

# Association of Carotid Artery Intima Media Thickness with Traditional Risk Factors of Atherosclerosis in Patients with Type 2 Diabetes Mellitus and Hypertension

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**Abstract:** ***Objective:** To examine the association of common carotid intima media thickness (CCA-IMT) with risk factors of atherosclerosis in type 2 diabetes and hypertension patients. **Methods:** This cross-sectional descriptive study was carried out in 14 type 2 diabetes, 15 hypertension and 15 control subjects. CCA-IMT and ankle brachial index (ABI) were measured by ultrasonography. Anthropometric characteristics of each subject were also taken. **Results:** type 2 diabetes group had higher mean CIMT values as compared to the other two groups. ABI was significantly inversely related to CIMT in type 2 diabetes and hypertension group. **Conclusion:** CIMT showed association with ABI and duration in type 2 diabetes and hypertension groups*

**Keywords:** Atherosclerosis, type 2 diabetes, hypertension, ankle brachial index, ultrasonography

## 1. Introduction

Atherosclerosis is the leading cause of morbidity and mortality all over the world [1]. It is a slowly progressive disease with multiple risk factors, leading to ischaemic heart disease (IHD), cerebrovascular accidents and peripheral vascular diseases [2]. The first clinical manifestation of cardiovascular disease often arises in a stage of well-advanced atherosclerosis. However, arterial vessel wall changes occur during a presumably long subclinical lap phase characterized by endothelial dysfunction and gradual thickening of intima [3].

Type 2 diabetes appears to confer an excess risk of clinical cardiovascular disease [4], and atherosclerosis is one of the primary pathophysiologic processes underlying ischemic cardiovascular events, diabetics might be expected to have a greater degree of atherosclerosis than nondiabetics[5].

The epidemiology of hypertension, in terms both of its importance as a risk factor for cardiovascular and other diseases and of its own etiology [6].It is also a potent promoter of atherosclerosis[7]. In recent years, research on atherosclerosis has been mainly towards identifying markers of early atherosclerosis[3]. Prevalence of atherosclerotic vascular disease is markedly increased among individuals with diabetes-mellitus and hypertension. Dyslipidemia, hyperinsulinemia and central obesity seem to be associated with increased risk of atherosclerosis, along with the development of hypertension and diabetes (NIDDM)[8].

Various non-invasive markers of early arterial wall alteration are currently available, such as arterial wall thickening and stiffening, endothelial dysfunction and coronary artery calcification[9]. Of them, intima-media thickness (IMT) of large peripheral arteries, especially

carotid, can be assessed by B-mode ultrasound in a relatively simple way. This technique yields information on atherosclerotic wall changes that cannot be obtained by conventional contrast angiography or MRI. Owing to its non-invasive character and easy applicability, quantitative carotid B-mode ultrasonography has emerged as one of the methods of choice for determining the anatomic extent of atherosclerosis and its progression, and for assessing cardiovascular risk[10]. CCA-IMT is associated with all the subtypes of ischaemic stroke, carotid plaque, and cardiovascular deaths[11].However, Geroulakos G et al[12] and Kanters SD[13] were unable to find statistical significant correlation of CCA-IMT with age, gender, duration of DM, serum total cholesterol and triglyceride levels in patients with type 2 diabetes mellitus[2].Thus there are conflicting reports in the literature regarding the association of CCA-IMT with traditional risk factors of atherosclerosis.

Therefore, with this background, the aim of the current study was to examine if an association of CIMT with other traditional risk factors indeed exists in type 2 diabetes and hypertension patients. The population we considered, to examine this association was a cohort of the above patients in the North Indian population in Amritsar.

## 2. Methodology

This descriptive, cross-sectional study was conducted over a period of 1 year in Faculty of Sports Medicine and Physiotherapy, Guru Nanak Dev University, Amritsar. We included DM2 and hypertensive patients between the age group of 35 and 60 years. The sample comprised of 14 DM 2 patients (8M, 6F), 15 hypertensives (8M, 7F) and 15 controls (10M, 5F) individuals who had neither of these diseases at their time of enrolment in the study. The protocol

was approved by Ethics Committee, Faculty of Sports Medicine and Physiotherapy, Guru Nanak Dev University, Amritsar. All patients signed the informed consent form. An inclusion criterion for type 2 diabetes patients was diagnosed disease duration >1 year with no disease or condition (e.g. diagnosed PAD, uncontrolled hypertension, diabetic complications, surgical revascularization of lower limb arteries or carotid arteries). Inclusion criterion for hypertension patients was diagnosed disease duration >1 year with no disease or condition (e.g. diagnosed/ clinical presentation PAD, uncontrolled diabetes, surgical revascularization of lower limb arteries or carotid arteries). Patients with symptomatic terminal liver disease, any associated cardiac illness and past history of stroke, present technical impossibility of measuring the ankle-brachial index or carotid intima-media thickness and those submitted to limb amputation were excluded from the study[14].

ABI was measured using Doppler ultrasound ACUSON X150 with 8 linear array MHz transducer and a sphygmomanometer. All measurements were performed with the patient in the supine position after 10 minutes of rest. The sphygmomanometer cuff was tied just above the elbow in arms and just above medial malleolus in legs. The ultrasound transducer was used to locate the arterial Doppler signal distal to the cuff. The systolic pressure of the posterior tibial artery and brachial artery were measured bilaterally[14]. We divided the highest systolic pressure in the posterior tibial by the highest systolic pressure found in the brachial artery of the upper limbs, thus obtaining ABI[14]. The normal values for ABI are between 0.9 and 1.4. CIMT measurements were carried out in common carotid artery, with the subject in supine position, neck extended and head slightly turned in the direction opposite to the carotid artery being examined[15]. CIMT was measured in the far wall of common carotid artery, around 1 cm below the carotid bifurcation using high resolution B

mode ACUSON ultrasound machine with a linear array transducer of 7.5 to 12 MHz. CIMT was the distance between the leading edges of lumen-intima interface and media-adventitia interface. The value of IMT over the cut point of 0.68 mm correlated with obviously increased risk of carotid atherosclerosis[16]. Multiple measurements of ABI and CIMT were performed by a single operator[14], to improve precision and eliminate the risk of errors while measuring both non-invasive methods. Anthropometric and physiological characteristics like height, weight, BMI, waist circumference, hip circumference, blood pressure, resting heart rate were also measured using standard protocols.

3. Statistical Analysis

The data were analyzed using SPSS software version 17.0 (SPSS, Chicago, IL, USA). Demographic and clinical characteristics of all the three groups are represented as Mean ± SD. Pearson correlation coefficient was performed between independent variables in all the 3 groups, to establish the relationships among the variables measured with an alpha value of 0.05, considered as statistically significant.

Table 1: Mean descriptive characteristics of the 3 groups

Parameters	Group 1 T2DM(N=14)	Group 2 HYPER(N=14)	Group 3 Control(N=15)
AGE(yrs)	55±6.82	50±6.071	49.2±6.95
HEIGHT(cm)	168.39±9.88	168.57±10.196	161.65±10.47
WEIGHT(kg)	80.2±15.16	79.57±13.31	72.76±11.37
BMI(kg/m <sup>2</sup> )	27.97±4.92	27.94±4.83	26.84±4.21
SBP(mm/HG)	138.93±12.27	162.2±16.93	130.47±8.93
DBP(mm/HG)	90.86±13.30	102.87±11.53	80.73±8.9
RHR(beats/min)	80.71±11.23	84±4.78	72.53±7.03
ABI	0.68±0.38	0.72±1.25	1.05±0.27
CIMT(mm)	0.84±0.098	0.80±0.08	0.47±0.08

Table 2: Correlation of ABI and CIMT with traditional cardiovascular risk factors in DIABETIC GROUP=0

		AGE	D/D	WT	BMI	WAIST	HIP	WHR	SBP	DBP	RHR	ABI	IMT
AGE	Pearson Correlation	1	.894**	0.224	0.009	0.103	0.112	0.006	-0.059	-0.082	-0.088	0.091	0.047
	Sig. (2-tailed)		0	0.139	0.954	0.501	0.463	0.971	0.698	0.591	0.564	0.552	0.761
D/D	Pearson Correlation	.894**	1	0.198	-0.058	0.126	0.15	0.003	0.014	-0.098	-0.011	-0.055	.430**
	Sig. (2-tailed)		0	0.192	0.704	0.41	0.325	0.984	0.926	0.521	0.941	0.72	0.004
WT	Pearson Correlation	0.224	0.198	1	.551**	.660**	.748**	0.099	-0.029	0.076	-0.081	-0.054	-0.017
	Sig. (2-tailed)	0.139	0.192		0	0	0	0.517	0.85	0.619	0.598	0.724	0.911
BMI	Pearson Correlation	0.009	-0.058	.551**	1	.744**	.562**	.479**	-0.14	0.06	-0.009	0.015	.364*
	Sig. (2-tailed)	0.954	0.704	0		0	0	0.001	0.36	0.696	0.951	0.922	0.015
WAIST	Pearson Correlation	0.103	0.126	.660**	.744**	1	.787**	.577**	-0.027	0.038	-0.023	-0.147	0.015
	Sig. (2-tailed)	0.501	0.41	0	0		0	0	0.861	0.802	0.879	0.335	0.92
HIP	Pearson Correlation	0.112	0.15	.748**	.562**	.787**	1	-0.043	-0.168	-0.2	-0.203	-0.206	0.024
	Sig. (2-tailed)	0.463	0.325	0	0	0		0.78	0.271	0.189	0.18	0.174	0.875
WHR	Pearson Correlation	0.006	0.003	0.099	.479**	.577**	-0.043	1	0.192	.356*	0.249	-0.023	0.066
	Sig. (2-tailed)	0.971	0.984	0.517	0.001	0	0.78		0.207	0.016	0.099	0.882	0.664
SBP	Pearson Correlation	-0.059	0.014	-0.029	-0.14	-0.027	-0.168	0.192	1	.702**	.775**	-0.156	0.253
	Sig. (2-tailed)	0.698	0.926	0.85	0.36	0.861	0.271	0.207		0	0	0.307	0.097
DBP	Pearson Correlation	-0.082	-0.098	0.076	0.06	0.038	-0.2	.356*	.702**	1	.760**	0.045	0.26
	Sig. (2-tailed)	0.591	0.521	0.619	0.696	0.802	0.189	0.016	0		0	0.77	0.089
RHR	Pearson Correlation	-0.088	-0.011	-0.081	-0.009	-0.023	-0.203	0.249	.775**	.760**	1	-0.255	0.108
	Sig. (2-tailed)	0.564	0.941	0.598	0.951	0.879	0.18	0.099	0	0		0.091	0.48
ABI	Pearson Correlation	0.091	-0.055	-0.054	0.015	-0.147	-0.206	0.023	-0.156	0.045	-0.255	1	-.615**
	Sig. (2-tailed)	0.552	0.72	0.724	0.922	0.335	0.174	0.882	0.307	0.77	0.091		0
IMT	Pearson Correlation	0.047	.430**	-0.017	.364*	-0.015	0.024	0.253	0.013	0.26	0.108	-.615**	1
	Sig. (2-tailed)	0.761	0.004	0.911	0.015	0.92	0.875	0.097	0.935	0.089	0.48	0	

\*\* . Correlation is significant at the 0.01 level (2-tailed). \* . Correlation is significant at the 0.05 level (2-tailed).

**Table 3:** Correlation of ABI and CIMT with traditional cardiovascular risk factors in HYPERTENSION GROUP=1

		AGE	D/D	WT	BMI	WAIST	HIP	WHR	SBP	DBP	RHR	ABI	IMT
AGE	Pearson Correlation	1	.768**	-0.051	-0.154	0.02	-0.02	0.093	-0.198	-0.024	-0.221	0.091	0.014
	Sig. (2-tailed)		0	0.77	0.371	0.909	0.907	0.588	0.248	0.891	0.195	0.597	0.935
D/D	Pearson Correlation	.768**	1	0.098	0.039	0.121	0.068	0.094	-0.056	0.015	-0.135	0.141	-0.036
	Sig. (2-tailed)	0		0.571	0.821	0.481	0.695	0.585	0.748	0.931	0.433	0.413	0.836
WT	Pearson Correlation	-0.051	0.098	1	.648**	.732**	.811**	-0.076	0.179	0.188	0.211	0.24	0.026
	Sig. (2-tailed)	0.77	0.571		0	0	0	0.659	0.295	0.273	0.216	0.159	0.883
BMI	Pearson Correlation	-0.154	0.039	.648**	1	.402*	.589**	-0.264	0.286	0.215	0.309	-.268	0.088
	Sig. (2-tailed)	0.371	0.821	0		0.015	0	0.119	0.09	0.209	0.067	0.079	0.608
WAIST	Pearson Correlation	0.02	0.121	.732**	.402*	1	.767**	.389*	0.074	0.071	0.048	0.223	-0.107
	Sig. (2-tailed)	0.909	0.481	0	0.015		0	0.019	0.666	0.682	0.78	0.191	0.533
HIP	Pearson Correlation	-0.02	0.068	.811**	.589**	.767**	1	-0.287	0.006	0.111	0.068	0.321	-0.093
	Sig. (2-tailed)	0.907	0.695	0	0	0		0.089	0.972	0.52	0.694	0.056	0.591
WHR	Pearson Correlation	0.093	0.094	-0.076	-0.264	.389*	-0.287	1	0.082	-0.062	-0.031	-0.114	-0.033
	Sig. (2-tailed)	0.588	0.585	0.659	0.119	0.019	0.089		0.635	0.72	0.856	0.508	0.848
SBP	Pearson Correlation	-0.198	-0.056	0.179	0.286	0.074	0.006	0.082	1	.371*	.853**	-0.02	.357*
	Sig. (2-tailed)	0.248	0.748	0.295	0.09	0.666	0.972	0.635		0.026	0	0.908	0.017
DBP	Pearson Correlation	-0.024	0.015	0.188	0.215	0.071	0.111	-0.062	.371*	1	.540**	-0.041	.382*
	Sig. (2-tailed)	0.891	0.931	0.273	0.209	0.682	0.52	0.72	0.026		0.001	0.813	0.01
RHR	Pearson Correlation	-0.221	-0.135	0.211	0.309	0.048	0.068	-0.031	.853**	.540**	1	0.269	0.253
	Sig. (2-tailed)	0.195	0.433	0.216	0.067	0.78	0.694	0.856	0	0.001		0.078	0.097
ABI	Pearson Correlation	0.091	0.141	0.24	-0.268	0.223	0.321	-0.114	-0.02	-0.041	0.269	1	-.510**
	Sig. (2-tailed)	0.597	0.413	0.159	0.079	0.191	0.056	0.508	0.908	0.813	0.078		0.001
IMT	Pearson Correlation	0.014	-0.036	0.026	0.088	-0.107	-0.093	-0.033	.357*	.382*	0.253	-.510**	1
	Sig. (2-tailed)	0.935	0.836	0.883	0.608	0.533	0.591	0.848	0.017	0.01	0.097	0.001	

**Table 4:** Correlation of ABI and CIMT with traditional cardiovascular risk factors in CONTROL GROUP=2

		AGE	WT	BMI	WAIST	HIP	WHR	SBP	DBP	RHR	ABI	IMT
AGE	Pearson Correlation	1	0.091	-0.157	-0.095	-0.012	0.111	-0.039	-0.052	-0.048	0.052	-0.245
	Sig. (2-tailed)		0.576	0.333	0.56	0.943	0.496	0.811	0.751	0.768	0.751	0.127
WT	Pearson Correlation	0.091	1	0.176	-0.091	.510**	0.16	0.119	0.202	0.08	-0.035	0.019
	Sig. (2-tailed)	0.576		0.277	0.576	0.001	0.299	0.466	0.211	0.624	0.829	0.908
BMI	Pearson Correlation	-0.157	0.176	1	.358*	0.27	-0.077	0.013	0.245	-0.077	-.354*	0.182
	Sig. (2-tailed)	0.333	0.277		0.023	0.092	0.635	0.937	0.128	0.638	0.025	0.261
WAIST	Pearson Correlation	-0.095	-0.091	.358*	1	-0.192	-0.03	-0.049	0.098	0.011	-0.168	-0.072
	Sig. (2-tailed)	0.56	0.576	0.023		0.236	0.855	0.765	0.548	0.946	0.3	0.659
HIP	Pearson Correlation	-0.012	.510**	0.27	-0.192	1	0.221	0.095	0.196	-0.051	-0.173	0.056
	Sig. (2-tailed)	0.943	0.001	0.092	0.236		0.15	0.561	0.224	0.754	0.286	0.717
WHR	Pearson Correlation	0.111	0.16	-0.077	-0.03	0.221	1	-0.049	-0.019	-0.105	-0.294	0.273
	Sig. (2-tailed)	0.496	0.299	0.635	0.855	0.15		0.766	0.909	0.518	0.066	0.325
SBP	Pearson Correlation	-0.039	0.119	0.013	-0.049	0.095	-0.049	1	0.301	.649**	-0.062	0.015
	Sig. (2-tailed)	0.811	0.466	0.937	0.765	0.561	0.766		0.059	0	0.706	0.928
DBP	Pearson Correlation	-0.052	0.202	0.245	0.098	0.196	-0.019	0.301	1	0.274	-0.172	0.187
	Sig. (2-tailed)	0.751	0.211	0.128	0.548	0.224	0.909	0.059		0.087	0.289	0.247
RHR	Pearson Correlation	-0.048	0.08	-0.077	0.011	-0.051	-0.105	.649**	0.274	1	-0.077	0.047
	Sig. (2-tailed)	0.768	0.624	0.638	0.946	0.754	0.518	0	0.087		0.635	0.773
ABI	Pearson Correlation	0.052	-0.035	-.354*	-0.168	-0.173	-0.294	-0.062	-0.172	-0.077	1	0.042
	Sig. (2-tailed)	0.751	0.829	0.025	0.3	0.286	0.066	0.706	0.289	0.635		0.798
IMT	Pearson Correlation	-0.245	0.019	0.182	-0.072	0.056	0.273	0.015	0.187	0.047	0.042	1
	Sig. (2-tailed)	0.127	0.908	0.261	0.659	0.717	0.325	0.928	0.247	0.773	0.798	

\*\* . Correlation is significant at the 0.01 level (2-tailed). \* . Correlation is significant at the 0.05 level (2-tailed).

**4. Results**

There were 44 patients divided into 3 groups: group 1 type 2 diabetes(8 males, 6 females) mean age 55±6.82 years, group 2 hypertension(8 males, 7 females)mean age 50±6.07 years and group3 controls(10 males, 5 females) mean age49.2±6.95 years. Group 1 had the highest mean CIMT value (0.82mm) followed by grou2 (0.71mm) and group 3(0.47mm). Similarly, the results of other variables according to the group division have been shown in table1.

In group 1 diabetes, strong association of duration of disease was seen with age(r=0.894) and CIMT(r=0.430). Waist circumference was seen to be positively associated with weight (r=0.660), BMI (0.744), hip circumference(r=0.787) and waist hip ratio(r=0.577).hip circumference was also seen to be positively associated weight(r=0.748) and BMI(r=0.562). Waist hip ratio had a fair association with diastolic blood pressure(r=0.356). Diastolic blood pressure had a strong association with systolic blood pressure(r=0.702) and resting heart rate(r=0.760). Resting heart rate was seen to be positively associated with systolic blood pressure(r=0.775). Modest association of CIMT was

seen with BMI( $r=0.364$ ) while, inverse correlation was seen with ABI ( $r=-0.615$ ) [Table-2].

In group 2 hypertension, duration of disease was seen to be strongly associated with age ( $r=0.768$ ). BMI was seen to be positively correlated to waist circumference ( $r=0.402$ ) and hip circumference( $r=0.589$ ) while an inverse correlation was seen with ABI( $r=-.372$ ). Also, waist circumference was seen to be positively associated with weight( $r=0.732$ ), hip circumference ( $r=0.767$ ) and waist hip ratio( $r=0.389$ ). Systolic blood pressure had a strong correlation with diastolic blood pressure( $r=0.371$ ), resting heart rate( $r=0.853$ ) and CIMT ( $r=0.357$ ). Similarly, diastolic blood pressure was seen to be positively associated with resting heart rate( $r=0.540$ ) and CIMT( $r=0.382$ ). Further, resting heart rate was also seen to be strongly associated to CIMT ( $r=0.569$ ) while, it had a strong inverse relation with ABI( $r=-0.572$ ). In addition, CIMT was found to have an inverse relation with ABI( $r=-0.510$ ) [table-3].

In group 3 Controls, weight was found to be associated with hip circumference( $r=0.510$ ) while, BMI was found to be correlated with waist circumference ( $r=0.358$ ) and inversely related to ABI( $r=-0.354$ ). Also, systolic blood pressure had a strong association with resting heart rate( $r=0.649$ )[Table-4].

## 5. Discussion

Our study showed that in type 2 diabetes group, patients had high CIMT values as compared to the other two groups[table-1]. The thickening of the intima-media complex is considered a marker of premature atherosclerosis and a predictor of cardiovascular disease risk[17,18]. It is also noteworthy that these patients with high mean value had low ABI values ( $<0.9$ ), a product of a quantitative reduction in systolic blood pressure in the lower limbs caused by proximal atherosclerotic occlusion<sup>5</sup> as well. (table-1). Therefore, our study corroborates with the findings of braselario et al[14] that the prevalence of carotid atherosclerosis was higher in these patients with low abnormal ABI levels.

Our study also supports the findings of Marcos-Gomez et al, 2011[15] that carotid IMT is greater in diabetics as compared to hypertensive and Bonora et al[19] who found that CCA-IMT was increased in diabetic patients as compared to controls and increased central obesity reflected by increased waist to hip ratio was an independent risk factor for carotid atherosclerosis. Further, it was also observed that in type 2 diabetes group, that increased CIMT values showed modest association with duration of disease( $r=0.430$ ) and BMI( $r=0.364$ ). We confirm the findings of Rehman et al[1] and Wagenknecht LE[20] showed duration of diabetes directly affects the CCA-IMT and also found that chronic hyperglycaemia was an independent risk factor for carotid atherosclerosis [artis 5]. Similar to our observation, Ciccone et al 21 and Rehaman et al found that BMI is strongly associated with the IMT of common carotid artery. Their results suggest that central fat accumulation may accelerate the development of earlier clinically silent stages of atherosclerosis. [artis 5]. Also, a strong relation was observed between resting heart rate and blood pressure(systolic and diastolic) in diabetic and hypertensive group suggesting that high blood pressure

(BP), obesity, and abnormal lipid profile, often coexist with diabetes and tend to be associated with preclinical cardiovascular abnormalities<sup>16</sup>[rhr and bp article]

In the hypertension group, systolic and diastolic blood were found to positively correlated to CIMT levels [table-3]. These results are in conformation with the previous studies which suggest that of all traditional risk factors, hypertension appears to have the greatest effects on IMT.55;57[ pavel]. Pavel et al reported that patients with essential hypertension, IMT was related to the level of systolic and diastolic blood pressure, 58 but the Plaque Hypertension Lipid Lowering Italian Study (PHYLLIS) suggested that the systolic and pulse pressure together with age were the most significant factors associated with an increased carotid IMT in hypertensive patients.55 [pavel artis]

Moreover, we wished to observe the association of between ABI and CIMT, and found a strong negative correlation with CIMT in the diabetic and hypertensive group. These results are in agreement with the findings of bresalin et al and Bots et al, who found an association between increased carotid IMT and atherosclerosis of the arteries of the lower extremities as assessed by ankle- arm index measurement. 83[pavel] [bresalin]. An inverse relation between ABI and CIMT shows that with progression of PAOD the IMT increases. 115,116 [pavel].

In conclusion our study shows the association of BMI and duration of disease with CIMT in type 2 diabetes group and association of blood pressure with raised CIMT levels in the hypertension group, while an inverse relation was seen between ABI and CIMT in diabetes and hypertension group. Lack of association of ABI with different covariates in both the groups suggests further investigation on a large sample size to find out the contribution of various factors in the development of carotid and peripheral atherosclerosis.

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## 8. Conflict of Interest

None

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