Journal of Clinical Lipidology (2017) ■, ■–■

Journal of Clinical Lipidology

Original Article

Changes in truncal obesity and fat distribution predict arterial health

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KEYWORDS:
Truncal obesity;
Body mass index;
Dual-energy X-ray absorptiometry;
Arterial stiffness;
Pulse wave velocity

BACKGROUND: Truncal obesity is associated with metabolic syndrome and cardiovascular risk. Although vascular health is influenced by weight, it is not known whether changes in fat distribution modulate arterial function.

OBJECTIVE: We assessed how changes in truncal (android) fat at 1 year affect arterial stiffness and endothelial function.

METHODS: We recruited 711 healthy volunteers (235 males, age 48 ± 11 years) into the Emory Predictive Health Study; 498 returned at 1 year. Measurements included anthropometric and chemistry panels, fat mass using dual-energy X-ray absorptiometry, arterial stiffness indices (pulse wave velocity [PWV], augmentation index [AIx], and subendocardial viability ratio [SEVR]; Sphygmocor), flow-mediated dilation (FMD), and reactive hyperemia index (Endo-PAT).

RESULTS: At baseline, measures of body mass correlated with PWV, AIx, SEVR, and FMD. In a multivariable analysis including body mass index (BMI) and traditional risk factors, BMI remained an independent predictor of PWV, AIx, SEVR, and FMD. In a model including BMI and measures of fat distribution, android fat remained an independent predictor of PWV ($\beta = 0.31$, $P = .004$), AIx ($\beta = 0.24$, $P = .008$), and SEVR ($\beta = -0.41$, $P < .001$). The 1-year change in android fat correlated negatively with change in SEVR ($\beta = -0.13$, $P = .005$) and FMD ($\beta = -0.13$, $P = .006$) after adjustment for change in gynoid fat.

CONCLUSION: In addition to BMI, android fat is a determinant of arterial stiffness, independent of traditional risk factors. Changes in android fat over time are associated with simultaneous changes in vascular function, indicating fat distribution's effect on vascular health.

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Submitted May 2, 2017. Accepted for publication August 23, 2017.

1933-2874/
http://dx.doi.org/10.1016/j.jacl.2017.08.013

Introduction

Excessive abdominal or visceral fat, known as truncal obesity, is associated with metabolic syndrome and cardiovascular risk.[1–5] Obesity and the metabolic syndrome contribute to a systemic proinflammatory and oxidized milieu leading to arterial stiffness and endothelial dysfunction. Adipokines are associated with upregulation of profibrotic factors and promote the synthesis of proteins in the extracellular matrix of the vessel wall.[6–8] Furthermore, dysfunctional perivascular adipose tissue is related to a local proinflammatory state.[9,10] Recent data suggests that changes in visceral fat may influence cardiovascular risk factors.[11] Specifically, increasing visceral fat over time has been associated with a higher likelihood of hypertension, hyperlipidemia, and metabolic syndrome.[12] Vascular endothelial dysfunction is a precursor for the development of atherosclerosis and predicts incident risk of cardiovascular morbidity and mortality.[13,14] Although arterial health is influenced by weight, it is not known whether changes in fat distribution modulate arterial function. In our study, we hypothesized that changes in truncal (android) fat as measured by dual-energy x-ray absorptiometry (DXA) would predict changes in arterial stiffness and endothelial dysfunction.

Methods

Seven hundred eleven healthy volunteers (469 females and 235 males, mean age 48 ± 11 years) were recruited as part of the Predictive Health Institute from December 2007 to December 2010 at the Emory-Georgia Tech Center for Health Discovery and Well Being. At the baseline visit, each subject was assigned a health partner trained to use subjects' data profiles and collaboratively generate a health goal and personalized action plan at each visit. Participants with acute illness, cerebrovascular disease, heart failure, and coronary or valvular heart disease were excluded. Vascular testing and blood draws were performed after an overnight fast. Four hundred ninety-eight subjects returned at 1 year for repeat testing. The study was approved by the Emory University Institutional Review Board and informed consent was obtained from all subjects. Our analysis is a substudy of the overall Emory Predictive Health Initiative focused on the evaluation of cardiovascular risk factors and risk factor reduction in a relatively healthy population.

Hypertension, hypercholesterolemia, and diabetes mellitus were self-reported by questionnaire on each examination. Medication lists were reviewed and subjects were reclassified as having hypertension, hypercholesterolemia, or diabetes mellitus if the medication list reflected medications treating these conditions. Tobacco use was self-reported by questionnaire on each examination. Blood pressure was measured in the seated position 3 times at 5-minute intervals by an automatic device (Omron, Kyoto, Japan) and documented as the mean value. Fasting lipid profile, metabolic panel, and high-sensitivity C-reactive protein were measured at each visit (Quest Diagnostics, Madison, NJ). The 10-year risk of coronary death or nonfatal myocardial infarction was estimated by the Atherosclerotic Cardiovascular Disease in Adults pooled cohort equations.[15]

Body mass index (BMI) was calculated as weight in kilograms/height in square meters. Waist and hip circumferences were measured in centimeters and recorded as the mean of 2 measurements. The waist-to-hip ratio was calculated by dividing the mean waist circumference by the mean hip circumference at each visit. Body composition variables were calculated by DXA (GE Lunar Densitometry, iDXA). DXA is considered a gold standard for body composition analysis and can identify whole-body fat mass within 2% coefficient of variation.[16] The android region included an area from the top of the iliac crest to 20% of the distance from the iliac crest to the bottom of the subject's head. The gynoid region extended from the top of the greater trochanter down a distance twice the height of the android region.[17] Measures of android and gynoid fat were reported as fat mass in kilograms from which the android-to-gynoid fat ratio was derived.

Endothelium-dependent brachial arterial flow-mediated dilation (FMD) is a noninvasive measure of conductance vessel endothelial function and nitric oxide bioavailability and its measurement has been previously described.[18,19] In our laboratory, the mean difference in FMD between assessments performed in 11 subjects on consecutive days was 1.26% (standard deviation [SD] 0.76), with a correlation coefficient of 0.75. The mean difference in the FMD between 2 readings of the same 11 measurements was 0.82% (SD 0.48, r = 0.97).

Pulse wave velocity (PWV), the central augmentation index (AIx), and the subendocardial viability ratio (SEVR) are measured by application tonometry and provide noninvasive indices of arterial stiffness, arterial wave reflections, and myocardial workload and perfusion, respectively. Both PWV and AIx are independent predictors of adverse cardiovascular outcomes.[20] SEVR has been associated with coronary artery disease and decreased coronary flow reserve.[21] PWV, AIx, and SEVR were estimated by the SphygmoCor device (AtCor Medical, Australia), which records pressure waveforms peripherally using a high-fidelity tonometer.[19,22,23] AIx was standardized to a heart rate of 75 beats/min and divided by the subject's height yielding a height and heart rate–corrected value (AIx). Reproducibility studies in our laboratory on 9 subjects on consecutive days have demonstrated a coefficient of variation of 3.8%, 13.8%, and 20.3% for PWV, SEVR, and AIx, respectively.[22]

The reactive hyperemia index (RHI) provides an index of postischemic microvascular vasodilation that is reflective of endothelial function. Low RHI is associated with adverse cardiovascular events.[24] Digital pulse amplitude tonometry is a plethysmographic device allowing detection of pulsatile arterial volume changes by a pressure transducer (Endo-PAT; Itamar Medical, Israel).[25] Full details of the probe