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Predictive Value of Carotid Ultrasonography in Coronary Artery Diseases

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Abstract
Background: As a real-time imaging technique, carotid ultrasonography is gaining popularity among doctors due to its accessibility, low cost, speed, safety, and lack of invasiveness. **This study aimed to** Determine non-invasive carotid ultrasonography parameters indicative of coronary artery disease by assessing the correlation between carotid artery disease and coronary artery disease using coronary CTA and invasive coronary angiography through cardiac catheterization. **Methods:** Forty patients were recruited for this prospective research after their doctors sent them to the radiology department of Benha university hospital for coronary computed tomography and carotid ultrasonography due to their suspicion of having CAD. Patients were separated into three groups (n=20 with a single lesion, n=10 with two lesions, and n=10 with three lesions) based on the number of lesions present in their coronary arteries. Carotid ultrasonography, CCT, and ICA, as well as a comprehensive history and physical examination, were performed on all patients. **Results**: Patients were on average 67.75.54 years old, and 62.5% were male. Patients with two or more coronary lesions had a larger carotid plaque burden than those with a single lesion. Neither the prevalence nor the location of plaques differed significantly across the groups. A cut of level more than 1.33 mm in IMT has an 80% sensitivity and an 87% specificity for predicting the severity of coronary artery disease (P0.001). **Conclusion:** IMT is the only marker having a substantial predictive value in individuals with coronary artery disease. The prevalence of coronary lesions increases with increasing Intima-media thickness diameter.

Keywords: Carotid ultrasonography's predictive value for diagnosing coronary artery disease.

1. Introduction

Coronary heart disease (CHD) is the largest cause of death in the world, and atherosclerosis is to blame. Identifying risk factors for CHD at an early stage is crucial for prevention and has the potential to save healthcare costs. It is generally agreed that risk assessment in atherosclerosis is an important first step in the prevention of cardiovascular events, since it pinpoints individuals who would benefit most from targeted diagnostic and therapeutic interventions.[1].

Atherosclerosis is a systemic vascular condition, which is a crucial feature of the disease. Ischemic events far away may be predicted by atherosclerotic lesions close to the site of the occurrence. [2].

Despite new recommendations from the European Society of Cardiology recommending noninvasive imaging for the first diagnostic care and risk assessment of patients with suspected CAD, invasive coronary angiography remains the gold standard for diagnosis at now. [3]. And yet, a recent American[4] and Canadian guidelines [5] ultrasonography is not mentioned as a possible diagnostic technique for cardiovascular disease, and instead only coronary artery calcium (CAC) scoring is used for risk assessment and interventional CVD decision making. However, recent developments in ultrasonography have renewed its use as a stratification modality. [6, 7]. In instance, ultrasonography for identification of subclinical atherosclerosis is widely used in clinical decision-making for both at-risk and prevalent CAD patients. This is especially true for carotid plaque evaluation and, more recently, femoral plaque assessment.

As a real-time imaging technique, carotid ultrasonography is gaining popularity among doctors due to its accessibility, low cost, speed, safety, and lack of invasiveness. This approach offers information on the common carotid arteries (CCA), bifurcation, internal carotid arteries (ICA), and external carotid arteries (ECA), and it may be used as an early detector and a follow-up tool.

Enhanced intima-media thickness (IMT) in the carotid arteries is one example of how ultrasonography probes may be used to immediately identify early arterial wall remodelling. The risk of coronary artery re stenosis may be assessed by IMT, and it is non-invasive and repeatable.[8].

This study aimed to identify carotid ultrasound parameters predictive of coronary artery disease as a non-invasive method by analysing the relationship between carotid artery disease as

detected by ultrasound and coronary artery disease as detected by CTA and invasive coronary angiography by cardiac catheterization.

2. Patients and methods

Forty patients with suspected coronary heart problems were recruited for this prospective research, with their doctors referring them to the radiology department at Benha university hospital for coronary computed tomography and carotid ultrasonography. Patients were enrolled between January 2022 and January 2023 from the Internal Medicine department at Benha University Hospital with the agreement of the hospital's ethics board. Patients gave their informed consent after being given all of the study's details.

Inclusion criteria were patients suspected of having CHD who have been allowed to participate in the trial.

Exclusion criteria were subjects with a known history of allergic response, renal failure, malignant arrhythmia, or pregnancy were excluded from the research.

The studied patients divided into three groups according to number of lesions in the coronary vessels: Single lesion n=20, Two lesions n=10 and Three lesion n=10.

All patients were subjected to the following:

Full history taking (sex, age, Smoking history, hypertension (defined as systolic BP 140 mmHg or diastolic BP 90 mmHg or use of antihypertensive drugs), diabetes, and stroke were also recorded. Comprehensive medical checkup including systolic, diastolic, and heart rate readings. Total cholesterol (TC), high-density lipoprotein (HDL-C), and low-density lipoprotein (LDL-C) levels were measured in the lab at the start of the study.

Carotid ultrasonography: Correlation between carotid ultrasonography and invasive coronary angiography is performed on the same day as coronary computed tomography. Subclinical atherosclerosis risk assessment and atherosclerosis progression monitoring are two areas where CIMT has received much research as a surrogate sign. Plaque was defined as an ultrasound-detected increase in the carotid intima-media thickness (CIMT), which is the distance between two echogenic lines representing the lumen-intima interface and the media-adventitia interface of the carotid arterial wall. Plaque in the carotid artery was defined as an echoic focal wall thickening that was at least 1.5mm bigger than the IMT in the rest of the carotid artery and protruded into the lumen.

In order to standardise picture capture, interpretation, and data gathering, we measured the carotid artery as part of our normal examination. Plaques in the carotid artery were looked for along its short and long axes, from the clavicle to the temporomandibular joint caudally to cranially, and by anterior, anterolateral, lateral, and posterolateral insonation on both sides to the extent that they were apparent. The GE Logiq 8 ultrasound scanner's 8–12 MHz transducer was used for the high-resolution carotid ultrasound imaging (GE Healthcare, Chicago, IL).

Patients were scanned while lying on their backs with their heads turned to the side. Multiple longitudinal and transverse perspectives were employed to look at the alterations in the vessel's far wall. Each side of the neck was filmed, and the distal common carotid artery and proximal internal carotid artery and bulb were imaged and measured as part of a thorough procedure (three projections on each side).

The common carotid artery (CCA), the bifurcation of the CCA, the internal carotid artery (ICA), and the external carotid artery (ECA) were all evaluated (ECA). According to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) guidelines, carotid artery stenoses were classified as mild (50%), moderate (51%- 70%), or severe (>70%) based on the percentage diameter of the stenosis.

Carotid IMT may be measured via ultrasound imaging. The far-wall IMT was calculated by averaging the far-wall IMT measurements taken from the outer wall (adventitia) of the left and right CCAs beginning below the bulb. The median of the left and right CCA values was the near-wall IMT. The average of the four CCA IMTs was used to get the mean IMT. The IMT of the distal wall was measured as the mean distance from the luminal-intimal to the medial-adventitial interfaces at three separate locations 1.0 cm proximal to the carotid bifurcation. An IMT more than 1.0 mm was considered abnormal based on data from healthy Chinese participants.

Coronary computed tomography: By providing three-dimensional view of the coronary lumen, stenoses, and plaque characteristics, coronary CT angiography (CCTA) has revolutionised the non-invasive evaluation of CAD (3D). These records may now be obtained with little X-ray exposure (typically on par with CACS) and rapid acquisition times, eliminating the need for patients to hold their breath or use beta-blockers to lower their heart rates. However, there is still significant variation in the degree to which protocols are optimised

across different facilities throughout the world. The night before their CTA, all patients were given metoprolol succinate, and during the test, they were given either intravenous metoprolol or diltiazem as required to keep their heart rates below 60 beats per minute.

The first is a non-contrast test used for calcium scoring, while the second is a contrast-enhanced CTA test used to assess coronary artery health. (J.F.) examined all CT examinations of the coronary tree for calcified plaque and used the Agatston-Janowitz (AJ130) technique to construct an overall CAC score for quantifying coronary atherosclerosis. Risk for cardiovascular disease (CVD) was classified according to the CAC score as low (100), intermediate (100-399), high (400+), or very high (400).[9].

In order to do a contrast-enhanced CTA scan Coronary segments were identified using a modified American Heart Association categorization after a weight-dependent bolus of 70-90ml iodine contrast agent (Ultravist, Bayer). Segments were labelled as either normal (having smooth parallel margins), having non-significant stenosis (luminal stenosis 50%), or having considerable stenosis (luminal stenosis 50%). (50 percent).

Angiography of the coronary arteries (ICA): CT findings are then confirmed and compared to the gold standard, invasive coronary angiography. As the gold standard for identifying obstructive CAD, ICA also makes it possible to do coronary revascularization at the same time. It has been observed that only 38% to 50% of patients who have elective ICA are found to have obstructive CAD, and that the surgery is linked with infrequent but substantial procedure-related complications3.

Statistical analysis

IBM SPSS Statistics Version 25 was used to examine the data. The Shapiro-Wilk test was used to examine the data for signs of non-normality. Mean and standard deviation (SD) were determined for numerically regularly distributed data, whereas median and range were derived for numerically non-normally distributed data. Non-numerical data was presented using frequency and percentage. Statistical significance of differences between groups and correlations between qualitative variables were assessed using analytical statistics such one-way ANOVA, Kruskal-Wallis, and Chi-Square tests. The degree of relationship between two numerical variables was evaluated using correlation analysis. The sensitivity and specificity of diagnostic tools were calculated using the ROC curve. Generalized linear models were used for the logistic regression analysis, and odds ratios (OR) were determined to forecast risk factors. The cutoff for significance was set at 95% confidence level, or p 0.05.

3. Results

Patients were on average 67.75.54 years old, and 62.5% of the sample was composed of men. Twenty-seven percent of the participants were smokers, 25% were diabetic, and 42.5% were hypertensive. Patients with a prior stroke history made up 27.5% of the total. Total cholesterol is within the usual range for this patient (Mean Standard Deviation = 141.89 15.05 mg/dl), but LDL-C is somewhat raised (Mean Standard Deviation = 95.59 11.25 mg/dl) and HDL-C is below the ideal range (Mean Standard Deviation = 46.3 10.88 mg/dl). According to the patient's clinical data, they have high blood pressure (mean standard deviation [MSD] = 147.88 mmHg systolic, MSD = 91.69 mmHg diastolic). Their average heart rate is 79.998.02 beats per minute, which is well within acceptable limits. Table 1 shows the study participants separated into three categories based on the number of coronary artery lesions they had. Demographic data, risk variables, laboratory tests, and clinical evaluations were compared across all individuals. There were statistically significant variations in mean age, mean total cholesterol, and mean LDL-cholesterol levels between the two groups. Table 2 shows that the prevalence of carotid plaques is greater in individuals with two or more coronary lesions compared to those with only one. Neither the prevalence nor the location of plaques differed significantly across the groups. Table 3 shows that there was a statistically significant difference in intima media thickness (IMT) across the groups. The number of coronary lesions increases with increasing IMT diameter. Figure 1 shows that a higher number of coronary lesions is correlated with a higher calcium accumulation and severity CAC score, as determined by CT angiography. A significant p value (0.001) was found using a cut of level greater than 1.33 mm in IMT in the ROC curve study of IMT prediction of coronary artery disease severity (Figure 2). As can be seen in Figure 3, there is a negative connection between IMT and both Total and LDL-C. There was a statistically significant positive association between IMT and CAC scores. In Table 4, we see that IMT, hypertension, and total cholesterol were all significant predictors of coronary artery disease severity in univariate analysis.

Multivariate research reveals that IMT is the sole predictive signal. **Table 5**

Table (1) Baseline criteria of the studied subjects

	Total studied subjects n=40
Demographic data	
Age years, n(%)	67.7±5.54
Gender, n(%)	25(62.5)
Cardiovascular risk factors	
Smoking, n(%)	11(27.5)
DM, n(%)	10(25)
Hypertension, n(%)	17(42.5)
Stroke, n(%)	11(27.5)
Laboratory investigations	
Total cholesterol (mg/dl), M±SD	141.89±15.05
LDL-C (mg/dl), M±SD	95.59±11.25
HDL-C (mg/dl), M±SD	46.3±10.88
Clinical data	
SBP, M±SD	147.88±9.33
DBP, M±SD	91.69±5.11
Heart rate	75.99±8.02

Table (2) Baseline criteria of the studied subjects

	Single lesion n=20	Two lesions n=10	Three lesion n=10	p	test
Demographic data					
Age, years	66.23±4.26	66.24±5.61	73.48±5.56	0.001*	8.033
Gender "Males"	12(60%)	7(70%)	6(60%)	0.852	x^2=0.320
Smoking	5(25%)	3(30%)	3(30%)	0.939	x^2=0.125
Cardiovascular risk factors					
DM	6(30%)	2(20%)	2(20%)	0.766	x^2=0.533
Hypertension	5(25%)	6(60%)	6(60%)	0.082	x^2=5.013
History of stroke	6(30%)	3(30%)	2(20%)	0.829	x^2=0.376
Laboratory investigations					
Total cholesterol, mg/dl	148.77±15.85	136.33±8.29	131.57±6.08	0.003*	Z=11.782
LDL-C, mg/dl	100.93±12.72	93.72±6.94	88.92±4.12	0.01*	5.246
HDL-C, mg/dl	47.84±14.26	42.6±2.94	42.65±3.99	0.544	Z=1.219
Clinical data					
SBP, mmHg	150.44±10.17	145.88±11.06	142.39±8.67	0.118	2.266
DBP, mmHg	91.34±5.08	90.42±6.56	91.13±5.53	0.913	0.091
Heart rate	79.14±4.89	75.95±7.98	73.64±9.11	0.08	Z=58.54

Oneway Anova test, x^2=Chi-square test, Z= Kruskal Wallis.

Table (3) Plaque criteria differences between of the studied subjects

Carotid ultrasonography findings	**Single lesion n=20**		**Two lesions n=10**		**Three lesions n=10**		**p**	**Test**
	N	**%**	**N**	**%**	**N**	**%**		
Number of carotid plaques								
1	10	50.0%	4	40.0%	2	20.0%	0.079	11.325
2	10	50.0%	5	50.0%	4	40.0%		
3	0	0.0%	1	10.0%	2	20.0%		
4	0	0.0%	0	0.0%	2	20.0%		

Plaque type								
Soft plaque	7	35.0%	2	20.0%	2	20.0%		
Hard plaque	8	40.0%	5	50.0%	5	50.0%	0.889	1.131
Mixed plaque	5	25.0%	3	30.0%	3	30.0%		
Plaque distribution								
Common carotid artery bifurcation	10	50.0%	4	40.0%	3	30.0%		
Common carotid artery	4	20.0%	3	30.0%	3	30.0%	0.967	1.380
Internal carotid artery	4	20.0%	2	20.0%	3	30.0%		
External carotid artery	2	10.0%	1	10.0%	1	10.0%		

Chi-Square test

Table (4) Pearson correlation between IMT and other studied parameters in the studied patient

	r	p
Age	0.174	0.28
Smoking	0.076	0640
Gender	-0.014	0.933
total cholesterol	-.438	0.004*
LDL-C	-.329	0.038*
HDL-C	-0.218	0.174
Hypertension	-0.268	0.094
CAC score	0.750	<0.001*

Table (5) Logistic regression analysis for prediction of coronary artery disease severity

	Univariable			Multivariable		
	p	**OR**	**95% CI**	**p**	**OR**	**95% CI**
Age	0.053	0.886	0.783-1.001			
Hypertension	0.029*	0.222	0.057-0.857			
IMT	0.004*	0.034	0.004-0.376	0.04*	0.026	0.00-0.102
Total cholesterol	0.006*	1.120	1.032-1.213			

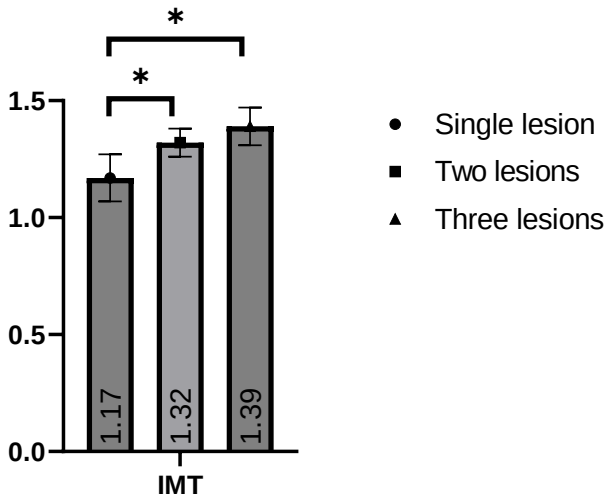

Fig. (1) Intima media thickness differences between three groups of study

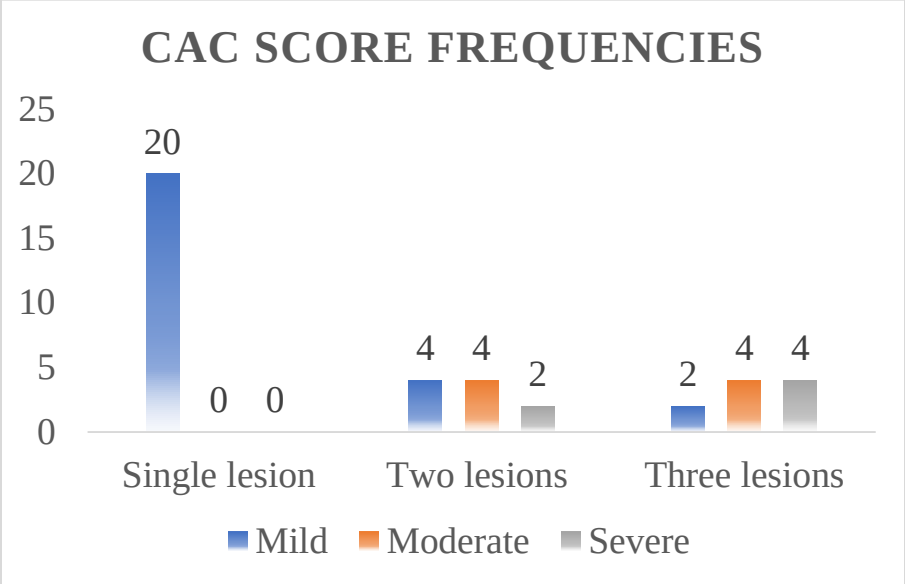

Fig. (2) CAC score frequencies in the studied groups

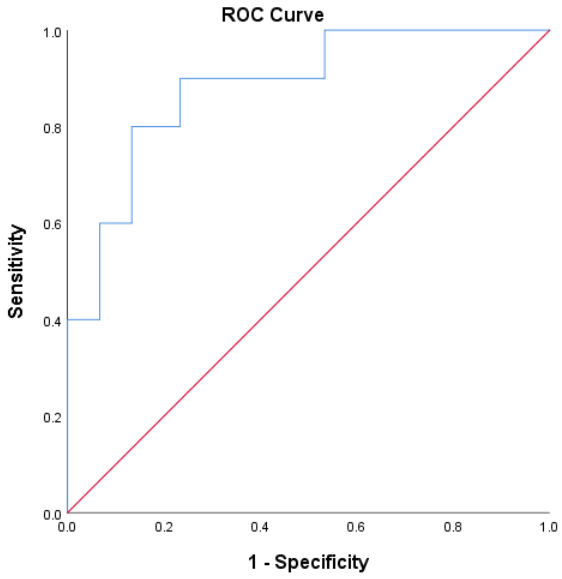

Fig. (3) ROC curve analysis of IMT prediction of coronary artery disease severity

Cases:

Case 1: A CT coronary angiography was sought for a 48-year-old male patient who was experiencing usual chest discomfort. Diffuse ectasia of the left anterior descending (LAD) and right carotid (RCA) arteries, left main (LMA) and left circumflex (LCX) mega-coronary artery stenosis, normal carotid doppler save for increased intima media thickness measuring 0.1 centimetres. **Figure 4**

Case 2: We were sent a 65-year-old male with hypertension and unusual chest discomfort for CT coronary angiography. PCI-confirmed diagnosis of proximal LAD partial occlusion and severe distal occlusion. A tiny lesion in the mid-RCA region that is consistent with PCI. Right internal carotid artery (ICA) carotid doppler shows considerable mixed plaque with 55% stenosis, measuring about 0.81 x 0.21 cm. **Figure 5 and 6**

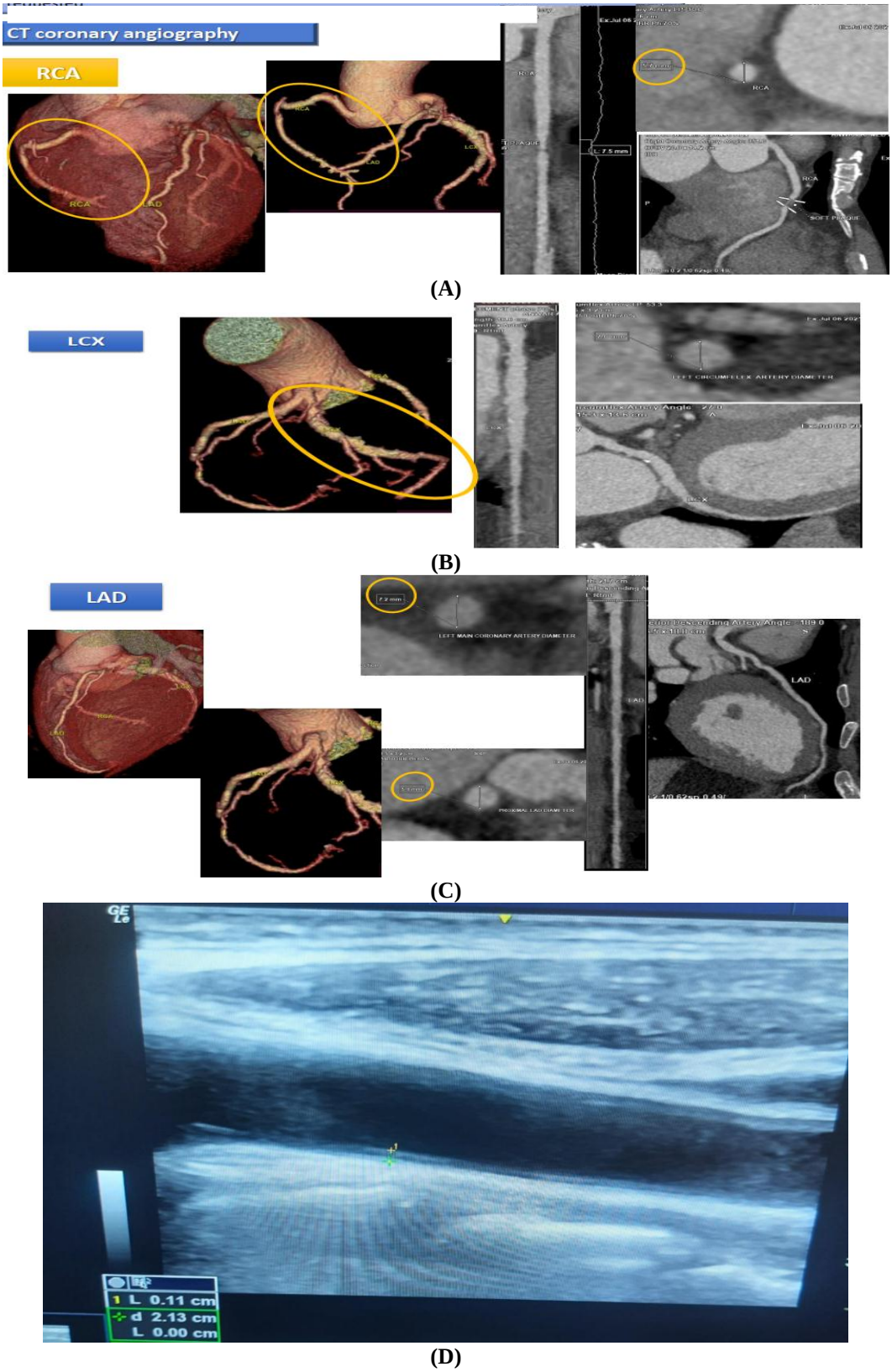

Fig. (4) (A-C) CT coronary angiography, (D) Carotid doppler

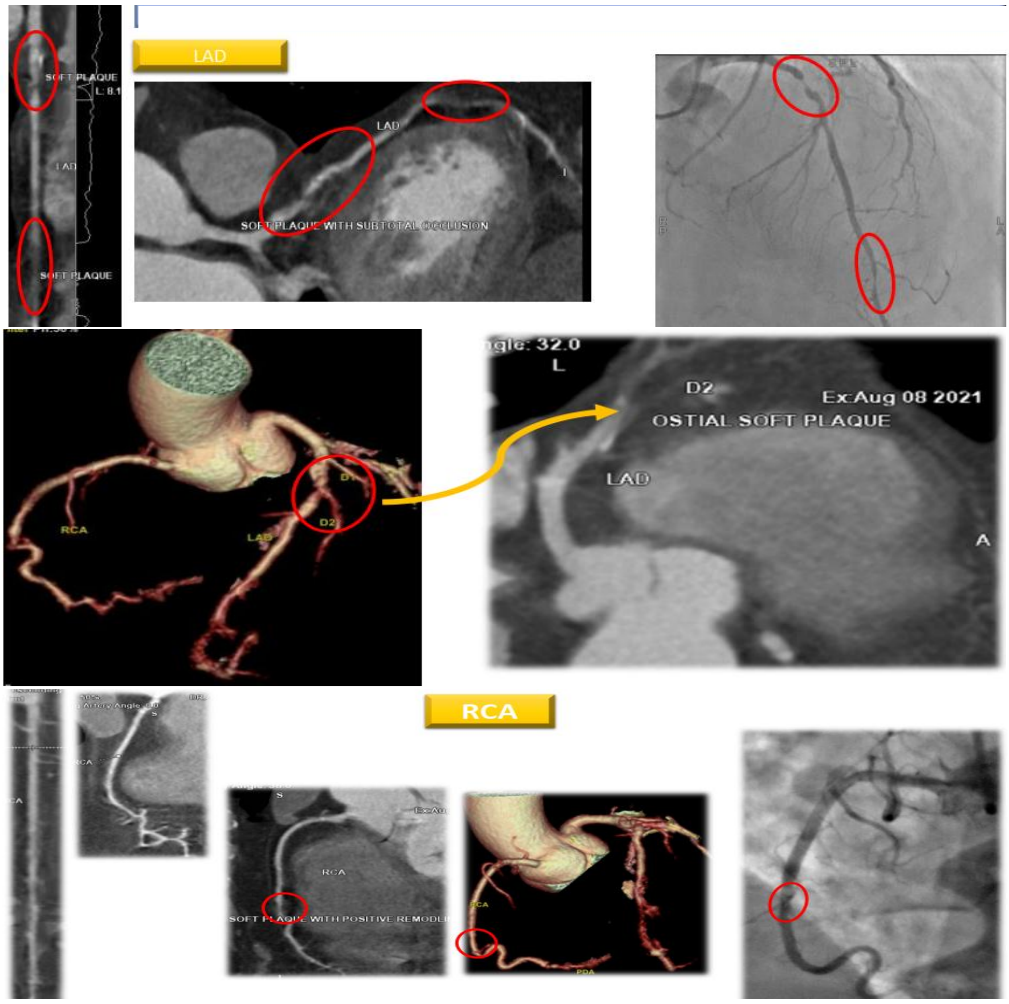

Fig. (5) CT coronary angiography

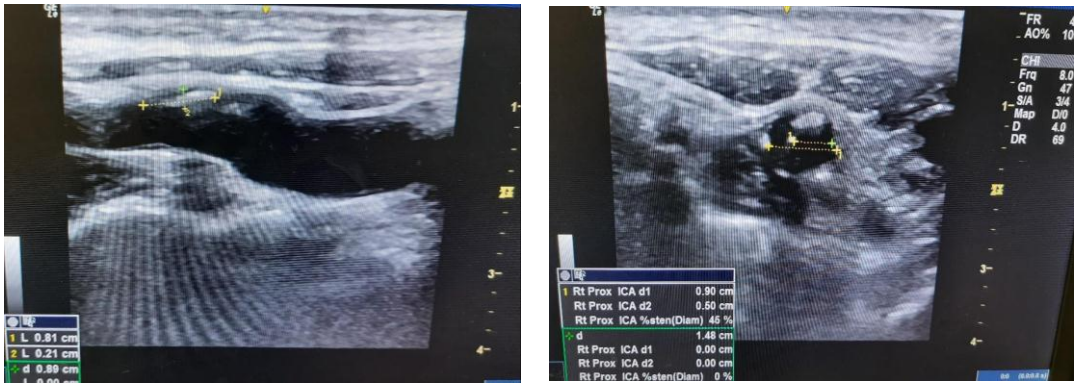

Fig. (6) Carotid doppler

4. Discussion

Forty individuals with a history of CHD suspicion participated in this investigation. Laboratory testing, carotid ultrasonography, and coronary computed tomography were performed on all individuals. According to the amount of coronary lesions, the patients were separated into three categories: Twenty patients had a single lesion, ten had two lesions, and ten had three.

Age, total cholesterol, and LDL-cholesterol all differed significantly (P0.001, 0.003, and 0.01) between the groups in our research.

Consistent with our results, another research looked at the backgrounds of 480 people with

CHD suspicions and did duplex Doppler ultrasonography of the carotid arteries and coronary angiography or CT. Based on the existence of coronary lesions, patients were placed in either the CHD or control group. Single coronary lesion patients (n = 145), double coronary lesion patients (n = 90), and triple coronary lesion patients (n = 90) made up the CHD subgroups. Researchers found that there was a statistically significant difference in age between the groups they compared (P 0.001). [10].

More carotid plaques were seen in individuals with two or more coronary lesions than in those with only one. Neither the prevalence nor the location of plaques differed significantly across the groups.

Consistent with our findings, another research looked at the incidence of plaque in the carotid arteries and its importance, particularly in individuals with coronary atherosclerosis. Patients included 1,705 people who had high-resolution ultrasound scans of their carotid arteries and coronary arteries on consecutive days. Significant coronary artery stenosis was found to be more common in individuals with carotid plaque (75.4 percent vs. 58.3 percent, p0.001), particularly multi-vessel disease (46.3 percent vs. 27.2 percent, p0.001). [11].

Further, Zhu et al. Plaque quantity and incidence differed significantly between the control group and all CHD subgroups **(Table 2).**[10].

Our research revealed statistically significant differences in intima media thickness (IMT) (p0.001) between the groups we compared. The number of coronary lesions increases with increasing IMT diameter.

Similarly, 333 asymptomatic type 2 diabetes individuals with no history of CAD received exercise electrocardiography or myocardial perfusion scintigraphy to identify silent myocardial ischemia; those with positive test findings had coronary computed tomography angiography or coronary angiography. They came to the conclusion that maximal IMT was noticeably higher in patients with severe CAD who required coronary revascularization.[12].

The purpose of this meta-analysis was to examine the correlation between coronary and carotid atherosclerosis phenotypic manifestations utilising currently accessible imaging modalities. Twenty-two thousand six hundred and eighty-three individuals were analysed from eighty-nine articles that compared carotid and coronary atherosclerosis. Regardless of the severity of CAD, there was a linear rise in CIMT (P0.001). Patients with CAD had a greater CIMT than controls (P0.001).[13].

After CT angiogram analysis, we found that a higher CAC score was related with a greater number of severe coronary lesions.

CAC scoring has emerged as an easily accessible, reliable, and effective means of assessing the risk of major cardiac events, especially in asymptomatic people planning for primary prevention interventions like aspirin and statins, based on single-center and multicenter clinical and population-based studies with short-term and long-term outcomes.[14].

Cut of level greater than 1.33 mm in IMT revealed a significant p value (0.001) with 80% sensitivity and 87% specificity in ROC curve study of IMT prediction of coronary artery disease severity.

A prospective study was conducted on 229 individuals who were free of cardiovascular complications and who had at least one extra cardiovascular risk factor, which is similar to our study. Only individual differences in IMT were shown to be a significant predictor of cardiovascular events (P = 0.045).[15].

Out of a total of 6814 MESA patients, 6739 underwent a baseline carotid artery assessment. Of them, 6614 participants reached farwall mean CCA IMT values (99.7 percent) while 6628 participants received the maximum ICA IMT (96.4 percent) (98.2 percent). Only 6500 were included in the statistical analysis since 114 people didn't have full information on their risk factors. They found that the IMT percentile was a robust independent predictor of CHD occurrences across all models.[16].

We found that IMT had a statistically significant inverse relationship with both total cholesterol and LDL-C when compared to the other variables we looked at. There was a statistically significant positive association between IMT and CAC scores.

The predictive value of IMT assessment and carotid plaque detection in relation to cardiovascular risk variables for clinically severe CAD was studied. However, in multiple regression analysis, only age (P=0.15), IMT (P0.01), high density lipoprotein (HDL) cholesterol (P=0.02), and, less significantly, total cholesterol (P=0.09) were found to be independent parameters for the prediction of significant CAD, while presence of carotid plaques in common carotid artery (P0.001) and male sex (P0.005) were found to be categorical risk factors.[17].

Adding a positive coronary artery calcium score to the model improved the area under the curve from 0.7627 to 0.7714 (P=0.02), and the IMT score boosted it from 0.7210 to 0.7396 (P=0.0008). [16].

Univariate analysis revealed that IMT, hypertension, and total cholesterol were all significant predictors of coronary artery disease severity in the current study's logistic regression analysis. Multivariate research reveals that IMT is the sole predictive signal.

According to one research, severe CAD may be identified when the intermaxillary distance (IMT) is at least 0.75 mm (sensitivity 78 percent , specificity 79 percent , positive predictive value 95 percent , negative predictive value 41 percent , odds ratio 12.9, 95 percent CI 3.5 to 47.6)[17].

5. Conclusion

Intima-media thickness (IMT) is the only measure in individuals with coronary artery disease that has a substantial predictive value. The prevalence of coronary lesions increases with increasing Intima-media thickness diameter. A greater number of coronary lesions was correlated with a higher calcium score in the coronary arteries, which was measured using CT angiography.

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Author contribution

The authors shared equal responsibility for the research.

Conflicts of interest

There are no competing interests.

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