Intima Media Thickness of Carotid and Femoral Artery as predictor of Cardiovascular Events

Original Article

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ABSTRACT

Objective: To establish the correlation between IMT (presence and severity) of carotid and femoral artery detected on Doppler study and presence of subclinical CAD in asymptomatic patients for early detection of CAD and risk stratification by a non-invasive method.

Methodology: This cross-sectional analytic study was conducted in the Cardiology department of Mayo Hospital Lahore for a period of 1 year. One hundred and twenty asymptomatic subjects with and without conventional risk factors for CAD were included The thickness of the intima-media of carotid and the femoral artery was assessed by high-resolution B mode Ultrasonography. The patients enrolled in our study underwent coronary angiography. Data was entered and analyzed through SPSS (Statistical package for social science) version 16. **Results:** There were a total of 120 patients with a male-to-female ratio of 1.8:1 The mean age of patients was 32.40 ± 10.74 years, minimum age of patients was 20years while the maximum age was 40 years. Most of our patients were overweight, smokers, and had established family history of heart disease. Most of the patients had a single-vessel disease and had severe CAD at the time of presentation. There were 93 patients whose IMT was >0.8 mm. There were 16 patients whose CMIT was <0.8 mm. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of B-mode USG (using CIMT and FA-IMT) were calculated as 85.32%, 72.73%, 96.88%, 33.33% and 84.17% respectively for CMIT. For FA-IMT sensitivity, specify, PPV, NPV and Diagnostic accuracy of B-mode USG was 84.4%, 54.55%, 94.85%, 26.09% and 81.67% respectively.

Conclusion: The increased IMT is a predictor of coronary vascular disease, measured non-invasively with B-mode ultrasound. It can be used to predict future cardiovascular events and risk stratification. If patients are diagnosed in the earlier stages then timely treatment can prevent or regress the progression of the disease.

INTRODUCTION

Ultrasonographic measurement of carotid intima-media (also called intimal-medial or intima-media) thickness (CIMT) refers to the utilization of ultrasound (B-mode) to determine the thickness of intima and media of carotid artery (two innermost layers of the carotid artery wall). The intima-media thickness of the femoral artery (FA-IMT) has also been acquired and studied. Detection and monitoring of IMT (atherosclerosis) may provide an opportunity to intervene earlier in atherogenic disease and/or monitor the disease.[1] The mortality due to Coronary Heart Disease (CHD) is 274 per 100'000 population.[2] Established major risk factors for CHD have been identified by a panel of experts of the National Cholesterol Education Program (NCEP). These risk factors include raised levels of LDL-C and total cholesterol, and decreased levels of HDL-C in the serum. Tobacco consumption, raised blood pressure, premature CHD in the family, and advanced age is among other risk factors. The treatment strategies to modify the risk of CHD, with emphasis on target goals of LDL cholesterol were highlighted in the ATP III study.[3] Pathological investigative reports show that the magnitude and degree of atherosclerosis are linked with the presence of conventional risk factors. There are significant variabilities in the degree of atherosclerosis at each stage of exposure to risk factors.

There has been a growing interest in identifying a

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technique that can improve the ability to diagnose those at risk of developing CHD, as well as to measure disease progression, particularly for those at intermediate risk. ATP III recommends the use of Framingham criteria to further stratify those patients with two or more risk factors for more intensive lipid profile management.[3]

The carotid and femoral arteries can be well visualized by ultrasonography, and their respective IMTs acquired by using the same have been investigated as a technique to identify and monitor subclinical atherosclerosis. B-mode ultrasound is most commonly used, and the IMT is measured and averaged over several sites in each carotid artery. Distant (far) wall images of each common carotid artery yield more accurate and reproducible IMT measurements than imaging of the near wall. Two echogenic lines are produced, representing the media-adventitia interface and lumen intima interface. IMT is the interval between these two lines.[4]

A limitation of IMT as a surrogate for CAD is that it does not accurately assess the total atherosclerotic burden and therefore cannot predict the severity of CAD or distinguish the patients with single-vessel, double vessel, or multiple vessels CAD. Given these limitations, more recent research has used the combined carotid artery IMT and femoral artery IMT measurements to more accurately determine the atherosclerotic burden of the coronary arteries.[5]

In October 2009, the United States Preventive Services Task Force (USPSTF) published a systematic review of the measurement of CIMT within the scope of a larger recommendation statement entitled "Using Nontraditional Risk Factors in Coronary Heart Disease Risk Assessment". Based on one fair- and two good-quality studies, the USPSTF states that CIMT, independently of Framingham risk factors, predicts CHD in asymptomatic patients. ARIC study revision was done and found that CIMT measurement can be used to predict the future risk of CVD.[6]

The association of raised carotid IMT with conventional risk factors were studied in the Atherosclerosis Risk in Communities (ARIC) study in 15,800 subjects. The relationship between CIMT and elevating quartiles of total cholesterol, LDL cholesterol, and triglycerides was graded. CIMT was then also correlated with the incidence of CHD in a subgroup of patients enrolled in the trial after 4 to 7 years of follow-up. The presence or absence of plaque was judged by experts only if two out of the three criteria were present (CIMT>1.5mm), abnormal wall texture (brighter echoes), and abnormal shape. The site-specific reliability coefficient was measured as 0.77, 0.73 & 0.70 for the mean carotid far wall IMT at the carotid bifurcation, ICA, CCA respectively. The incidence of future CHD can be predicted noninvasively by measuring mean carotid IMT.[7]

An association between cardiac incidents and CCA-IMT in a group of 1288 middle-aged men of Finnish origin was seen by Salonen and Salonen. IM thickening of the arterial wall was defined as a distance of more than 1.0 mm from the intima-luminal interface and media-adventitia interface in the CCA below the carotid bulb. This association was built based on follow up of 12 months and 24 events in total, structural changes in CCA or carotid bulbs was linked with 3.29 times, IMT with 2.17 times, small plaques with 4.1 times and big plaques (stenotic) with a 6.71 times more risk of acute MI in comparison to the normal carotid artery wall.[8]

The Rotterdam Study in 1989, recruited 7,983 individuals, both male and female of 55 years of age or more. The primary purpose of this study was to inquire into the prevalence and frequency of major risk factors for chronic diseases in the elderly, including CVD. Whether the progression of atherosclerosis in asymptomatic elderly subjects can harbinger cardiovascular events, was one of the features of this study. Measurements of CIMT were used to assess the progression of atherosclerosis.

Increasing CIMT from 0.6 mm - 1.0 mm was associated with increased risks of stroke and MI.[9,10] O'Leary and colleagues performed CIMT in 4,476 asymptomatic subjects aged 65 years or older without clinical CVD. There was a correlation between the occurrence of CVD events and IMT thickness of carotid arteries; and it was notably significant even after adjusting conventional risk factors. The authors concluded that CCA-IMT progression from EDIC (Epidemiology of Diabetes intervention and complications) 1 to 6 years it was 0.019 millimeters lower in intensive as opposed to conventional (p-value < 0.0001) & 01-12 years it turned out to be 0.014 mm lower (p-value = 0.048), but changes from 6-12 years were comparable (0.005 millimeter, p-value = 0.379) The Carotid Atherosclerosis Progression Study (CAPS) was a longitudinal study of 4,904 subjects. Conventional risk factors were noted and CIMT measurements were taken at baseline and were followed over 10 years (mean follow-up 8.5 years, range 7.1-10.0 years). Adverse outcome events were MI in 73 patients (1.5%), angina or MI in 271 patients (5.5%), and death in 7 subjects (1.5%). Different researchers have recently published a retrospective review of the data from the

CAPS.[11-13]

MATERIAL AND METHODS

Setting

The study was conducted on an outpatient basis in the Cardiology department in collaboration with the Radiology department at Mayo Hospital, Lahore, Islamic Republic of Pakistan. It was a cross-sectional analytical study that started in January 2017 and concluded in January 2018. A total of 120 male and female asymptomatic subjects (Age 20-40 years) with and without known CAD conventional risk factors, who gave informed consent were included in this study. The sample size was calculated by using WHO standard software by taking a 26.9% prevalence of CAD with a 95 % level of significance and an 8 % margin of error. Patients with primary CAD, primary dyslipidemia, severe co-morbid disease e.g. (CLD, CKD), and peripheral vascular disease were excluded.

Data Collection

Presence or absence of conventional risk factors for CVD was recorded. Weight, height and waist circumference were measured to calculate BMI. Blood sugar level (fasting and random) was done to detect DM in patients who are not known to have it. B.P was noted. Following lab. investigations were done:

CBC, RFT's, LFT's, FASTING LIPID PROFILE, CXR, ECG, Doppler, Coronary Angiography (who gave consent for)

Carotid & femoral doppler analysis

The thickness of the intima-media of the carotid and the femoral artery was assessed by Ultrasonography B-mode (High Resolution) with GE Logic 7 System using a linear probe of 7.5 MHz.All patients who fulfilled the inclusion criteria underwent Doppler evaluation. This was performed by an experienced radiologist who is unaware of clinical history and other relevant findings.

The Doppler criteria used to diagnose the IMT thickness:

- 1 longitudinal and 1 short-axis image of the CA and FA each was needed.
- The interval between the interface of lumen and intima and interface between the media and adventitia

For carotid artery

The maximum CCA IMT described on both sides (right and left), as the mean of the maximum IMT far and near the wall, calculated ten millimeters proximal to the common carotid bulb. The thickening of IM greater than 0.8mm was considered abnormal.

For Femoral Artery

In the femoral artery, a 15mm long segment just proximal to the bifurcation of common FA into superficial and profunda artery, IMT was measured. The mean FA-IMT was 0.8mm and considered abnormal if its value above this value.[12]

Analysis of coronary arteries by angiography

Coronary arteries were imaged with the digital Toshiba infrex DSA/DA System (Japan), utilizing a quantitative assessment of CAD in selected individuals. The angiographic images were assessed by 02 senior cardiologists to determine the severity of CAD, without knowing the clinical features of the patients.

Data Analysis

Data was entered and analyzed through SPSS (Statistical package for social science) version 16. Numerical data were presented in mean ± S.D. For the variation of quantitative data standard deviation (S.D) and range were used. The qualitative variables were presented in the form of frequency, percentage, pie chart, and bar chart where appropriate. 2x2 table was generated to calculate sensitivity, specificity, PPV, NVP and diagnostic accuracy of B-mode USG by using CIMT and FA-IMT taking coronary angiography as the gold standard.

RESULTS

There were 77 (64.17%) male and 43 (35.83%) female patients in the study. The male-to-female ratio was 1.8:1 [Figure 1]. We included 120 cases of with no obvious symptoms suggestive of CAD with mean age of 32.40±10.74years. Minimum age of patients was 20years while maximum age was 40 years [Table 1]. There were 47 (39%) patients who were unemployed in which house wives were also included while 22 (18%) were employed as watchman or private job, 19 (16%)
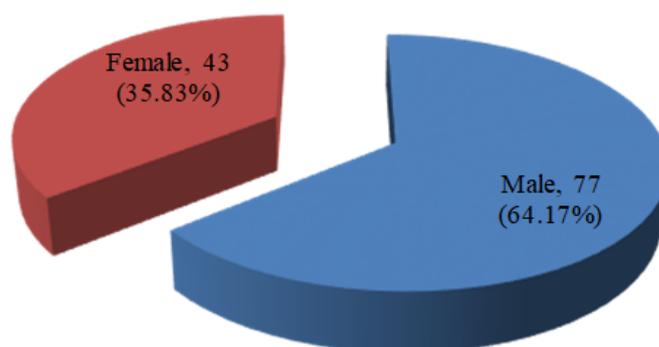

Figure 1: Gender wise distribution of subjects

Age (Years)		Male	Female	Total
	N	87	77	120
	Mean	31	34	32.40
	SD	9	8	10.74
	Minimum	20	23	20
	Maximum	40	37	40

Table 1: Descriptive statistics of age (years) of patients

		Frequency	Percentage
Occupation	Unemployed	47	39%
	Other Jobs	22	18%
	Labour	19	16%
	Businessman	32	27%
	Total	120	100%

Table 2: Occupation of subjects

were labor and 32 (27%) were business.

In this study, there were 83 (69%) patients who belonged to lower SES, 34 (28%) patients belonged to middle SES while 3 (3%) belonged to high SES [Figure 2]. There were 21 (18%) patients who were illiterate, 23 (19%) patients had education <5 class, 34 (28%) patients had education >5 class and 42 (35%) patients had education >metric [Figure 3].

The mean height, weight and waist of patients was 163.9±6.4cm, 73.33±11.24kg and 95.57±17.14cm, respectively. Mean BMI of patients was 28.07±4.43 [Table 3].

In this study, we observed DM in 25 (20.83%) cases, HTN in 28 (23.33%) cases, 70 (58.33%) were smokers, 66 (55%) had dyslipidemia while 36 (30%) reported family history of CAD [Table 4].

The hematology and biochemistry reports of our subjects is shown in Table 5. Table 6 describes various risk factors present in patients. There were 25 patients who were diabetic, 28 were hypertensive, 70 were smokers, 66 had dyslipidemia and 36 patients had family history of CAD.

In Male patients CMIT & FA-IMT was 0.84±0.16 and 1.2±0.4 mm. While in female patients mean CMIT & FA-IMT was 0.83±0.15 and 0.90±0.40 mm respectively [Table 7].

Angiography findings showed that 5 patients had LM involvement, 47 had LAD, 35 had LCX, 22 had RCA and 11 patients were having normal findings [Table 8].

Vessel involvement showed that 28 patients had SVD, 58 had DVD and 23 patients had TVD while 11 patients had normal findings on angiography [Table 9].

There were 17 patients who had mild disease, 25 had moderate and 67 patients had severe CAD [Table 10].

There were 93 patients whose IMT was >0.8 mm. Among these patients 24 had SVD, 49 had DVD and 20 had TVD. While there were 16 patients whose CMIT was <0.8 mm among these patients 4 had SVD, 9 had DVD and 3 patients had TVD respectively [Table 11].

Sensitivity, specificity, PPV, NPV and diagnostic accuracy of B-mode USG (using CIMT and FA-IMT) were calculated as 85.32%, 72.73%, 96.88%, 33.33% and 84.17% respectively for CMIT. For FA-IMT sensitivity, specify, PPV, NPV and Diagnostic accuracy of B-mode USG was 84.4%, 54.55%, 94.85%, 26.09% and 81.67% respectively [Table 12].

DISCUSSION

The process of atherosclerotic plaque formation starts from early childhood and progresses gradually over the years. Clinical symptoms of CVD and angina occur only when coronary arteries have narrowed to the extent that they result in the limitation of coronary blood flow or due to the formation of thrombus on a pre-
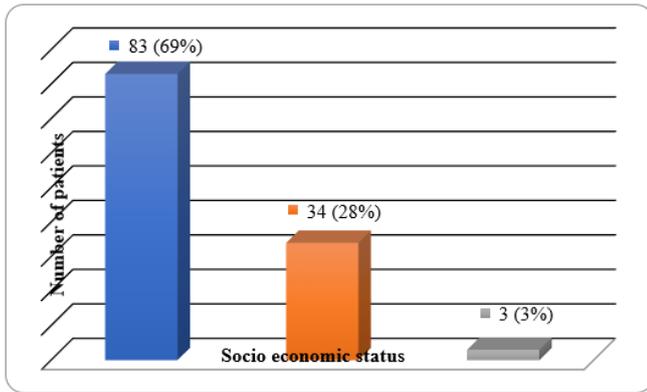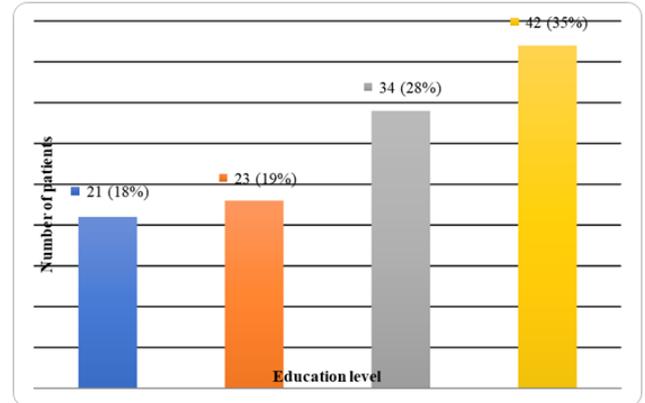
Figure 2: Socioeconomic Status of the subjects

Figure 3: Educational status of subjects

		Height (cm)	Weight (Kg)	Waist (cm)	BMI
Anthropometric measurements	Mean	163.9	73.33	95.57	28.07
	SD	6.4	11.24	17.14	4.43
	Minimum	152.4	60	53	23
	Maximum	173.7	90	190	34
	Range	21.3	30	137	11

Table 3: Descriptive statistics of anthropometric measurements of patients
Criteria for BMI (WHO Criteria) Normal: 19 to 25, Under Weight: less than 18.5, Normal weight: 18.5 to 24.9
Over Weight: 25 to 29.9, Obese: more than30.

Risk factors		Frequency	Male=n(%)	Female=n(%)
	DM	25(20.83%)	16(13.33%)	9(7.50%)
	HTN	28(23.33%)	20(16.67%)	8(6.67%)
	Smoking	70(58.33%)	66(55%)	4(3.33%)
	Dyslipidemia	66(55%)	45(37.50%)	21(17.50%)
	Family History	36(30%)	27(22.50%)	9(7.50%)

Table 4: Distribution of risk factors of CAD in patients

Laboratory parameters	Laboratory Report
Hemoglobin (gm/dl)	13.7±1.5
Alanine Aminotransferases (U/L)	33.1±21.6
Aspartate Aminotransferases (U/L)	27.5±10.6
Serum cholesterol (mg/dl)	158.8±37.6
HDL (mg/dl)	47.1±26.3
Blood Sugar Random (gm/dl)	124.5±40.2
HbsAg Negative	100%
Anti-HCV Negative	100%

Table 5: Descriptive statistics of laboratory investigations

existing plaque that suddenly ruptures or gets eroded. Although a clinical CVD event doesn't occur in all the individuals with atherosclerotic plaque, the risk for future cardiovascular events is directly proportional to the extent of subclinical atherosclerosis. The identification of asymptomatic patients with elevated risk for CVD and the presence of atherosclerosis is paramount importance, as future CVD events and morbidity can be decreased by timely medical interventions.[6,8,13-16]

CVD risk can be further assessed by imaging arteries to identify and calculate the presence of subclinical vascular disease. It is of utmost importance that imaging modality for screening is affordable, safe, sensitive and guide to interventional options that can change the natural course of CVD favorably.

Risk factors		Frequency	IMT	
			CA	FA
	DM	25(20.83%)	0.82±0.36	1.20±0.45
	HTN	28(23.33%)	0.80±0.32	1.2±0.55
	Smoking	70(58.33%)	0.80±0.30	1.3±0.52
	Dyslipidemia	66(55%)	0.79±0.4	0.99±0.56
	Family History	36(30%)	0.77±0.32	0.98±0.66

Table-6: Risk Factors distribution among patients with IMT

	Male		Female	
	CMIT	FA-IMT	CMIT	FA-IMT
Mean	0.84	1.2	0.83	0.90
SD	0.16	0.4	0.15	0.40
Minimum	0.80	0.84	0.8	0.84
Maximum	1.2	2.4	1.2	1.91

Table-7: CIMT & FA-IMT in patients

		Frequency	Percentage
Angiography Findings	LM	5	4.17%
	LAD	47	39.17%
	LCX	35	29.17%
	RCA	22	18.33%
	Normal	11	9.17%
	Total	120	100

Table-8: Distribution of coronary angiography findings in patients

		Frequency	Percentage
Angiography Findings	SVD	28	23.33%
	DVD	58	48.34%
	TVD	23	19.16%
	Normal	11	9.17%
	Total	120	100

Table-9: Distribution of vessel involvement in patients

Measurement of CIMT with Ultrasound (B-mode) to calculate C-IMT is a sensitive, non-invasive, and reproducible method for identification and quantification of atherosclerotic burden and CVD risk. As a research tool, it is well verified and is used in clinical practice in abundance.[13,17-22]

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		Frequency	Percentage
Angiography Findings	Mild <50%	17	14.17%
	Moderate: 50-70%	25	20.83%
	Sever: >70%	67	55.83%
Total		109	100%

Table-10: Severity of Stenosis

		SVD	DVD	TVD	Total
IMT	>0.8	24	49	20	93
	<0.8	4	9	3	16
Total		28	58	23	109

Table-11: IMT in relation to diseased vessels

		CORONARY ANGIOGRAPHY					
		+	-			+	-
CIMT	>0.8	93	3	FA-IMT	>0.8	92	5
	<0.8	16	8		<0.8	17	6
	Total	109	11			109	11

Sensitivity	85.32%	84.4%
Specificity	72.73%	54.55%
Positive Predictive	96.88%	94.85%
Negative Predictive	33.33%	26.09%
Diagnostic Accuracy	84.17%	81.67%

Table-12: Diagnostic Accuracy of USG (CMIT & FA-IMT)

change the natural course of CVD favorably. Measurement of CIMT with Ultrasound (B-mode) to calculate C-IMT is a sensitive, non-invasive, and reproducible method for identification and quantification of atherosclerotic burden and CVD risk. As a research tool, it is well verified and is used in clinical practice in abundance.[13,17-22]

Numerous studies in middle-aged (40-65) have shown that the major risk factor for CHD (which includes cholesterol level, Blood Pressure, and cigarette smoking) is predictive of long term outcomes in these age groups. However, equally compelling data from observational studies are almost non existing in young adults.[2]

Autopsy studies showed that atherosclerosis of coronary arteries can start in the second decade of life and a recent study found severely stenotic coronary arteries (narrowing >40%) in 19% of men in their early 30s.[42] Based on national cholesterol education programmed recommended cholesterol screening in all adults 20 years of age or older. Similarly, JNC-VI on identification, prevention, and management of high blood pressure recommends screening for HTN in person 18 years or older.

However, guidelines in the prevention of CAD in young adults have not been uniformly accepted, in part because data on risk prediction and prevention of CVD is scarce in individuals less than forty years of age.[2] Therefore, we conducted a cross-sectional study with 120 cases with no obvious symptoms suggestive of CAD. Most cases of CAD become clinically apparent in patients aged 40 years or older, that's why we included patients having a mean age of 32±10.74 years. The mean ages of male patients were 31±9 and that of females was 34±8 years.

The mean CIMT in male patients who were involved in this study were 0.84±0.16 and that of female were 0.83±0.1.5 mm. The mean FA-IMT for male patients was 1.2±0.4 and that of female patients was 0.90±0.40. [23,24] Salonen and Salonen documented that a single measurement of the maximum CCA-IMT >1mm was predictive of future acute MI over a 1 month to 3 years period.[25]) Belcaro and colleagues also documented that 1-time IMT measurement of carotid and femoral arteries of >1 mm in asymptomatic patients was able to successfully predict CVD events over a period of 6 years.[26] In our study, there was a clear male preponderance (64.17%) which is in

agreement with the previous studies suggesting that CAD is predominately a disease of men.[27]

In our study hypertension was present in 23.33%, DM 20.83%, Smoking 58.33%, Dyslipidemia 55%, and family history of CAD in 30% patients respectively. The diabetic patients had the highest abnormal CIMT and in smokers, abnormal FA-IMT was highest. This is in contrast to previous studies that showed hypertensive patients had greater IMT in the carotid artery. As observed in the previous studies there was an increased degree of IMT in tobacco consumers, our study found similar results.[28]

The CIMT and FA-IMT in male patients were more as compared to female patients. The mean CIMT in male patients was 0.84±0.14 and in female patients was 0.83±0.15.

While in FA mean IMT in male and female patients was 1.2±0.4 and 0.90±0.40 respectively. Twelve studies (case-control) showed that median IMT was comparable (0.83-1.05 mm) and in the 06 studies (cohort),(0.73-1.08 millimeter). The meta-analysis of these studies showed that with advanced age,

screening may become less reliable. But David S Wald and Jonathan P Bestwick weren't able to confirm this pattern and there is a likelihood that results of screening can be better.[29]

It clearly shows that IMT is a primarily a surrogate parameter for the inherent process of atherogenesis and therefore appear to be approximate means of identifying and possibly monitoring of young healthy adults at significantly high risk of future vascular events.[30]

The angiographic analysis revealed that 23.33% of patients had SVD, 48.34% had DVD and 19.16% had TVD, and 9.17% of patients had normal angiography. The involvement of LM was 4.17%, LAD was seen in 39.17%, LCX in 29.17%, and RCA in 18.33% patients. The results are in contrast to another study which showed the involvement of LAD as 42%, LCX 26%, and RCA 22%.[31,32] In our study, the majority of patients suffered from DVD disease. i.e. 48.34% and single-vessel disease 23.33%. Sridevis et al reported 27.4% and Akanda et al have reported 42.1% that majority of patients have TVD.[31,32]

The frequency of Left Mainstem disease was 4.17% while Soleimani A et al showed that LM disease to be 3.6-6.4%.[33] The published literature showed that LAD is the most commonly affected artery which is similar to our study. The normal angiogram in our study was 9.17% which is contrary to MAK Akanda et al who reported 25% normal angiograms. The reported

difference in our study is that LCX is the second most commonly affected artery as compared to RCA in Previous studies.[31] The severity of stenosis observed in our study was mild 14.1%, moderate in 20.83%, and severe in 55.83% patients.

The prognostic importance of CIMT and FA-IMT was significantly linked to the hazard of development of CAD as compared to patients who had normal IMT. CVD events or MI are linked to the formation of thrombus after erosion or rupture of plaque& there is an increasing body of evidence that those plaques which look less stenotic on angiographic views are more susceptible to progress or rupture as compared to more stenotic lesions at the time of revascularization. Outcomes from pathoanatomic studies have shown that during the early stages of coronary atherosclerosis, vessels may undergo compensatory enlargement.[28]

Due to a strong body of evidence that CVD events and IMT are co-related, FDA has accepted two-dimensional ultrasound as a tool to quantify the degree of atherosclerosis. Ludwig M et al proposed the utilization of Duplex Ultrasound for the quantification of IMT and to detect the presence of plaques and stenosis.[34]

CONCLUSION

In our study, the sensitivity, specificity, PPV, NPV, and diagnostic accuracy of B-mode USG (using CMIT and FA-IMT) were calculated as 85.32%, 72.73%, 96.88%, 33.33%, and 84.17% respectively for CMIT. For FA-IMT sensitivity, specify, PPV, NPV and Diagnostic accuracy of B-mode USG was 84.4%, 54.55%, 94.85%, 26.09% and 81.67% respectively. It was concluded from the results of the study that the use of B-mode USG is accurate enough to measure the risk of CAD in patients presented in OPD for a regular check-up. It is concluded that mean CMIT and FA-IMT >0.8 mm were associated with CAD as compared to patients who had less than these values. So asymptomatic patients appearing in OPD for regular checkups can be screened by a noninvasive method and can help predict future CAD. These patients can be treated by aggressive risk factors management, lifestyle modification to prevent further development/progression of CAD and to prevent acute MI and stroke which could lead to disability.

High-resolution duplex ultrasonography appears encouraging for the identification, measurement and serial investigation of structural changes of the arterial wall non invasively.

LIMITATIONS OF THE STUDY

Our research team made a thorough effort for this study, although, but just like any other study few

limitations can be attributed to the same.

First of all, it was a single-center study so the number of the patient enrolled were limited. Secondly, we only used Doppler ultrasound to assess the degree of thickness of the intima-media of both carotid and femoral arteries. Another factor that wasn't taken into consideration was whether patients were already on medication (statins, ACEI/ARBs, etc.) that regress atherosclerotic process or not. As it is Doppler ultrasound-based study and measurement depend on the operator, so there are inter-operator variations that we should take into account.

CONTRIBUTIONS TOWARDS SCIENTIFIC KNOWLEDGE

The measurement of Intima-media thickness is a well-validated and accepted marker and method for establishing a diagnosis of subclinical atherosclerosis. This can help the physicians and cardiologists in classifying the sizeable fraction of intermediate CVD risk patients into lower and higher risk groups. As it is a non-invasive method to detect cardiovascular disease in patients with intermediate-risk category, it can be easily performed by using the standard measurement techniques. If patients are diagnosed in the earlier stages, then timely treatment can prevent or regress the progression of the disease. In this way, many patients can be treated medically and the burden of interventional cardiologists, as well as an economic burden, can be reduced.

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CONFLICT OF INTERST

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