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Assessment of CIMT and correlating it with ABPM in overweight and obese individuals

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Abstract

Introduction: The correlation between excess body weight and elevated blood pressure is well known. However, the correlation between carotid intima-media thickness (CIMT) and 24 hr ambulatory blood pressure monitoring (ABPM) remains to be established. Thus, the present study intended to examine the possible correlation between CIMT and 24 hr ABPM in overweight and obese participants.

Materials and methods: The present study was prospective and cross-sectional in nature. It included 95 non-hypertensive participants attending the Department of Medicine King George’s Medical University, Lucknow over a period of 1 year. Anthropometric measures such as weight, height, body mass index (BMI), and waist circumference (WC) were recorded. The 24 hr ABPM was performed in each individual and values were recorded. The quantitative estimation of CIMT was performed using a high-resolution B-mode ultrasound scanner with a 7 MHz linear transducer. Chi-square test was used to assess the association between the categorical variables. Pearson’s correlation coefficient was used to test the strength of correlation. A p-value of < 0.05 was regarded as statistically significant.

Results: Increase in BMI and WC was associated with a significant increase in proportion of participants with increased CIMT and pulse pressure (all p-values <0.05). Increase in CIMT was associated with the significant increase in proportion of participants with rise in 24 hr SBP, Day SBP, and Night SBP (all p-values<0.001). Similarly, increase in CIMT was associated with significant increase in the proportion of systolic and diastolic Non-Dippers or Inverse Dippers participants and participants with negative Day Systolic Load (SL), positive Night SL,and negative Night Diastolic Load) (all p-values <0.05).A positive, moderate, and statistically significant correlation was observed between CIMT and average SBP, average DBP, day SBP, day SBP load variability (SBPLV), and night SBPLV. Moreover, a positive, mild, and statistically significant correlation was between CIMT and day diastolic BPLV, and night diastolic BPLV.

Conclusions: The study suggests that overweight and obese participants have a significantincrease in CIMT values. Moreover, increased CIMTvalues were

positively and significantly correlated with increase 24 hr ABPM parameters.

Keywords: ABPM; Body mass index; BMI; Carotid artery intima–media thickness; CIMT; Obesity; Waist circumference

Introduction

Over the past 50 years, the global prevalence of obesity has increased in pandemic proportions[1]. Based on the estimates of World Health Organisation (WHO), in 2016, there were around 1.9 billion overweight adults, of which more than 650 million were obese[2]. Obesity has resulted in premature morbidity and mortality by raising the chances of cardio-metabolic diseases, osteoarthritis, depression, dementia, and some types of cancers[1].

Obesity has been identified as a modifiable risk factor of hypertension[3,4]. Moreover,findings of various studies have suggested that increased body mass index (BMI) results in higher chances of developing hypertension and new-onset hypertension[5,6]. The global prevalence of hypertension amongst adults, estimated in 2015, was found to be around 30 - 45%[3]. Moreover, as per the latest data, about 36 - 47% of obese patients suffer from hypertension, compared to around 20% individuals with normal BMI[5].

The global health data (GHD) reported over 7.5 million deaths due to raised blood pressure, accounting for 12% of the total global deaths[7]. The diagnosis and follow-up of HTN usually depends on the measurement of office blood pressure (BP),aimed to assess the true usual BP levels. However, intra-individual variations in office systolic BP (SBP) at different clinic visits is 10 to 20 mm Hg. Moreover, the measurements in the office may not reflect the true BP levels. It also do not reflect the diurnal variation and nocturnal BP levels. The 24hr ambulatory BP monitoring (ABPM) is a precise method to quantify BP levels and diagnose HTN. Studies have shown that 24 hr ABPM is more accurate than office BP measurements in predicting cardiovascular (CV) morbidity and mortality[8].

Recently, carotid artery intima media thickness (CIMT), as measured by vascular ultrasound, has emerged as a potential marker of hypertensive vascular damage. In adults, increased CIMT is an indicator of generalized atherosclerosis and a strong predictor of future CV morbidity and mortality[9,10]. Numerous studies have demonstrated that CIMT correlate with traditional risk factors of cardiovasculardisease (CVD)[11,12]. There is data which shows that obesity and metabolic syndrome are associated with increased CIMT[13,14].

Although the association of excess body weight with elevated BP has been known for a long time[15,16], the correlation between CIMT and 24 hr ABPM has not been evaluated with respect to Indian population. Thus, the purpose of the present study was to examine the possible correlation between CIMT and 24 hr ABPM in overweight and obese participants.

Materials and methods

The present study is a further analysis of the datafrom our original study[17]. It included 95 participants who attended the Departmentof Medicine, King George's Medical University, Lucknow over a period of 1 year. Prior to initiating the study, the study protocol was approved by the Institutional Ethics Committee. After explaining the study procedures, a written informed consent was obtained from the participants.

Male and female participants, aged between 20-60 years, and having BMI of > 25 and < 40 Kg/m^{2}were included in the study. However,the participants with age > 60 years; history of hypertension and on antihypertensive medication; receiving lipid lowering medication; receiving medication that increases BP such as anti-migraine medication (sumatriptan), amphetamines, corticosteroids, erythropoietin, estrogens (birth control pills), tricyclic antidepressants, chronic use of cough or coldmedication (ephedrine and psedoephedrine), tranylcypromine; history of endocrine disorders (acromegaly, Cushing's disease, hyperthyroidism, Type-2 Diabetes mellitus); pregnant women; clinical neurological disease with autonomic dysfunction; obstructive sleep apnoea;and morbid obesity (BMI > 40 Kg/m^2) were excluded.

History, Baseline investigations, and Methodology

All the eligible participants were enrolled in the study and baseline details were recorded in an especially designed proforma, including: age, sex, height, weight, body mass index (BMI),and waist circumference (WC). Baseline investigations included random blood sugar (RBS), serum creatinine, serum urea, and lipid profile (TotalCholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG)). According to International classification of overweight and obesityconsidering BMI, subjects were categorized in three groups as normal weight (18.5-24.9kg/m^2), overweight (25-29 kg/m^2), and obese (≥30 kg/m^2)[2]. Based on WC, the subjects wereconsidered as obese, if WC was >94 cm (men) and > 80 cm (women)[18]. Following a detailed history and clinical examination, the patients were further evaluated during the study.

Measurement of carotid artery intima–media thickness (CIMT)

CIMT was performed using a high-resolution B-mode ultrasound scanner with a 7 MHz linear transducer (Aloka Pro Sound Alpha 6, Hitachi Aloka Medical America, Wallingford, CT, USA). All subjects in the study were examined by the same radiologist; with the participants in the supine position, the head overextended and turned 45° away from the examined side. Measurement of IMT was made on the posterior wall of common carotid artery at 1 cm proximal to the bifurcation, in the segment that were free of plaque. For each participant, the CIMT was determined as the average of 4 measurement of intimo-medial thickness measured at far wall of both the left and right carotid. The best images of the distal wall were used to calculate the IMT of the common and internal carotid arteries. The value of the IMT was defined as the mean value of measurements between the right and the left carotid arteries. Normal values of CIMT in males and females were 0.458±0.116 mm and 0.47±0.104 mm, respectively. Based on age groups, there are different cut-off values of CIMT thickness viz., 20-29 years, 30-39 years, 40-49 years, and 50-59 years had cut-off values of 0.402 mm, 0.466 mm, 0.586 mm, and 0.692 mm, respectively.[19]

Ambulatory blood pressure monitoring (ABPM)

Ambulatory BP measurements were recorded usingCONTEC 06 C oscillometric device. ABPM device was programmed to take readings at every 15 and 30 minutes during day-time and night-time, respectively. Procedure followed, precautions to be taken by the subjects and the medical personal, and interpretation of the findings are described elsewhere[17].

Circadian parameters

The mean day-time SBP and DBP values and meannight-time SBP and DBP values were estimatedusing BP values obtained from 6 am to 10 pm, and 10 pm to 6 am, respectively. Finally, night-timedipping (ND) was estimated by the formula: [(day-time mean SBPnight-time mean SBP)/day-time mean SBP] × 100[20].Based on ND, circadian BP patterns were categorized intothree types: the dipper (a positive day-night ratio between10% and 20%); the non-dipper (ratio of less than 10%),and the inverse dipper (a negative day-night ratio)[21].

The validity of ABPM device was ensured, by taking at least 3 simultaneous recording, with a calibrated sphygmomanometer connected to ABPM device with the help of Y connector. The ABPM device was used, if the average readings for ABPM device and sphygmomanometer were foundnot to be differing by > 5 mmHg.

Statistical analysis

The data was represented in terms of frequency. Chi-square test was used to assess the association between the categorical variables. Correlation analysis was performedusing Pearson's bivariate correlation. The correlation wasgraded as r < 0.3: weak or negligible; r = 0.3-0.5:mild; r = 0.5-0.7: moderate; and r > 0.7:strong. SPSS version 19.0 (IBM SPSS Inc.,Chicago, IL, USA) was used for the statistical analysis. A probability value of less than 0.05 signified the statistical significance.

Results

A total of 95 participants were enrolled in the study. With BMI as the criteria, 20, 50, and 25 participants were found to be normal, overweight, and obese, respectively. While, with WC as the criteria, 26 and 69 participants were observed to be normal, and obese, respectively.

Table 1 depicts association of BMI and WC with CIMT and pulse pressure. Increase in BMI was associated with a significant increase in proportion of participants with increased CIMT (p-value = 0.001) and pulse pressure (p-value <0.001). Similarly, increase in WC was associated with a significant increase in proportion of participants with increased CIMT (p-value = 0.045) and pulse pressure (p-value = 0.001).

Table 2 depicts association of CIMT with age and pulse pressure. No statistically significant association was observed between CIMT and age (p-value = 0.377). However, significantly greater proportion of participants with pulse pressure >50 mm Hg had increased CIMT (p-value = 0.007).

Table 3 depicts association of CIMT with parameters of systolic ambulatory BP. Increase in CIMT was associated with the significant increase in proportion of participants with rise in 24 hr SBP (p-value <0.001), Day SBP (p-value <0.001), and Night SBP (p-value <0.001). Similarly, increase in CIMT was associated with the significant increase in the proportion of Non-Dippers or Inverse Dippers participants (p-value = 0.042) and participants with negative Day Systolic Load (p-value <0.001) and positive Night Systolic Load (p-value <0.001).

Table 4 depicts association of CIMT with parameters of diastolic ambulatory BP. In contrast to the findings of systolic ambulatory BP, increase in CIMT was associated with the significant increase in the proportion of Non-Dippers / Inverse Dippers participants (p-value = 0.022) and participants with negative Night Diastolic Load (p-value = 0.036).

Table 5 depicts correlation of CIMT with parameters of AMBP. A positive, moderate, and statistically significant correlation was observed between CIMT and Average SBP (r = 0.69; p-value = 0.0001), Average DBP (r = 0.51; p-value = 0.0001), Day SBP (r = 0.66; p-value = 0.0001), Day-time systolic blood pressure load variability (SBPLV) (r = 0.68; p-value = 0.0001), and Night-time SBPLV (r = 0.60; p-value = 0.0001). Moreover, a positive, mild, and statistically significant correlation was between CIMT and Day-time diastolic BPLV (r = 0.48; p-value = 0.0001), and Night-time diastolic BPLV (r = 0.42; p-value = 0.0001).

Discussion

Researchers have observed a strong correlation between hypertensionand BMI. Moreover, obesity is considered as a major controllable risk factor and has been reported as a good measure for predicting the incidence of hypertension[22].In high risk individuals such as overweight and obese, measurement of CIMT is recommended, as it useful in identifyingthe chances of end organ damage resulting from hypertension, which maynot be evident by other investigation including the electrocardiogram (ECG)[23].

Measurement of CIMT with ultrasound has resulted in a remarkably increased incidences of identifying the subclinical cases of atherosclerosis as well as increased ability to track the progression of CVD.The use of CIMT has increased due to its feasibility, reliability, non-invasive, and inexpensive nature. Researchers have reported that increase inCIMT isstrongly associated with atherosclerotic lesions involving various arteriesincluding aorta, coronary, cerebral, and peripheral arteries. Moreover, increase in CIMT is observed to be positively correlated with the rise in the risk of stroke, myocardial infarction MI, and cardiovascular (CV) death, particularly in patients belonging to the elderlyage group[24]. Increased CIMT has also been documented to be associated with overweight andobesity[25]. Similar findings were observed in the present study.

Increase in BMI and WC was associated with a significant increase in proportion of participants with increased CIMT and pulse pressure. Similar to the present study, Diggikar et al. reported statistically significant increase in CIMT withincrease in both BMI ($p < 0.05$) and WC ($p < 0.01$)[26]. Similarly, El-Hafez et al. observed significant increase in mean CIMT in obese subjects as compared to non-obese subjects[27]. Jinet al. reported that individuals who were obese ($p < 0.001$) or centrally obese ($p = 0.003$) had significantly increased CIMT, as compared with those who were not obese or not centrally obese[14]. Similar to the present study, De Pergola et al. reported that obesity is associated with significant increase in the incidence of rise in mean pulse pressure[28,29].

In the present study, no statistically significant association was observed between CIMT and age (p-value = 0.377). However, various studies have reported that, compared to young adults, middle-aged and older individuals have a higher CIMT[30,31]. A recent systematic review, involving healthy individuals, reported a strong positive association between age and CIMT, thereby, highlighting the fact that a gradual, linear increase in CIMT did not differ between age decades ($r = 0.91$, p-value < 0.001). Moreover, this relationship was not affected by CVD or risk factors[32]. However, significantly greater proportion of participants with pulse pressure >50 mm Hg had increased CIMT (p-value = 0.007). Similarly, Geraci et al. evaluated hypertensive patients and reported a statistically significant correlation between CIMT and 24 hr pulse pressure ($r = 0.229$; p-value < 0.001)[33].

In the present study, the CIMT was evaluated as a mean of 4 measurement of intimo-medial thickness of both the left and right common carotid artery. However, certain studies involving general and hypertensive adult individuals have reported higher CIMT on the left than the right side[34,35]. This may be due, at least in part, to the greater hemodynamic stress on the left carotid system (direct origin from the aortic arch), which is probably aggravated in hypertension states[35].

In the present study, increase in CIMT was associated with the significant rise in proportion of participants with increase in parameters of 24 hr ABPM such as 24 hr SBP, Day SBP, and Night SBP, systolic and diastolic Non-Dippers or Inverse Dippers, negative Day Systolic Load, positive Night Systolic Load, and negative Night Diastolic Load (all p-values <0.05). Moreover, a positive correlation was observed between CIMT and Average SBP, Average DBP, Day SBP, Day-time SBPLV, Day-time DBPLV, Night-time SBPLV, and Night-time DBPLV (p-value < 0.001).

Fouad et al. observed that changes in CIMT are very well predicted by ABPM, but office BP remains inconclusive for hypertension-induced changes in CIMT. Moreover, the changes in CIMT, caused by hypertension, were significantly related to 24 hr ABPM. The parameters of ABPM such as SBP and DBP, in accordance to the findings of the present study,were found to be significantly correlated with hypertension-induced changes in CIMT[36]. Similar to the findings of the present study, Xiong et al. reported a highly linear correlation between CIMT and variability in 24 hr SBP, 24 hr DBP, and daytime SBP[37]. However, Kollias et al. reported that SBP was independently correlated with increased CIMTin adolescents[38]. Similarly, Dawson et al. observed that SBP was independently associated with CIMT in adolescents[39]. It suggests that SBP is strongly related to the vascular lesions.The linear correlation between CIMT and parameters of 24 hr ABPM revealed that the severity of systolic hypertension may play a significant role in causing early vascular lesions and is recognized as a significant prognostic factor for morbidity and mortality from coronary artery disease and stroke in adult populations.

Moreover, as compared to the dipper hypertensives, non-dipper hypertensive individuals have higher left ventricular mass, cerebrovascular disease, and CV morbidity[40,41]. In the present study, an association between increased CIMT and systolic and diastolic non-dipping pattern was found amongst the participants. This is supported by the findings of earlier studies. Pierdomenico et al. observed significantly increased CIMT amongst non-dippers than in dippers[42]. Similarly, Salvetti et al. reported significantly greater prevalence of increased CIMT in non-dippers than in dippers individuals[43].

The present study has certain limitations.Firstly, it was a single centre study and had a small sample size, so results of the studycannot be extrapolated to the general population. Secondly, measurement of CIMT was carried out manually andthus, has a risk of bias and limited reproducibility. Lastly, irrespective of the arm circumference, BP cuff of same size was used in all the subjects, thereby, affecting the BP readings.

Conclusions

Findings of this study indicates that overweight and obese participants had a significant increase in CIMT values. Increase in CIMT was not significantly associated with age of the participants. However, it was positively correlated with parameters of 24 hr ABPM. Moreover, increase in CIMT positively correlated with non-dippers or inverse dippers, thus, identifying non-hypertensive participants at an increased risk of cerebrovascular disease, and cardiovascular morbidity.

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Legends Tables

Table 1: Association of BMI and WC with CIMT and Pulse Pressure

Groups	CIMT		Pulse pressure	
	Increased	Normal	≤50 mm Hg	>50 mm Hg
BMI				
Group I (n=20)	0 (0)	20 (100)	20 (100)	0 (0)
Group II (n=50)	13 (26)	37 (74)	35 (70)	15 (30)
Group III (n=25)	12 (48)	13 (52)	11 (44)	14 (56)
*p-value	0.001		<0.001	
WC				
Group A (n=26)	3 (11.5)	23 (88.5)	25 (96.2)	1 (3.8)
Group B (n=69)	22 (31.9)	47 (68.1)	41 (59.4)	28 (40.6)
*p-value	0.045		0.001	

Data expressed as percentages; BMI: Body Mass Index; WC: Waist circumference; CIMT: Carotid artery intima-media thickness; * - Chi-square test p-value < 0.05 was considered as statistically significant

Table 2: Association of CIMT with Age and Pulse Pressure

Characteristic	Increased CIMT (n=25)		Normal CIMT (n=70)		p-value*
	No.	%	No.	%	
Age					
<40 yrs	11	44.0	38	54.3	0.377
≥40 yrs	14	56.0	32	45.7	
Pulse Pressure					
≤50 mm Hg	12	48.0	54	77.1	0.007
>50 mm Hg	13	52.0	16	22.9	

Data expressed as percentages; CIMT: Carotid artery intima-media thickness; * - Chi-square test p-value < 0.05 was considered as statistically significant

Table 3: Association of CIMT with Systolic Ambulatory Pressure Parameters

Characteristic	Increased CIMT (n=25)	Normal CIMT (n=70)	p-value*
	n (%)	n (%)	
SBP 24 hr			
High	12 (48.0)	7 (10.0)	<0.001
High Normal	9 (36.0)	35 (50.0)	
Normal	4 (16.0)	28 (40.0)	
Day SBP			

Characteristic	Increased CIMT (n=25)	Normal CIMT (n=70)	p-value*
	n (%)	n (%)	
High	11 (44.0)	4 (5.7)	<0.001
High Normal	9 (36.0)	35 (50.0)	
Normal	5 (20.0)	31 (44.3)	
Night SBP			
High	17 (68.0)	17 (24.3)	<0.001
High Normal	4 (16.0)	31 (44.3)	
Normal	4 (16.0)	22 (31.4)	
Systolic Dipping			
Dipper	5 (20.0)	30 (42.9)	0.042
Non-Dippers / Inverse Dippers	20 (80.0)	40 (57.1)	
Day Systolic Load			
Negative	14 (56.0)	67 (95.7)	<0.001
Positive	11 (44.0)	3 (4.3)	
Night Systolic Load			
Negative	9 (36.0)	54 (77.1)	<0.001
Positive	16 (64.0)	16 (22.9)	
Circadian variation SBP			
Absent	20 (80.0)	42 (60.0)	0.071
Present	5 (20.0)	28 (40.0)	

Data expressed as percentages; CIMT: Carotid artery intima-media thickness; SBP: Systolic blood pressure; * - Chi-square test p-value < 0.05 was considered as statistically significant

Table 4: Association of CIMT with Diastolic Ambulatory Pressure parameters

Characteristics	Increased CIMT (n=25)	Normal CIMT (n=70)	p-value*
	n (%)	n (%)	
DBP 24 hr			
High	6 (24.0)	8 (11.4)	0.259
High Normal	7 (28.0)	18 (25.7)	
Normal	12 (48.0)	44 (62.9)	
Day DBP			
High	6 (24.0)	7 (10.0)	0.215
High Normal	2 (8.0)	6 (8.6)	
Normal	17 (68.0)	57 (81.4)	

Characteristics	Increased CIMT (n=25)	Normal CIMT (n=70)	p-value*
	n (%)	n (%)	
Night DBP			
High	9 (36.0)	10 (14.3)	0.065
High Normal	8 (32.0)	32 (45.7)	
Normal	8 (32.0)	28 (40.0)	
Diastolic Dipping			
Dipper	8 (32.0)	41 (58.6)	0.022
Non-Dippers/ Inv. Dippers	17 (68.0)	29 (41.4)	
Day Diastolic Load			
Negative	21 (84.0)	66 (94.3)	0.112
Positive	4 (16.0)	4 (5.7)	
NightDiastolic Load			
Negative	20 (80.0)	66 (94.3)	0.036
Positive	5 (20.0)	4 (5.7)	
Circadian variation DBP			
Absent	14 (56.0)	32 (45.7)	0.377
Present	11 (44.0)	38 (54.3)	
>50 mm Hg	13 (52.0)	16 (22.9)	

Data expressed as percentages; CIMT: Carotid artery intima-media thickness; DBP: Diastolic blood pressure; * - Chi-square test p-value < 0.05 was considered as statistically significant

Table 5: Correlation of CIMT with ABPM parameters

Variable	"r"	"p"	Strength	Significance
Average SBP	0.69	0.0001	Moderate	S
Average DBP	0.51	0.0001	Moderate	S
Day SBP	0.66	0.0001	Moderate	S
% Change in SBP	-0.18	0.079	Weak	NS
% Change in DBP	-0.09	0.409	Weak	NS
BPLV Sys Day	0.68	0.0001	Moderate	S
BPLV Dias Day	0.48	0.0001	Mild	S
BPLV Sys Night	0.60	0.0001	Moderate	S
BPLV Dias Night	0.42	0.0001	Mild	S
Circadian SBP Night	-0.11	0.269	Weak	NS
Circadian DBP Night	-0.09	0.392	Weak	NS

Pearson's correlation coefficient: r; r< 0.3: Weak or negligible correlation; r=0.3-0.5: Mild correlation; r=0.5-0.7: Moderate correlation; r>0.7: Strong correlation; "-" sign indicates a negative correlation; CIMT: Carotid artery intima-media thickness; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BPLV: Blood pressure load variability; Sys: Systolic; Dias: DiastolicNS:notsignificant; S: significant; p-value < 0.05 was considered asstatistically significant