female patient aged 48 years old with body mass index 28, presented by atypical chest pain & dyspnea referred to rule-out coronary artery disease.

**Findings:**

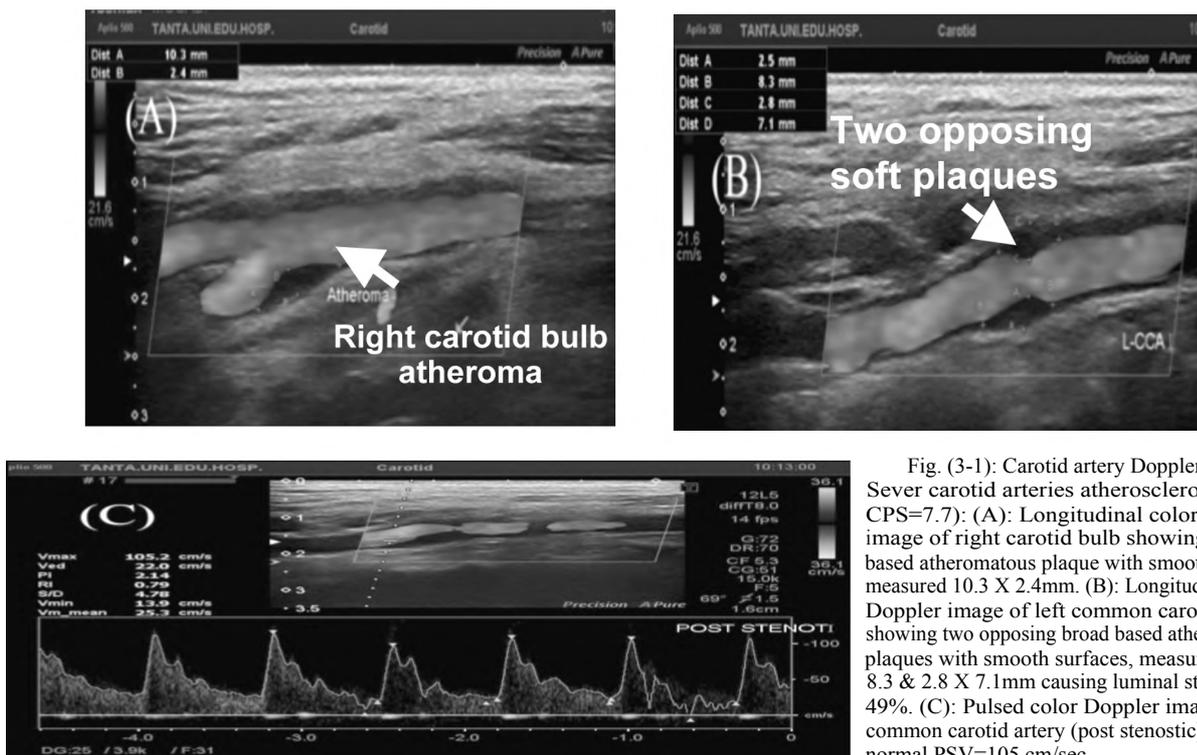


Fig. (3-1): Carotid artery Doppler revealed Sever carotid arteries atherosclerosis (high CPS=7.7): (A): Longitudinal color Doppler image of right carotid bulb showing a broad based atheromatous plaque with smooth surface measured 10.3 X 2.4mm. (B): Longitudinal color Doppler image of left common carotid artery showing two opposing broad based atheromatous plaques with smooth surfaces, measured 2.5 X 8.3 & 2.8 X 7.1mm causing luminal stenosis by 49%. (C): Pulsed color Doppler image of left common carotid artery (post stenotic) revealed normal PSV=105 cm/sec.

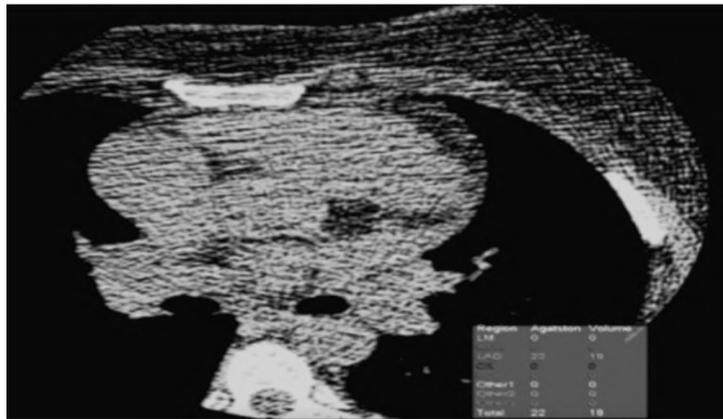


Fig. (3-2): Unenhanced cardiac CT axial image demonstrating CACS by Agatston units which equal 22 (low score).

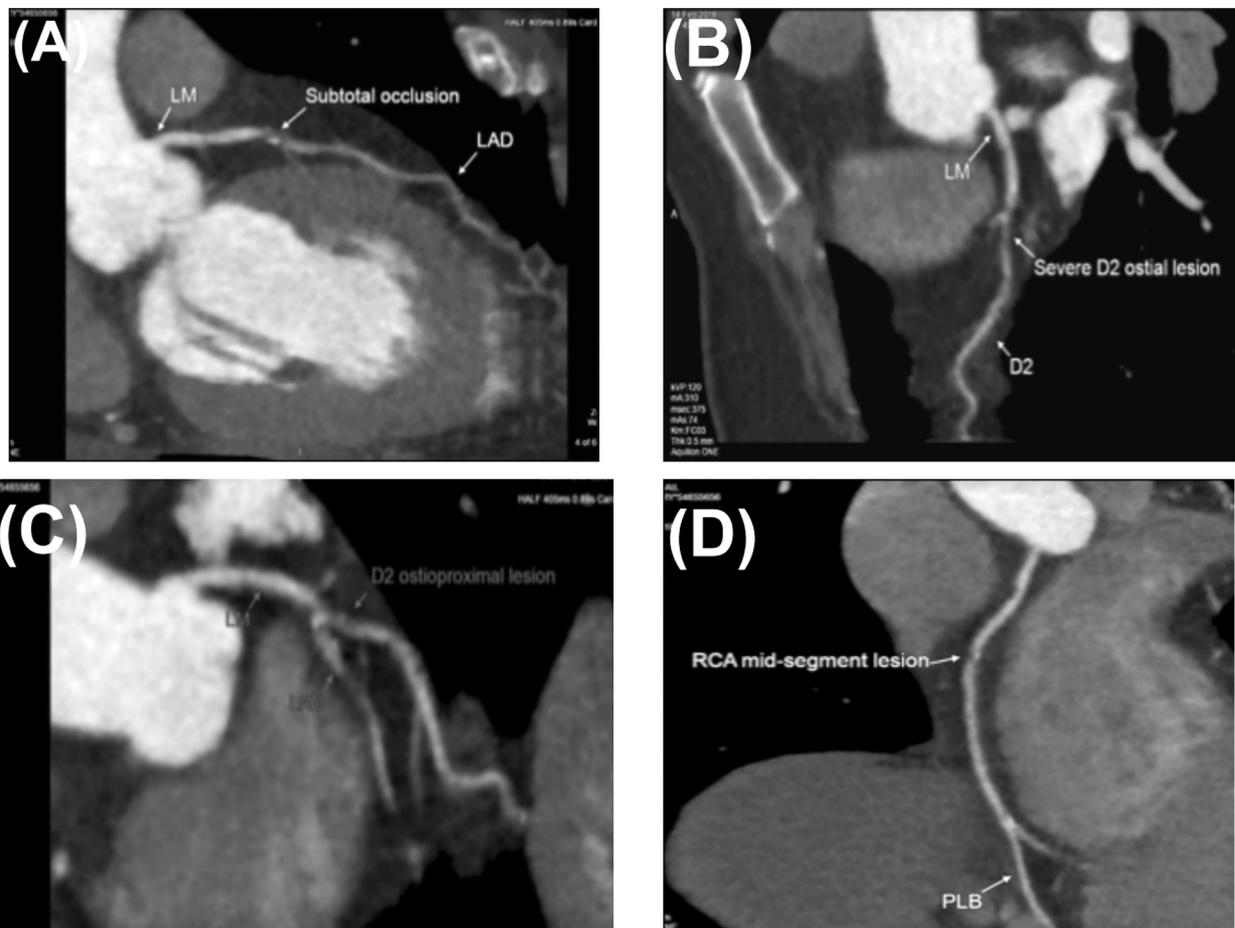


Fig. (3-3): Multidetector coronary CT angiography revealed severe coronary artery disease (Gensini score=30): (A): Left oblique image showing a mixed eccentric plaque at proximal to mid-segment of LAD exerting subtotal occlusion measured about 6mm. (B & C): Curved MPR images showing soft eccentric plaque at ostio-proximal segment of D2 exerting severe stenosis about 70% & measuring about 9mm in length. (D): Curved MPR image showing a mixed eccentric plaque at mid-segment of RCA exerting moderate stenosis (60%, length: 6mm).

Fig. No. (4):

Hypertensive smoker male patient aged 68 years old, with body mass index 22, presented by atypical chest pain, referred to rule-out coronary artery disease.

Findings:

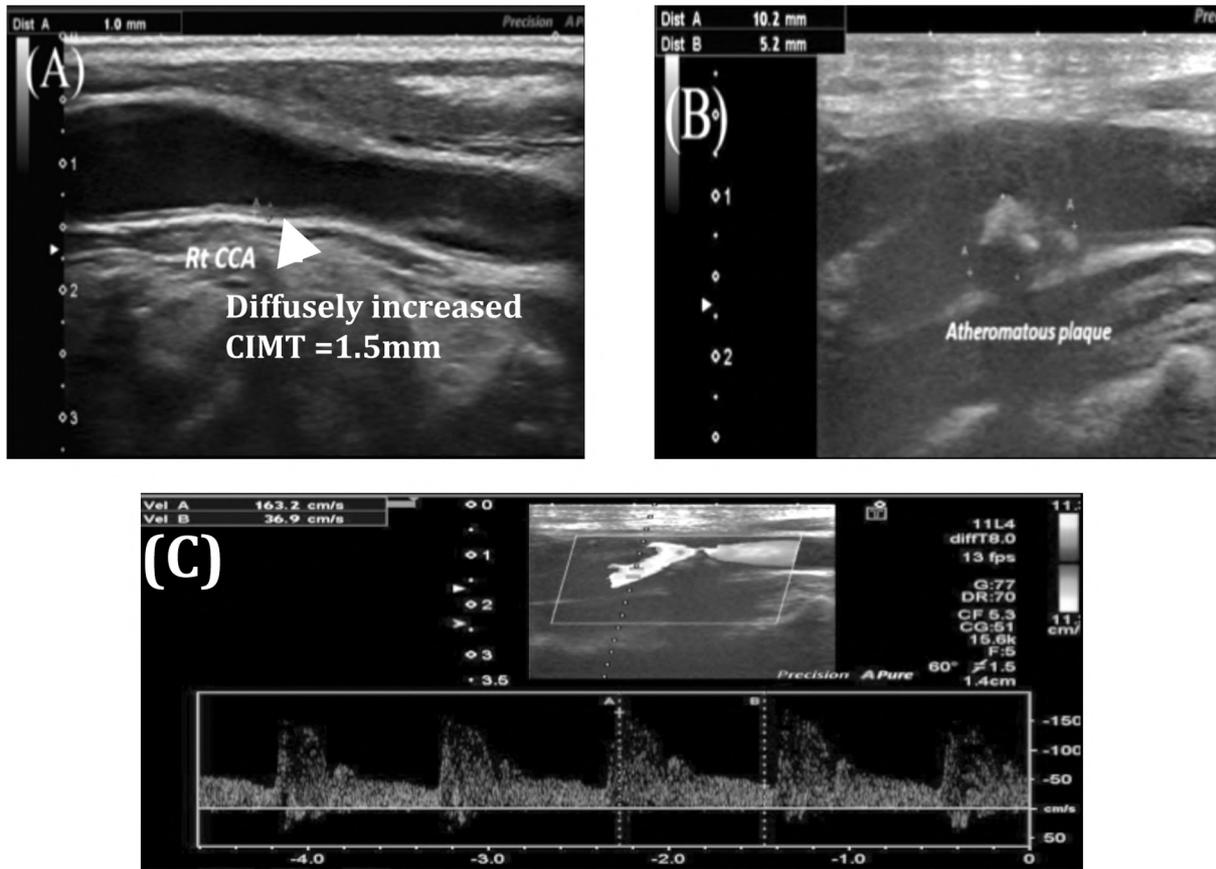


Fig. (4-1): Carotid artery Doppler revealed severe carotid arteries atherosclerosis (high CPS=5.2): (A): Longitudinal gray-scale image of R-CCA showing increased intimal-media complex thickening measured 2mm. (B): Longitudinal gray-scale image showing a calcified heterogeneous broad based plaque at the posterior wall of right carotid bulb measuring 10.2 X 5.2mm causing luminal stenosis by 68%. (C): Duplex of the right common carotid artery (post stenosis) showing increased PSV=163cm/sec (post stenotic jet) indicating moderate stenosis.



Fig. (4-2): Unenhanced CT axial image demonstrating CACS by Agatston units which equal 237 (moderate scoring).

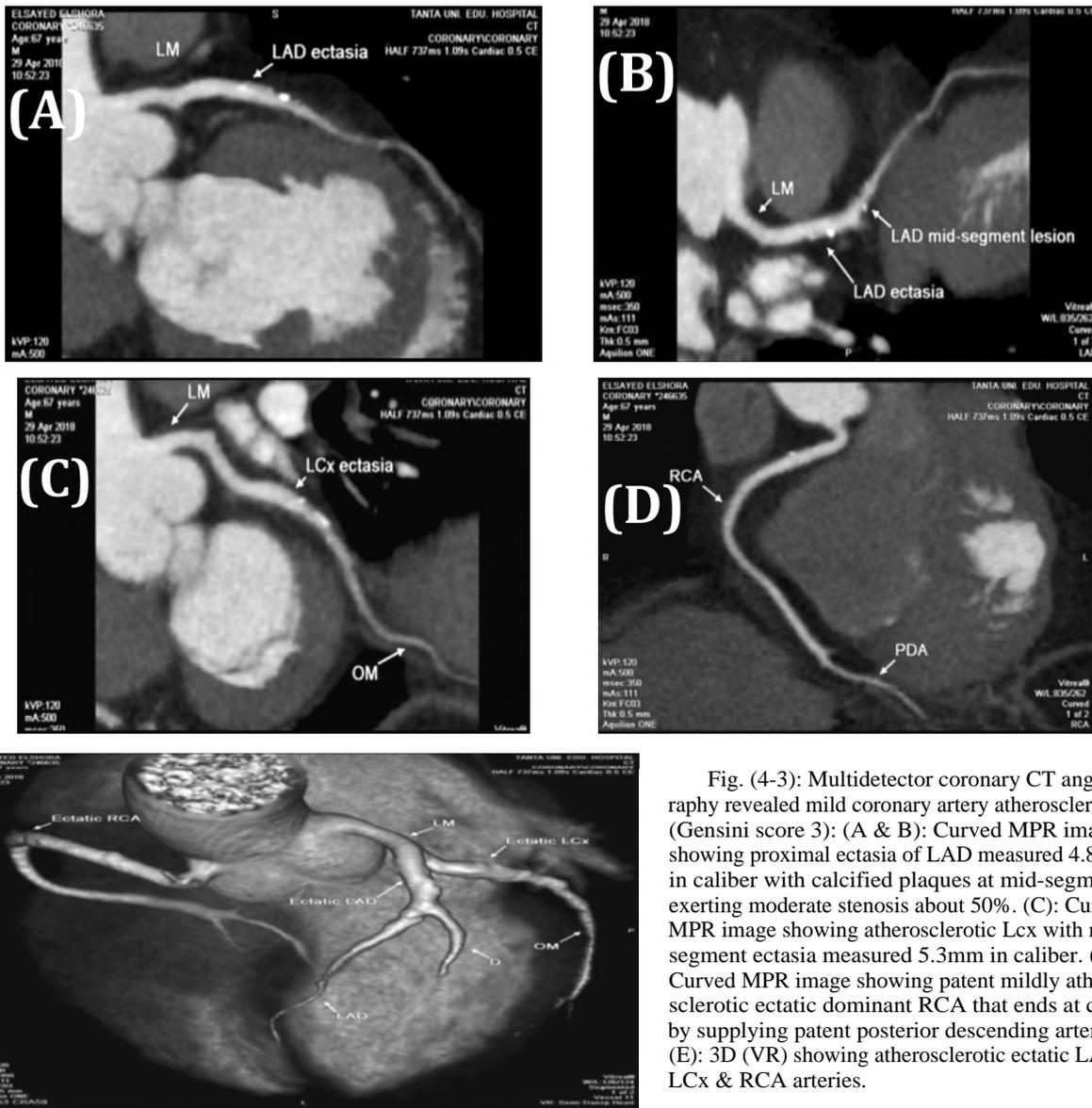
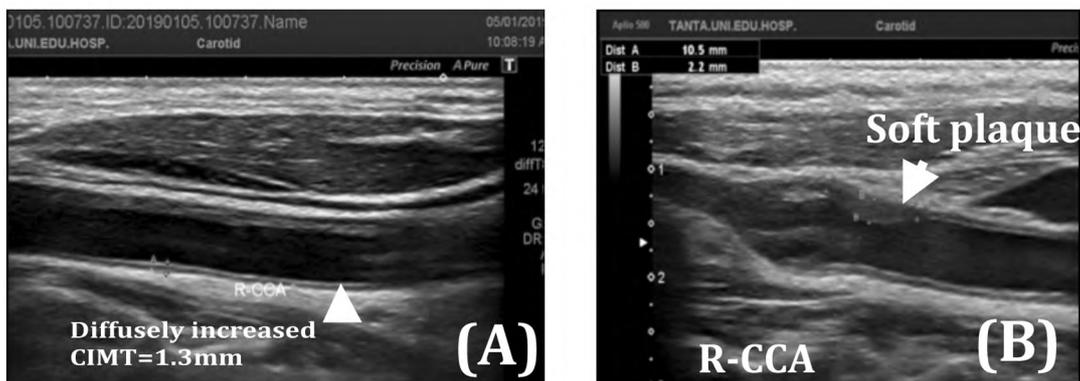


Fig. (4-3): Multidetector coronary CT angiography revealed mild coronary artery atherosclerosis (Gensini score 3): (A & B): Curved MPR images showing proximal ectasia of LAD measured 4.8mm in caliber with calcified plaques, exerting moderate stenosis about 50%. (C): Curved MPR image showing atherosclerotic LCx with mid-segment ectasia measured 5.3mm in caliber. (D): Curved MPR image showing patent mildly atherosclerotic ectatic dominant RCA that ends at crux by supplying patent posterior descending arteries. (E): 3D (VR) showing atherosclerotic ectatic LAD, LCx & RCA arteries.

Fig. No. (5):

Male smoker patient aged 50 years old with body mass index 40 complained of atypical chest pain, referred to rule-out coronary artery disease.

Findings:



Diffusely increased CIMT=1.3mm (A)

R-CCA (B)

Soft plaque

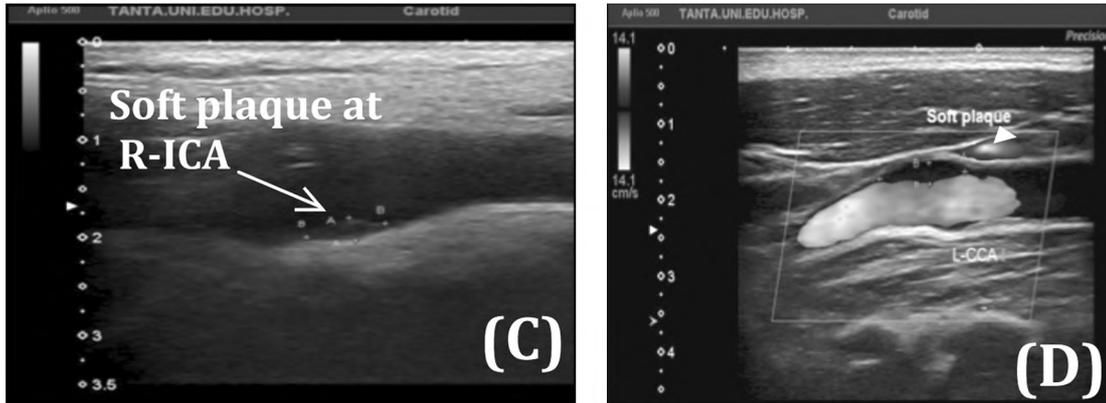


Fig. (5-1): Carotid artery Doppler revealed sever carotid arteries atherosclerosis (high CPS=7.4): (A): Longitudinal gray-scale image of R-CCA showing increased intimal- media complex thickening measured 1.3mm. (B): Longitudinal gray-scale image showing a broad based soft homogenous plaque at the anterior wall of distal part of the R-CCA measuring 10.5 X 2.2mm with no significant stenosis. (C): Longitudinal gray-scale image showing small soft homogenous atheroma with smooth surface at the beginning of the R-ICA measuring 6.3 X 2.4mm. (D): Color Doppler image showing an echolucent broad based plaque at anterior wall of distal L-CCA 13.4 X 2.8mm.

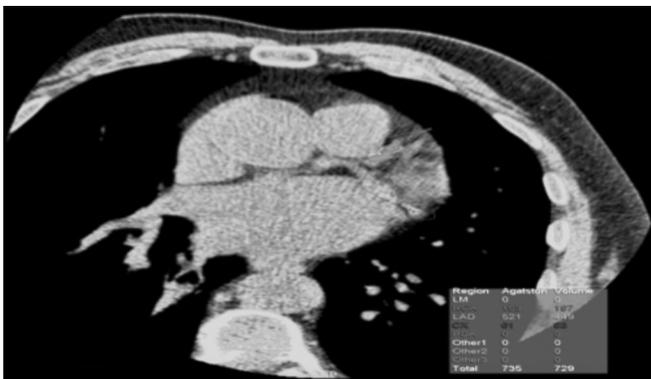


Fig. (5-2): Unenhanced cardiac CT axial image demonstrating CACS by Agatston units which equal 735 (high scoring).

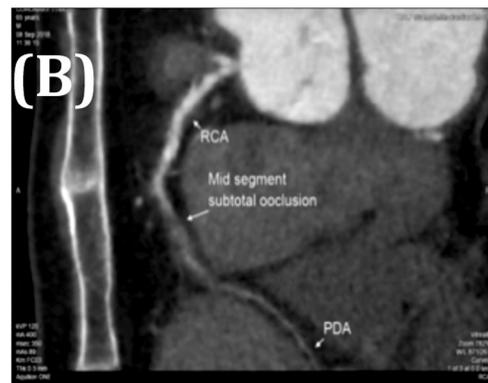
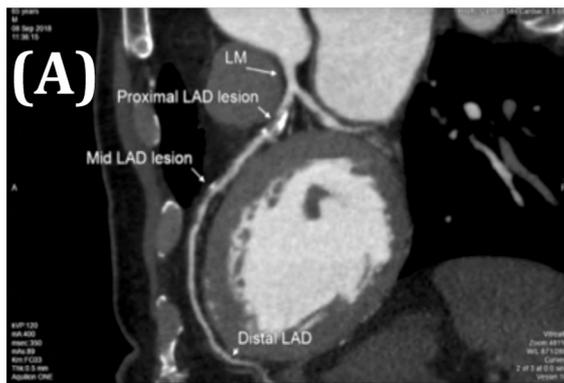


Fig. (5-3): Multidetector coronary CT angiography revealed sever coronary atherosclerosis (Gensini scor=28): (A): Curved MPR image showing 'multiple soft and mixed plaques along the entire LAD exerting moderate stenosis about 60% for 2cm length its proximal segment. (B): Curved MPR image showing stenosis about 50% for 8mm length at distal segment RCA mid-segment subtotal occlusion caused by soft eccentric plaque measured about 1.3cm. (C): 3D VR image showing atherosclerotic LAD lesions & subtotal occlusion of the RCA.

Fig. No. (6):

Male patient aged 51 years old complained of dyspnea and atypical chest pain with body mass index 28 referred to rule-out coronary artery disease.

Findings:

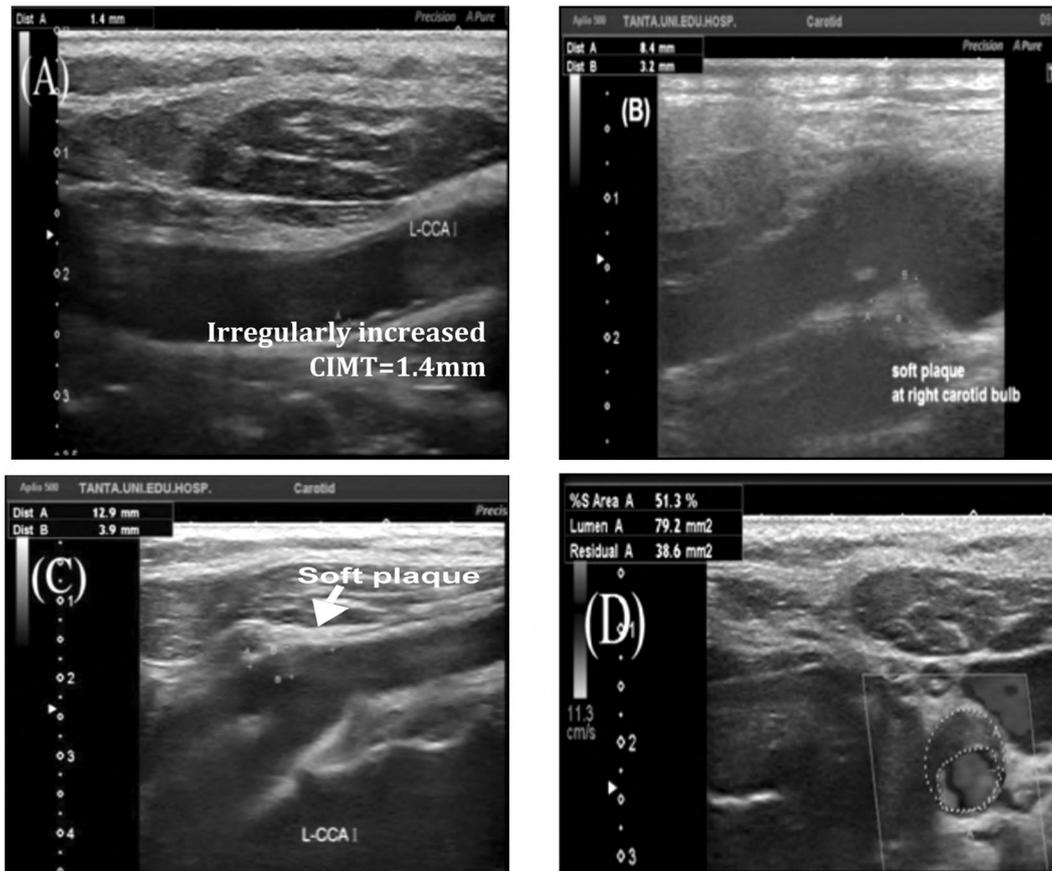


Fig. (6-1): Carotid artery Doppler revealed severe carotid arteries atherosclerosis (CPS=6.1): (A): Longitudinal gray-scale image of L-CCA showing fine irregular thickened intimal wall measured 1.4mm. (B): Longitudinal gray-scale image of R-CCA showing small soft plaque measured 4.3 X 2.2mm at its posterior wall (C): Longitudinal gray-scale image showing a broad based atheromatous plaque at the anterior wall of left carotid bulb measuring 12.9 X 3.9mm. (D): Transverse color Doppler image showing reduction of L-CCA lumen about 51% caused by soft atheromatous plaque.



Fig. (6-2): Unenhanced CT axial image demonstrating CACS by Agatston units which equal 223 (moderate scoring).



Fig. (6-3): Multidetector coronary CT angiography revealed severe coronary atherosclerosis (Gensini score=48): (A): Curved MPR image showing a totally occluded mid-segment of LAD measured about 3cm by mixed plaques. (B): 3D (VR) showing severe stenosis of the mid-segments of LAD artery.

Fig. No. (7):

Female patient aged 48 years old with body mass index 25 complained of atypical chest pain, referred to rule-out coronary artery disease.

Findings:

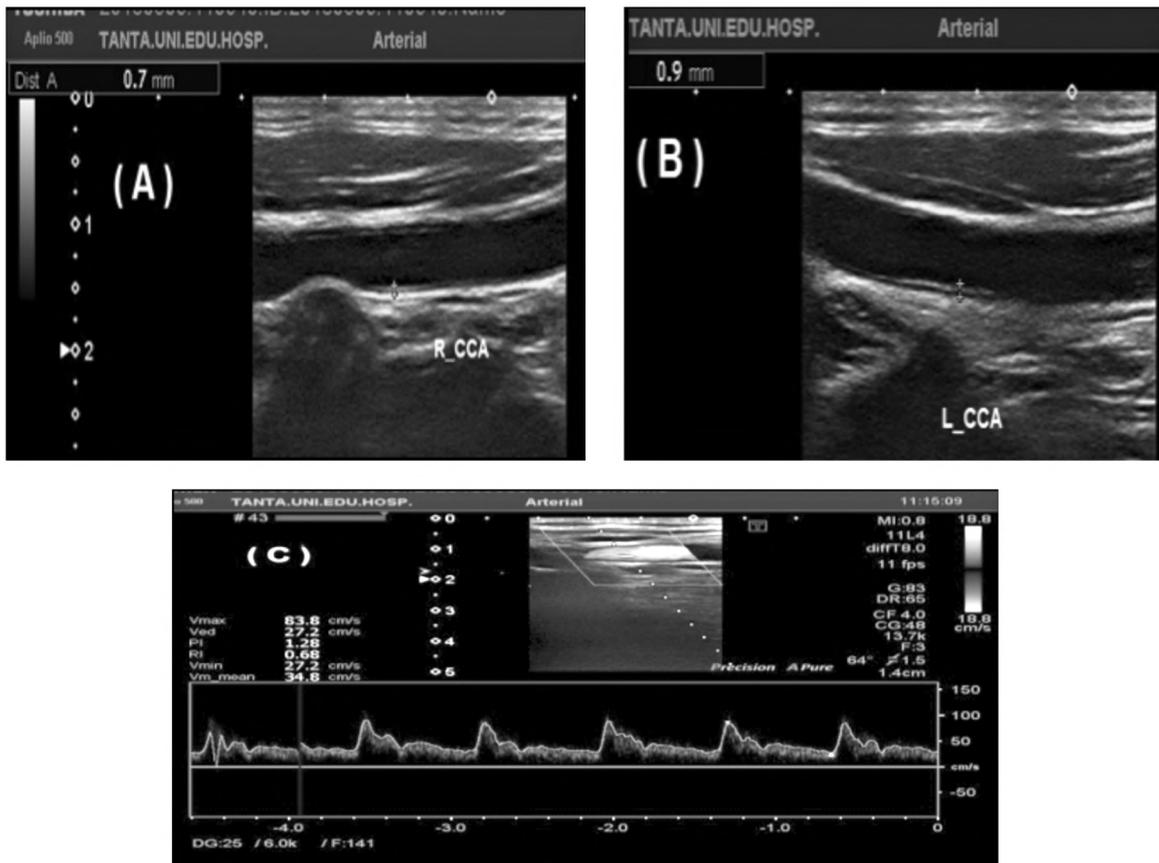


Fig. (7-1): Normal Carotid artery Doppler. (A & B): Longitudinal gray-scale images showing normal intimal-media complex thickening measured 0.7mm on R-CCA & 0.9mm on L-CCA. (C): Duplex of the right common carotid artery showing normal PSV=83cm/sec.



Fig. (7-2): Unenhanced cardiac CT axial image demonstrating CACS by Agatston units which equal 2 (low scoring).

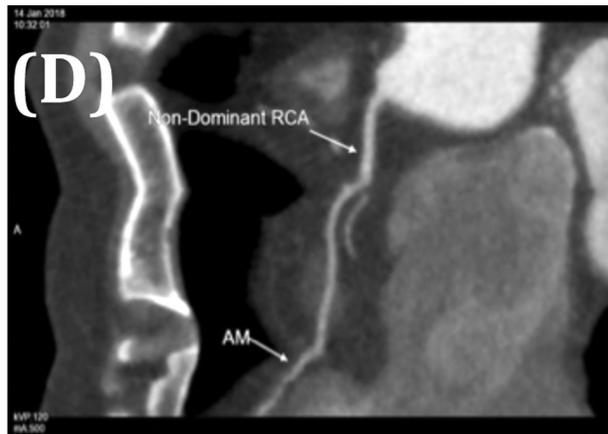
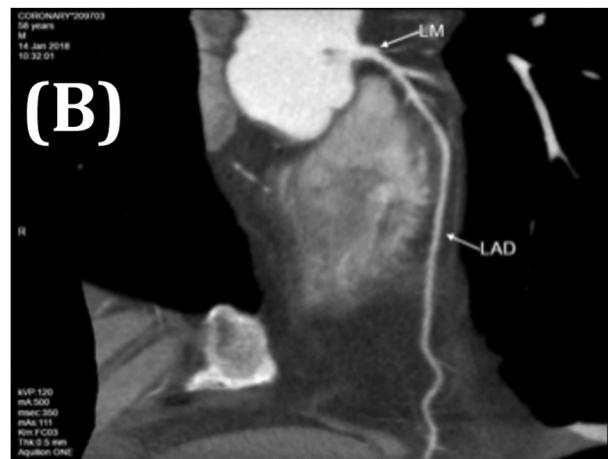
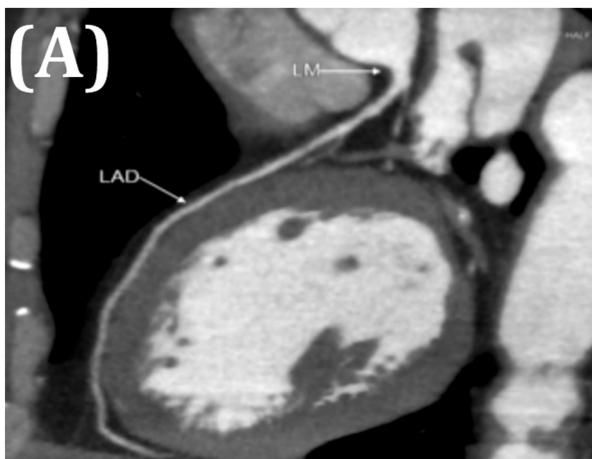


Fig. (7-3): Multidetector coronary CT angiography. (A & B): Curved MPR images showing average caliber patent LM & LAD with no definite athermanous plaque. (C): 3D (VR) showing branches of LM: LCX of average caliber patent dominant vessel supplying two OM branches, posterior LV branch & LAD supplying three diagonal branches and ends distally beyond the apex. (D): Curved MPR image showing average caliber patent RCA that supplies acute marginal branch. (E): 3D (VR) showing course and branches of RCA.

## Discussion

Our results showed significant relation between CIMT and severity of coronary artery disease evaluated by Gensini score ( $p < 0.045$ ). One of the first longitudinal studies of association between the carotid morphology with the risk of acute coronary events was based on the analysis of the population-based Kuopio Ischaemic Heart Disease (KIHD) study [9], an extensive epidemiologic research project that was launched in the 1980s and involved around three thousand middle-aged males from the Eastern Finland. The study also showed 11% increased risk of myocardial infarction with each 0.1mm incremental increase of CIMT and that the presence of intimal-medial thickening was associated with a 2.17-fold risk of acute myocardial infarction compared with men free of any structural changes in the carotid artery wall at baseline. Following this study, Sugathan et al., 2000 [10] found that a CIMT of 1mm is associated with an increased risk of having a significant coronary stenosis using intravascular ultrasound as reference.

Different following studies findings are of different levels of significance with regards to adding CIMT to conventional cardiovascular risk scores, Oord et al., 2013 [11] concluded in his systematic review that the addition of CIMT to traditional CVD risk prediction models does not lead to a statistical significantly increase in performance of those models. Guaricci et al., 2014 [12] focused on the relationship between CIMT and presence, severity and features of CAD detected by CCTA in intermediate risk and symptomatic patients showing that CIMT predicts the CACS, the presence of obstructive CAD and the extension of CAD expressed as SIS and Gensini's score.

The literature has stated that such contradicting results are probably stemming from the differences in study design, differences techniques in CIMT measurements, such as measuring the common or internal segment and whether plaques are included or excluded from analyses, as covered in a review by Naqvi & Lee, 2014 [13]. Another explanation to such phenomenon is that CIMT is correlated positively & strongly with CVD risk, yet adding it to a prediction model with other CVD risk factors might not add to the score because of collinearity, specially that all the risk predictor in traditional risk are proven linear predictors of atherosclerosis and CIMT [14].

As expected, the carotid plaque score was significantly different between those with unobstructed

coronary arteries and those with obstructive CAD, as we found significant correlation between carotid plaque score and Gensini score ( $p < 0.004$ ), in agreement with Jialin et al., 2018 [15] who found that the patients with high Gensini Score possessed higher levels of maximum carotid plaque area, suggesting that carotid plaque quantification may serve as a useful screening tool for assessing the extent of significant coronary atherosclerosis. Hirata et al., 2018 [6] whose study showed that high CPS was significantly associated with an increase in cardiovascular mortality in cohort of oldest old individuals with an extremely low CVD risk.

In the current study we found high prevalence of mixed plaques in coronary and carotid arteries representing 54.3% and 43.3% respectively with significant relation between type of plaques them ( $p < 0.02$ ). These findings are in agreement with Grutta et al., 2017 [16] who found that mixed plaque in 84% of carotid plaques and 56% of coronary arteries plaques with significant correlation between coronary and carotid plaques types, so atherosclerosis should be considered as a systemic disease with heterogeneous extent and pattern across anatomic districts. Furthermore, atherosclerotic plaque imaging performed by CCT and carotid US may refine quantitative data of coronary calcium score and CIMT.

The coronary artery calcium CAC score is a direct measure of the amount of calcified atheroma and is highly correlated with total coronary atheroma that includes the measured calcified plaque and unmeasured non-calcified plaque [17]. Previous studies have considered the association between coronary artery disease and CAC, especially in asymptomatic patients. The prognostic value of CAC in asymptomatic patients has been shown to be independent of traditional risk factors in studies such as the Multi-Ethnic Study of Atherosclerosis (MESA) [18].

Zhao et al., 2018 [19] whose study reported that coronary calcification is the strongest predictor of significant stenosis irrespective of the continent or geographical origin of the patients. In addition a significant correlation between coronary artery calcium score and coronary artery disease ( $p$ -value  $< 0.016$ ) with sensitivity 92.3 was detected in our study, in agreement with Greenland et al., 2018 [20] who reported that coronary artery calcification has emerged as the most predictive single cardiovascular risk marker in asymptomatic persons, capable of adding predictive information beyond the traditional cardiovascular risk factors.

In the current study, we found that the presence of carotid artery lesions was associated with incident positive CAC score and, from a statistical point of view, both CIMT and CPS showed a strong relationship with extensive coronary artery calcification ( $p < 0.048$ ) and ( $p < 0.025$ ) respectively. These associations should be taken into consideration when plaque is identified during a carotid artery examination.

These findings are consistent with Jeevarethnam et al., 2017 [21] who observed that carotid plaque and increased CIMT both were associated with the presence of coronary calcification. Gaibazzi et al., 2016 [22] found that the prevalence of carotid plaque was approximately double (71.5 Vs. 34.8%,  $p = 0.001$ ) and CACS and CIMT significantly higher ( $p = 0.001$ ) in patients with CAD compared with the group without CAD. Guaricci et al., 2014 [12] also reported a significant correlation was found between CIMT and CACS ( $p < 0.01$ ).

Some limitations occur in this study. First, the results should be confirmed in a larger population on a multicenter basis, despite our cohort was highly selected and underwent CCT and carotid US in a very limited temporal window. Second, our patients were not studied with intravascular US, which is considered the gold standard for plaque characterization. Third, CCA was used only to confirm coronary artery disease; the study was not designed to assess the diagnostic accuracy of CCT which is known to be high. Fourth, a somewhat biased referral population was studied, since we analyzed symptomatic patients with indication to CCT; in this regard, the referral population may explain the relative high prevalence of obstructive CAD.

#### Conclusion:

Our study assessed subclinical atherosclerosis as defined by CIMT, CPS and CACs to develop simple, non-invasive yet sensitive risk-prediction tools to promptly identify those individuals at risk of CVD as valuable clinical strategy that can be more widely implemented in everyday primary care practice.

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## الدوبلر على الشريان السباتي ودرجة تكلس الشرايين التاجية في تقييم تصلب الشرايين في المرضى محتملي الإصابة بأمراض الشرايين التاجية

تعد أمراض القلب والأوعية الدموية السبب الرئيسي للإعتلال والوفيات في كل من البلدان الصناعية وذات الدخل المنخفض إلى البلدان متوسطة الدخل. وحيث أن تصلب الشرايين هو الحالة المرضية الكامنة وراء غالبية أمراض القلب والأوعية الدموية في جميع أنحاء العالم. ويظل تصلب الشرايين بدون أعراض حتى يتطور إلى مرض يحد من التدفق الدم (ضيق الشريان بنسبة 70-80%) أو عندما تتشكل جلطة على تمزج أو تآكل ترسبات موجودة سابقاً. ومع ذلك، فإن نسبة كبيرة من المرضى تتدهور حالتهم الصحية فجأة نتيجة إحتشاء عضلة القلب أو الموت المحتمل.

وقد جمعت العديد من الدراسات بين مؤشرات المباشرة (مثل درجة تكلس الشريان التاجي) ومؤشرات غير مباشرة لتصلب الشرايين (مثل قياس سمك الطبقة الداخلية السباتية ودرجة الترسب السباتي).

إشتملت هذه الدراسة على ثلاثين مريضاً يعانون من أعراض الإصابة بمرض الشرايين التاجية وكان هناك إرتفاع معدل إنتشار تصلب الشرايين السباتية في المرضى الذين يعانون من أمراض تصلب الشرايين التاجية (91.7%). ووجد إرتباط كبير بين مرض تصلب الشريان السباتي الذي يقدر بحساب سمك جدار الشريان السباتي CIMT ودرجة الترسب للشريان السباتي CPS وشدة الإصابة بمرض شرايين القلب التاجية. كان هناك إرتفاع في درجة تكلس الشريان التاجي في المرضى الذين يعانون من أمراض الشرايين التاجية (95.8%). وجدنا أيضاً إرتباط هام بين درجة تكلس الشريان التاجي CACS وشدة الإصابة بمرض شرايين القلب التاجية.

في الختام: تقييم الدراسة تصلب الشرايين تحت الإكلينيكي وذلك بإعتبار سمك جدار الشريان السباتي CIMT ودرجة الترسب للشريان السباتي CPS ودرجة تصلب الشرايين التاجية CACS أداة بسيطة للتنبؤ بالمخاطر غير الغازية لتحديد الأشخاص الذين يتعرضون لخطر الأمراض القلبية الوعائية على الفور كإستراتيجية سريرية قيمة يمكن تنفيذها على نطاق أوسع في ممارسة الرعاية الأولية اليومية.