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Comparison of regional body composition and its relation with cardiometabolic risk between BMI-matched young and old subjects

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ABSTRACT

Objective: Difference in regional body composition between young and old people may be related with differential cardiometabolic risks. We investigated regional body composition in BMI-matched young and old subjects to compare its relation with cardiometabolic risk.

Methods: We recruited 1:3 gender- and BMI-matched 86 young subjects (mean age 27.3 ± 2.9 years) and 258 older subjects (75.6 ± 8.2 years) from a community. Abdominal visceral (VAT) and subcutaneous adipose tissue (SAT) and muscle area at mid-thigh level were evaluated by computed tomography. Fat depots in the gynoid area and lower extremity were measured by dual energy X-ray absorptiometry. Adiponectin, retinol binding protein-4 (RBP-4), and C-reactive protein (CRP) concentrations, pulse wave velocity (PWV) and ankle-brachial index (ABI) were measured for cardiometabolic risk.

Results: VAT was greater in older subjects while SAT was almost the same, resulting in twice higher VAT/SAT ratio in older men and women (1.03 ± 0.37 and 0.57 ± 0.18) than younger counterparts (0.55 ± 0.24 and 0.23 ± 0.23) (both $P < 0.01$). Fat mass in the gynoid area and lower extremity was smaller in older subjects than younger subjects. The VAT correlated with adiponectin level negatively and RBP-4 level positively while gynoid fat correlated with them in opposite direction. The CRP levels negatively correlated with mid-thigh muscle in older subjects. Older subjects had higher PWV and lower ABI compared to BMI-matched younger counterparts.

Conclusion: In conclusion, older adults in this cohort had increased visceral fat and decreased gynoid and lower extremity fat, along with less muscle mass. These findings may help explain the worse cardiometabolic profiles in the elderly who have the same BMI as the young.

1. Introduction

Compositional changes associated with aging point to possible differences in body fat distribution, metabolic profile, and the degree of associated cardiovascular and metabolic risks between young and old people [1]. Thus, regional fat distribution, rather than overall fat volume, is considered to be more important in understanding the link between obesity and cardiometabolic disorders [2,3].

Although body mass index (BMI) has long been an important tool in approximating obesity and metabolic derangement [4], it has a limited value in distinguishing between fat and muscle mass and identifying regional body composition. Since various adipose

Abbreviations: VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; DXA, dual energy X-ray absorptiometry; CT, computed tomography; CRP, C-reactive protein; RBP-4, retinol binding protein-4; PWV, pulse wave velocity; ABI, ankle-brachial index.

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tissue depots are known to have different biologic functions [5] the same BMI can mask different cardiometabolic risk profiles. A recent large prospective study has demonstrated an increased risk of coronary heart disease with increasing BMI within the normal range of BMI [6].

Currently, advanced technologies with computed tomography (CT) or dual energy X-ray absorptiometry (DXA) can be used to measure regional fat mass. CT has an advantage in distinguishing between visceral (VAT) and subcutaneous adipose tissue (SAT) [5], which are pertinent given the sizable differences in VAT between individuals with the same BMI [7]. There is substantial evidence linking VAT with metabolic abnormalities as well as full-blown manifestations of cardiovascular diseases [8,9]. DXA can measure gynoid (lower body or peripheral) fat compartments. In contrast to VAT, gynoid fat may induce metabolic benefits by increasing energy consumption [10]. Many studies with simple anthropometric measurements have given more weight to the central adiposity in the association with cardiometabolic risks [4], but studies directly characterizing gynoid fat in cardiometabolic perspective are limited.

Some studies show aging is associated with gain of fat mass and loss of muscle mass [3]. However, other studies show inverse correlation between aging and fat mass [11]. Most of these studies employed indirect methods like bioelectrical impedance for body composition measurement and did not control for BMI.

Recently, various diagnostic methods have been used to investigate the presence of atherosclerosis in asymptomatic subjects. Pulse wave velocity (PWV) has been frequently used as an index of atherosclerosis because it is very simple, reproducible, and noninvasive [12]. The ankle brachial index (ABI) is also a surrogate marker for generalized atherosclerosis because lower levels have been associated with risk of coronary and cerebrovascular diseases [13].

Based on these findings, we hypothesized that there would be a sizeable difference in visceral and subcutaneous fat and muscle mass between young and old people with the same BMI, which might contribute to varying degrees of cardiometabolic risks. For this, we investigated the whole and regional body composition in gender-specific, BMI-matched young and old subjects and compared how different fat characteristics contribute to varying cardiometabolic risk and subclinical atherosclerosis.

2. Methods

2.1. Study subjects

The Korean Longitudinal Study on Health and Aging (KLoSHA) began at Seongnam city in 2005 and consisted of two groups: 1) 1000 elderly subjects aged over 65 years for original cohort and 2) 100 healthy young subjects aged 20–35 years as a young adult reference group. The proportion of people aged ≥65 in Seongnam was 6.2%. Anticipating a low response rate in the oldest group aged ≥85, we have recruited subjects in two stages. In the first stage, 698 people were recruited using age and sex-stratified random sampling from a roster of 56,993 people aged 65–84 years. In the second state, we contacted everyone aged ≥85 ($n = 3459$) and 302 subjects were enrolled for this group. In all, 439 men and 561 women were enrolled in KLoSHA. Detailed information about recruitment has been published previously [14]. At the same time, 100 healthy young subjects aged 20–35 years were recruited from the same community as a young adult reference group for KLoSHA. None of the study subjects had been previously diagnosed with cardiovascular disease or any chronic wasting diseases such as malignancy, tuberculosis, and malnutrition. After excluding 14 subjects whose weight changed more than 3 kg in the 3 months prior to analysis, 39 males and 47 females were included in the current study.

Based on these 39 male and 47 female young subjects, 117 male and 141 female older participants from KLoSHA were randomly obtained by 1:3 BMI-matching by using a range of ±0.5 kg/m^2. Demographics and biochemical characteristics of the selected subjects were similar to the cohort population. This study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (SNUBH, B-0609/037-014). Written informed consent was also obtained from every subject.

2.2. Anthropometric and biochemical parameters

Height, body weight, and waist circumference were measured by standard methods. Various biochemical parameters and surrogate indices of cardiometabolic risk were evaluated. A 75-g oral glucose tolerance test (OGTT) was done and fasting and postload 30, 60, 90 and 120 min glucose levels were measured. Area under the curve for glucose ($AUC_{glucose}$) was calculated by a trapezoidal method. Plasma insulin concentration was measured by radioimmunoassay (Linco, St Charles, MO, USA). The homeostasis model assessment of insulin resistance (HOMA-IR) and beta-cell function (HOMA-B) was calculated as reported previously [15]. HbA_{1c} was measured by Bio-Rad Variant II Turbo HPLC analyzer (Bio-Rad, Hercules, CA) in SNUBH, the National Glycohemoglobin Standardization Program (NGSP) level II certified laboratory. Fasting plasma concentrations of lipids were measured on a Hitachi 747 chemistry analyzer (Hitachi, Tokyo, Japan). Circulating adiponectin and retinol binding protein-4 (RBP-4) concentrations were measured using enzyme-linked immunosorbent assay kits (AdipoGen, Seoul, Korea). The concentration of hsCRP was measured by immunonephelometry (Dade Behring, Marburg, Germany).

After taking the average of two consecutive systolic/diastolic blood pressure (SBP/DBP) measurements, hypertension was defined as ≥140/90 mmHg or taking antihypertensive medication. Diabetes mellitus (DM) was defined as ≥126 mg/dL of fasting or ≥200 mg/dL of postload 120 min glucose or taking antidiabetic medication.

2.3. Abdominal and thigh fat and thigh muscle areas by CT scan

CT images were obtained using a 64-detector-row machine (Brilliance; Philips Medical Systems, Cleveland, OH, USA). Fat and muscle areas were identified as tissues with attenuation from −190 to −30 Hounsfield units (HU) and 30–100 HU, respectively, using a commercially available software (Rapidia 2.8; Infinitt Co., Seoul). At the level of the umbilicus, VAT was defined as fat area inside the abdominal wall musculature. After subtracting VAT from the total fat area at the umbilicus, the remainder was defined as SAT (Fig. 1B). Muscle and fat areas were also measured at the mid-thigh (Fig. 1C).

2.4. Regional body composition analysis by DXA

Regional body composition was measured with a DXA (Lunar, GE Medical systems, Madison, WI, USA). Precision was excellent for lean tissue mass (root mean square of 0.21 kg; coefficient of variation [CV] of 0.4%). A high correlation between consecutive measurements was observed for all three compartments of body composition: total body bone mineral content, lean mass, and fat mass (standard error ranges: 0.993–1.002, all $r^2 = 0.99$). We used a workstation program (GE Medical systems) to analyze regional body composition. The regions of interest (ROI) for regional body composition were identified using the following criteria (Fig. 1A):

- Trunk ROI (T): from the pelvis cut to the neck cut.
- Android ROI (A): from the pelvis cut to above the pelvis cut by 20% of the distance between the pelvis and neck cuts.