CAROTID ARTERY INTIMA-MEDIA THICKNESS AND 10-YEAR RISK OF HEART DISEASE IN DIABETIC PATIENTS: A COMPARATIVE STUDY

VINODKUMAR MUGADA*, RAJ KIRAN KOLAKOTA

Department of Pharmacy Practice, Vignan Institute of Pharmaceutical Technology, Visakhapatnam, Andhra Pradesh, India.
Email: mugadavinodkumar18@gmail.com

ABSTRACT

Objective: The aim of the present study was to assess the factors affecting carotid artery intima-media thickness (CIMT) and 10-year risk of heart disease in diabetic patients classified according to CIMT.

Methods: This was an analytical cross-sectional study conducted on 92 patients for 1 year. 10-year risk of heart disease was calculated using the American College of Cardiology/American Heart Association Guideline on the Assessment of Cardiovascular Risk. Based on CIMT, the subjects were classified into two groups. Group 1 contains subjects with CIMT <0.9 and Group 2 contains subjects with CIMT ≥0.9. The Mann–Whitney U-test, Pearson's correlation, and descriptive statistics were used to compare and describe the data. The level of statistical significance was taken at p<0.05.

Results: Patients with 51–60 years of age group are high in number. Males were predominantly high than their counterparts. There is a statistically significant association between total cholesterol (p=0.001), high-density lipoproteins (p=0.000), low-density lipoproteins (p=0.001), postprandial blood sugar (p=0.000), and hemoglobin 1Ac (p=0.035) with CIMT. The mean 10-year risk of heart disease in Groups 1 and 2 is 13.13±15.40 and 23.63±17.57, respectively. There is statistically highly significant association (p=0.000) of 10-year risk of heart disease between two groups. There is a positive correlation (r=0.45, p<0.0001) between CIMT and risk of heart disease.

Conclusion: Our study found that greater the CIMT, greater the risk of the heart of disease.

Keywords: Total cholesterol, High-density lipoproteins, Low-density lipoproteins, Blood pressure, diabetes, Carotid artery intima-media thickness.

INTRODUCTION

The carotid artery intima-media thickness (CIMT) can be used as an important parameter to detect and assess atherosclerosis and for evaluating the risk of cardiovascular disease (CVD) [1,2]. In individuals with type 1 or type 2 diabetes, per 0.1 mm increase in common CIMT, the hazard ratio for a cardiovascular event is 1.12 (95% confidence interval: 1.07–1.16) [3]. Values of CIMT >0.9 mm are considered abnormal and values >1 mm correlate with increased the incidence of atherosclerosis and cardiovascular events [4,5]. Several traditional modifiable cardiovascular risk factors including obesity, high blood pressure, high blood sugar, dyslipidemia, and cigarette smoking had been correlated with elevated CIMT by population-based studies [6]. A study showed higher values for atherogenic factors such as age, body mass index (BMI), systolic and diastolic blood pressure, and low-density lipoproteins (LDL) with respect to thickness [7]. CIMT has been independently associated with coronary artery disease in Indian subjects [8]. Another study reported that increased CIMT determines the risk of future coronary heart disease and stroke [9]. Therefore, predicting CIMT can be used for diagnosing premature CVD.

The aim of the present study was to know the association of CIMT and 10-year risk of heart disease in diabetic patients.

METHODS

Study design

The information about CIMT and risk of heart disease was observed at the same time. There is no need to follow-up. The subjects were categorized into two groups based on CIMT. The factors affecting CIMT and risk of heart disease were compared between two groups. The features of our study best suit with analytical and comparative cross-sectional study. Hence, our study design was analytical and comparative cross-sectional study.

Ethical approval

Our study was approved by the Institutional Ethical Committee (RKHEC/RC NO. Clinicals/Pharm.D/N2/2017, Dt 03/05/2017). The objective of the study was clearly explained to the patient and a patient consent form was obtained.

Study duration

This study was conducted on 92 diabetic patient's Inpatient Department of Medicine, RK Hospital, Gajuwaka, for 10 months, that is, from May 5, 2017 to February 28, 2018.

Participants

- Patients with the age group between 40 and 70 years, patients with diabetes alone and diabetes along with hypertension and dyslipidemia were included in the study.
- Patience with the age group of <40 and >70 years, critically ill patients were excluded from the study.

Sampling technique and sample size

Stratified random sampling (disproportionate) was used to select the diabetic patients. The patients were classified into two groups based on CIMT. The sample size was estimated from Raosoft Inc., sample size calculator. The sample size was 92. Group 1 (n=37) contains subjects with CIMT <0.9, whereas Group 2 (n=55) contains subjects with CIMT ≥0.9.

Data analysis

A prestructured data collection form was prepared to obtain demographic and clinical data from the patient. The data regarding

CIMT were obtained from laboratory reports. The 10-year risk of heart disease was calculated using guidelines form the American College of Cardiology/American Heart Association on assessment of cardiovascular risk. The 10-year risk of heart disease was represented in percentage. Descriptive statistics were calculated for quantitative data such as age, total cholesterol (TC), and systolic blood pressure. Frequency and percentage were calculated for qualitative data. Data were represented in tables to compare and contrast between the two groups. The normality of numerical data was tested using the Shapiro–Wilk test. Independent t-test is used for numerical data when the normality of data confirms normal distribution. Non-parametric tests like Mann–Whitney U-Test were used wherever applicable. Pearson's correlation coefficient test was used to find the correlation between two variables. The level of significance was considered at p<0.05. If the level of significance was p<0.01, then it was considered statistically highly significant.

RESULTS

As shown in Table 1, 51–60 years age group was high in number in both groups. Males are predominantly higher than females in both the groups. The percentage of hypertensives, dyslipidemic patients, and non-smokers is high in the number in both the groups. The prevalence of the absence of cerebrovascular accident and coronary artery disease was high in both the groups. The proportion of non-alcoholics and non-smokers was high in both groups.

There was a statistically highly significant relation between TC (p=0.001), high-density lipoproteins (HDL) (p=0.000), LDL (p=0.001), postprandial blood sugar (PPBS) (p=0.000), BMI (p=0.007), age (p=0.008), 10-year risk of heart disease (p=0.000), waist–hip ratio (WHR) (p=0.001), LDL/HDL ratio (<0.0001), and TC/HDL ratio (<0.0001) with CIMT. Hemoglobin (HB) 1Ac (p=0.035) had statistically significant association with CIMT.

As shown in Table 2, CIMT was having statistically highly significant correlation with age (p=0.000), HDL (p=0.000), LDL (p=0.007), SBP (p=0.005), PPBS (p=0.006), WHR (p=0.002), LDL/HDL ratio (p=0.000), TC/HDL ratio (p<0.0001), duration of diabetes (p<0.0001), and 10-year risk of heart disease (p<0.0001). TC and Hb1Ac found to have statistically significant correlation (p=0.011 and p=0.038, respectively).

DISCUSSION

As shown in Table 1, 51–60 years age group patients were predominantly high. There was a statistically significant association between age and CIMT (p=0.004). Males were higher than their counterparts. Non-smokers were high in number and dyslipidemia was high in both groups. Tripathy *et al.* reported a high prevalence of diabetes in patients aged 25–44 years [10]. A statistically significant difference was reported in age difference by Bharati *et al.*, the prevalence of diabetes is higher in the age group of ≥50 years than in persons aged between 20 and 49 years [11]. Diabetes in India was rising and women are more affected than males [12]. Bharati *et al.* [11] also reported a high prevalence of diabetes mellitus in females. Non-alcoholics are high in both the groups. The percentage of non-hypertensive patients, the percentage of patients with the absence of cerebrovascular accident and coronary artery disease was high. Duration of diabetes was significantly correlated (p<0.001) with CIMT in our study. It may suggest an increase in the risk of CVD in patients. However, Mounika *et al.* [13] reported a 36% of the onset of renal and cardiac complications in patients with 1–5 years of the duration of diabetes, whereas 31.6% of the onset of renal and cardiac complications in patients with 6–10 years of duration.

The mean blood lipid profile values of Group 1 are higher than Group 2 as shown in Table 3. There was a statistically highly significant association between TC, HDL, LDL, LDL/HDL ratio, and TC/HDL ratio, with CIMT, wherein triglycerides did not show any statistically significant association with CIMT in our study (Table 1). Similar associations were reported by Yang *et al.* [14]; however, triglycerides and TC did not show any significant association in his study. He observed a close correlation between CIMT and LDL/HDL cholesterol ratio than LDL cholesterol levels even after the adjustment of age. Furthermore, LDL/HDL cholesterol ratio showed a positive association with the prevalence of carotid plaques.

Table 1: Sociodemographic and clinical characteristics of patients

S. No.	Characteristic	Group 1 (n=37) Frequency (%)	Group 2 (n=55) Frequency (%)	p value
1	Age in years			
	40–50	14 (37.84)	7 (12.72)	0.004*
	51–60	15 (40.54)	24 (43.63)	
	61–70	5 (13.51)	15 (27.30)	
	71–80	3 (8.10)	9 (16.36)	
2	Gender			
	Females	12 (32.43)	23 (41.82)	0.109
	Males	25 (67.57)	32 (51.18)	
3	Alcoholism			
	Alcoholic	6 (16.22)	12 (21.81)	0.506
	Non-alcoholic	31 (83.78)	43 (71.18)	
4	Hypertension			
	Non-hypertensive	7 (18.91)	19 (34.55)	0.102
	Hypertensive	30 (81.09)	36 (65.45)	
5	Cerebrovascular accident			
	Present	7 (18.91)	20 (36.4)	0.715
	Absent	30 (81.09)	35 (63.6)	
6	Coronary artery disease			
	Present	6 (16.22)	11 (20)	0.646
	Absent	31 (83.78)	44 (80)	
7	Dyslipidemia			
	Present	21 (56.76)	47 (85.5)	0.002
	Absent	16 (43.24)	8 (14.5)	
8	Smoking			
	Smokers	7 (18.91)	14 (25.45)	0.461
	Non-smokers	30 (81.09)	41 (74.55)	

*Mann–Whitney U-test

Our study reported a statistically significant association between BMI, WHR, and HbA1c levels. In contrast, Yang *et al*. reported no significant difference with these parameters. The combined application of LDL cholesterol and HDL cholesterol was superior to separate lipid parameters for assessing the risk of early-stage atherosclerosis in apparently healthy people from the general population [14]. Enomoto *et al*. [15] found a significant association between IMT and proatherogenic lipoprotein measurements, and it was reported that the LDL/HDL ratio was found to be the strongest predictor for IMT progression. Some studies suggested that cholesterol ratios can better predict the risk of CVD than individual lipid profile parameters [16-20]. Katakami *et al*. [21] observed that cholesterol ratios can be good risk indicators for early-stage atherosclerosis, even if the conventional lipid parameters are within normal range.

Our study found a statistically significant association between BMI and CIMT. Some studies reported a significant association between BMI and CIMT [9,22,23]. Ozdemir *et al*. [24] did not find a correlation between BMI and CIMT when comparing participants with normal BMI to overweight subjects. One study reported an increase of one BMI unit caused a 0.009 mm increase in CIMT and an increase of 1 year in age caused a 0.011 mm increase in CIMT in their study [23]. Butt *et al*. [25] reported that overweight patients significantly took dominance in a low-risk category and he did not found a significant correlation between HDL, LDL, TC, TG, and BMI.

Systolic blood pressure was having a statistically significant correlation with CIMT ($p=0.005$) in our study. Norbert *et al*. [26] reported that the mean CIMT of newly diagnosed hypertensives was significantly higher than the mean CIMT values of the drug-treated hypertensives. Hong *et al*. [27] reported higher CIMT values in prehypertensives than normotensives. Bashir *et al*. [28] reported a strong positive correlation of CIMT with systolic blood pressure ($p=0.000$) and a moderately positive correlation with diastolic blood pressure.

There is a highly significant correlation of CIMT with duration of diabetes ($p<0.0001$) in our study. Bashir *et al.* [28] reported a highly significant correlation of CIMT with duration of diabetes ($p=0.000$). The strong relationship between CIMT with duration of diabetes reflects the detrimental effect on arterial wall thickening through ongoing

Table 2: Correlation analysis of demographic and clinical variables with CIMT

S. No.	Parameter	r value	95% CI	p value
1	TC	0.26	0.06–0.44	0.011
2	HDL	−0.34	−0.51–0.14	0.000
3	LDL	0.28	0.07–0.45	0.007
4	TG	0.07	−0.13–0.27	0.512
5	SBP	0.29	0.09–0.46	0.005
6	DBP	0.09	−0.11–0.28	0.407
7	FBS	0.16	−0.04–0.35	0.129
8	PPBS	0.28	0.08–0.45	0.006
9	HbA1c	0.22	0.01–0.40	0.038
10	Age	0.34	0.14–0.50	0.000
11	Duration of diabetes	0.40	0.21–0.56	<0.0001
12	10-year risk of heart disease	0.45	0.27–0.60	<0.0001
13	BMI	0.16	−0.04–0.35	0.121
14	WHR	0.15	0.09–0.24	0.002
15	LDL/HDL ratio	0.36	0.17–0.53	0.000
16	TC/HDL ratio	0.49	0.31–0.63	<0.0001

CIMT: Carotid artery intima-media thickness, CI: Confidence interval, HDL: High-density lipoproteins, TC: Total cholesterol, LDL: Low-density lipoproteins, TGs: Triglycerides, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBS: Fasting blood sugar, PPBS: Postprandial blood sugar, HB: Hemoglobin, BMI: Body mass index, WHR: Waist–hip ratio

Table 3: Association of variables of patients with CIMT

S. No.	Parameter	Group 1 (n=37)	Group 2 (n=55)	p value
1	TC	195.3±44.87 mg/dL (95% CI: 181.7–209.0)	222.8±40.57 mg/dL (95% CI: 211.9–233.6)	0.001*
2	HDL	49.13±7.63 mg/dL (95% CI: 45.55–50.27)	41.58±8.68 mg/dL (95% CI: 39.26–43.92)	0.000
3	LDL	123.59±34.35 mg/dL (95% CI: 108.3–128.9)	139.29±30.67 mg/dL (95% CI: 130.2–146.8)	0.001
4	Triglycerides	156.9±69.86 (95% CI: 133.6–180.2)	185.7±99.05 (95% CI: 159.0–212.5)	0.108
5	LDL/HDL ratio	2.49±0.65 (95% CI: 2.28–2.71)	3.27±1.02 (95% CI: 2.99–3.55)	<0.0001*
6	TC/HDL ratio	4.11±0.80 (95% CI: 3.84–4.38)	5.53±1.31 (95% CI: 5.17–5.88)	<0.0001*
7	Systolic blood pressure	130±15.27 mmHg (95% CI: 124.9–135.1)	135.63±16.64 mmHg (95% CI: 131.1–140.1)	0.081
8	Diastolic blood pressure	84.32±5.02 mmHg (95% CI: 82.65–86.00)	82.16±11.12 mmHg (95% CI: 79.16–85.17)	0.401
9	FBS	148.6±51.83 mg/dL (95% CI: 132.9–164.4)	162.2±62.25 mg/dL (95% CI: 145.6–178.9)	0.265
10	PPBS	216.1±59.73 mg/dL (95% CI: 197.9–234.3)	276.4±92.46 mg/dL (95% CI: 251.7–301.2)	0.000*
11	HbA1c	7.268±0.675 (95% CI: 7.06–7.47)	7.691±1.077 (95% CI: 7.40–7.97)	0.035
12	10-year risk of heart disease	13.13±15.40 (95% CI: 7.99–18.26)	23.63±17.57 (95% CI: 18.88–28.38)	0.000*
13	BMI	22.76±3.64 (95% CI: 21.55–23.97)	25.42±4.59 (95% CI: 24.18–26.66)	0.007
14	WHR	0.87±0.06 (95% CI: 0.85–0.89)	0.93±0.11 (95% CI: 0.90–0.95)	0.001
15	Duration of diabetes	7.83±5.08 (95% CI: 6.14–9.53)	9.34±4.92 (95% CI: 8.01–10.6)	0.140

*Independent t-test. CIMT: Carotid artery intima-media thickness, TC: Total cholesterol, HDL: High-density lipoproteins, LDL: Low-density lipoproteins, FBS: Fasting blood sugar, PPBS: Postprandial blood sugar, HB: Hemoglobin, BMI: Body mass index, WHR: Waist–hip ratio

atherosclerotic events. In our study, PPBS levels and Hb1Ac levels have significant association and correlation with CIMT (Tables 2 and 3). One study reported no significant association of CIMT with Hb1Ac levels [28]. Few studies reported that blood pressure control was more important for all the endpoints, especially cardiovascular complications in diabetic patients as compared to the glycemic control [29,30].

In our study, the 10-year risk of heart disease was statistically highly significant association and correlation with CIMT. IMT measurements could help in predicting the risk of CVD because thickening of arteries is a known hallmark feature of atherosclerosis. Several studies have shown this association between CIMT and risk of CVD in future. However, recommendations regarding the use of CIMT for predicting the risk of CVD events are conflicting. Lorenz *et al.* [31] found an increase in relative risks of CVD events by a factor of 1.15 for every 0.1-mm increase in CIMT. In contrast, den Ruijter *et al.* [3] found no meaningful addition to CVD event prediction when CIMT was added to conventional risk prediction models. However, many other studies showed an increase in the risk of CVD events with an increase in CIMT [7,32,33].

CONCLUSION

Age, duration of diabetes, TC, LDL, HDL, LDL/HDL ratio, TC/HDL ratio, PPBS levels, Hb1Ac levels, systolic blood pressure, and WHR affect the CIMT. The risk of heart disease increases with increase in the CIMT.

AUTHORS' CONTRIBUTION

Vinodkumar Mugada - concept, design, literature search, data acquisition, manuscript preparation, and editing. Raj Kiran Kolakota - concept, design, the definition of intellectual content, and review.

CONFLICTS OF INTEREST

The authors declared that they have no conflicts of interest.

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