Original Research Article

A study to compare the relationship between the presence of coronary artery disease and carotid intima media thickness in COPD and other various risk factors

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Abstract

Introduction: The burden of coronary artery disease (CAD) continues to rise globally, as developing nations, including India, are adopting to lifestyle changes with predisposition to cardiovascular diseases (CVD). During the past 30 years, coronary artery disease(CAD) rates have doubled in both urban and rural India while they have been halved in the United states. **Materials and Methods:** Patients admitted in Department of General Medicine, GIMSR,GITAM (Deemed to Be University), Visakhapatnam from January 2020 to December 2020 for a period of 12 months. 100 cases, 100 controls were included in the study. Outcome measures were Relationship between risk factors and IMT (Intima Media Thickness) Relationship between IMT and coronary artery disease. **Results:** The statistical analysis was done using the t-test and ANOVA and p-value of <0.001 was considered to be significant. The mean age of cases is 49.81 years and that of controls is 47.93 years. There were 71 males and 29 females in the case group. There were 60 males and 40 females in the control group. Both the correlation and regression analyses indicate that BMI and AVCIMT have a moderate positive relationship that is statistically significant. **Conclusion:** Cardiovascular risk factors, diabetes, smoking, hypertension, hypercholesterolemia are associated with increased CIMT. This study suggests a significant association between carotid IMT and the presence of CAD in Indian population also which differs from our Western counterparts in risk factor profile, mortality and morbidity. For all these reasons, and the wealth of experience with this approach, external carotid external ultrasound is likely to remain among the most widely employed imaging technique for the quantification and tracking of subclinical atherosclerosis.

Key Words: coronary artery disease, CVD, CIMT, BMI, IMT.

Introduction

The burden of coronary artery disease (CAD) continues to rise globally, as developing nations, including India, are adopting to lifestyle changes with predisposition to cardiovascular diseases (CVD) [1]. During the past 30 years, coronary artery disease(CAD) rates have doubled in both urban and rural India while they have been halved in the United states. By 2015, cardiovascular diseases are expected to account for 34% of male deaths and 32% of female deaths, amounting to a total of 1.5million deaths[2].

It is imperative to shift the focus to disease prevention rather than palliation. Prevention requires early identification of individuals at risk of developing cardiovascular disease but clinically asymptomatic, so that intensive preventive measures may be instituted to arrest the progression of disease. Cardiovascular disease is an end result of atherosclerotic process. The various diagnostic modalities used currently (exercise electrocardiography, stress echocardiography, thallium scanning, coronary angiography) can detect atherosclerotic disease only when it becomes well advanced and occlusive [3].

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The common carotid artery thickness was demonstrated to be related to cardiovascular risk factors and to the occurrence of coronary heart disease. An increase in the carotid intimal media thickness (IMT) is associated with an increased risk of Ischemic heart disease and cerebrovascular disease[4].A widely accepted, convenient marker of atherosclerosis is carotid artery intima-media thickness (IMT)which is significantly associated with prevalent and incident carotid plaques. Carotid intima media thickness (IMT) measurement is a promising tool for detecting atherosclerosis in its pre-occlusive phase[7-10].

Atherosclerosis is an inevitable accompaniment of ageing and its rate of development depends on several factors. Well known risk factors for accelerated atherosclerosis includes smoking, hypertension, dyslipidemia and dysglycemia. Atherosclerosis is a slow and progressive disease of the arterial wall that underlies the majority of cardiovascular events. Several investigations have provided evidence of an association between increased IMT and classical risk factors associated with the development of atherosclerotic disease and the occurrence of cardiovascular events. IMT regression or delayed IMT progression can be observed when risk factors are controlled via lifestyle modifications or inhibited by different pharmacologic therapies. These findings demonstrate the usefulness of repeated IMT measurements in the evaluation of a patient's response to therapy. The burden of coronary artery disease (CAD) continues to rise globally, as developing nations, including India, are adopting to lifestyle changes with predisposition to cardiovascular diseases (CVD). During the past 30 years, coronary artery disease (CAD) rates have doubled in both urban and rural India while they have been halved in the United states. Atherosclerosis, unless in a severe form is often asymptomatic, so that a direct examination of the vessel wall is necessary to detect

affected individuals in the early stages. It has been suggested by International atherosclerosis project that the atherosclerotic process occurs at the same time in carotid, cerebral and coronary arteries. Measurement of the carotid intima-media thickness (CIMT) of the common carotid artery (CCA) by B-mode ultrasound was found to be a suitable non invasive method to visualize the arterial walls and to monitor the early stages of the atherosclerotic process[6]. The purpose of this study is to correlate carotid intima medial thickness and the extent of CAD as well as the effect of various risk factors on IMT.

Aims and objectives

- To study the usefulness of B-mode ultrasound as a non-invasive marker to examine the association between carotid intima media thickness (IMT) and the extent and severity of coronary artery disease.
- To study the effects of traditional vascular risk factors on atherosclerotic changes in the carotid artery.
- To assess the severity of atherosclerosis.

Materials and methods

Study design

Cross-sectional study.

Study setting

Patients admitted in Department of General Medicine, GIMSR, GITAM (Deemed To Be University), Visakhapatnam

Study population

Cases and age, sex matched controls in the age group 30-65 years.

Study duration

January 2020 to December 2020, a period of 12 months

Estimated sample size

100 cases, 100 controls

Outcome measures

Relationship between risk factors and IMT (Intima Media Thickness)
Relationship between IMT and coronary artery disease.

Data collection

Inclusion criteria

Cases

- Known cases of coronary artery disease
- H/o angina
- H/o Myocardial infarction
- Those who have undergone elective coronary angioGraphy

Controls

- No h/o heart disease
- No h/o diabetes mellitus
- No h/o hypertension
- Normolipidemia

Exclusion criteria

1. Patients with insulin dependent diabetes mellitus.
2. Patients with history of pancreatitis, pancreatectomy, hemochromatosis, cushing's syndrome, glucagonoma, hyperthyroidism, hypothyroidism.
3. Patients on medications which can elevate blood glucose levels- glucocorticoids, thyroid hormones, diazoxide, diuretics, Beta adrenergic agonists and nicotinic acid.
4. Patients with history of CABG, carotid surgery, endarterectomy, cerebrovascular accident, PVD.

Ultrasound evaluation

B mode ultrasound using 7 MHz linear array transducer was done, scanning includes left and right carotid arteries. The carotid artery is focused in the far wall and the 3 segments are identified on each side: the distal 1.0cm of the common carotid proximal to the bifurcation, the carotid bulb and the proximal 1.0 cm of the internal carotid artery.

Biochemical studies

Fasting sample is collected in the morning for the analysis of the following parameters using standard techniques:

- FBS(FASTING BLOOD SUGAR)
- TC(TOTAL CHOLESTEROL)
- TG(TRIGLYCERIDES)
- HDL(HIGH DENSITY LIPOPROTEIN)
- LDL(LOW DENSITY LIPOPROTEIN)

Pulmonary evaluation:

All smokers of the study participants underwent pulmonary evaluation tests by using spirometry.(SpiroWin Plus Spirometer). Following parameters recorded.

- FEV1 (Forced Expiratory Volume 1st Second)
- FVC (Forced Vital Capacity)
- FEV1/FVC (Ratio of FEV1 & FVC)

Patients were classified into NO COPD, Mild, Moderate, severe and very severe based on 2020 GOLD guidelines of COPD.

Statistical methods

Statistical analysis was done by using various statistical methods like t test, ANOVA, correlation and regression. Quantitative variables were expressed as mean ± standard deviation and qualitative variables as percent incidence.

Limitations

The study was done within a select group of sub population and hence may not reflect the actual prevalence in general population.

Ethical issues

Informed oral consent was taken from the patients. The study was cleared by the approved ethical committee of the Institution. The rights and welfare of human subjects on whom the study was conducted was adequately protected.

Results

The statistical analysis was done using the t-test and ANOVA and p-value of <0.001 was considered to be significant. The mean age of cases is 49.81 years and that of controls is 47.93 years. There were 71 males and 29 females in the case group. There were 60 males and 40 females in the control group.
Cases Vs controls: Basic statistics
Sample size:
Controls: 10
Cases: 100

Table 1: Risk factors

Parameter	Control	Case
HTN	-	85%
SMOKING	-	42%
COPD	-	22%
DM	-	78%
BMI	21.7	24.5
SBP	115.5	166.3
DBP	73.1	95.2
FBS	82.9	143.8
TC	141.2	224.2
HDLC	44.6	35.4
LDLC	53.9	168.5

The mean values of cardiovascular risk factors is higher in cases as compared to controls.

Table 2: AVCIMT

	Control	Case
Value	0.48	0.91
CI (90%)	± 0.007	± 0.019

The AVCIMT of controls is 0.48 mm and that of cases is 0.91 mm.

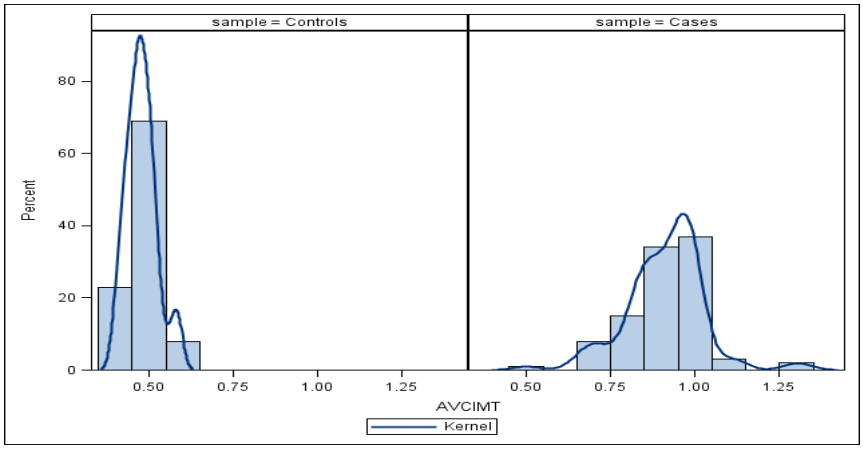


Fig 1: AVCIMT of Controls and Cases.

Table 3: CAD

	Control	Case
SVD	-	24%
DVD	-	34%
TVD	-	36%

Among the cases, 24% had SVD (Single Vessel Disease), 34% had DVD (Double Vessel Disease) and 36% had TVD (Triple Vessel Disease).

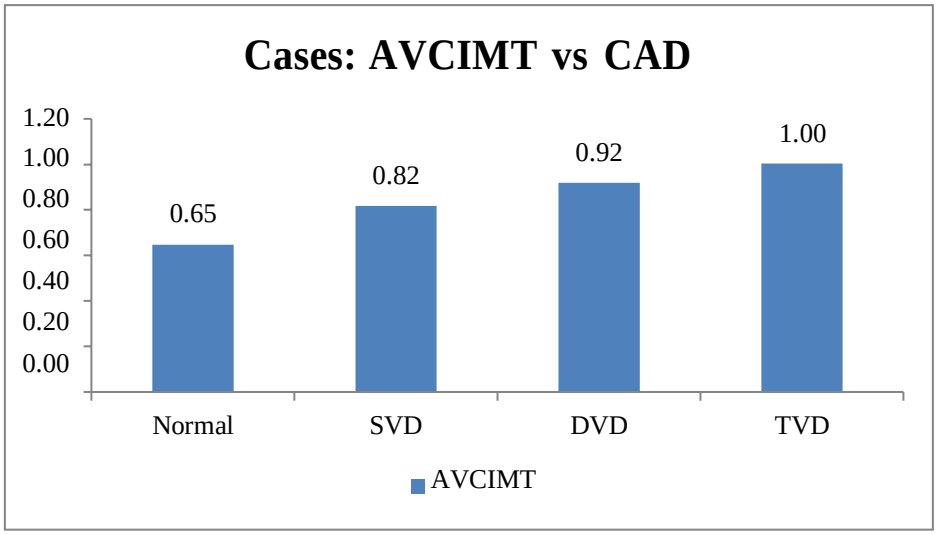


Fig 2: Relationship between AVCIMT & CAD

The AVCIMT increased as the number of involved vessels increased.

Table 4: Statistical Analysis: ANOVA

Source	DF	SS	MSS	F Value	Pr > F
Model / CAD	3	0.87	0.29	57.75	**<.0001**
Error	95	0.48	0.01		
Corrected Total	98	1.34			

As the above ANOVA analysis indicates, the relationship between AVCIMT and CAD is very significant ($p < 0.0001$).

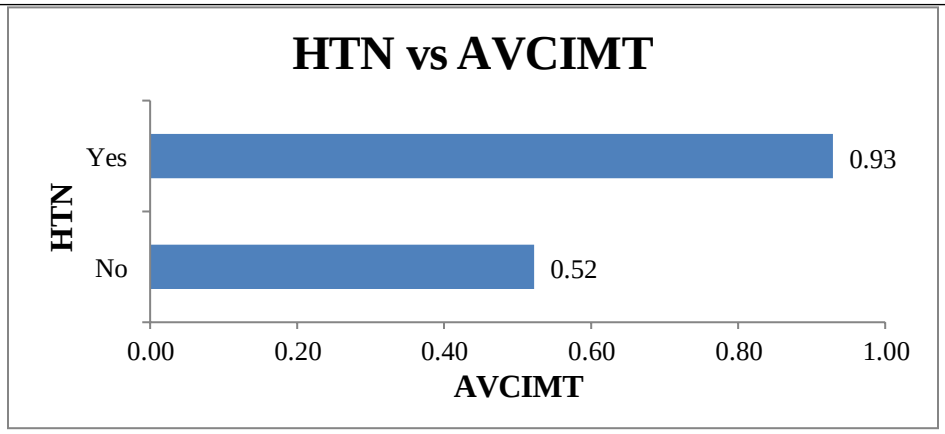


Fig 3: Relationship between HTN &AVCIMT

The AVCIMT in Hypertensives is 0.93 mm and in Non Hypertensives it is 0.52 mm.

Table 5: Statistical Analysis: T-test

HTN	N	Mean	StdDev	t-value	p-value
No	114	0.52	0.13	-23.17	**<.0001**
Yes	79	0.93	0.11		

As the above t-test indicates, the higher value of AVCIMT observed among people with hypertension compared to those without hypertension is statistically highly significant.

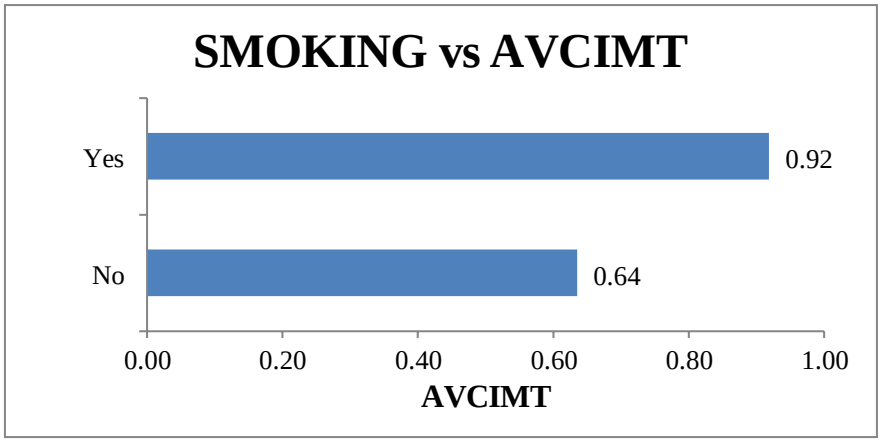


Fig 4: Relationship between SMOKING & AVCIMT

The AVCIMT in Smokers is 0.92 mm and in Non Smokers it is 0.64 mm.

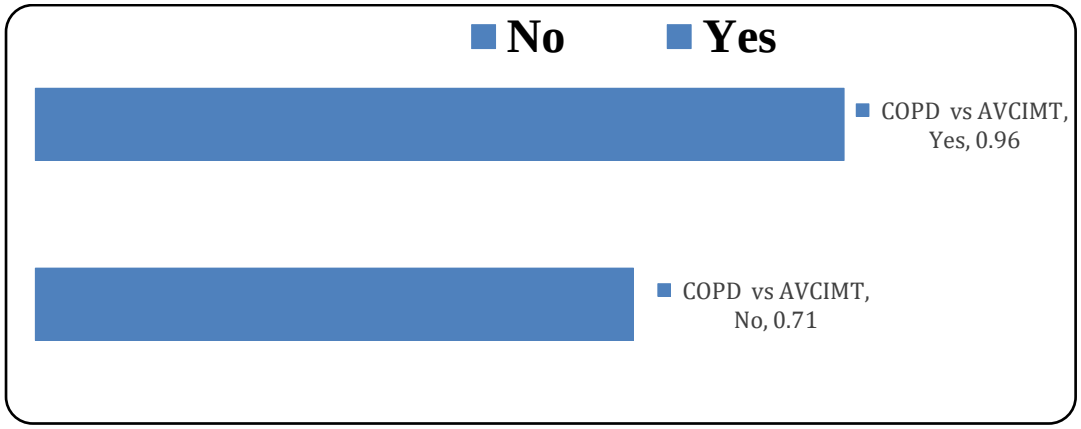
Table 6: Statistical Analysis: T-test

SMOKING	N	Mean	Std Dev	t-value	p-value
No	158	0.64	0.23	-12.84	**<.0001**
Yes	42	0.92	0.08		

As the above t-test indicates, a higher value of AVCIMT is observed among smokers as compared to non-smokers is statistically very significant.

Table showing stages of COPD among smokers with AVCIMT		
Classification	**Number (n)**	**AVCIMT**
No COPD	20	0.71
Mild COPD	6	0.79
Moderate COPD	8	0.88
Severe COPD	5	0.91

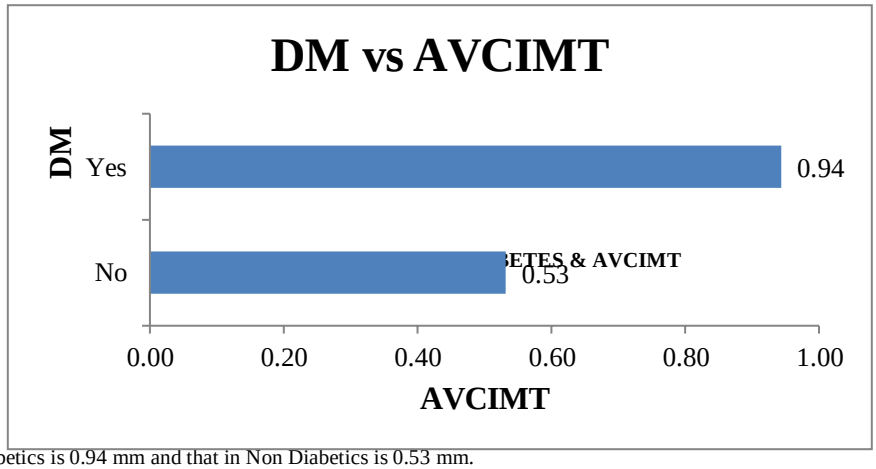
Very severe COPD	3	1.08
Total Smokers	42	



COPD	N	Mean	Std.Dev	t-value	P-value
No	20	0.71	0.07	-21.73	<0.001
Yes	22	0.96	0.09		

Table showing Statistical analysis among Smokers: T -test

As the above t-test indicates, a higher value of AVCIMT is observed among COPD as compared to non-COPD is statistically significant.



The AVCIMT in Diabetics is 0.94 mm and that in Non Diabetics is 0.53 mm.

Table 7: Statistical Analysis: T-test

DM	N	Mean	Std Dev	t-value	p-value
No	119	0.53	0.14	-23.3	**<.0001**
Yes	69	0.94	0.10		

As the above t-test indicates, the higher value of AVCIMT observed among people with diabetes compared to those without diabetes is statistically very significant.

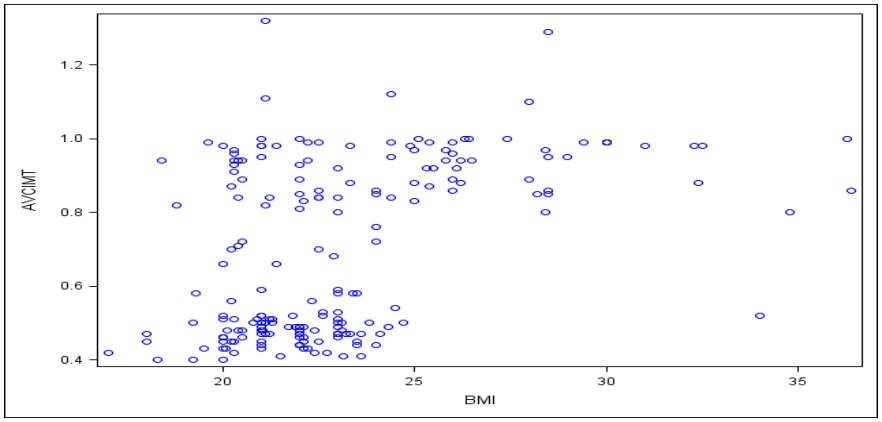


Fig 6: Relationship between BMI & AVCIMT

Increase in BMI is associated with an increase in AVCIMT.

Table 8: Statistical Analysis: Correlation and Regression

Correlation	p-value
0.45	**<.0001**

Regression	Coefficient	Std Err	t-value	p-value
Intercept	-0.02	0.10	-0.23	0.82
BMI	0.03	0.00	**7.08**	**<.0001**

Both the correlation and regression analyses indicate that BMI and AVCIMT have a moderate positive relationship that is statistically significant.

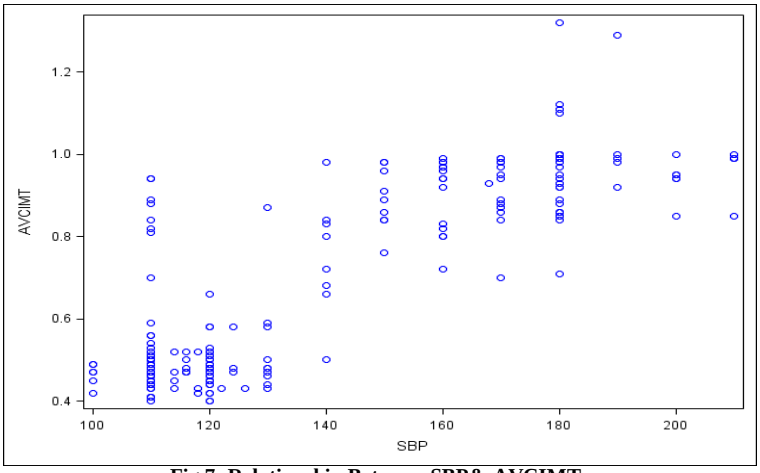


Fig 7: Relationship Between SBP& AVCIMT

Increased SBP is associated with increase in AVCIMT.

Table 9: Statistical Analysis: Correlation and Regression

Corr	p-value
0.84	**<.0001**

Regression	Coefficient	Std Err	t-value	p-value
Intercept	-0.19	0.04	-4.49	<.0001
SBP	0.01	0.00	**21.75**	**<.0001**

Both the correlation and regression analyses indicate that SBP and AVCIMT have a positive relationship that is statistically significant.

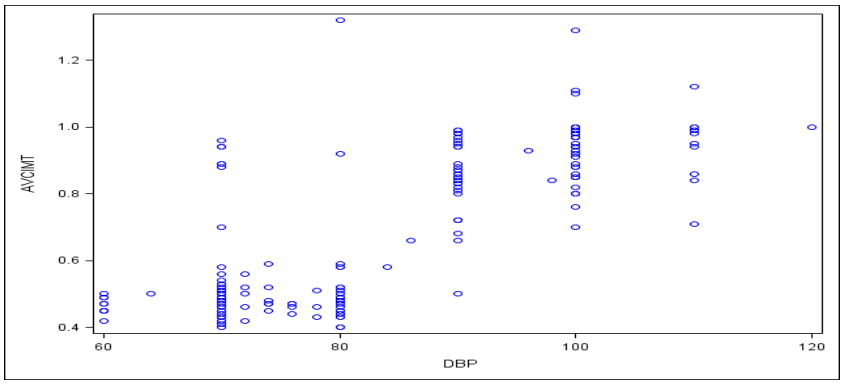


Fig 8: Relationship between DBP& AVCIMT

Increased DBP is associated with increase in AVCIMT.

Table 10: Statistical Analysis: Correlation and Regression

Corr	p-value
0.79	**<.0001**

Regression	Coefficient	Std Err	t-value	p-value
Intercept	-0.41	0.06	-6.60	<.0001
DBP	0.01	0.00	**17.97**	**<.0001**

Both the correlation and regression analyses indicate that DBP and AVCIMT have a positive relationship that is statistically significant.

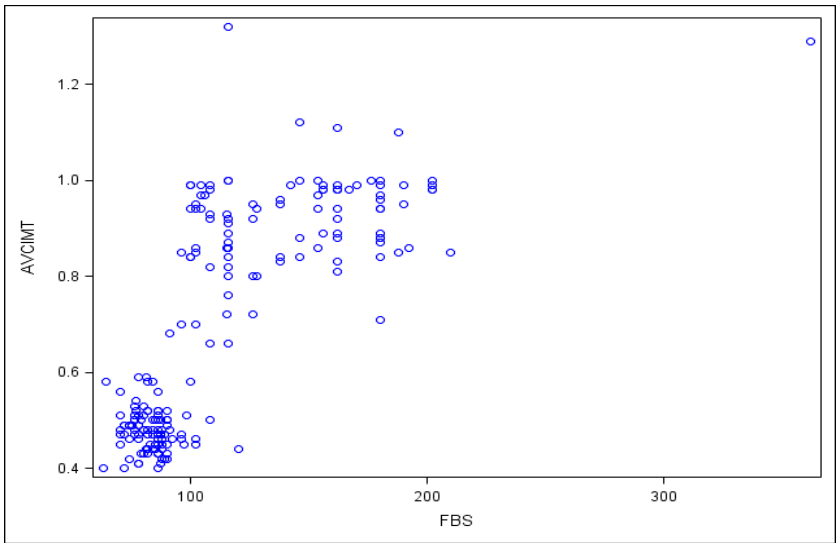


Fig 9: Relationship between FBS& AVCIMT

Increased FBS is associated with increase in AVCIMT.

Table 11: Statistical Analysis: Correlation and Regression

Corr	p-value
0.77	**<.0001**

Regression	Coefficient	Std Err	t-value	p-value
Intercept	0.21	0.03	6.68	<.0001
FBS	0.00	0.00	**16.93**	**<.0001**

Both the correlation and regression analyses indicate that FBS and AVCIMT have a positive relationship that is statistically significant.

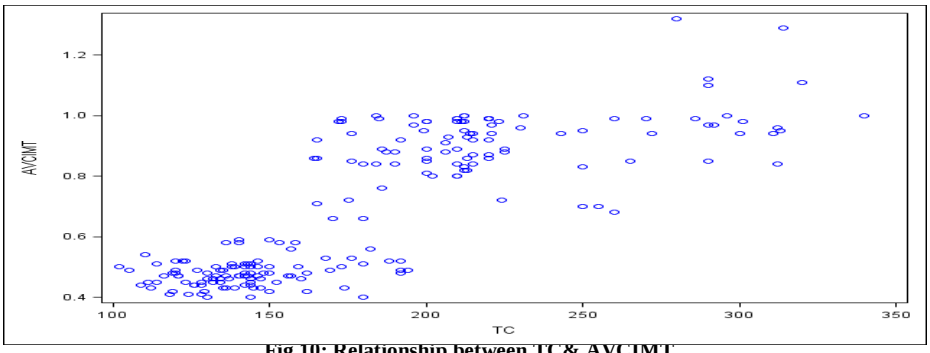


Fig 10: Relationship between TC& AVCIMT

Increased TC is associated with increase in AVCIMT.

Table 12: Statistical Analysis: Correlation and Regression

Corr	p-value
0.81	**<.0001**

Regression	Coefficient	Std Err	t-value	p-value
Intercept	0.05	0.03	1.30	0.19
TC	0.00	0.00	**19.43**	**<.0001**

Both the correlation and regression analyses indicate that TC and AVCIMT have a positive relationship that is statistically significant.

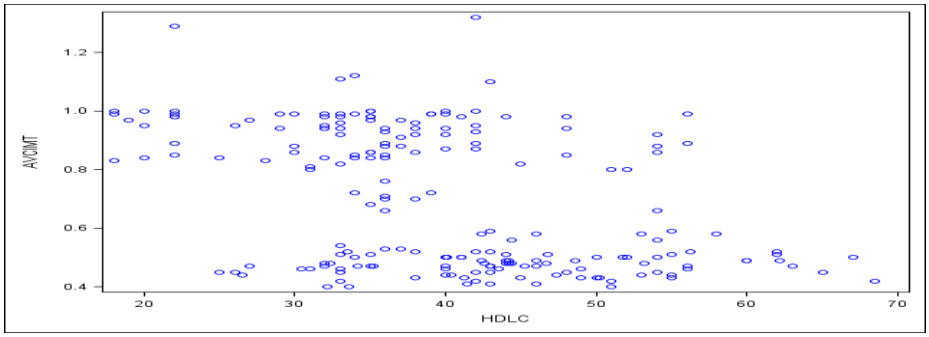


Fig 11: Relationship between HDLC& AVCIMT

High HDLC (High Density Lipoprotein) is associated with low AVCIMT.

Table 13: Statistical Analysis: Correlation and Regression

Corr	p-value
-0.44	**<.0001**

Regression	Coefficient	Std Err	t-value	p-value
Intercept	1.10	0.06	18.48	<.0001
HDLC	-0.01	0.00	**-6.99**	**<.0001**

Both the correlation and regression analyses indicate that HDLC and AVCIMT have a moderate negative relationship that is statistically significant.

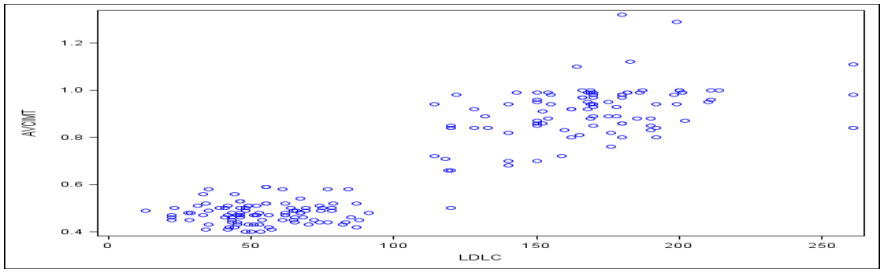


Fig 12: Relationship between LDLC& AVCIMT

High LDLC (Low Density Lipoprotein) is associated with high AVCIMT.

Table 14: Statistical Analysis: Correlation and Regression

Corr	p-value
0.91	**<.0001**

Regression	Coefficient	Std Err	t-value	p-value
Intercept	0.32	0.01	22.12	<.0001
LDLC	0.00	0.00	**30.53**	**<.0001**

Both the correlation and regression analyses indicate that LDLC and AVCIMT have a positive relationship that is statistically significant.

The AVCIMTs associations with the HTN, Smoking, Diabetes Mellitus, SBP, FBS, serum total cholesterol and LDL were found to be statistically significant ($p<0.001$).The statistical significance implied that the Framingham's traditional risk factors indeed had a role in contributing to CIMT.

The AVCIMT was found to be higher in triple vessel disease (1.00mm) >double vessel disease (0.92mm) >single vessel disease (0.82mm) >normal (0.65mm). Hence, a significant association between the extent of the carotid atherosclerosis and the presence of coronary artery disease was found.

Discussion

Interventional and non-interventional methods to detect atherosclerosis are widely used in clinical practice. CIMT measurement has been recommended by the American Heart Association as the most useful method to identify atherosclerosis.[7] Carotid intima media thickness is a valid marker of early atherosclerosis and thus has the potential to detect cardiovascular disease in its subclinical phase. A number of longitudinal studies examined the relationship between CIMT and future events, most arterial system. The advantage of B-mode ultrasound lies in its ability to image atherosclerosis within the arterial wall rather than the lumen of the artery. Its acceptance by medical researchers as a continuous measure of localized atherosclerosis is reflected in its use in ongoing cohort studies and clinical trials.In 2002, the Food and Drug Administration recognized the progression of CIMT as measured by B-mode ultra-sound as a marker of atherosclerosis. In 2003 the European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension recommended the use of IMT measurements in high-risk patients to help identify target organ damage and in 2010 the American Heart Association and the American College of Cardiology advocated the use of IMT on intermediate risk patients if usual risk classification was not satisfactory[9].The role of CIMT as an indicator of CAD has been assessed in various studies. Increased CIMT is associated with other well-known cardiovascular risk factors, including diabetes, smoking, hypertension, hypercholesterolemia, and the metabolic syndrome. Bots demonstrated a graded relationship between the number of traditional risk factors and increased CIMT. Crouse in the Journal of Lipid Research compiled an extensive list of both traditional and nontraditional risk factors associated with CIMT. ·In the Atherosclerosis Risk In Communities study (ARIC) which included 13,870 subjects, carotid IMT was consistently greater in those with clinical cardiovascular disease than in disease free controls. In a study of 75 male patients undergoing coronary angiography for chest pain, Geroulakos and colleagues showed that the common carotid IMT was not only higher in patients with CAD, but also had a significant linear relationship with the number of involved arteries ($r=0.54, p<0.001$).

In an analysis of data of 468 patients undergoing cardiac catheterization and B-mode ultrasound of the carotid arteries, Wofford *et al*. showed that patients with more severe extra cranial carotid artery atherosclerosis are several times more likely to have multiple vessel CAD.Hulthe *et al*. reported a significant correlation between the IMT of the carotid bulb and diameter stenosis of the included coronary segments (r = 0.68). Thus, the degree of carotid atherosclerosis correlates with that of coronary atherosclerosis, and the latter might be estimated to some extent by assessing the former. Demircan et al. found that the CIMT of patients with acute coronary syndrome were significantly increased compared to patients with stable angina pectoris. It has been reported in another study that a maximal CIMT value of 0.956 mm had 85.7% sensitivity and 85.1% specificity to predict angioFigic CAD. In this respect the results of our study are in agreement with previous studies showing significant association between raised IMT and the presence of CAD. Paroiartérielle et Risqué Cardiovasculaire in Asia Africa/Middle East and Latin America (PARC-AALA) is another important large-scale study, in which 79 centers from countries in Asia, Africa, the Middle East, and Latin America participated, and the distribution of CIMT according to different ethnic groups and its association with the Framingham cardiovascular score was investigated. Multi-linear regression analysis revealed that an increased Framingham cardiovascular score was associated with CIMT, and carotid plaque independent of geographic differences. Even in this present study we have found significant association between the extent of carotid atherosclerosis measured by B-mode ultrasound and the presence and its extent or absence of coronary atherosclerosis documented by coronary angiography. In the multivariate modeling which included analysis between risk factors (HTN, DM, Smoking, Dyslipidemia) and CIMT, it was found to be statistically significant ($p<.001$). Among the risk factors carotid intima media thickness seemed to be a better predictor for the presence of coronary artery disease.

Another advantage of B-mode ultrasound was that we were able to analyze the morphology of the carotids, among the 36 who had triple vessel disease, 14 were found to have plaques in their carotids which reflect the severity of atherosclerosis[10]

Although the normal CIMT values are debated in various studies ranging from 0.7+/-0.1mm,[17] our control population had a mean of 0.48+/-0.007mm, $p<0.001$.

Conclusion

We concluded through this study that the easy applicability and the non invasive nature of B-mode ultrasonography make it suitable for use as a surrogate endpoint in measuring the atherosclerotic burden in people with cardiovascular risk factors.

Carotid Doppler ultrasonography can be utilized as a valuable screening tool due to its several advantages, including ease of application, reproducibility, low cost and strong correlation with atherosclerosis.Its advantage over coronary calcium scoring and coronary CT angiography is the lack of ionizing radiation and the ability to detect disease at a young age when coronary calcium score is often zero. CIMT is predictive of MI and stroke. Cardiovascular risk factors, diabetes, smoking, hypertension, hypercholesterolemia are associated with increased CIMT. This study suggests a significant association between carotid IMT and the presence of CAD in Indian population also which differs from our Western counterparts in risk factor profile, mortality and morbidity.For all these reasons, and the wealth of experience with this approach, external carotid external ultrasound is likely to remain among the most widely employed imaging technique for the quantification and tracking of subclinical atherosclerosis.

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