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Association between sonographically measured mesenteric fat thickness and brachial artery flow-mediated dilation in Chinese young male adults

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Abstract

Objective: To investigate the potential correlation between sonographically measured mesenteric fat thickness (MFT) and brachial artery flow-mediated dilation (FMD) in a sample of healthy Chinese male young adults.

Methods: Healthy male participants were recruited from Hong Kong Polytechnic University for this prospective observational study. The physical activity readiness questionnaire and ultrasound measurements of carotid intima media thickness were used to screen for clinically healthy subjects. MFT and brachial artery FMD were measured by ultrasound, and body mass index (BMI) was recorded.

Results: A total of 34 healthy male subjects, aged 19–26 years (mean $\pm$ SD BMI, 21.7 ± 3.2 kg/m^2) were included. Pearson's correlation coefficient test showed that brachial artery FMD had a statistically significant inverse relationship with BMI and with Log (MFT). Further stepwise multiple linear regression analysis showed that Log (MFT), and not BMI, was an independent predictor of impaired brachial artery FMD.

Conclusions: Sonographic measurements of MFT were an independent predictor of brachial artery FMD in Chinese male young adults.

Keywords

Body mass index, sonography, mesenteric fat thickness, flow-mediated dilation; carotid intima media thickness

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Introduction

Mesenteric fat, a type of visceral adipose tissue that drains free fatty acids directly into the portal circulation, is metabolically more active than other adipose tissues, such as subcutaneous or extraperitoneal fat.[1] Previous studies by the present authors demonstrated that mesenteric fat thickness (MFT) was correlated with multiple cardiovascular risk factors and was an independent determinant of fatty liver disease, polycystic ovarian syndrome, metabolic syndrome and obstructive sleep apnoea.[2–4] MFT was also found to be associated with carotid intima media thickness, which is well recognized as a surrogate marker for atherosclerosis.[5]

Endothelial dysfunction is characterized by an intricate imbalance between vasodilators (e.g. nitric oxide) and vasoconstrictors (e.g. angiotensin II and endothelin-1), and is thought to play a central role in the pathogenesis of atherosclerosis and cardiovascular disease (CVD).[6] Brachial artery flow-mediated dilation (FMD) has been demonstrated to have prognostic significance in the assessment of endothelial functionality in older adults[7] and patients who undergo vascular surgery.[8] Impaired FMD has been associated with abdominal adiposity, independent of body weight,[9,10] underscoring the fact that central obesity is considered to be a more potent parameter than general obesity for assessing risk of CVD.[5]

Adipose tissue is highly heterogeneous and complex in nature.[11,12] For example, portal (mesenteric fat) and non-portal adipose tissues (extraperitoneal fat or subcutaneous fat) have different metabolic characteristics and so exert different effects on cardiovascular risks such as endothelial dysfunction.[11] To the present authors' knowledge, there are no published studies regarding the correlation between sonographically measured MFT and endothelium-dependent vasodilation. Thus, the aim of the present study was to investigate the association between sonographically measured MFT and brachial artery FMD in a sample of healthy Chinese male young adults.

Subjects and methods

Study population

This prospective observational study was conducted at the Ultrasound laboratory, Department of Health Technology and Informatics, Hong Kong Polytechnic University, between January 2015 and June 2015, and included healthy Chinese male volunteers recruited from Hong Kong Polytechnic University. One week prior to the start of the study, participants were asked to complete a physical activity readiness questionnaire (PAR-Q),[13] a simple, self-administered form that contains that seven yes/ no questions focused on symptoms of heart disease and bone or joint problems. Demographic information and previous medical history were also collected. Following a 15-min rest period, blood pressure was determined as the mean of two or three measurements obtained using an HEM-762 monitor (Omron Corporation, Kyoto, Japan) with the participant in a sitting position. Body mass index (BMI) was calculated from height and weight measurements obtained with participants wearing light clothing without shoes.

Exclusion criteria comprised: (1) previous history, signs and symptoms, or self--declaration, of coronary heart disease, diabetes, CVD and/or kidney disease; (2) taking any form of medication; (3) presence of hypertension (i.e., systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg); (4) obesity (i.e., BMI > 30 kg/m^2); (5) a ‘yes’ answer to any of the seven questions in the PAR-Q; and (6) carotid intima media thickness > 0.8 mm (cut off value for a marker of cardiovascular risk) measured by sonography.[14] Prior to ultrasound assessments, participants were asked to abstain from cigarette smoking, and caffeine and alcohol intake for at least 12 h and to abstain from any food or soft drink intake for at least 6 h.

The study was reviewed and approved by the Human Subjects Ethics Subcommittee of Hong Kong Polytechnic University (approval No. HSEARS20141017004) and written informed consent was obtained from each participant.

Image acquisition

All ultrasound examinations were performed by two trained researchers (SPYS and PSCW) in the Hong Kong Polytechnic University, using an HD11 XE ultrasound unit (Philips Medical Systems, Bothell, WA, USA), according to published procedures for measuring mesenteric fat.[5,11,15] Briefly, a Philips C8-5 MHz broadband curved transducer (Philips Medical Systems) was used to perform a complete survey around the paraumbilical area. Due to the highly reflective nature of peritoneal surfaces, mesenteric fat appears as elongated structures with strong echoes in the periphery called mesenteric leaves. The mesenteric leaves are separated by echoic peritoneal surfaces, and tiny blood vessels of approximately 1–2 mm diameter are visible within the spaces between the echoic peritoneal surfaces. The mesenteric leaves, unlike small bowel loops, show no peristalsis. In the present study, MFT was defined manually as the perpendicular distance between two successive mesenteric leaves. Approximately 7–9 measurements were made on each ultrasound examination and the mean of the three thickest mesenteric leaves was used for analysis (Figure 1).

Brachial artery FMD was calculated by measuring brachial artery diameter using a Philips L12-5 MHz linear transducer (Philips Medical Systems) as follows. Subjects were instructed to rest for at least 10 min prior to measurements, to ensure a stable vascular condition. Measurements were obtained with subjects lying a supine position with the right arm slightly abducted from the body, and the transducer was placed at a position 5–10 cm above the antecubital fossa, as previously described.[16] Longitudinal images of the right brachial artery were visualized under B-mode ultrasound. The lumen diameter of the artery was defined as the perpendicular distance between the near wall and far wall of the tunica media. Anatomical landmarks were clearly identified to ensure consistency of the imaging plane and image quality throughout the whole examination.

Baseline brachial lumen diameter was measured without applying a sphygmomanometer cuff. To measure reactive lumen diameter, a sphygmomanometer cuff (Omron Corporation) was placed on the right forearm, 1–2 cm distal to the elbow crease.[17] Cuff occlusion pressure was set at 50 mmHg above the systolic blood pressure of each subject for a duration of 5 min. Occlusion duration was set at 5 min, as FMD has been shown to increase linearly with increasing cuff occlusion durations up to 4.5 min.[17] Following cuff deflation, vasodilation was noted and the brachial artery reactive lumen diameter was measured at intervals of 30 s, 60 s, 90 s, 120 s, 150 s and 180 s following pressure cuff release. Baseline (Figure 2a) and reactive (Figure 2b) lumen diameters were determined during diastole. Brachial artery FMD was calculated as the mean of three measurements of reactive lumen diameter change from baseline expressed as a percentage of baseline diameter: ([maximal lumen diameter during reactive phase – baseline lumen diameter] / baseline lumen diameter) $\times$ 100.

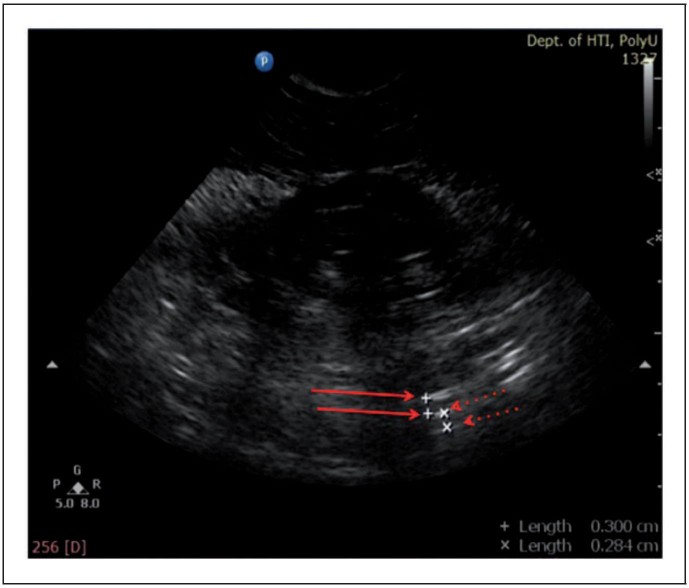

Figure 1. Representative grey-scale sonogram from a healthy Chinese male young adult, showing measurement of mesenteric fat thickness: the periphery of mesenteric leaves and mesenteric fat thickness were measured using callipers, and defined as the perpendicular distance between two successive mesenteric leaves. Two layers of mesenteric leaf thickness were determined by the distance between two '+' markers (solid line arrow) and between two 'x' markers (dotted line arrow), corresponding to 3 mm and 2.84 mm, respectively, in the present figure

A Philips L12-5 MHz linear transducer was also used for carotid intima media thickness measurements. Near and far arterial walls were displayed as two white lines separated by a hypoechogenic space. Measurements were taken at the thickest point on the far wall of the distal common carotid artery, approximately 1 cm proximal to the bifurcation of the common carotid artery, in a plaque-free section.[18] The carotid intima media thickness was determined as the distance between the leading edge of the first hyperechogenic line of the posterior wall (the lumen-intima interface) and the leading edge of the second hyperechogenic line (the media-adventitia interface). Measurements were taken in triplicate during diastole on the left and right common carotid arteries, and the mean of the three largest carotid intima media thickness values was used for screening. Subjects with carotid intima media thickness >0.8 mm (the cut-off value for a marker of cardiovascular risk) were excluded from the study, as previously described.[14]

Statistical analyses

The primary objective of the study was to determine if there was a correlation between brachial artery FMD and MFT. Using G*Power statistical software, version 3.1 for Windows® (www.gpower.hhu.de),[19] the required sample size was estimated to be 34 subjects with alpha $= 0.05$, power $= 80\%$, coefficient of determination $R^2 = 0.2$, and a two-tailed design.

Interclass and intraclass correlation coefficient (ICC) analyses were used to confirm that inter- and intrarater reliability of the

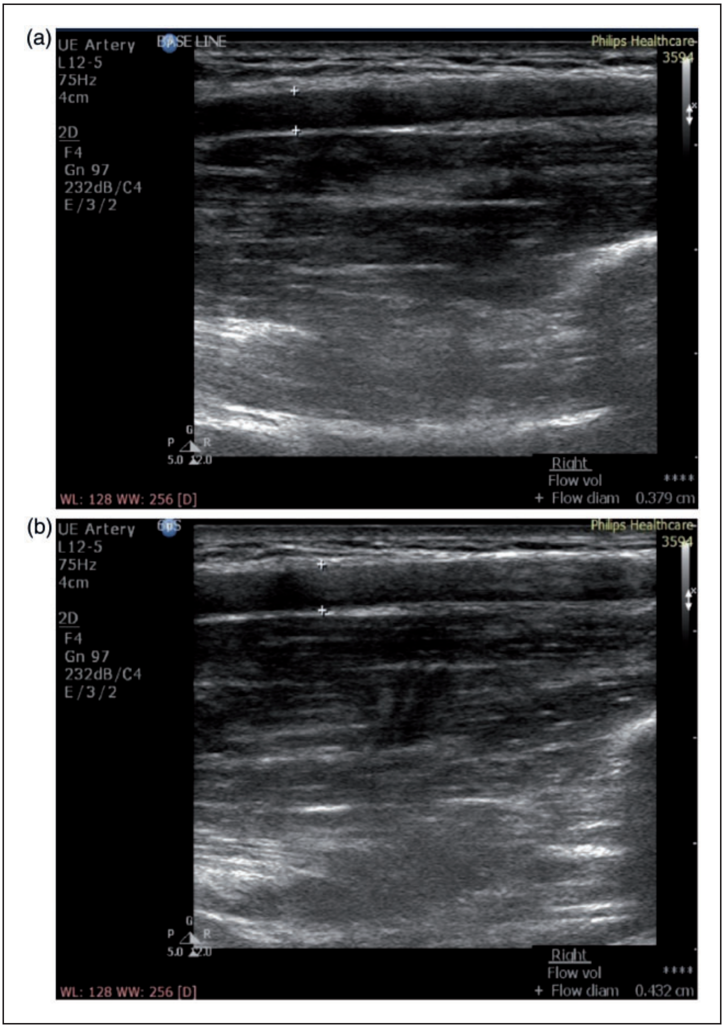

Figure 2. Representative grey-scale sonograms from a healthy Chinese male young adult showing measurement of: (a) baseline diastolic brachial artery diameter, where lumen diameter was defined as the perpendicular distance between the tunica media of the near and far artery wall (shown between the callipers '+'), corresponding to 0.379 cm in the present figure; and (b) reactive diastolic brachial artery diameter (during hyperaemia), obtained 60 s following deflation of a sphygmomanometer cuff at 50 mmHg above the systolic blood pressure of the subject for a duration of 5 min, corresponding to 0.432 cm (shown between the callipers '+'). Thus, brachial artery FMD for this patient was 14%

ultrasound measurements made by two trained researchers did not exceed 0.9.[20] Normality of the datasets was assessed using Shapiro–Wilk test. MFT data with skewed distribution were logarithmically transformed (Log (MFT) prior to statistical analyses. Associations between brachial artery FMD and BMI or Log (MFT) were analysed using Pearson's correlation coefficient. Stepwise multiple linear regression analysis was used to test whether BMI and Log (MFT) were independent determinants

Table 1. Demographic and clinical characteristics of 34 healthy Chinese male young adults.

	Study cohort data			
Characteristic	Mean ± SD	Median	Minimum–Maximum	Statistical significance
Age, years	21.4 ± 1.3	—	19.0–26.0	NS
CIMT, mm	0.4 ± 0.1	0.4	0.3–0.7	NS
BMI, kg/m^2	21.7 ± 3.2	20.8	15.5–30.3	NS
Brachial FMD, %	12.5 ± 3.5	12.7	6.2–18.6	NS
MFT, mm	3.8 ± 1.2	3.4	2.2–6.7	$P < 0.05$
Log (MFT), mm	0.6 ± 0.1	0.5	0.3–0.8	NS

BMI, body mass index; FMD, flow-mediated dilation; CIMT, carotid intima media thickness; MFT, mesenteric fat thickness; Log, logarithmic scale.
NS, not statistically significant ($P > 0.05$; Shapiro–Wilk test for normality).

of brachial artery FMD: BMI and Log (MFT) were the independent variables and brachial artery FMD was the dependent variable in the model.

Data analyses were performed using IBM SPSS software, version 19.0 (IBM Corp, Armonk, NY, USA) for Windows®. A two-tailed P-value <0.05 was considered to indicate statistical significance.

Results

A total of 34 healthy Chinese male volunteers, aged 19–26 years, were recruited for the study, among whom, three were underweight (BMI $< 18.5\,kg/m^2$), 21 had a BMI in the range 18.5–22.9 kg/m^2, six had BMI in the range 23.0–24.9 kg/m^2 and four were overweight (BMI, 25.0–29.9 kg/m^2). All ICC scores ranged from 0.90–0.99, indicating a reliability of >90% for ultrasound measurements.

Clinical and demographic characteristics are presented in Table 1. Shapiro–Wilk test for normality showed that the MFT dataset was negatively skewed ($P < 0.05$) and so Log (MFT) values were used in subsequent statistical analyses (Table 1).

Using Pearson's correlation coefficient test, brachial artery FMD was found to have a statistically significant inverse relationship with BMI ($P = 0.027$) and with Log (MFT) ($P = 0.003$; Figure 3). Stepwise multiple linear regression analysis showed that Log (MFT) was the only independent predictor for brachial artery FMD ($P = 0.003$) and approximately one-third of the sample were found to fit into this liner regression relationship ($R^2 = 0.267$; Table 2). The unstandardized coefficient (i.e., how much the dependent variable varies with the independent variable when all other independent variables are held constant) indicated that for every 1 unit of Log (MFT) increase, 13.724 units of brachial artery FMD would decrease.

Discussion

In the present study, sonographically measured MFT, and not BMI, was shown to be an independent predictor of brachial artery FMD, suggesting that assessment of central obesity may be more useful than general obesity and BMI in predicting early signs of CVD and its ensuing complications. To the authors' knowledge, the present study is the first to demonstrate a correlation between MFT and brachial artery FMD in healthy Chinese young adults using ultrasound techniques, and measurements were shown to

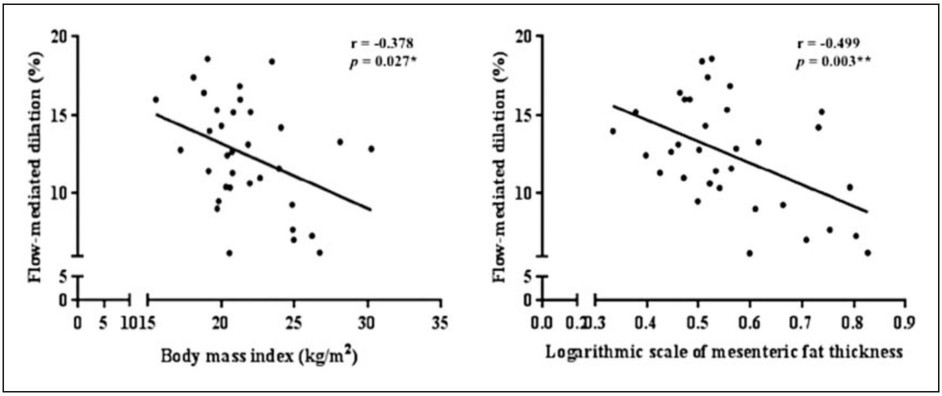

Figure 3. Pearson's correlation coefficient analysis of the association between brachial artery flow-mediated dilation and body mass index or Log mesenteric fat thickness in healthy Chinese male young adults ($n = 34$): brachial artery flow-mediated dilation exhibited a statistically significant inverse relationship with both variables (*body mass index, $P = 0.027$ and **Log [mesenteric fat thickness], $P = 0.003$)

Table 2. Stepwise multiple linear regression analysis to determine whether body mass index (BMI) and sonographically measured mesenteric fat thickness (MFT) are independent determinants of brachial artery flow-mediated dilation in 34 healthy Chinese male young adults.

	Coefficient of Determination					
Parameter	R^2	Adjusted R^2	Unstandardized Coefficient	Standardized Coefficient	t	Statistical Significance
Log (MFT)	0.267	0.220	−13.724	−0.499	−3.259	$P = 0.003$
BMI	n/a	n/a	n/a	−0.157	−0.886	NS

Log, logarithmic scale; n/a, not assessed.
NS, not statistically significant ($P > 0.05$).

have excellent reliability between two investigators (all ICCs >0.9).[20]

Although BMI provides a rough estimate of obesity-associated chronic disease risk,[21] it does not assess body composition. The expansion of visceral fat mass in humans represents a progressive pathological status largely characterized by increasing production of pro-inflammatory molecules including interleukin (IL)-6 and tumour necrosis factor (TNF)-α, which are implicated in the development of CVD and overt disease states, such as type 2 diabetes mellitus.[22] The majority of fat storage occurs in the subcutaneous compartment of the body (approximately 80% of total body-fat mass), however, free fatty acids, C-reactive protein, IL-6 and TNF-α are at higher levels in visceral fat compared with subcutaneous fat.[12] These inflammatory cytokines in visceral fat augment endothelial reactive oxygen species production, leading to reduced nitric oxide bioavailability and impaired bioactivity of the endothelial isoform of nitric oxide synthase, resulting in loss of vascular motile phenotypes.[6] In accordance with these findings, the present study showed that increased MFT was associated with decreased brachial artery FMD. These results suggest that sonographic examinations of MFT may confer a non-invasive means of predicting brachial artery FMD, and may, therefore, be useful as a prognostic indicator for CVD.

The results of the present study may be limited by several factors. First, the study included a convenience sample of male student volunteers, possibly conferring a systematic bias, and may not fully represent the entire population. Secondly, a previously published study of ultrasound mesenteric fat measurements by the present authors,[11] demonstrated that thicker mesenteric fat was positively correlated with the presence of several cardiovascular risk factors including total cholesterol, low-density lipoprotein cholesterol, triglycerides and fasting plasma glucose.[11] These factors, and other relevant demographic details (e.g., waist-to-hip ratio), were not investigated in the present study, and thus, the present authors suggest that further studies are required to collect more demographic data from the subjects, together with additional biochemical and haemodynamic markers. Thirdly, because men tend to have higher visceral fat volume and thicker mesenteric fat depots than women,[11] only male subjects were recruited. The present results, therefore, need to be confirmed in female subjects. Fourthly, the present study was limited to the measurement of endothelium dependent dilation, and did not measure glyceryl trinitrate or methacholine induced dilation for the determination of endothelium independent vasodilation.[9,10] Finally, the absence of an automatic measurement system for tracking the vessel wall and MFT, and the lack of adjustment on brachial artery FMD using blood flow data at reactive hyperaemia, may have contributed to measurement bias.

In conclusion, the present study showed a statistically significant association between sonographically measured MFT and brachial artery FMD in a sample of healthy Chinese young male adults. The present results suggest that sonographic surveillance of MFT may be a useful tool in the assessment of cardiovascular risk.

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Declaration of conflicting interests

The authors declare that there are no conflicts of interest.

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