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BMI vs. body composition and radiographically defined osteoarthritis of the knee in women: a 4-year follow-up study[1]

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Summary

Objective: To elucidate the role of body mass index (BMI) and knee osteoarthritis (OAK) by evaluating measures of body composition including fat mass and skeletal muscle mass (SMM).

Methods: Data are from 541 women enrolled in the Michigan Bone Health Study, a longitudinal, population-based study. At visits in 1998 and 2002, radiographs were taken of both knees and were evaluated for the presence of OAK (≥2 on the Kellgren–Lawrence (K–L) scale). Joint space width (JSW) was measured with electronic calipers. Fat mass and SMM were determined using bioelectrical impedance analysis.

Results: In 2002, the prevalence of OAK was 11% in this population of women whose mean age was 47 years. Fat mass, lean mass, SMM, waist circumference and BMI were greater in women with OAK compared to those without OAK. In multiple variable analyses adjusted for age, fat mass and SMM explained OAK prevalence and increasing OAK severity better than models with BMI; further SMM explained more variation than did fat mass. SMM was positively associated with level of left and right medial JSW while there was no consistent association of JSW and BMI or fat mass.

Conclusion: Fat mass and SMM were associated with K–L OAK score and the amount of joint space, with more variation explained by SMM. SMM was highly associated with JSW. Therefore, though obesity, frequently characterized by BMI, is a frequently reported risk factor for OAK, this mis-attribution may mean that interventions that focus on weight loss as treatment for osteoarthritis should be aware that this may negatively impact muscle mass.

Key words: Osteoarthritis, Body mass index, Body composition, Fat mass, Skeletal muscle mass.

Introduction

Obesity, usually characterized by body mass index (BMI), is considered a major risk factor for prevalent osteoarthritis (OA)[1–7]. Data from the Chingford general population survey suggest that women in the highest tertile of BMI have six-fold increased odds of knee osteoarthritis (OAK), and nearly 18 times increased odds of bilateral OAK, compared to women in the lowest tertile of BMI[3]. Longitudinal studies show that increased weight precedes the presentation of OAK. In a longitudinal study of men and women aged 40–64 years, Manninen *et al.*[5] found that every standard deviation (SD) increase in BMI (3.8 kg/m^2) was associated with a relative risk of 1.4 (95% CI, 1.2–1.5) for developing OAK.

However, not all obese persons develop OAK, nor are all individuals with OAK obese, suggesting that other factors aside from obesity, defined by BMI, are important. It has also been proposed that muscle mass or muscle strength is protective for the development of OA[8–10].

Because BMI is a measure of both fat and lean mass, the relative contribution of adipose tissue and muscle mass and their contribution to muscle strength, cannot be disaggregated. Studies limited to the use of BMI as a measure of body composition may unduly impede our understanding of the mechanisms associated with the development and progression of OAK. Use of BMI does not adequately provide a means of understanding the physiological role that could be relevant for OA including joint loading or more systemic biochemical factors. For example, muscle strength, assessed as torque, reflects the capacity to do work and is strongly influenced by body mass, but is differentially expressed with respect to skeletal muscle mass (SMM) vs. total body mass.

Based on an anticipation of the constraints of BMI, we related body composition measures to the development and progression of OA of the knee. We addressed the following hypotheses: (1) In middle-aged women, variation in the development and progression of radiographically determined OAK is better explained by individual body composition measures such as fat mass, SMM and waist circumference as compared to BMI, a generalized measure of obesity; and (2) body composition measures would explain more variation in two measures of OAK, including the osteophyte-based Kellgren–Lawrence (K–L) OA ordinal classification

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or the amount of joint space width (JSW) and its change than would BMI.

Materials and methods

STUDY POPULATION

This sample is from women enrolled in the Michigan Bone Health Study (MBHS), a longitudinal, population-based study conducted among women living in and around Tecumseh, Michigan. The sampling frames for the study were the historical family records of the Tecumseh Community Health Study (TCHS) which was a population-based, prospective cohort study established in 1959 to study the risk factors for common chronic and infectious diseases. Women eligible for MBHS were the daughters of TCHS participants who, in 1988, were between the ages of 20 and 40 years, not pregnant and premenopausal. These women were contacted using letters, telephone calls and in-person visits. There were 539 women successfully recruited into the MBHS, a participation rate in excess of 80%. In 1992, a second sampling frame based on a community census of Tecumseh was developed to include women whose parents had not participated in the TCHS. As a result, an additional 121 women in the desired age range of 24−44 years (of a possible 135 eligible) were recruited (90% participation rate), for a total of 660 participants.

Knee X-rays were taken as a part of the 1992, 1995/1996, 1998/1999 and 2002/2003 annual data collections, with the 1998 and 2002 collections taken using a semi-flexed positioning[11]. To avoid drawing conclusions that may be based on positioning alone, only the 1998 and 2002 time points are used for these analyses and included a total of 541 women. For the purposes of this study, women could be either lost or recovered between the 1998 and 2002 visits. However, the cohort was stable; of those women in the 1998 data set with OA and body composition measures, 88% of them had data in the 2002 group.

Further, women lost to follow-up or recovered were similar to each other in terms of OA prevalence, overweight prevalence and age. For example, of the women lost to follow-up (i.e., had data in 1998 but not in 2002), 13% of them had OA compared to 16% of those recovered in 2002. The weights were also similar: 62.1% of those lost to follow-up were overweight in 1998 (as defined by BMI $\geq$ 25) while of those recovered in 2002, 66% were overweight.

Women were ineligible for an annual data collection if they were pregnant; participants who were excluded for pregnancy became eligible again for subsequent data collection as long as they were not pregnant. The University of Michigan Institutional Review Board approved the study protocol, and written informed consent was obtained from each participant.

OA MEASURES

Weight-bearing anterio-posterior radiographs in a semi-flexed position[11] were taken of both knees using General Electric radiographic equipment (model X-GE MPX-80; General Electric Medical Systems, Milwaukee, WI, USA) and Kodak film (X-DA with Kodak rare earth intensifying screens, Eastman Kodak, Rochester, NY, USA). The source film distance was 40 inches and standard radiographic techniques were used. Radiographs were evaluated by at least two readers with a third consensus reader for the presence of OA defined by the K−L scale depicted in the Atlas of Standard Radiographs of Arthritis (0 = normal, 1 = doubtful OA, 2 = minimal OA, 3 = moderate OA, and 4 = severe OA)[12]. This scale is based on the degree of osteophyte formation, joint space narrowing, sclerosis, and joint deformity. OA was defined as the presence of at least one knee with a grade of 2 or higher. Apart from the K−L criteria, joints could also be classified as showing changes consistent with rheumatoid arthritis, missing or unable to evaluate.

To promote reproducibility over the period of observation, readers reviewed the K−L grading criteria and evaluation films that were representative of each K−L level of OA. There were 25 knee radiographs that were evaluated independently by each reader and their results were compared for consistency. After standardization procedures were completed, two readers (JJ, DJ), both board-certified musculoskeletal radiologists, independently evaluated X-rays and classified both knees. Scores from two readers were compared and any score that was not congruent was reread and, if necessary, subjected to consensus evaluation. Further, a sample of 110 knee radiographs that had been used in previous evaluations was again read to assess the potential for drift in scoring over time. Films were not read side-by-side to minimize the likelihood of having correlated errors.

JSW was measured on both the medial and lateral aspect of each knee radiograph with electronic calipers. Measurement locations were ascertained by identifying the centerline of each joint using the medial and lateral tibial condyle edge and then establishing points that were 50% and 75% between the centerline and the condyle edge. Ten percent of radiographs were remeasured for quality control. The 4-year difference in JSW was established by subtracting the JSW values in 1998 images from those ascertained in 2002.

BODY COMPOSITION MEASURES

Fat mass and SMM were determined from the impedance and conductance measures of the bioelectrical impedance analysis (BIA). BIA is based on measurement of the transmission speed of a 0.25 V electrical pulse between electrodes attached at the feet and across the knuckles of the hand. Because fat-free mass comprises water, proteins and electrolytes, conductivity is greater in fat-free mass than in fat mass[13]. Resistance and reactance are used to estimate total body water, and by extension, fat mass and lean mass, with the latter including bone[14]. The coefficient of variation percent of the resistance and reactance measures are less than 2% each in a reproducibility study of 20 women similar to the population being characterized. SMM was calculated by the method of Janssen[15] who subsequently indexed SMM to height for a skeletal muscle index (SMI) and developed cut points relating to the risk of disability associated with SMI[16]. These variables were available from annual assessments and were treated as time-varying covariates.

Weight and height, measured annually with a calibrated balance beam scale and stadiometer, were used to calculate BMI [weight (kg)/height (m)^2]. Waist circumference (cm) was measured annually with a non-stretching tape at the narrowest point of the mid-torso at maximum inhalation. Elbow breadth (cm) was assessed as an index of skeletal frame size using a Martin calipers.

DATA ANALYSIS

Univariate distributions of the eight continuous measures of body composition were examined for normality. To meet the assumptions of normality and to reduce skewness, natural log transformations were applied to the body composition measures of fat mass, SMM, and waist circumference. The frequencies of the K−L score for OAK and categorical covariates were examined overall and by year of visit.

Repeated measures mixed-effects logistic model (SAS, Proc NLMixed, SAS Institute, Cary, NC) was used to evaluate the relationship *across time* (i.e., between 1998 and 2002) between the presence of OAK (a dichotomous variable, K−L $\geq$ 2 vs. K−L $<$ 2) and continuous measures of BMI and body composition (fat mass, SMM, and waist circumference). Non-proportional odds models were used to evaluate the relationship *across time* between the (ordinal) K−L OA severity measure (scale) and measures of BMI and body composition (fat mass, SMM, and waist circumference). A random slope model was tested and found to be non-significant, so random intercept models were analyzed.

Analyses of covariance (ANCOVA) (SAS, Proc GLM, SAS Institute, Cary NC) were used to evaluate the relationship between measures of JSW for 2002 as well as changes from 1998 and measures of BMI and body composition (fat mass, SMM, and waist circumference) as well as age.

Covariates were retained in models if their inclusion changed the β coefficients by 10% or more. The appropriateness of model fitting was assessed both graphically and using model r^2 (for ANCOVA) and Akaike Information Criterion (AIC) for mixed-effects models.

Results

In 1998, the frequency of knee OA, defined as a K−L score $\geq$2 was 11.6% among women who had X-ray data at this visit. In 2002, the frequency of knee OA was 11% in the population of women whose mean age was 47 years (Table I). These frequencies differ slightly due to the fact

Table I
Age and body size characteristics of the MBHS population coincident with X-rays for OAK

	1998 (n = 485)		2002 (n = 483)	
	Mean	SD	Mean	SD
Age (years)	43.1	4.85	46.9	4.85
Body composition measures				
Fat mass (kg)	28.9	12.40	29.6	13.80
$_{log}$(Fat mass)	3.3	0.39	3.3	0.43
Lean mass (kg)	45.8	6.93	47.6	7.53
SMM (kg)	20.5	2.73	21.0	2.98
$_{log}$(SMM)	3.0	0.13	3.0	0.14
Waist circumference (cm)	85.9	14.40	89.3	15.40
$_{log}$(Waist circumference)	4.44	0.16	4.48	0.17
Elbow breadth (cm)	6.14	0.32	6.17	0.30
SMM:Fat mass ratio	0.81	0.29	0.83	0.33
BMI (kg/m^2)	28.3	6.23	29.00	6.85
$_{log}$(BMI)	3.32	0.21	3.34	0.23