Variation Of Carotid Intima Media Thickness With Anthropometric Measures In Healthy Adults Of Hong Kong Chinese Population

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Abstract
Objective:
To investigate the association of several obesity anthropometric indices, including body mass index (BMI), waist circumference (WC) and waist-hip ratio (WHR), with carotid intima media thickness (CIMT) in local Chinese population; and to examine the variation of CIMT with age in local Chinese population.
Methods:
This is a cross-sectional prospective study in 184 Chinese patients in a local Accident and Emergency Department (AED) aged ≥ 18 years without risk factors for atherosclerosis. Subjects' common carotid artery intima media thickness was measured with a 4.5-15MHz linear ultrasound transducer at a point 10mm proximal to the carotid bulb. All subjects' age, gender, anthropometric (WC and hip circumference (HC) from which WHR was calculated, weight and height from which BMI was calculated) and CIMT values were recorded on a pro forma. Descriptive and inferential statistic methods such as *t* test and chi-square were carried out. Correlation coefficients were used to determine the relationship between age, BMI, WC, WHR, and CIMT.
Results:
The right, left, and average CIMT of both sides in our study subjects were 0.55+/-0.14mm, 0.58+/-0.15mm, and 0.56+/-0.14mm respectively, with no significant difference between the right and left sides ($p>0.05$). The left, right and average CIMT did not differ significantly between men and women ($p>0.05$). WC ($r=0.313$, 0.271, 0.309; all $p<0.001$) and WHR ($r=0.359$, 0.312, 0.355; all $p<0.001$) showed moderate positive correlations with right, left, and average CIMT. BMI ($r=0.188$, 0.160, 0.184; $p<0.05$) showed weak positive correlations with right, left, and average CIMT. Correlations between BMI with right, left, and average CIMT in male was found to be stronger than in female. There was a linear relationship between age and CIMT ($r=0.557$, 0.509, 0.564 for right, left and average CIMT respectively; all $p<0.001$), for which in female was stronger than in male.
Conclusions:
Ultrasonic CIMT measurement can be useful for refining CVD risk assessment in some symptomatic patients. It detects subclinical vascular disease and identifies patients at increased risk of CVD, and thus aids in risk stratification and patient management especially in the primary care setting and AED. This study provides evidence of a positive association of WC, WHR, BMI and age with CIMT in Hong Kong Chinese population. The association of WC and WHR was found to be stronger than that of BMI with CIMT. WC and WHR may be used as supplemental indices for redefining obesity and an alternative tool for further refining discrimination of early atherosclerotic burden. CIMT increases with age, and this factor should be considered in the sonographic assessment of CIMT.

Keywords
Carotid intima media thickness, ultrasound, anthropometric index, cardiovascular disease

Introduction

Atherosclerosis is a leading cause of ischemic cardiovascular diseases (CVD). It is a process that begins in childhood and remains asymptomatic for decades before manifestation to clinical events at a later age. Epidemiological evidence suggests that abdominal obesity accelerates atherosclerotic progression. Yet, current evidence on the topic is still limited and inconsistent [1][2]. Obesity is an established risk factor for clinical CVD. Several studies suggest that anthropometric measures of abdominal adiposity, such as waist circumference (WC) and waist-hip ratio (WHR), are better predictors of cardiovascular risk than body mass index (BMI), the primary marker of general adiposity [3][4][5].

Carotid intima-media thickness (CIMT) is an established marker for subclinical atherosclerosis as well as an independent predictor for cardiovascular risk. It is measured non-invasively by ultrasonography.Carotid ultrasound helps in CVD risk assessment. An increase in CIMT is associated with an increased risk of ischemic heart disease and cerebrovascular disease [6][7]. This test can be considered if additional information about the burden of subclinical vascular disease or future CVD risk is needed but the degree of preventive measures is uncertain[6]. Exercise tolerance test (ETT) is a widely used test for evaluation of ischemic heart disease. Previous study observed significant positive association between CIMT with ETT results in type 2 diabetic patients [8]. It was found that mean CIMT was useful for screening patients with an inconclusive ETT result to exclude coronary heart disease [9]. CIMT could also be used to stratify risk in women, younger men and in African American individuals, where coronary artery calcium scoring may have limited discriminatory power because of a high prevalence of a zero calcium score [10]. CIMT values greater than or equal to 75th percentile are considered high and indicative of increased CVD risk [11]. In the emergency department, this value helps in risk stratification of patients presenting with symptoms such as chest pain, and aids in the disposition of these patients. In primary care, primary prevention of CVD can be achieved with potentially screening the patients with thicker wall by life style modifications such as diet control and regular exercise.

The association between various anthropometric indices of obesity and CIMT has been examined in a few studies, but most of them were conducted among mostly overweight or obese subjects [1][12][13][14]. In addition, previous evidence was derived from European and Western Caucasian populations, with limited evidence from Asians [15][16]. Studies on anthropometric indices and CIMT may help the detection and prediction of subclinical atherosclerosis and early CVDs associated with obesity [17]. In the present study, we investigate the association of several anthropometric indices of obesity, including BMI, WC and WHR, with CIMT in local Chinese population.

Nomograms for CIMT values and age-related changes have not been reported in Hong Kong. In this study, we also examine the normal variation of age related increase of CIMT in Hong Kong Chinese population.

Methods

A prospective cross sectional study was performed. The study was approved by the Hospital Authority Research Ethics Committee (HA REC), and written informed consents were obtained from all the study participants. Local Chinese patients aged ≥ 18 who presented to a local AED, and had no risk factors for atherosclerosis, were included. Subjects who had a history of past or current smoking and alcohol consumption, hypertension, diabetes mellitus, use of lipid lowering medications, and renal disease were excluded from the study. We also excluded subjects with BMI > 40kg/m^2, a history of bariatric surgery and known body dystrophies and abdominal hernias. Subjects with signs and symptoms suggesting peripheral artery disease, myocardial infarction, or stroke and those with a history of angioplasty or coronary artery bypass surgery were also excluded.

<u>CIMT measurement</u>

Images of the right and left common carotid arteries (CCA) were acquired using Electric LOGIQ S7 (General Electric Healthcare; Boston, Massachusetts, USA) ultrasound machine equipped with a matrix linear probe with operating frequency 4.5-15MHz by three emergency physicians with at least six years clinical experience in point-of-care ultrasound. The CIMT measurement conformed to the European Society of Cardiology's guideline [18]. With the patient lying in the supine position, the neck was rotated to the opposite side for examination. Longitudinal and transverse sonograms of the CCA were obtained and IMT measurements were taken in the CCA at a point 10mm proximal to the bulb, which was the reference point of measurement for all study participants (Figure 1). Thickness of the intima media was defined as the distance between the leading edge of lumen intima and the leading edge of media adventitia echo. On transverse view, the far wall CIMT was taken as the transverse IMT measurement. The CCA was also scanned by two longitudinal views: anterolateral, with transducer positioned parallel to the anterior border of the sternocleidomastoid muscle and posterolateral, with the transducer positioned parallel to the posterior border of the sternocleidomastoid muscle. The far wall CIMT readings were taken. An average of the anterolateral and posterolateral planes was obtained as the longitudinal IMT measurement. The average longitudinal and transverse measurements gave the main single CIMT measurement for the study on each side of the neck. All images used for measurements were frozen at end diastole.

Indicators of abdominal adiposity
Anthropometric measurements were obtained using standardized equipment and techniques.Body weight, heightand BMI were measured using Ultrasonic Scales SK-V7 (SONKA, China). WC was measured at midpoint between the inferior border of the costal arch and the iliac crest, at the median axillary line. HC was measured at the maximal protrusion of the gluteal muscle. The ratio between WC and HC was calculated as WHR.

Outcomes
The primary outcome was the association between CIMT and the anthropometric indices of obesity, including BMI, WC and WHR, in adult local Chinese patients without risk factors for atherosclerosis. Secondary outcome was the variation of CIMT with age in adult local Chinese patients without risk factors for atherosclerosis.

Statistical Analysis
All the data were entered on a spreadsheet and analyzed using IBM SPSS (version 26; IBM Corp., Armonk, NY). Continuous variables are presented as mean +/- standard deviation and ranges. Categorical variables are presented as frequency and percentages. Descriptive and inferential statistic methods such as *t* test and chi-square were carried out. Correlation coefficients were used to determine the relationship between age, BMI, WC, WHR, and CIMT. A 2-tailed p value of 0.05 or less was considered as statistically significant.

Results
A total of 184 participants were enrolled in this study. Baseline characteristics and anthropometric measurement are shown on Table 1. The mean age of the participants was 44+/-16.4 (range 18-92) years. Participants less than 25 years of age constituted 16.7%, 26-35 years constituted 18.3%, 36-45% constituted 16.7%, 46-55 years constituted 21.5%, 56-65 years constituted 16.7%, and those older than 65 years constituted 9.1%.

The male-to-female ratio was 0.8:1. The mean BMI of the study population was 22.49+/-3.82 kg/m^2. More than one half (58.2%) of the study population was normal weight, while about one fifth (21.7%) were overweight. The underweight subjects constituted 16.3%, while obese constituted 3.8%. The mean WC was 79.12+/-13.55cm, and the mean WHR was 0.84+/-0.10cm.

Mean right and left CIMT
CIMT ranged 0.30 to 1.13mm on the right side and 0.33 to 1.23mm on the left side, with mean values of 0.55+/-0.14mm on the right and 0.58+/-0.15mm on the left (Table 2). There was no statistically significant difference between the values of the right and left sides (p=0.22).

Comparison of CIMT between sexes
The left, right, and average CIMT values did not differ between male and female on both sides (p>0.05) (Table 3).

Comparison of CIMT between age groups
There was a graded increase in the right, left, and average CIMT with increasing age (p<0.05), which remained significant among all age groups after matching for intergroup differences (Table 4).

Correlation of CIMT With BMI, WC and WHR
WC (r=0.313, 0.271, 0.309; all p<0.001) and WHR (r=0.359, 0.312, 0.355; all p< 0.001) showed moderate positive correlations with right, left, and average CIMT (Graphs 1 & 2). BMI (r=0.188, 0.160, 0.184; p<0.05) showed weak positive correlations with right, left, and average CIMT (Table 5, Graph 3). Correlations between BMI with right, left, and average CIMT in male (r=0.278, 0.321, and 0.319; p<0.05) was found to be stronger than in female (r=0.106, 0.019, 0.064; p>0.05) (Table 6).

Correlation of CIMT with age
Age (r=0.557, 0.509, 0.5; all p<0.001) showed positive correlations with right, left, and average CIMT (Table 5, Graph 4). Correlations between age with right, left, and average CIMT in female (r=0.618, 0.621, 0.658; all p<0.001) was found to be stronger than in male (r=0.489, 0.373, 0.454; all p<0.001) (Table 6).

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Discussion

The reported normal reference values for CIMT vary. Mean CIMT values in previous studies have ranged from 0.4 to 1.0mm [19][20]. The mean CIMT in this study was 0.562+/-0.136mm. In a study conducted in rural China, the mean CIMT was 0.57mm with population aged ≥ 45 years (average age 59.92 years). A Taiwan study found mean CIMT in non-CAD population to be 0.65+/-0.02mm for <60 years and 0.72+/-0.04mm for ≥ 60 years [21], whereas we found mean CIMT to be 0.54+/-0.12mm for <60 years and 0.67+/-0.15mm for ≥60 years. Heterogeneity in the methods used by different studies at the site of measurement of carotid artery IMT could account for this variation. In this study, measurement of the CIMT in the longitudinal and transverse planes was employed, and the average of these 2 planes was used as a single CIMT value for each side, which is similar to previous studies [19][22][21]. The anterolateral and posterolateral planes, in relation to the sternocleidomastoid muscle, were used for the longitudinal measurement due to clarity and easy accessibility to the CCA [19][20]. The majority of previous studies related to CIMT were conducted in Western populations. According to a consensus statement from the American Society of Echocardiography, CIMT values greater than or equal to 75^{th} percentile are considered high and indicative of increased CVD risk [11]. The 75^{th} percentile of average CIMT in our population is 0.64mm, and that in different age groups is shown in Table 4.

Our study is one of the few studies evaluating the associations between anthropometry and CIMT, a valid clinical surrogate for atherosclerosis. WC and WHR were found to have moderate positive correlations with right, left, and average CIMT in this study. Ge et al. found a positive significant association of WC and WHR with CIMT in a lean Asian population [17]. BMI was found to have a weak positive correlation with right, left, and average CIMT in this study. One study also reported a weak positive correlation between BMI and CIMT, which was not statistically significant [24]. Ge et al. observed no association between BMI and CIMT [17], which may be due to the lower BMI of the participants recruited in their study. Stronger positive correlation with CIMT in WC and WHR than in BMI was observed in this study. Ge et al, and several studies conducted in different populations [1][12][15][25][26], found WC and WHR but not BMI showed a positive significant association with CIMT. Caution is recommended while using BMI as a screening tool for detecting CVD risk, as abdominal adiposity may initiate atherosclerotic progress ahead of weight gain. This in turn affects the relationship between CIMT and BMI. A large European cohort study (EPIC) reported that the association of WC and WHR with the risk of death was stronger among participants with a lower BMI than among those with a higher BMI. Correlation between BMI with right, left, and average CIMT in male was found to be stronger than in female in the present study. This could partially be explained by the differential hormonal profile between male and female. Fat storage in men tends to be around the abdomen, whereas it tends to be around the lower body in women of childbearing age.

Increase of CIMT with increasing age was observed in this study. This agreed with earlier findings in different studies carried out in different regions of Nigeria and Bangladesh [17][19][23][24][27][28]. This is presumably due to the increased adaptive response of arterial wall to tensile stress in the absence of arteriosclerosis [24].

Correlation between age with right, left, and average CIMT in female was found to be stronger than in male. Several studies showed that endogenous estrogens protect against the atherosclerotic process, and the level of which has been known to decline with age [29][30]. One study found that serum dehydroepiandrosterone (DHEA) and androgens in women declined with age, and that normal hormonal concentrations had no apparent negative effects on cardiovascular risk factors. Higher DHEA and androstenedione were found to be associated with lower carotid wall thickness [31].

This study is subjected to the usual limitations of cross-sectional studies. The sample size of this study was not large. We did not include metabolic indicators such as plasma lipids in the data analysis, as they were unavailable in this study. But we consider metabolic abnormalities as part of the pathological linkage between abdominal obesity and atherosclerosis. There are possible inter-investigator measurement differences. As we used data based on one-time measurement of CIMT and anthropometric measures, measurement errors may have resulted in an underestimation of the true association. Despite both WC and WHR provide information on intra-abdominal fat, they do not

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appear to well distinguish between intra-abdominal and subcutaneous fat that have been shown to contribute differentially to metabolic syndrome risk factors [32]. Although we controlled for risk factors for CVD, the possibility of residual confounding or unmeasured confounders cannot be excluded. We recruited subjects from a local AED, where people attend for health problems. But the subjects were those without risk factors for atherosclerosis, implying the results can be generalized to such patients.

An increase in CIMT is associated with increased CVD risks, as found in some previous studies. With the use of data from this study, a longitudinal study may be conducted on the prediction of acute coronary syndrome (ACS) by CIMT with the use of data from this study. WC and WHR were found to show a positive significant association with CIMT. CIMT values greater than or equal to 75th percentile are considered high and indicative of increased CVD risk. If WC and WHR are translated to a CIMT value, the WC and WHR corresponding to the 75th percentile of CIMT may probably be a simple stratification tool for CVD risks especially in the primary care setting where ultrasound machines are usually not available. This potential association, however, needs to be confirmed by another study in the future.

Conclusion

Ultrasonic CIMT measurement can be useful for refining CVD risk assessment in some symptomatic patients. It detects subclinical vascular disease and identifies patients at increased risk of CVD, and thus aids in risk stratification and patient management especially in the primary care setting and the AED. This study provides evidence of a positive association of WC, WHR, BMI and age with CIMT in Hong Kong Chinese population. The association of WC and WHR was found to be stronger than that of BMI with CIMT. WC and WHR may be used as supplemental indices for redefining obesity and an alternative tool for further refining discrimination of early atherosclerotic burden. CIMT increases with age, and this factor should be considered in the sonographic assessment of CIMT.

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Ethics approval

The study was approved by the Hospital Authority Research Ethics Committee.

Conflict of interest

All authors have disclosed no conflict of interest.

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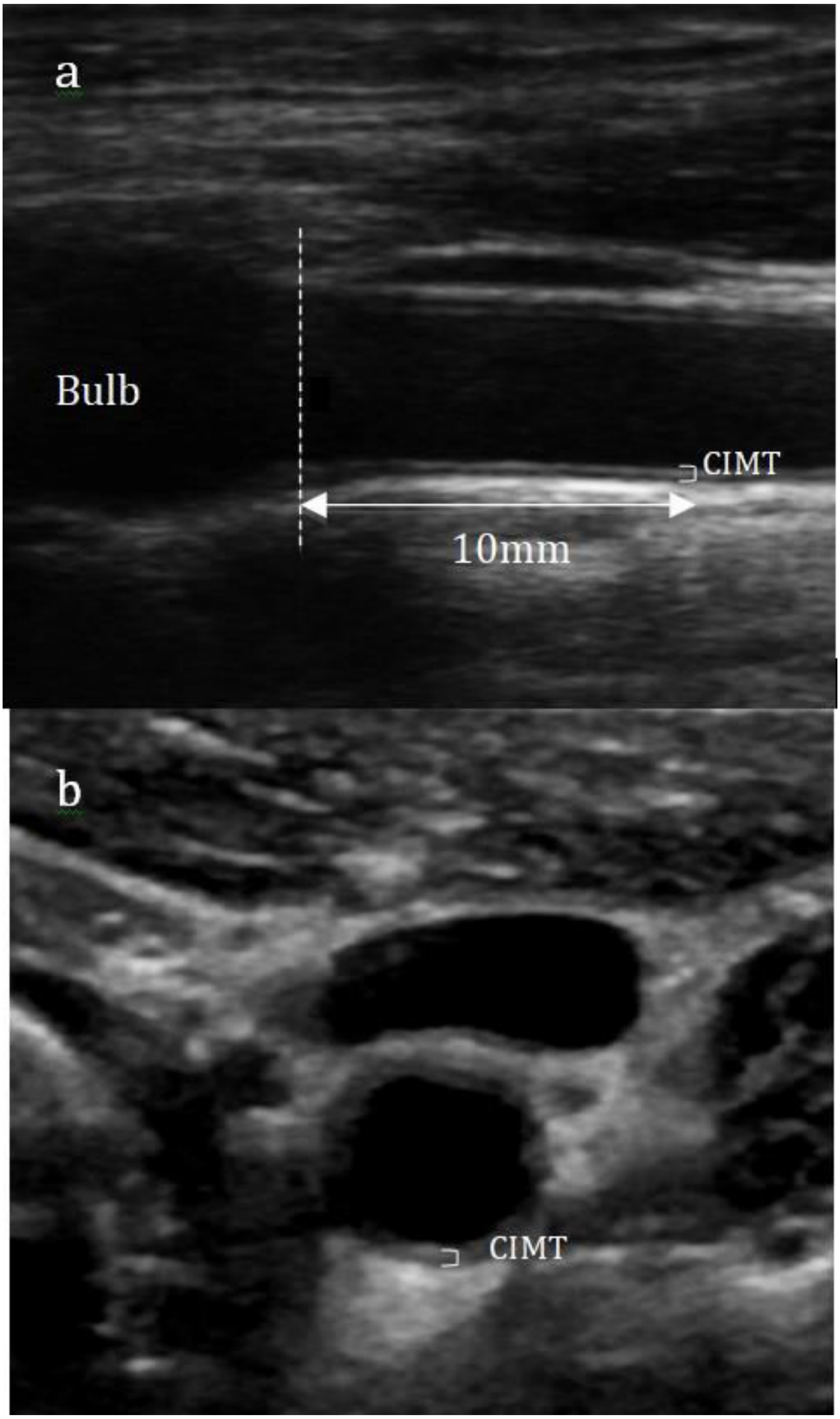

Figure 1: (a) Longitudinal plane of common carotid artery. (b) Transverse plane of common carotid artery 10mm proximal to the bulb.
CIMT: Carotid intima media thickness
Bulb: Carotid bulb

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	N (%)
Age, year (mean +/- SD) Range	44.4 +/- 16.4 18-92
Age group, year 18-25 26-35 36-45 46-55 56-65 >65	 31 (16.7) 34 (18.3) 31 (16.7) 40 (21.5) 31 (16.7) 17 (9.1)
Sex Male Female	 83 (44.6) 101 (54.3)
BMI, kg/m^2 (mean +/- SD)	22.49 +/- 3.82
BMI categories Underweight (<18.5) Normal (18.5-24.9) Overweight (25.0-29.9) Obese (>30)	 30 (16.3) 107 (58.2) 40 (21.7) 7 (3.8)
Waist circumference, cm (mean +/- SD)	79.12 +/- 13.55
Waist-hip ratio (mean +/- SD)	0.84 +/- 0.10

Table 1: Baseline characteristics and anthropometric measurement

SD: Standard deviation
BMI: Body mass index

	Range (mm)	**Mean +/- SD (mm)**
Right CIMT	0.30 – 1.13	0.55 +/- 0.14
Left CIMT	0.33 – 1.23	0.58 +/- 0.15
Average CIMT	0.33 – 1.15	0.56 +/- 0.14

Table 2: Right, left and average CIMT

CIMT: Carotid intima media thickness
SD: Standard deviation

	N	**Mean +/- SD**	**p-value**
Right CIMT			0.531
Male	83	0.55 +/- 0.14	
Female	101	0.54 +/- 0.14	
Left CIMT			0.475
Male	83	0.59 +/- 0.15	
Female	101	0.57 +/- 0.16	
Average CIMT			0.475
Male	83	0.57 +/- 0.13	
Female	101	0.56 +/- 0.14	

Table 3: Left and right CIMT based on sex distribution

CIMT: Carotid intima media thickness
SD: Standard deviation

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	N	Right CIMT Mean +/- SD	Left CIMT Mean +/- SD	Average CIMT Mean +/- SD	75th percentile of average CIMT
Age group					
<25	31	0.45 +/- 0.08	0.48 +/- 0.07	0.47 +/- 0.07	0.51
26-35	34	0.49 +/- 0.09	0.52 +/- 0.13	0.50 +/- 0.10	0.59
36-45	31	0.50 +/- 0.10	0.51 +/- 0.11	0.51 +/- 0.09	0.57
46-55	40	0.59 +/- 0.13	0.62 +/- 0.15	0.61 +/- 0.13	0.66
56-65	31	0.64 +/- 0.12	0.65 +/- 0.15	0.64 +/- 0.12	0.71
>65	17	0.67 +/- 0.15	0.73 +/- 0.18	0.70 +/- 0.16	0.78
p-value		0.005	0.006	0.001	

Table 4: Right, left and average CIMT based on age group distribution

CIMT: Carotid intima media thickness
SD: Standard deviation

	Average CIMT		Right CIMT		Left CIMT	
	r	p-value	r	p-value	r	p-value
BMI	0.184	<0.05	0.188	<0.05	0.160	<0.05
WC	0.309	<0.001	0.313	<0.001	0.271	<0.001
WHR	0.355	<0.001	0.395	<0.001	0.312	<0.001
Age	0.564	<0.001	0.557	<0.001	0.509	<0.001

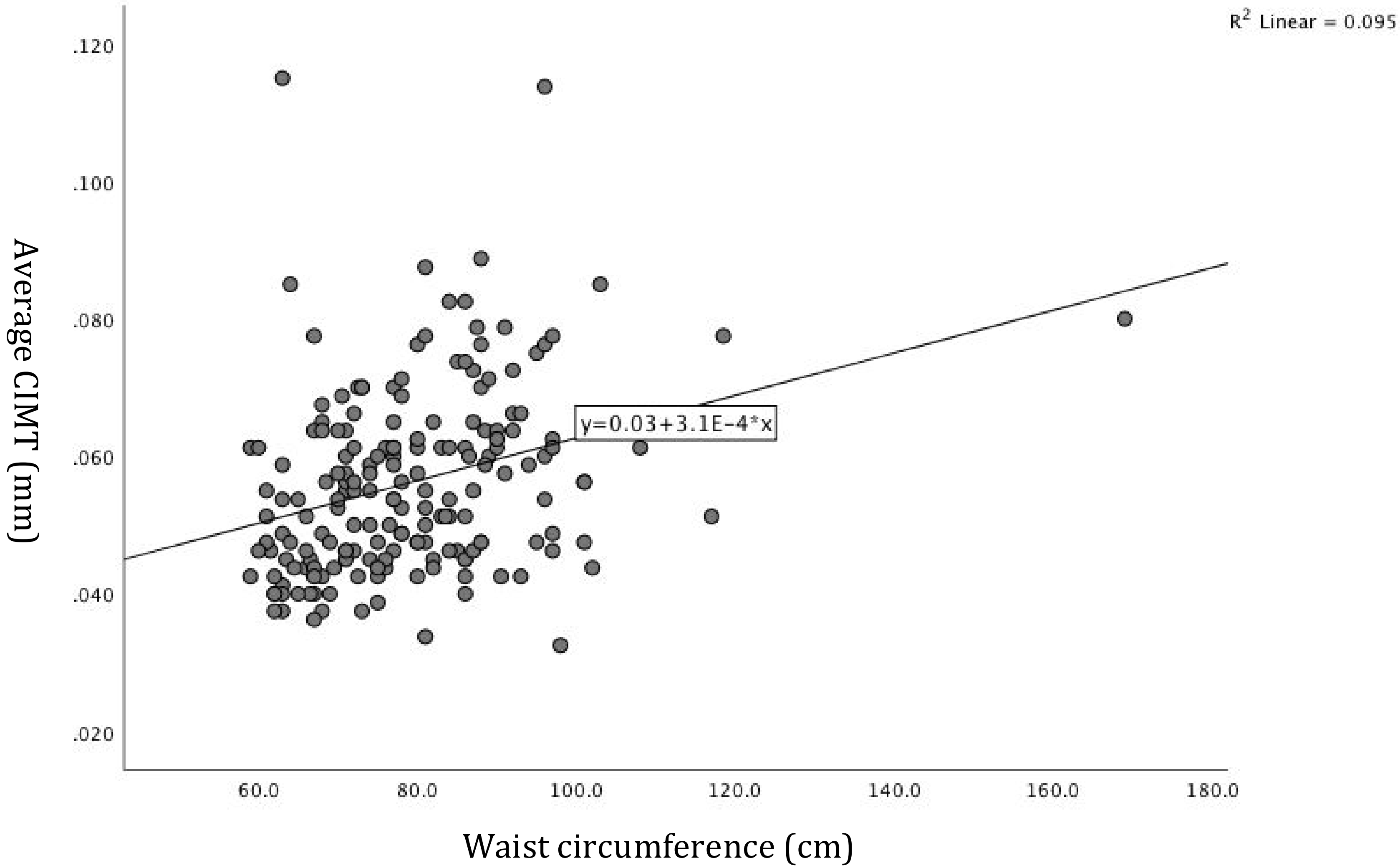
Table 5: Relationship of BMI, WC, WHR, age with CIMT

r: Pearson correlation coefficient
BMI: Body mass index
WC: Weight circumference
WHR: Waist-hip ratio
CIMT: Carotid intima media thickness

	Average CIMT		Right CIMT		Left CIMT	
	r	p-value	r	p-value	r	p-value
BMI						
Male	0.319	<0.05	0.278	<0.05	0.321	<0.05
Female	0.064	>0.05	0.106	>0.05	0.847	>0.05
Age						
Male	0.454	<0.001	0.489	<0.001	0.373	<0.001
Female	0.658	<0.001	0.618	<0.001	0.621	<0.001

Table 6: Relationship of BMI and age with CIMT on sex distribution

r: Pearson correlation coefficient
BMI: Body mass index
CIMT: Carotid intima media thickness



Graph 1: Correlation between WC and average CIMT

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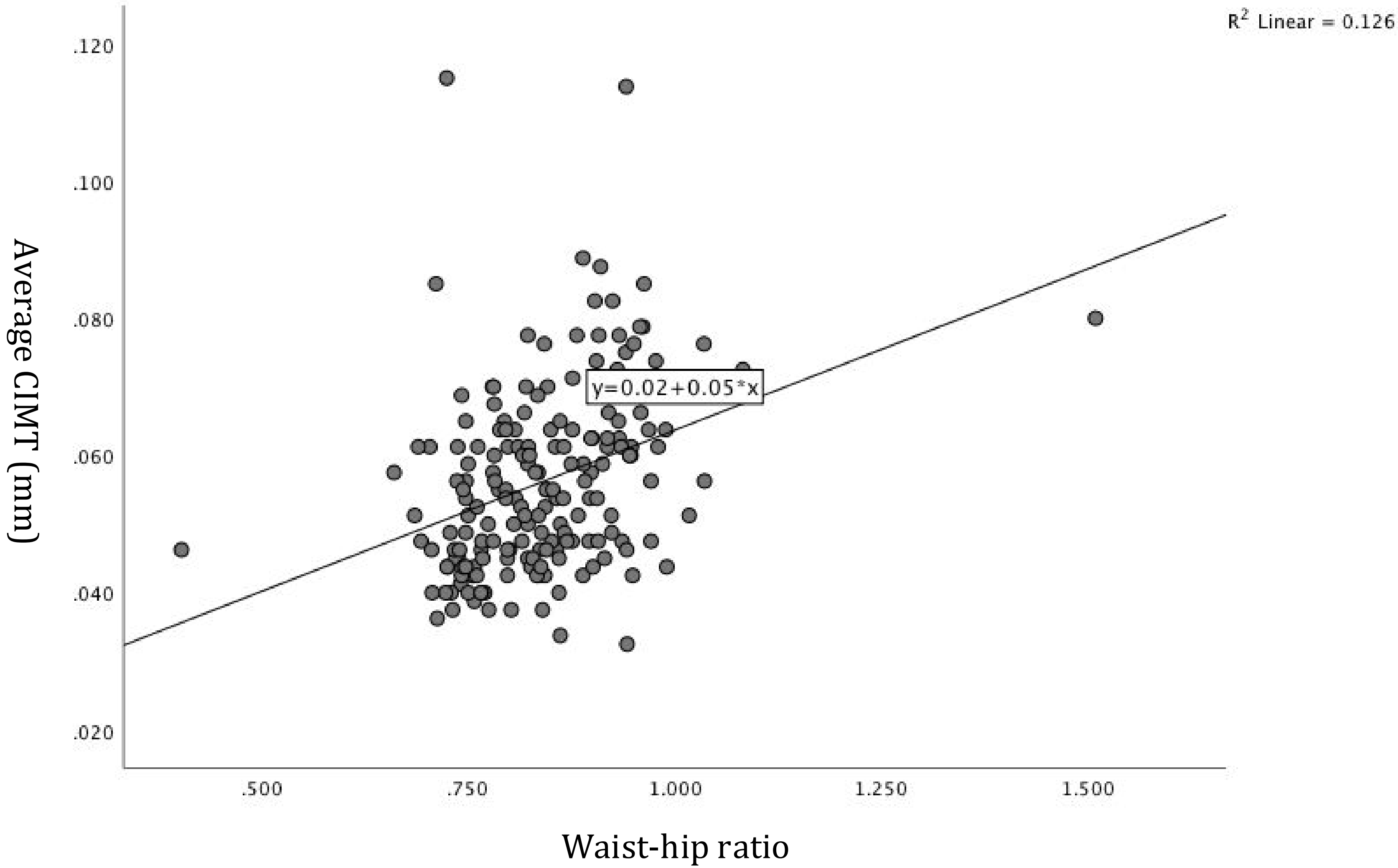

Graph 2: Correlation between WHR and average CIMT

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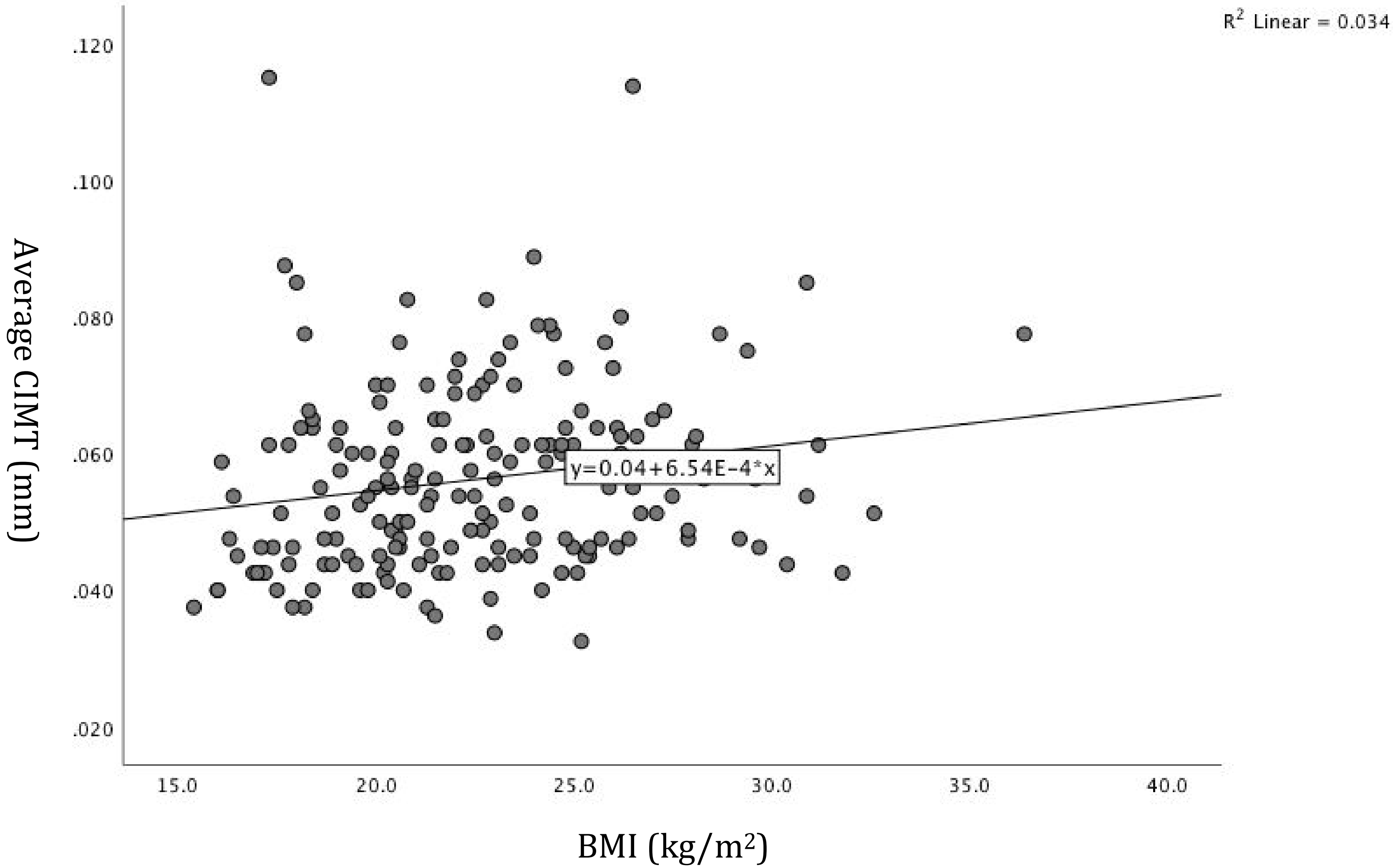

Graph 3: Correlation between BMI and average CIMT

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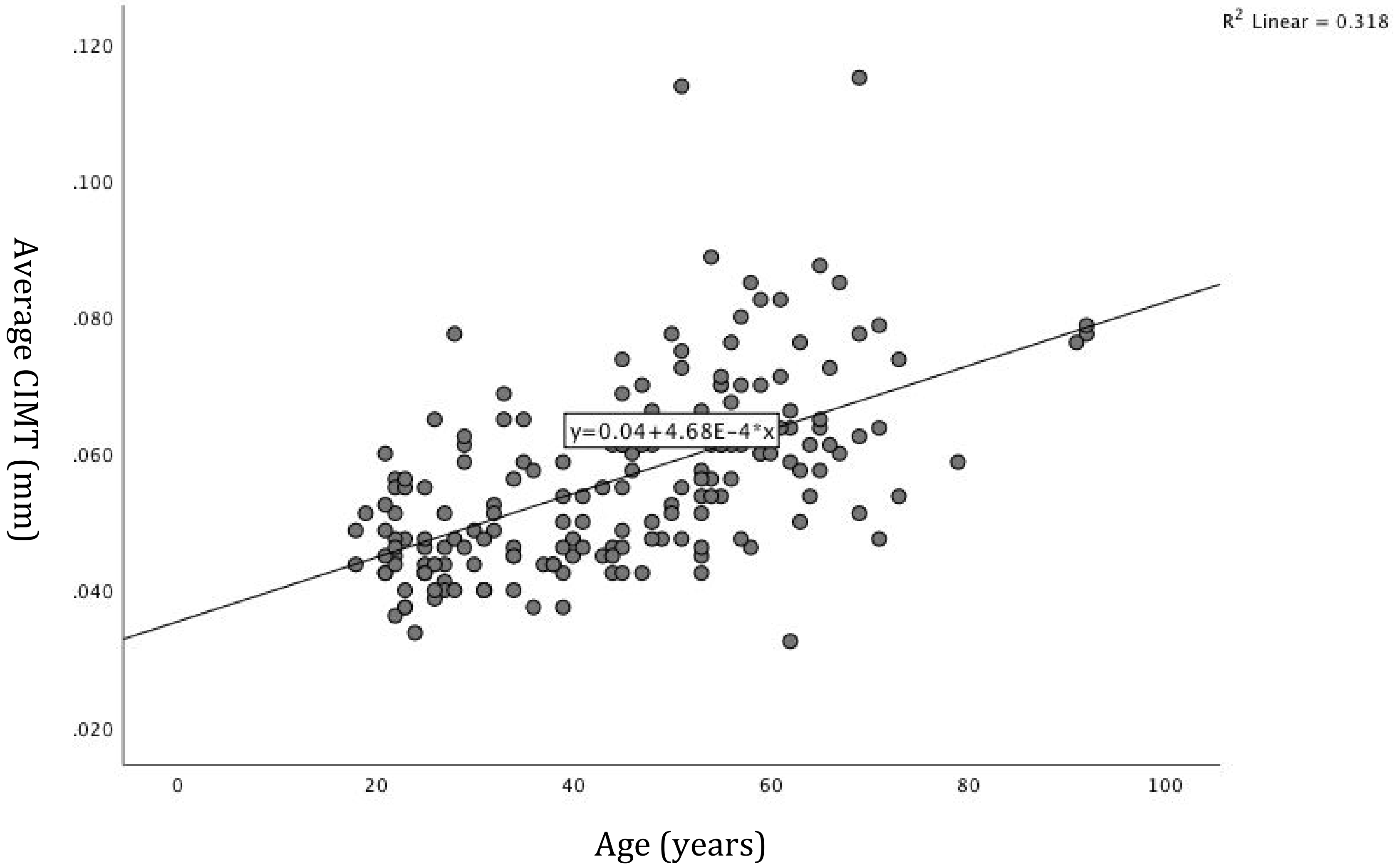

Graph 4: Correlation between age and average CIMT