IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 2 Ser. 6 (February. 2019), PP 64-71
www.iosrjournals.org

A Study to Compare Carotid Intima-Media Thickness with Conventional Risk Factors for Atherosclerosis.

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Date of Submission: 29-01-2019 Date of acceptance: 14-02-2019

Atherosclerosis is a disease of large and medium-sized muscular arteries and is characterized by endothelial dysfunction, vascular inflammation, and the buildup of lipids, cholesterol, calcium, and cellular debris within the intima of the vessel wall. This buildup results in plaque formation, vascular remodeling, acute and chronic luminal obstruction, abnormalities of blood flow and diminished oxygen supply to target organs.

Atherosclerosis- Atherosclerosis (ath"er-o-skleh-RO'sis) comes from the Greek words athero (meaning gruel or paste) and sclerosis (hardness}[1]

Atherosclerosis remains the major cause of death and premature disability in developed societies. Moreover, current predictions estimate that by the year 2020 cardiovascular diseases, notably atherosclerosis, will become the leading global cause of total disease burden. Although many generalized or systemic risk factors predispose to its development, atherosclerosis affects various regions of the circulation preferentially and yields distinct clinical manifestations depending on the particular circulatory bed affected. Atherosclerosis of the coronary arteries commonly causes myocardial infarction and angina pectoris. Atherosclerosis of the arteries supplying the central nervous system

frequently provokes strokes and transient cerebral ischemia. In the peripheral circulation, atherosclerosis causes intermittent claudication and gangrene and can jeopardize limb viability. Involvement of the splanchnic circulation can cause mesenteric ischemia. Atherosclerosis can affect the kidneys either directly (e.g., renal artery stenosis) or as a frequent site of atheroembolic disease[2].

Table – 1[3]

Major Risk Factors for Atherosclerosis (Excluding LDL cholesterol)
Cigarette smoking
Hypertension (BP 140/90 mmHg or on antihypertensive medication)
Low HDL cholesterol[a] [<1.0 mmol/L (<40 mg/dL)]
Diabetes mellitus
Family history of premature CHD
CHD in male first-degree relative <55 years
CHD in female first-degree relative <65 years
Age (men 45 years; women 55 years)
Lifestyle risk factors
Obesity (BMI 30 kg/m^2)
Physical inactivity
Atherogenic diet
Emerging risk factors
Lipoprotein(a)
Homocysteine
Prothrombotic factors
Proinflammatory factors
Impaired fasting glucose
Subclinical atherogenesis(Can be measured by CIMT)

[a]HDL cholesterol ≥ 1.6 mmol/L (60 mg/dL) counts as a "negative" risk factor.

Heiss G, et al[4] assessed whether carotid atherosclerosis measured by B-mode ultrasound is related to cardiovascular risk factors. 386 cases with carotid artery wall thickening and an equal number of controls free of arterial intima-media thickening were drawn from the cohort of the Atherosclerosis Risk in Communities (ARIC) Study. Cases and controls were individually matched on sex, race, age group, study center, and date of examination. The mean values of total cholesterol, low density lipoprotein (LDL) cholesterol, total triglyceride, blood pressure, and pack-years of cigarette smoking were higher in cases than controls. Mean high density lipoprotein (HDL) cholesterol was lower in cases than controls. Case-control differences were all statistically significant.Prati P., et al study[5] showed the high prevalence of asymptomatic carotid atherosclerotic lesions in a general population (approximately 25% of adults) and its relation with the classic risk factors. It emphasized the value of ultrasonography in the detection of early atherosclerotic lesions. Hurst R.T., et al[6] reviewed the literature for clinical use of carotid intima-media thickness. They concluded that CIMT correlates with cardiac risk factors and is an independent predictor of future myocardial infarction and stroke risk.

Takashi W., et al[7] studied the Ultrasonic correlates of common carotid atherosclerosis in patients with coronary artery disease. Increased intima-media thickness and plaque development in the extra cranial carotid arteries reportedly correlate well with the prevalence of coronary artery diseases. The location of these atherosclerotic lesions in the carotid artery varies with age in patients with coronary artery atherosclerosis. Intima-media thickness, plaque, and calcification in the common carotid artery and bifurcation were assessed with high-resolution B-mode ultrasonography. . Intima-media thickness of at least 0.7 mm in the middle-age group and at least 1.0 mm in the old-age group was specific and positively predictive of coronary artery disease. In the middle-age group, intima media thickness in the common carotid artery was correlated with coronary atherosclerotic severity. Conversely, in the old-age group, the presence of plaque and calcification at the bifurcation was correlated with coronary atherosclerotic severity. The characteristic manifestation of the atherosclerotic lesion in the carotid artery varied with age in patients with coronary artery disease.

Blankenhorn D.H., et al[8] studied that Measurement of common carotid IMT is useful for the study of coronary artery risk factors and can augment studies of coronary artery intrusive lesions, because it is associated with coronary artery disease. B-mode measurement of common carotid IMT has the potential of serving as a noninvasive surrogate end point for clinical coronary events. Screening for peripheral vessel changes indicative of high risk for coronary artery disease is possible and cost-effective with the noninvasive procedures available.

Wang T.J., et al[9] studied that increased carotid intima-media thickness is associated with premature coronary heart disease concluded from the Framingham Heart Study. A family history of coronary heart disease (CHD) is an independent risk factor for cardiovascular events. However, the mechanisms underlying this susceptibility have not been fully elucidated. They hypothesized that an important mediator of the familial predisposition to CHD is subclinical atherosclerosis, which is detectable by noninvasive imaging (CIMT). Their findings suggest that subclinical atherosclerosis, assessed in the carotid arteries, is more prevalent in individuals with a family history of CHD. Early-onset parental CHD, in particular, identifies offspring with a strong familial predisposition to atherosclerosis.

Vemmos K.N., et al[10] studied relationship of Common Carotid Artery Intima-Media Thickness in Patients with Brain Infarction and Intracerebral Hemorrhage. They concluded that an increase in the intima-media thickness of the common carotid artery (CCA-IMT), as considered as an early marker of atherosclerosis and has been associated with a higher risk of stroke and myocardial infarction, was associated with risk of brain infarction. There was no evidence of an association between the IMT and cerebral bleeding.

Lorenz M.W., et al[11] studied the Prediction of Clinical Cardiovascular Events with Carotid Intima-Media Thickness. Carotid IMT is a strong predictor of future vascular events. The relative risk per IMT difference is slightly higher for the end point stroke than for myocardial infarction. They suggested that in future IMT studies, ultrasound protocols should be aligned with published studies.

Lester S.J., et al[12] studied Carotid Intima-Media Thickness and Coronary Artery Calcium Score as indications of subclinical atherosclerosis. They concluded that subclinical vascular disease can be detected by CIMT evaluation in young to middle-aged patients with a low FRS (Framingham risk score) and a CACS (coronary artery calcium score) of zero. They suggested that these findings have important implications for vascular disease screening and the implementation of primary prevention strategies.

Stein J. H., et al[13] studied the importance of determining vascular age (VA) by using carotid intima media thickness and integrating it with coronary risk assessment. Measurement of CIMT, a noninvasive estimate of current atherosclerotic burden, is feasible in a clinical setting and can be integrated into CHD risk assessment models. Determining VA using CIMT values may help individualize the age component of population-based CHD risk estimates.

AIM AND OBJECTIVES OF THE STUDY
1. Carotid artery IMT thickness (by B-mode USG scan) - Its association with CAD and stroke.
2. Comparison of carotid artery IMT with conventional risk factors for atherosclerosis.

METHODOLOGY
CASES - Patients admitted in Medical Wards of K.S. HEGDE CHARITABLE HOSPITAL under Medicine, Cardiology and Neurology and patients in M.I.C.U.(Medical Intensive Care Unit) and C.C.U.(Cardiac Care Unit) diagnosed as having stroke and / or CAD.
CONTROLS - Patients attending outpatient department in Medicine, Cardiology and Neurology.
Duration of study – From November 2008 to June 2010
50 cases of CAD
50 cases of stroke (CVA) (both ischemic and hemorrhagic)
50 controls
Controls - Healthy adults more than 30 years of age without present and past history of CAD, stroke and no risk factors for atherosclerotic disease like diabetes mellitus,hypertension, dyslipidemia, obesity.

INCLUSION CRITERIA
1. Age more than 30 years (both male and female).
2. Present or past diagnosis of CAD.
3. Present or past diagnosis of stroke.

EXCLUSION CRITERIA
1. Age less than 30 years of age.
2. Cases / controls who are not giving consent.
DIAGNOSIS OF CAD-Clinical features, ECG changes, increased cardiac enzymes, ECHO changes and coronary angiography suggesting CAD.
DIAGNOSIS OF STROKE Clinical features, CT brain (plain or contrast) or MRI brain (plain or contrast) suggesting stroke.

I. Methodology

After selecting the cases, a detailed questionnaire which includes a detailed history, physical examination and relevant investigations are done for each case.Controls are also analyzed with relevant investigations.After confirming the diagnosis of CAD and stroke (CVA), cases underwent measurement of IMT of distal CCA at its posterior wall bilaterally. Cases of CAD underwent coronary angiography to see the extent of the disease.Controls also underwent measurements of IMT of distal CCA at its posterior wall bilaterally.For measurement of IMT - B-mode USG scan using 7.5 MHz probe is used and whenever required to see plaques, plaque ulceration, lumen stenosis Colour Doppler scan is usedA written informed consent obtained from all CAD and stroke patients and from controls. Clinical examinations included blood pressure recording, assessment of cardiovascular status, height and body weight measurements. Biochemical assessment included fasting and postprandial blood sugar, and fasting lipid profile. Patients were evaluated for the presence and duration of conventional cardiovascular risk factors (hypertension, diabetes mellitus, family history of premature CAD, dyslipidemia, and current smoking). Hypertension was defined as systolic blood pressure > 140 mm Hg, or diastolic blood pressure > 90 mm Hg, or self-reported use of antihypertensive medications. Diabetes mellitus was defined as a fasting blood glucose > 110 mg·dL–1, or non-fasting blood glucose > 200 mg·dL–1 or pharmacological treatment for diabetes. Dyslipidemia was defined as low-density lipoprotein > 130 mg·dL–1, or high-density lipoprotein < 40 mg·dL–1, or triglycerides > 200 mg·dL–1. Family history was coded as positive if a first-degree relative had a coronary event before the age of 55 years in males or 65 years in females. Current smoking or tobacco use in any form was also considered a conventional risk factor.Carotid artery scanning was performed with a high resolution Sonos 5500 (Hewlett Packard, Inc., Anaheim, CA, USA) with a duplex B-mode scanner and a linear phased array transducer of 7.5 MHz frequency. Scanning was undertaken by a Radiologist who was unaware of the clinical status of the subjects. Intima-media thickness was taken as the distance between the leading edge of the first echogenic line of the far wall of the carotid artery (lumen intima interface) and the leading edge of the second echogenic line (media-adventitia interface). Measurements of IMT were made at end-diastole (peak of the R wave) at 3 segments on each side: the distal 1 cm of common carotid artery just before the bifurcation, the carotid bifurcation, and the proximal 1 cm of internal carotid artery and then average of all 3 taken into consideration, both right and left sides are measured like this method. Measurements were taken only on longitudinal scans and not on transverse scans.

TYPE OF STUDY – Case control study
STATISTICS - Multivariate logistic regression analysis using SPSS software version16

II. Results

There was no significant difference was found in three groups with respect to age, gender, history of smoking, history and duration of hypertension and diabetes mellitus, and family history of CVD risk factors, but there was significant difference in dyslipidemia.

Table 1: AVERAGE CIMT with CVD risk factors in all three groups

GROUPS	Number of CVD risk factors	Number of subjects	Mean CIMT	Std. Deviation	F	p
Control	0	28	.9911	.18260		
	1	18	1.1667	.17987		
	2	4	1.0875	.16520	5.225	.009 sig.
Stroke	0	2	1.0750	.17678		
	1	17	1.2235	.19374		
	2	22	1.3091	.15784	3.238	.031 sig.
	3	9	1.4444	.29309		
CAD	0	6	1.1250	.14053		
	1	13	1.2308	.10712		
	2	20	1.2850	.14699		
	3	9	1.4556	.17220		
	4	1	1.3500	.0		
	5	1	1.6500	.0	5.865	.000 sig.

CVD Risk factors-
- Smoking
- Family history of CVD
- Dyslipidemia
- Hypertension
- Diabetes mellitus

1. As number of risk factors increase CIMT increases in all three groups.
2. Increase in CIMT in all three groups in accordance with number of risk factors sometimes may not be apparent as number of patients may be a limiting factor

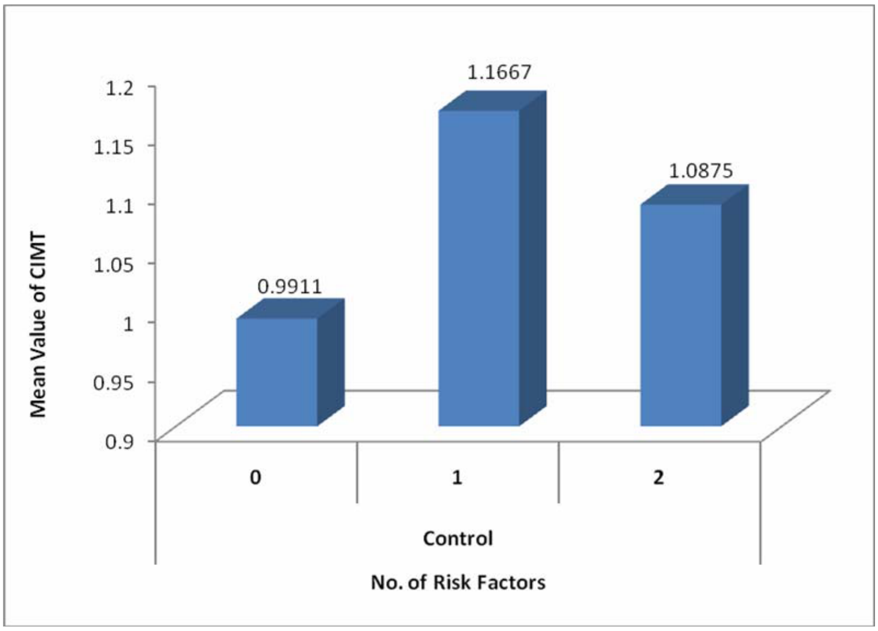

Fig. 1: AVERAGE CIMT with CVD risk factors in Control group

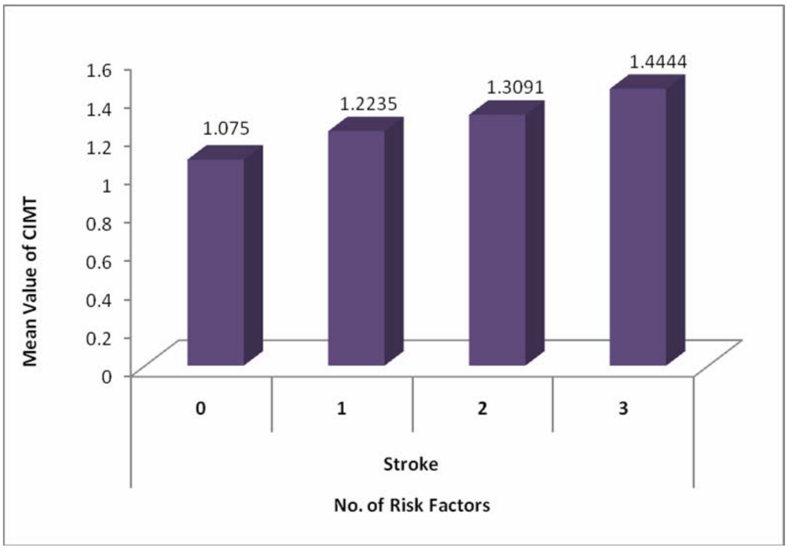

Fig. 2: AVERAGE CIMT with CVD risk factors in Stroke group

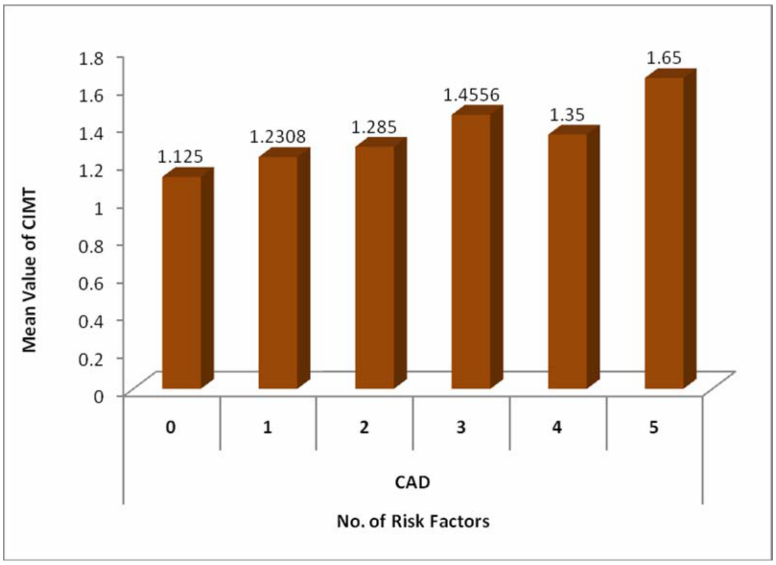

Fig. 3: AVERAGE CIMT with CVD risk factors in CAD group

Comparing table-20, table- 21, table- 22, it can be concluded that CIMT of healthy controls with one or two risk factors is significantly less than CIMT of stroke or CAD groups with similar number of risk factors.
So CIMT depends not only on conventional CV risk factors but also on other unknown atherosclerotic risk factors.
So CIMT should surrogate more appropriately for atherosclerotic diseases like stroke and CAD rather than conventional CV risk factors like hypertension, DM, etc.

Table 2: Multiple regression analysis
Stroke and CAD groups

	CVD risk factors	Unstandardized Coefficients		t	P(for Stroke and CAD)
		B	Std. Error		
	AGE	-.039	.007	-5.395	.000 vhs
	GENDER	.049	.164	.299	.765
	SMOKING	-.067	.171	-.391	.696
	FAM. H.	.252	.128	1.978	.050 sig
	Dyslipidemia	.441	.128	3.456	.001 vhs
	HTN	.071	.136	.526	.600
	DM	.051	.142	.361	.719
	AVER. CIMT	1.976	.388	5.095	.000 vhs

This table analyses demonstrating individual contribution by multiple variables as CV risk factors for clinical atherosclerotic diseases outcome as stroke and CAD.This table takes consideration of each CVD risk factor as independent risk factor for end point, atherosclerosis related morbidity (Stroke and CAD in our study). Here we see that most important determinants for end point of Stroke and CAD are age, family history of CVD, dyslipidemia, and average CIMT.But it is important to note that not all of these factors are independent from each other as average CIMT can be affected by many of these CVD risk factors.

Though hypertension, DM are not shown as significant contributors for stroke and CAD, probably this can be explained that these subjects had less CIMT hence did not have bad outcome. As CIMT is dependent on both conventional CV risk factors like hypertension, DM, etc and unknown risk factors of atherosclerosis, so CIMT is regarded to correlate better with stroke and CAD, than conventional CV risk factors like hypertension, DM, etc.

Table 3: Multiple regression analysis
CAD Group

	CVD risk factors	Unstandardized Coefficients		t	P(for CAD)
		B	Std. Error		
	AGE	-.039	.009	-4.300	.001 vhs
	GENDER	-.035	.224	-.155	.878
	SMOKING	-.103	.237	-.434	.665
	FAM .H.	.108	.158	.685	.495
	Dyslipidemia	.701	.189	3.708	.001 vhs
	HTN	.436	.218	1.999	0.049 sig.
	DM	.177	.222	.799	.427
	AVER. CIMT	2.094	.533	3.930	.001 vhs

Here we see that most important determinants for end point of CAD are age,dyslipidemia, hypertension and average CIMT

Table 4: Multiple regression analysis
Stroke Group

	CVD risk factors	Unstandardized Coefficients		t	P(for Stroke)
		B	Std. Error		
	AGE	-.011	.005	-2.271	0.026 sig.
	GENDER	.113	.103	1.094	.277
	SMOKING	.080	.108	.739	.462
	FAM. H.	.085	.089	.950	.345
	Dyslipidemia	.231	.098	2.362	0.02 sig.
	HTN	.431	.095	4.542	.001 vhs
	DM	.473	.095	4.963	.001 vhs
	AVER. CIMT	.572	.249	2.300	0.024 sig.

Here we see that most important determinants for end point of Stroke are age, dyslipidemia, hypertension, diabetes mellitus and average CIMT.
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III. Discussion

Carotid IMT is a valid marker of early atherosclerosis and thus has the potential to detect cardiovascular disease (CAD and CVA) in its subclinical phase. It possibly reflects the cumulative deleterious effects of various cardiovascular risk factors over time.In the current study the baseline characteristics of the 3 study groups are same to avoid confounding.

In our study following are the results-

1. CIMT is a marker of atherosclerosis as its value is raised in Stroke and CAD groups compared to age and gender matched controls. And raised values of CIMT are strongly associated with Stroke and CAD.
2. As risk factors for atherosclerosis, like age, family history of CVD,
dyslipidemia, hypertension, diabetes mellitus, increases value of CIMT increases in a proportional way.
3. Average CIMTControls-
1.0mm
Stroke- 1.3mm
CAD- 1.3mm

As average CIMT goes above 1 mm chances of having atherosclerotic diseases like Stroke and CAD increase.

4. In present study if we consider CIMT as independent variable for atherosclerosis/CVD, it is well comparable with other conventional risk factors for CVD like age, family history of CVD, dyslipidemia, etc. Clinical end points for atherosclerosis like Stroke and CAD, CIMT has statistically significant causal association.Our study is comparable with previous studies showing a significant association between raised IMT and the presence of significant atherosclerosis/cardiovasculardisease. But numbers of patients in different groups were less to draw any satisfactory conclusion. In India Gupta H. et al[2] study was done in 2003 to determine whether carotid intima-media thickness is associated with coronary artery disease and cardiovascular risk factors in the Indian population. 101 patients with coronary artery disease and 140 control .subjects were assessed for CIMT and other conventional CVD risk factors. Results showed that the average intima-media thickness was significantly higher in the coronary disease group. On multivariate logistic regression analysis, carotid intima-media thickness was the most important factor found to be an independent predictor of coronary artery disease. There was a significant association between number of CVD risk factors and the average intimamedia thickness values in both control and coronary artery disease groups. Similar results are also seen with our study but in our study we had three groups with separate Stroke and CAD groups.Another study from India, The Chennai Urban Population Study[14] reported significantly raised mean IMT values in diabetic patients compared to non-diabetic subjects. As diabetes is very strong risk factor for atherosclerosis we found very strong causal association of DM with stroke in our study.

But in case of CAD group strong association of DM with CAD is not established the reason being small sample size. This can also be explained on basis of less CIMT.Among western studies the Atherosclerosis Risk in Communities (ARIC) study[15], is worth mentioning. In this study carotid IMT was significantly higher in individuals with cardiovascular risk factors compared to normal controls. This is a population based study in which large cohort was followed up for at least 10 years. And in this population based cohort healthy controls without risk factors for atherosclerosis like family history of CVD, dyslipidemia, hypertension, DM were compared with people with risk factors for atherosclerosis. In our study we have compared **controls** with Non-modifiable risk factors for atherosclerosis like age, family history of CVD with **Stroke and CAD patients** who have both modifiable and Non-modifiable risk factors. We concluded similarly like ARIC study that CIMT increases linearly as number of risk factors for atherosclerosis increases.Like many studies in the past have shown that carotid IMT can indicate the presence and extent of CAD. Our study suggests a significant association between IMT and the presence and extends of CAD in the Indian population. However, more data are needed to establish carotid IMT as a noninvasive tool for the detection of CAD in symptomatic or asymptomatic individuals.CIMT role in predicting the risk of future cardiovascular events in Western populations has already been established by several large-scale prospective studies. But

CIMT role in India for prediction of future CVD has not been done on large randomized prospective studies. Our study was done on small number of patients with case-control nature, so it difficult to conclude on this aspect of CIMT role.

Finally it is said that the easy applicability and noninvasive nature of carotid Bmode ultrasonography make it suitable for use as screening tool for atherosclerosis burden. Which group of people should undergo measurement of CIMT is a little controversial issue but those with multiple risk factors for CVD should undergo for CIMT measurement after physician recommendation.

IV. Conclusion

CIMT can be used to assess atherosclerotic diseases burden.
It is well documented tool to see the vascular age of the person.
Large scale studies with randomization are required to establish a cut off value of average CIMT, according to age, gender and race, above which primary prevention of atherosclerosis can be started. CIMT can be used as monitoring tool for progression and regression of atherosclerosis process.

References

[1]. Mitchell R.S., Kumar V., Abbas, A.K., Fausto, N., *Robbins Basic Pathology:* Philadelphia: Saunders.2007; 8th edition: 345-355.
[2]. Gupta H., Bhargava K., Bansal M., et al. Carotid Intima Media Thickness and Coronary Artery Disease: An Indian Perspective, Asian Cardiovascular Thoracic Annuals 2003; 11:217-221.
[3]. Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, Loscalzo J. Harrison's principles of internal medicine. New York: McGraw-Hill Medical Publishing Division.2008; 17th edition: 1505.
[4]. Heiss G, Sharett AR, Barnes R, et al and the ARIC Investigators. Carotid atherosclerosis measured by B-mode ultrasound in populations: associations with cardiovascular risk factors in the ARIC study. Am J Epidemiol. 1991; 134: 250-256.
[5]. Prati P., Vanuzzo D., Casaroli M., et al. Prevalence and Determinants of Carotid Atherosclerosis in a General Population. *Stroke* 1992; 23:1705-1711.
[6]. Hurst R.T., Ng D.W.C., Kendall C., et al. Clinical Use of Carotid Intima-Media Thickness: Review of the Literature. J Am Soc Echocardiogr 2007; 20:907-914.
[7]. Takashi W, Tsutomu F, Kentaro F. Ultrasonic correlates of common carotid atherosclerosis in patients with coronary artery disease. Angiology. 2002; 53(2):177-83.
[8]. Blankenhorn D.H., Hodis H.N. Arterial Imaging and Atherosclerosis Reversal. *Arterioscler Thromb.* 1994; 14:177-192.
[9]. Wang T.J., Nam B.H., D'Agostino R.B., et al. Carotid Intima-Media Thickness Is Associated With Premature Parental Coronary Heart Disease. The Framingham Heart Study. *Circulation*. 2003; 108:572-576.
[10]. Vemmos K.N., Tsivgoulis G., Spengos K., et al. Common Carotid Artery Intima-Media Thickness in Patients with Brain Infarction and Intracerebral Hemorrhage. *Cerebrovasc Dis* 2004; 17:280-286.
[11]. Lorenz M.W., Markus H.S., Bots M.L., et al. Prediction of Clinical Cardiovascular Events with Carotid Intima-Media Thickness. A Systematic Review and Meta-Analysis. *Circulation*. 2007; 115:459-467.
[12]. Lester S.J., Eleid M.F., Khandheria B.K., et al. Carotid Intima-Media Thickness and Coronary Artery Calcium Score as Indications of Subclinical Atherosclerosis. Mayo Clin Proc. 2009;84(3):229-233.
[13]. Stein J.H., Fraizer M.C., Aeschlimaan S.E., et al. Vascular Age: Integrating Carotid Intima-Media Thickness Measurements with Global Coronary Risk Assessment. Clin. Cardiol. 2004; 27: 388–392.
[14]. Mohan V, Ravikumar R, Shanthi Rani S, et al. Intimamedia thickness of the carotid artery in South Indian diabetic & non-diabetic subjects: the Chennai Urban Population Study (CUPS). Diabetologia 2000; 43:494–9.
[15]. ARIC (Atherosclerosis risk in communities) Study.

Dr Mayank Sarawag,Dr.Manju Bhaskar. "A Study to Compare Carotid Intima-Media Thickness with Conventional Risk Factors for Atherosclerosis." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 2, 2019, pp 64-71.