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Correlation between Carotid Intima-Media Thickness and Coronary Artery Disease in Patients Evaluated by Coronary Computed Tomography Angiography

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Abstract

Background: The carotid intima-media thickness (CIMT) is increasingly used as surrogate marker for atherosclerosis worldwide. It can be measured simply, noninvasively, and reproducibly by ultrasound. Although CIMT has been considered a tool to improve the estimation of coronary artery atherosclerosis, this application is still a matter of debate and remains unclear whether routine CIMT measurement is useful for the detection of subclinical atherosclerosis in clinical practice in addition there are racial/ethnic differences as many studies have been conducted and revealed different CIMT among various ethnicities or races, leading to a different incidence of (CAD).

Aim: The purpose of this study was to evaluate the correlation between CIMT by ultrasound and atherosclerotic CAD among Iraqi patients and to determine whether increased CIMT is predictive of the presence and severity of coronary atherosclerosis.

Patients and Methods: Carotid ultrasound was carried out on patients who had undergone coronary CT angiography (CCTA) due to suspected coronary artery disease (CAD). To explore the link between carotid IMT and CAD, measurements were taken from three segments on both the right and left common carotid arteries, as well as from the proximal part of the internal carotid arteries.

Result: Among 100 patients (52 men and 48 women) with a mean age (54+10), significant correlation was found between increased CIMT and coronary artery atherosclerosis burden including the calcium score, coronary artery plaque and the presence of significant stenosis. The validity criteria of right and left common carotid arteries intima-media thickness at a cut-off value 0.72 mm and AUC=0.77, revealed relatively high sensitivity (83%) but low specificity (48%). Additionally, a relatively higher AUC=0.82 was obtained from the right-side internal carotid at cut-off value 0.75mm, sensitivity (90%) and specificity (40%).

Conclusion: Carotid intima-media thickness is a sensitive predictor of coronary atherosclerosis detected in symptomatic intermediate-risk patients.

Keywords: atherosclerosis, carotid intima-media thickness, coronary artery disease, coronary computed tomography angiography.

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Introduction

Coronary artery disease (CAD) is the most common type of heart disease and is considered the major cause of morbidity and mortality worldwide. Although the incidence of CAD has decreased over time in developed countries, this condition still causes about one-third of all death in people older than 35 years along with fact that mortality is expected to continue increasing in developing countries (1).

Most patients with stable CAD don't exhibit any symptoms or warning signs for years until unexpected coronary events like MI happen. So , it is preferable to recognize clients with CAD at an early stage, to promote interventions as soon as possible (2). Detection, treatment, and prevention of CAD are critical challenges in those large populations who have no symptoms but are at risk of developing CAD (3).

Hypertension, diabetes mellitus, smoking, fibrinogen, and low-density lipoprotein are common risk factors for CAD. Although these traditional risk factors can predict the risk of future cardiovascular events but reported to be weak predictors of CAD and fail to identify the ongoing atherosclerotic process (4). Since atherosclerosis is a generalized process; all arterial beds including the carotid and coronary arteries will be affected. Thus, carotid artery atherosclerosis could reflect coronary involvement, a fact that has been confirmed histologically by autopsy studies (5). Increased intima-media thickness (IMT) reflects early atherosclerosis therefore a measurement of the carotid intima-media thickness (CIMT) by B-mode ultrasound was found to be a suitable non-invasive method for visualizing the arterial walls and for monitoring the early stages of atherosclerotic process (6).

Coronary computed tomography angiography (CCTA) provides noninvasive high-quality images of the heart, great vessels, and coronary vasculature. It is useful and reliable in the assessment of patients with chest pain of possible ischemic origin providing atherosclerotic plaque detection, characterization, and quantification (7). Coronary CTA characterize by its strong ability to effectively rule out CAD given its high negative predictive value (>95%), which makes it especially useful in patients with low to intermediate risk of CAD (8).

Patients and methods

This study represents a cross-sectional study among Iraqi adult patients who had been referred by their physicians to Al-Najaf center for cardiovascular surgery and cardiac catheterization for suspicion of ischemic heart disease. The study was carried out between January 2022 and October 2022. A multi-detector 64-slice coronary CT angiography (CCTA) was done for all the patients to detect presence of CAD, then all patients underwent US scanning for CIMT. The CCTA images were evaluated by an expert specialist radiologist who was blinded to ultrasound results. Patients Profile investigations included age, sex, occupation, and residence place, in addition to risk factors for coronary artery disease including hypertension, diabetes, hyperlipidemia (according to their current medication), smoking and any other history related to family . Participants were considered to have a history of smoking if they were currently smoking or had smoked in the past. Family history was marked positive if a first-degree male relative had coronary artery disease before the age of 55, or if a first-degree female relative had the disease before the age of 65. Patient’s height and weight were assessed, and the BMI was estimated.

Calcium Scoring through non-contrast CT scan was performed first with 0.5 mm slice thickness and 3 mm slice collimation (usually performed between the tracheal bifurcation and diaphragm) to measure calcium score and also for determining the scan range required for subsequent CCTA. Carotid ultrasonography (CIMT) measurement was performed for all included patients using a linear transducer (7.5 MHz) of GE LOGIC E9 XD Clear ultrasound system (GE Healthcare, 2019, USA.

SPSS version 23.0 used for date analysis. As descriptive and inferential. To determine the optimal cut-off points for ultrasound parameters in predicting the severity of coronary artery disease (CAD), a receiver operating characteristic (ROC) curve analysis was utilized. These findings were expressed in terms of the area under the curve (AUC), sensitivity, and specificity. The relationship between coronary artery calcium (CAC) and ultrasound measurements was examined using Spearman's rank correlation coefficient. Additionally, the associations of ultrasound parameters with categorical markers of coronary atherosclerosis—including CAC, luminal stenosis, and plaque—were evaluated using the Student's t-test.

Results:

Table 1 52% male, and 48% female. The patients age range was 19-70 year, mean age (54 +10 year), while body mass index (30+5. Hypertensive patients 58 %, diabetic patients 26%, patients with hyperlipidemia 40%, with smoking 28%, and those with positive family history of CAD were 12% .

Table 1: Demographic characteristics of Iraqi patients (N = 100)

Variable	Frequency (Percentage)
Male	52%
Female	48%
Hypertension	58%
Diabetes mellitus	26%
Hyperlipidemia	40%
Family history of CAD	12%
Smoking	28%

Calcium score median (IQR)=0(0-92), patients with no stenosis 49%, non-significant stenosis (< 50%) seen in 15%, significant stenosis (≥50%) seen in 36%, coronary plaques present in 51%, soft plaques were seen in 4%, calcified plaques in 10%, and mixed plaque seen in 37%. RT Common Carotid IMT mean (0.77 + 0.1mm), LT common carotid IMT mean (0.79+0.1mm), RT internal carotid artery IMT mean (0.81+ 0.1mm), LT internal carotid artery IMT mean (0.8+ 0.1mm) as shown in table 2.

Table 2: Coronary stenosis severity, plaque type and Carotid artery intima-media thickness (N = 100)

Coronary stenosis severity	
No stenosis	49%
Non-significant stenosis, <50%	15%
Significant stenosis, ≥50%	36%
Coronary plaque presence	51%%
Coronary plaque type	
Calcified	10%
Soft	4%
Mixed	37%
I ntima-media thickness (mm)	
RT Common Carotid artery	0.77 +0.1
LT Common Carotid artery	0.79 +0.1
Mean RT & LT CCA	0.78 +0.1

RT Internal Carotid artery	0.81 + 0.1
LT Internal Carotid artery	0.80 + 0.1

There was positive highly significant correlation between the mean intima-media thickness of both right and left Common Carotid artery with increased CAC score (r =0.4), (p> 0.0001) as in figures 1and 2.

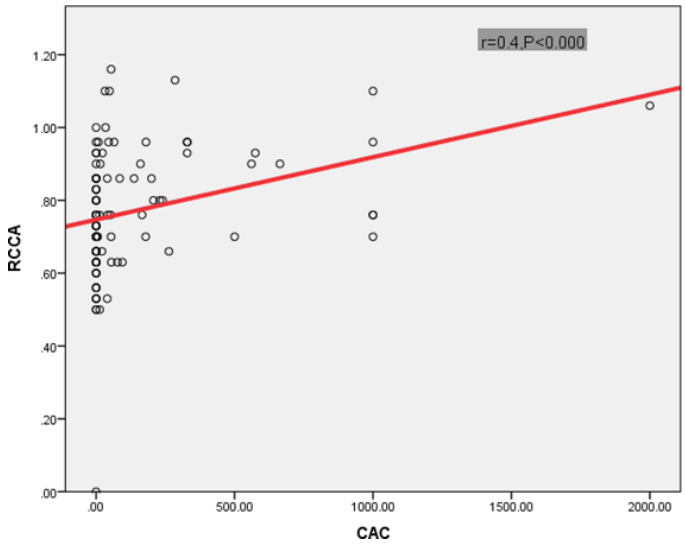


Figure 1: Correlation between Right Common Carotid Artery IMT(mm) and CAC

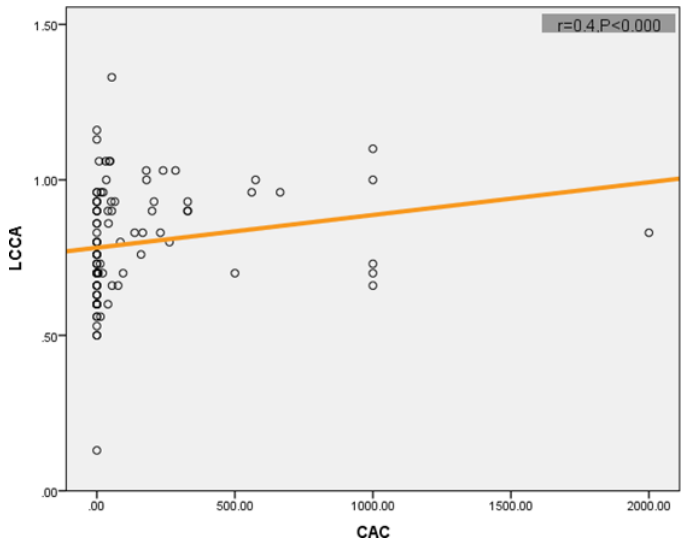


Figure 2: Correlation of left Common Carotid Artery IMT (mm) and CAC

Increased IMT was also associated with increased No. of vessels involved as in figures (3.5) & (3.6), P > 000.1.The analysis of data revealed that the mean RCCA – IMT of patients with coronary plaque was significantly higher than patients with no plaque (p<0.0001) as shown in figure (3.7), the same correlation was noticed for LCCA. Also, the RT and LT ICA – IMT of patients with coronary plaque was significantly higher than that of patients with no plaque (p<0.0001). There was no statistically significant difference of RCCA, LCCA, RICA and LICA -IMT and plaque types p= (0.8), (0.4), (0.5) & (0.5), respectively.

There was a clear and significant positive relationship between carotid IMT and the severity of coronary artery narrowing. Patients with more than 50% stenosis had noticeably higher IMT values compared to those with less than 50% stenosis, with the difference being highly significant (p<0.001). The validity criteria of R&LCCA in prediction of coronary stenosis at cut-off value 0.72 mm and AUC=0.77 revealed relatively high sensitivity (83%). The specificity (48%)as shown in (table 3) & figure 3.

Table 3: Validity criteria of CAD of the study sample

Variables	AUC	Cutoff value (mm)	Sensitivity	Specificity
RCCA	0.75	0.74	76%	45%
LCCA	0.76	0.74	77%	43%
Mean R&LCCA	0.81	0.72	88%	42%

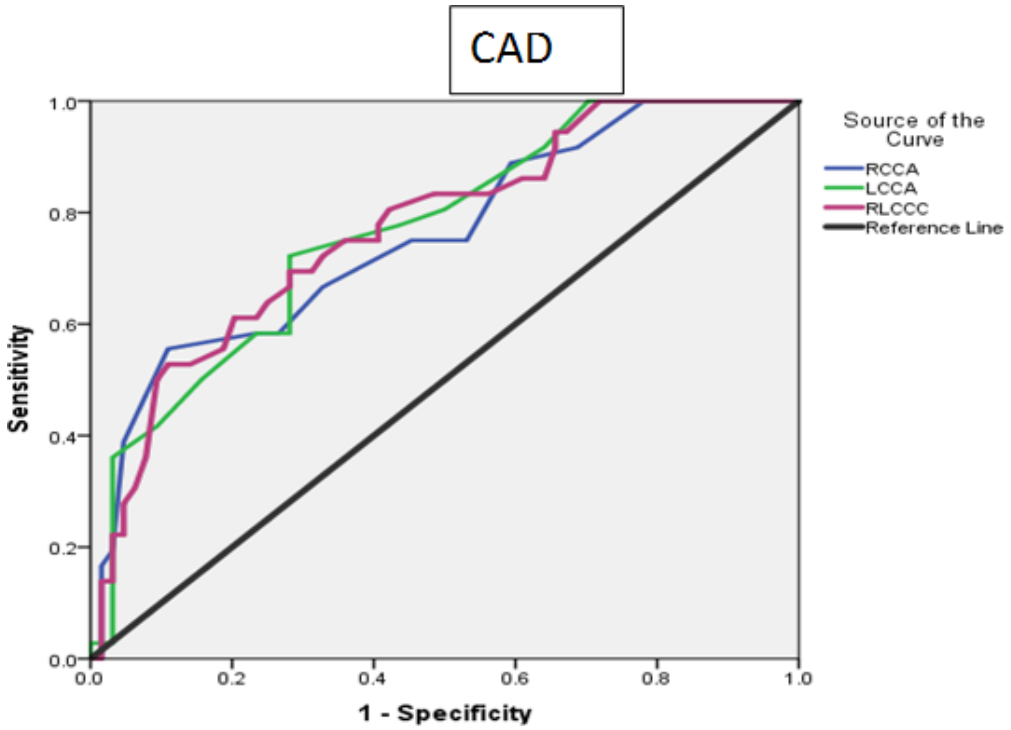


Figure 3: Receiver operator curve to estimate area under curve (AUC) for CCA_IMT to identify coronary artery stenosis risk.

The validity criteria of RICA in prediction of coronary stenosis at cut-off value 0.75mm and AUC=0.82, revealed relatively higher sensitivity (90%) but lower specificity (40%).

Table 4: Validity criteria of CAD of the study sample.

Variables	AUC	Cutoff value (mm)	Sensitivity	Specificity
RICA	0.82	0.75	90%	40%
LICA	0.80	0.75	83%	34%
R&LICA	0.81	0.72	88%	42%

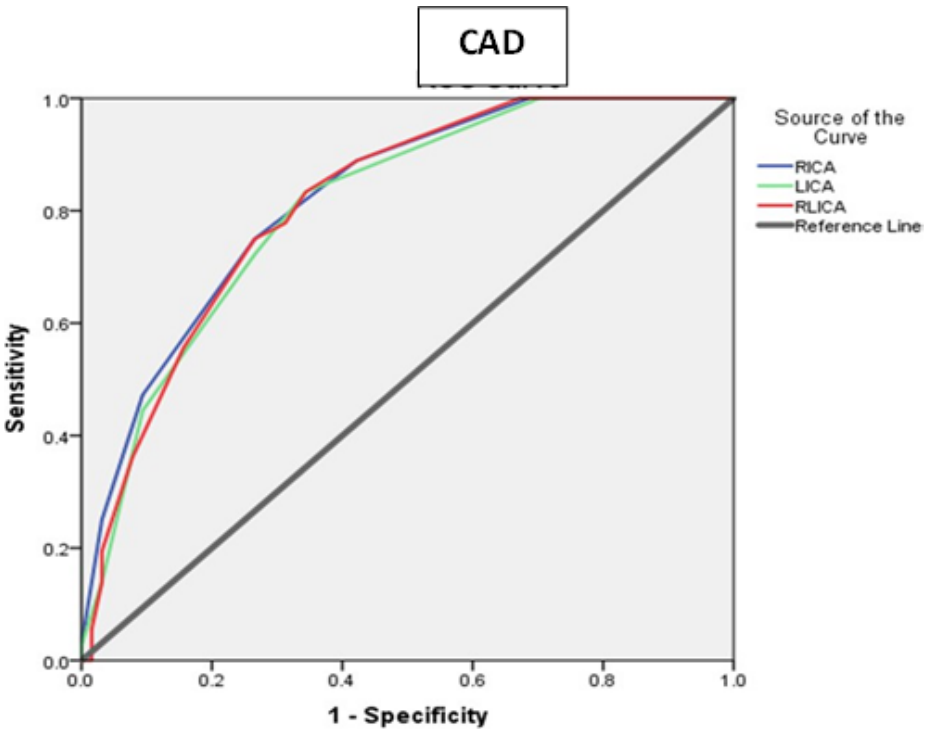


Figure 4: Receiver operator curve to estimate area under curve (AUC) for ICA_IMT identify coronary artery stenosis risk

Discussion

It is well known that atherosclerosis is a generalized process, however the two most common sites related to atherosclerosis are coronary and carotid arteries, and the relationship between them has been confirmed (9). The diagnostic methods commonly used today, typically detect atherosclerotic disease only once it has significantly progressed and started causing blockages. Likewise, many risk assessment tools can estimate the likelihood of future cardiovascular events but are unable to pinpoint active atherosclerosis at an early stage (5). Intima-media thickness (IMT) is a well-described marker for cardiovascular disease and extracranial carotid arteries provide excellent sites for IMT assessment because of their superficial location, adequate size, and limited movement (10). Racial differences in the size of the carotid IMT were considered and this will affect the prediction of CAD. Sekikawa et al. (11) After adjusting factors, the (IMT) of Caucasian men aged 40–49 years in the United States was found to be significantly greater compared to Japanese men of the same age group. In the present study, there is a significant positive correlation between increased CIMT and coronary atherosclerotic burden including CAC, presence of coronary artery plaque, and stenosis.

There is ongoing debate about which segment of the carotid artery is best for measuring intima-media thickness (IMT). Although measurements taken from the common carotid artery (CCA) tend to be more consistent and reproducible than those from the internal carotid artery (ICA) or the bifurcation, signs of disease progression often appear more clearly in the ICA and the bifurcation areas (13). Relying only on IMT measurements at the common carotid artery (CCA) may underestimate the actual burden of carotid atherosclerosis. In our study, we assessed IMT at both the CCA and the internal carotid artery (ICA) and found that both sites showed a positive association with (CAD). Though, IMT at ICA demonstrated a slightly stronger ability to predict CAD.

Guaricci and his colleagues in Italy in 2014, studied the relationship between CIMT and CAD distinguished through CCTA in symptomatic and middle-risk patients and concluded; similar to the present study; that CIMT is a good predictor of coronary atherosclerotic burden. They found that CIMT values significantly correlated with the number of coronary vessels with CAD ≥ 50 % ($p > 0.001$, overall number of plaques ($p> 0.001$), and CACS ($p>0.001$) (14). In addition, Jeevarethinam and his colleagues

in London, United Kingdom in 2015 also evaluated the relationship between carotid and coronary disease and find similar result (15).

Schroeder *et al*. (16) in Canada, 2013 and Cohen *et al*. (17) in US-Texas in 2013 similarly They investigated the link between carotid and coronary artery disease using coronary computed tomography angiography (CCTA). Their findings demonstrated a modest correlation between carotid intima-media thickness (IMT) and both coronary calcification and coronary artery disease (CAD) severity. However, their studies had some limitations: they included a mixed population consisting of asymptomatic, symptomatic, and high-risk individuals without considering the pre-test probability of disease. Additionally, the relatively small sample size in the study by Schroder et al. (50 patients) might have influenced the accuracy and reliability of the results.

A study conducted by Chang and colleagues in Taiwan in 2013 involved 120 patients who underwent (CCTA) appropriate to suspected (CAD). The researchers discovered that the predictive value of carotid intima-media thickness (CIMT) for detecting CAD varied with age. Specifically, they found that increased IMT at the carotid bifurcation served as an independent predictor of CAD in individuals over the age of 60, while this association was not observed in patients younger than 60. (18).

Several earlier studies have explored the relationship between carotid and coronary artery disease, but most relied on invasive coronary angiography as the reference method. One such study by Hussein H. J. (18) and colleagues in Iraq (2021) involved 132 patients who underwent invasive coronary angiography. Their findings showed a significant and direct correlation aligning with the results of the current study. However, these studies often lacked key details—such as the composition of arterial plaques and the degree of arterial remodeling—which are important when assessing atherosclerosis. As a result, invasive coronary angiography may have limitations as a comparison tool when the main focus is the atherosclerotic process itself. Moreover, because patients referred for invasive angiography are typically considered high-risk, it's unclear whether these findings apply to individuals with an intermediate likelihood of CAD—the group that makes up the largest portion of those targeted for primary prevention.

Conclusion: Carotid IMT showed positive correlation with coronary atherosclerosis burden including coronary artery calcification $p<0.0001$, presence of plaques $p<0.0001$, and significant stenosis $p<0.0001$. The validity criteria of mean R& LCCA- IMT at cut-off value 0.72 mm and AUC=0.77 revealed high sensitivity (83%) and relatively higher AUC=0.82 was obtained from RT internal carotid- IMT at cut- off value 0.75mm, sensitivity (90%) for prediction of <50% coronary artery stenosis.

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