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PREDICTIVE UTILITY OF CAROTID ARTERY ULTRA'SONOGRAPHY IN IDENTIFYING RISK FOR CORONARY ARTERY ATHEROSCLEROTIC DISEASE: A STUDY IN THE PAKISTANI POPULATION

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BACKGROUND:
Carotid artery ultrasonography is a non-invasive, cost-effective, nonradioactive imaging technique that allows for the visualization and measurement of the carotid arteries. **Objective**: To detemtine the sensitivity, specificity, and positive predictive value of carotid artery ultrasound using both B mode and doppler ultrasound, in predicting the presence of significant coronary artery disease in a cohod of Pakistani adults. **Methods:** It's a cross sectional study that was held at Department of Radiology, CMH, Malir-Karachi, that enrolled 103 patients through non-probability consecutive sampling. After informed consent, demographic details of all patients were documented. Both males and females were enrolled having cardiac symptoms with age ranging from 35-75years were enrolled. However, patients with prior history of coronary intervention (PCI, CABG) or diagnosed case of coronary artery disease were excluded. All the data was processed by SPSS v28.0. Quantitative variables were presented as mean ± SD. Qualitative variables was presented as frequencies and percentages. Evaluation among groups according to Fisher's exact and chi-square tests were applied with p-value of ≤0.05 was taken significant. **Results**: Mean age of the patients was 48.4 ± 10.3 years. The mean CIMT was 0.83 ± 0.12 mm. The diagnostic performance of carotid ultrasound in detecting significant CAD showed a sensitivity of 85.0%, specificity of 65.1%, accuracy of 76.7%, PPV of 77.3%, and NPV of 75.7%. **Conclusion**: We concluded that carotid artery ultrasound is an accurate, highly sensitive, non-invasive imaging investigation for detecting coronary artery disease with low specificity. **Key words**: Carotid atherosclerosis, Carotid Artery ultrasonography, Carotid artery diseases and Atherosclerosis plaque.

INTRODUCTION:
Risk factors like atherosclerosis, poor lipid profile cause various cerebro-vascular (CV) diseases like stroke and Coronary artery disease thus causing high mortality and long-term morbidity worldwide.[1] One previous study documented that stroke caused 6.5 million deaths globally in 2013 as a second most common disease.[2] According to one survey, Pakistan carries a high burden of this disease that drains all resources thus affecting economy.[3] There are various factors that contribute to its high prevalence that include late or undiagnosed risk factors for disease, false believes regarding disease and hakeem medications.
There are two types of stroke (ischemic and hemorrhagic) that have different pathologies and etiological factors. However, carotid artery atherosclerosis is a significant and theoretically avoidable risk factor for ischemic stroke. Degree and severity of atherosclerosis are directly correlated with the risk of stroke.[4] Risk of further ischemic cerebro-vascular episodes can be considerably decreased by early detection and timely treatment of carotid atherosclerosis.[5] Depending on the severity of the stenosis, there are three different treatment options that include medicinal therapy, endovascular repair and surgical reconstruction. Medical therapy or repeated follow-up exams are typically used to treat patients with less than 50% carotid stenosis.[6]
Carotid ultrasound (USG) is a non-invasive diagnostic modality for evaluating carotid atherosclerosis.[7] This technique helps to measure carotid intima-media thickness (CIMT), detect the presence and nature of atherosclerotic plaques and assess the percentage of carotid artery stenosis.[4] However, computed tomographic angiography is

associated with an injection of an intravenous contrast agent. The primary benefit of CTA is that it evaluates the carotid and coronary arteries' intracranial and extra-cranial segments and is utilized before end arterectomy surgery. The intravenous use of iodinated contrast material and the radiation risks are CTA's primary drawbacks. Consequently, a relative contraindication to CT angiography is abnormal renal function.[8]

Due to the high prevalence of cardiovascular risk factors and limited access to advanced diagnostic tools in Pakistan, there is a critical need for accessible screening methods. Thus we planned current project with aim to evaluate carotid ultrasonography as diagnostic tool for early detection of coronary artery disease enabling timely intervention and potentially reducing coronary artery disease related morbidity and mortality in the local population.

METHODS:

It's a cross sectional study that was held at Department of Radiology, CMH, Malir-Karachi, following ethical approval from CPSP. It enrolled 103 patients through non-probability consecutive sampling. Both males and females were enrolled having cardiac symptoms with age ranging from 35-75years were enrolled. However, patients with prior history of coronary intervention (PCI, CABG) or diagnosed case of coronary artery disease, pregnancy, CKD, CLD, malignancy and auto-immune diseases were excluded.[9]

After informed consent, demographic parameters of all patients were documented. Anthroprometric measurements like height, weight and BMI, were recorded in cardiology OPD of CMH-Malir than patients were referred to radiology department for carotid ultrasound. Blood pressure and heart rate were measured using standard procedure. Fasting blood samples were

collected by the Cardiology OPD staff to analyze lipid profile, fasting blood glucose, and other relevant biomarkers of the participants.

All participants underwent carotid artery ultra-sonography. It was done with high-resolution B-mode, color Doppler, and pulsed wave Doppler ultra-sonography, using a GE logic P7 ultrasound machine equipped with a 3-11- MHz linear array transducer. CIMT was measured at standardized locations on both the right and left common carotid, internal and external carotid arteries, and the mean values were used for analysis. Atherosclerotic plaque analysis if present was done that documented the presence or absence of plaque, its location and composition.

Percentage stenosis was calculated using preset settings of the ultrasound machine using percentage stenosis and velocity criteria. Angiograms were assessed for the presence and severity of coronary artery stenosis, using quantitative coronary CT angiography.

Data Analysis:

All the data was processed by SPSS v28.0. Quantitative variables like age, BMI, systolic and diastolic blood pressure and cholesterol levels were presented as mean ± SD. Qualitative variables like smoking status, alcohol intake, exercise habits, marital status, and family history of CAD was presented as frequencies and percentages. Evaluation among groups according to Fisher's exact and chi-square tests were applied with p-value of ≤0.05 was taken significant.

RESULTS:

103 cases from the cardiology outpatient clinic at CMH Malir, Karachi over a period of six months. They were then referred to radiology department for carotid ultrasound. The mean age of patients was 48.4 ± 10.3 years. The mean BMI was 28.4 ± 12.5 kg/m². There were 58(56.3%) males and 45(43.7%) females. Hypertension was present in 34 (33.0%), diabetes mellitus in 41 (39.8%), and current smoking in 16 (15.5%) patients as shown in table-1.

Table 1: Demographics and Co-morbidities of the patients

Gender	Frequency (n)	Percentage
Male	58	56.3%
Female	45	43.7%
Hypertensive	34	33.0%
Diabetic	41	39.8%
Smoker	16	15.5%

The mean CIMT was 0.83 ± 0.12 mm. Carotid plaque was detected in 47 (45.6%) patients, while carotid stenosis ≥50% was observed in 29 (28.2%) patients. Based on the predefined criteria (CIMT ≥0.8 mm, carotid ultrasound

was positive in 66 (64.1%) patients as shown in table-2. However, On CT coronary angiography, significant CAD was identified in 60 (58.3%) cases.

Table-2: Carotid Ultrasound Findings		
Carotid Ultrasound Findings	Frequency (n)	Percentage
CIMT ≥ 0.8 mm	66	64.1%
Carotid Plaque Present	47	45.6%
Carotid Stenosis ≥50%	29	28.2%
Carotid Ultrasound Positive*	66	64.1%
CT Coronary Angiography Findings		
CT Coronary Angiography Findings	Frequency (n)	Percentage
Significant CAD Present	60	58.3%
No Significant CAD	43	41.7%

* Positive if CIMT ≥0.8 mm

Cohen's Kappa value of 0.511 ($p < 0.001$) indicates moderate agreement between carotid ultrasound and CT coronary angiography in detecting significant CAD as shown in table-3.

Table-3: Diagnostic Performance of Carotid Artery Ultrasound Compared to CT Coronary Angiography					
		CT Coronary Angiography		**Kappa Value**	**p-value**
		CAD Present	CAD Absent		
Carotid Artery Ultrasound	Positive	51 (85.0%)	15 (34.9%)	0.511	< 0.001*
	Negative	9 (15.0%)	28 (65.15)		

*Statistically significant

The diagnostic performance of carotid ultrasound in detecting significant CAD showed a sensitivity of 85.0%, specificity of 65.1%, positive predictive value of 77.3%, and negative predictive value of 75.7% as shown in table-4.

Table-4: Diagnostic accuracy of carotid artery ultrasound		
Statistic	**Value**	**95% CI**
Sensitivity	85.0%	73.4% to 92.9%
Specificity	65.1%	49.1% to 79.0%
Positive Predictive Value	77.3%	69.0% to 83.8%
Negative Predictive Value	75.7%	62.1% to 85.5%
Accuracy of carotid artery ultrasound	76.7%	67.3% to 84.5%

The area under the curve (AUC) was 0.82 (95% CI: 0.74–0.90), indicating good discriminatory ability of carotid intima–media thickness in identifying patients with significant coronary artery disease as shown in fig-1.

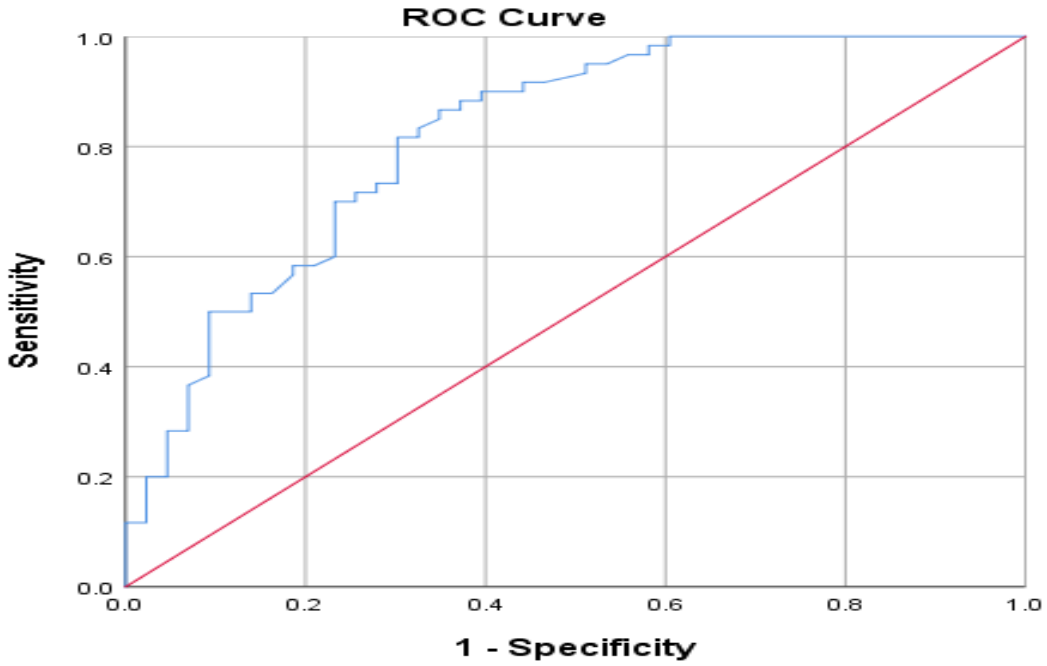

Figure-1: AUC Depicting Carotid-Intima-Thickness

DISCUSSION:

Degree and severity of carotid artery atherosclerosis (AS) is a strong predictor of ischemic heart disease.[4] The risk of further ischemic cerebro-vascular episodes can be considerably decreased by early detection and timely treatment of carotid atherosclerosis.[5] It affects any segment of the carotid arteries thus diagnostic imaging has an important role in patient's management with carotid atherosclerosis.

Atheromatous plaques at the carotid bifurcation can now be diagnosed non-invasively due to the development of Doppler ultrasound in the 1980s. Despite being the "gold standard" for assessing the severity of carotid artery disease, conventional angiography is an invasive procedure.[10] The probability of peri-procedural complications, such as thromboembolic phenomena, is 0.3–1% with CT-angiography as documented previously by literature review.[11] Similarly, it is associated with risks like radiation exposure and contrast media reactions.

Carotid Doppler ultrasound, on the other hand, is a precise, affordable, and radiation-free imaging technique. As a result, it is now widely used for both the initial screening of asymptomatic patients with risk factors for atherosclerosis and the diagnosis of clinically severe carotid artery disease in symptomatic patients as well as for coronary artery disease.[12] Because pre-clinical carotid atherosclerosis detection can help avoid future ischemic stroke and coronary artery disease thus early screening of high-risk patients is very crucial.

Results of present study showed that diagnostic performance of carotid ultrasound in detecting significant coronary artery disease has a sensitivity of 85.0%, specificity of 65.1%, accuracy of 76.7%, PPV of 77.3%, and NPV of 75.7% as shown in table-4. Similarly, one previous study concluded that the pooled estimates for sensitivity and specificity of Carotid Doppler ultrasound were 0.97 and 0.99, respectively.[13] Another study showed that sensitivity, specificity and diagnostic accuracy of Carotid Duplex Ultrasonography in detecting significant carotid atherosclerosis was 92.0%, 89.0% and 91.1% respectively.[11] Thus our results were in line with previous studies but low sensitivity may be contributed by ethnicity and genetic differences.

Our results showed that mean CIMT was 0.83 ± 0.12 mm. Carotid plague was detected in 47 (45.6%) patients, while carotid stenosis ≥50% was observed in 29 (28.2%) patients. Based on the predefined criteria (CIMT ≥0.8 mm, carotid ultrasound was positive in 66 (64.1%) patients as shown in table-2. However, On CT coronary angiography, significant coronary artery disease (CAD) was identified in 60 (58.3%) patients. Similarly, on previous study documented that CT coronary angiography confirmed clinically significant coronary artery stenosis in 50.5% cases.[11] Similarly, another study concluded that participants in their study had a mean CIMT of 0.85+0.14 mm. The mean CIMT was significantlyhigher in triple vessel disease (0.97+0.16 mm) versus double vessel disease (0.85+0.11 mm) and single vessel disease (0.78+0.10 mm).[14] Thus our findings were in line with previously above mentioned studies. Similarly, area under the curve (AUC) was 0.82 (95% CI: 0.74–0.90), indicating good discriminatory ability of carotid intima–media thickness in identifying patients with significant coronary artery disease as shown in fig-1.

Doppler ultrasonography is typically the first step in treating individuals with suspected carotid stenosis. Medical therapy and repeated follow-up ultrasounds are used to monitor the course of stenosis in patients with clinically non-significant stenosis (i.e., <50% stenosis).

LIMITATIONS:
Composition and morphology of atherosclerotic plaques was not studied. Moreover, this was a single centre study and lack of human resources, financial constrains and genetic workup added to its limitations.

CONCLUSION:
We concluded that carotid artery ultrasound is an accurate, highly sensitive, non for detecting coronary artery disease with low specificity. It has a good discriminatory ability of carotid intima–media thickness in identifying patients with significant coronary artery disease thus it's a reliable tool in early detection of coronary artery disease in the absence of CT-coronary angiography.

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IM, HH: Conceptualization of Project, Data Collection, Write-up
HZ, KAK: Literature Search, Drafting and write-up, Proof read
FA, MOA: Statistical Analysis, Drafting, Revision
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