Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. ■, no. ■, 1–9, 2016

1094-6950/■:1–9/$36.00
http://dx.doi.org/10.1016/j.jocd.2016.07.009

Original Article

Muscle Mass and Body Fat in Relation to Cardiovascular Risk Estimation and Lipid-Lowering Eligibility

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Abstract

This cross-sectional population-based study aimed to evaluate the relationships of muscle-mass and body-fat phenotypes to 10-yr risk of cardiovascular disease (CVD) events and eligibility for lipid management. Participants were Korean adults (N = 7315; 3163 men, 4152 women) aged 40–79 yr, free from stroke and coronary heart disease, who provided complete data for estimating 10-yr CVD risk and body composition during the Fifth Korea National Health and Nutrition Examination Survey (2009–2010). Four levels of combined muscle mass and body fat were determined using sex-specific quintiles of appendicular skeletal muscle mass divided by height squared, and sex-specific quintiles of total body fat percentage. Ten-year CVD risk was calculated using Pooled Cohort Equations and Framingham risk scores. Lipid-lowering medication eligibility was determined using American College of Cardiology/American Heart Association (ACC/AHA) and Adult Treatment Panel (ATP) III guidelines. Compared with the reference group, the risk of CVD events was higher in men with low muscle mass, high body fat, or the 2 factors combined. CVD risk was lower in women with low muscle mass, higher in women with high body fat, and nonsignificant in women with the 2 factors. Participants with low muscle mass and high body fat had higher odds for medication eligibility using the ACC/AHA guidelines but not the ATP III guidelines. Higher estimated 10-yr CVD risk was associated with combined phenotypes of low muscle mass and high fat in men but not in women. Also, the relationship of these phenotypes to lipid-lowering medication eligibility was guideline-specific.

Key Words: Body composition; cardiovascular disease risk; fat mass; lipid-lowering medication; muscle mass.

Introduction

Phenotypes combining lower muscle mass with higher body fat could confer a higher risk of cardiovascular disease (CVD) *(1)*. High levels of body fat play a major role in the development of CVD risk factors, including hypertension, dyslipidemia, and diabetes mellitus, as well as in increasing the risk of developing CVD *(2)*. Because the muscular system and other body systems, including endocrine and cardiovascular systems *(3)*, are interrelated, lower muscle mass also could adversely affect CVD.

Received 05/23/16; Revised 07/29/16; Accepted 07/29/16.
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However, evidence is insufficient that shows the relationship between the combination of lower muscle mass and higher body fat and the risk of CVD. Although cross-sectional, population-based studies have found combined phenotypes of lower muscle mass with obesity or nonobesity to be positively associated with cardiometabolic risk factors *(4–8)* and elevated Framingham coronary heart disease (CHD) risk scores *(9)*, prospective studies in the elderly did not find the combined phenotype group to be at higher risk of cardiovascular events *(10,11)*.

Because of the paucity of evidence showing the relationship between these combined phenotypes and CVD risk, we hypothesized that evaluating these relationships using a recently analyzed estimation of CVD risk *(12)*, as well as of individuals eligible for lipid-lowering treatment, would uncover valuable information on the health consequences of those combined phenotypes. Therefore, the present study investigated the relationships between combined muscle

mass and body fat phenotypes with 10-yr risk of a hard atherosclerotic cardiovascular disease (ASCVD) event, defined as a nonfatal myocardial infarction or CHD death, or fatal or nonfatal stroke *(12)* and CHD development *(13)*. The present study also examined these phenotypes for their relationship to eligibility for lipid management using data from the Fifth Korea National Health and Nutrition Examination Survey (KNHANES).

Methods

Study Participants

The participants were a representative sample of the civilian, noninstitutionalized Korean population of KNHANES, conducted in 2009–2010. The survey used a multistage, stratified, systematic sampling method and a rolling survey sampling design of household units. The current study included 7315 Korean adults from KHNANES (3163 men and 4152 women), aged 40–79 yr *(14,15)*, who were not diagnosed with stroke, angina pectoris, or myocardial ischemia and who provided information required for estimating a 10-yr risk of ASCVD and CHD and body composition. All participants signed an informed consent and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in the a priori approval by the institution's human research committee *(16)*.

Measurements of Muscle Mass and Body Fat

Whole-body dual-energy X-ray absorptiometry (Discovery QDR4500W; Hologic Inc., Bedford, MA) was used to measure total fat mass, total fat-free mass, and fat-free mass and bone mass at the 4 extremities. The within-day percentage coefficients of variation for duplicate measurements in 30 adults were 0.84–2.29 among 4 examiners. Appendicular skeletal muscle mass (ASM, in kilogram) was calculated as (fat-free mass at the 4 extremities – bone mass at the 4 extremities)/height squared (in square meter) using the formula of Baumgartner et al *(17)*. Two muscle groups were established: those with low muscle mass and those with normal muscle mass. The 2 groups were respectively assigned to 2 lower and 3 upper sex-specific quintiles of ASM/height^2 found in the study population *(18)*. Total fat percentage was calculated as total fat mass/(total fat mass + total fat-free mass) × 100. Individuals with normal body fat and high body fat were categorized based on the 3 lower and 2 upper sex-specific quintiles of total fat percentage in the study population, respectively *(18)*. Consequently, the 4-level study groups consisted of a reference group, a low-muscle-mass group, a high-body-fat group, and a combined low-muscle-mass and high-body-fat group.

Calculation of 10-Yr Risks of ASCVD and CHD and Determination of Lipid-Lowering Medication Eligibility

Blood pressure was measured 3 times using a standard manual sphygmomanometer with the participants seated. The average of the second and third blood pressure values was used for the analyses. Body mass index was calculated as weight (kg)/height (m)^2 and measured according to standard procedures. Antecubital venous blood samples were taken from each subject after a 12-h overnight fast. The levels of high-density lipoprotein cholesterol (HDL-C), triglyceride, total cholesterol, and fasting glucose were measured using an automatic analyzer (Automatic Chemistry Analyzer 7600; Hitachi, Tokyo, Japan). The level of low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald equation *(19)* or directly measured in the blood when the triglyceride level was >5.65 mmol/L. Self-reported questionnaires were used to assess the participants' medical history (diagnosis and treatment) of hypertension, diabetes mellitus, angina pectoris, myocardial ischemia, and stroke as well as smoking status (current smoker vs noncurrent smoker). An individual was defined as having diabetes mellitus based on either a high fasting blood glucose level of ≥6.99 mmol/L, having been diagnosed with diabetes mellitus by a physician, or currently being treated for diabetes mellitus *(14,15)*.

The 10-yr risk of developing ASCVD was defined as the risk of developing the first ASCVD event (i.e., a nonfatal myocardial infarction or death due to CHD, or a fatal or nonfatal stroke) within a 10-yr period *(12)*. The risk of ASCVD was calculated using the Pooled Cohort Equations for non-Hispanic whites, which included age, total cholesterol level, HDL-C, systolic blood pressure, current smoking status, and presence or absence of diabetes mellitus for each sex. The 10-yr risk of CHD was calculated using the Framingham 10-yr risk assessment equations, which included age, sex, blood pressure, HDL-C, LDL-C, diabetes mellitus, and current smoking status *(13)*.

Individuals eligible for lipid-lowering medication were determined using the American College of Cardiology/American Heart Association (ACC/AHA) blood cholesterol guideline *(20)* and the National Cholesterol Education Program Adult Treatment Panel (ATP) III guidelines *(21)*. According to the ACC/AHA guideline, treatment-eligible groups were those with an LDL-C level of ≥4.92 mmol/L, those who were ≥40 yr old with diabetes, and those with an ASCVD risk of ≥7.5%. Based on the ATP III guidelines, treatment-eligible groups were those with a CHD risk >20% or diabetes, those with an LDL-C level of ≥4.92 mmol/L, those with a 10%–20% CHD risk and a LDL-C level of ≥3.37 mmol/L, and those with a CHD risk <10% and a LDL-C level of ≥4.14 mmol/L.

Statistical Analyses

All analyses were conducted separately by sex. Using a linear regression analysis, a linear trend was examined for the relationships of sex-specific quintiles of ASM/height^2 and total body fat percentage to 10-yr risks of ASCVD and CHD. The relationships between the 4-level study groups and 10-yr risks of ASCVD and CHD (and components of those risk formulae) were examined using a polynomial test (for a trend) and a Scheffé post hoc