Is Femur Length the Key Height Component in Risk Prediction of Type 2 Diabetes Among Adults?

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OBJECTIVE — To examine the diabetes risk association with femur length, standing height, and height without femur length (HWFL) (HWFL = standing height − femur length).

RESEARCH DESIGN AND METHODS — We used data from three time periods of the National Health and Nutrition Examination Survey (1999–2000, 2001–2002, and 2003–2004) for this cross-sectional analysis and confined the eligible subjects to 6,188 adults aged 20+ years who had fasted ≥8 h and had no missing values of femur length or standing height. The outcome measure was type 2 diabetes.

RESULTS — Multivariate logistic regression analyses indicated that the odds of type 2 diabetes per 1-SD value increase in femur length, standing height, and HWFL were 0.73 (95% CI 0.61–0.86), 0.91 (0.75–1.10), and 1.09 (0.90–1.32) for men, respectively, and 0.82 (0.70–0.97), 0.99 (0.82–1.21), and 1.11 (0.93–1.33) for women.

CONCLUSIONS — Our study supports the hypothesis that femur length may be the key height component in diabetes risk association.

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A number of studies have observed that adult height is negatively associated with the risk of glucose intolerance, type 2 diabetes, and gestational diabetes mellitus (1–4). It has been suggested that short stature, in particular, adult short-leg length in relation to trunk length, is an indicator of poor childhood environmental conditions (intrauterine and/or early childhood) (5). This is considered to have modified some metabolic pathways and thus influenced the risk of developing diabetes. Recently, osteocalcin, one of the very few osteoblast-specific proteins, has been discovered to have an endocrine regulation effect on glucose homeostasis (6). It was found that mice lacking osteocalcin displayed decreased pancreatic β-cell proliferation, glucose intolerance, and insulin resistance. Because the femur bone is the longest and the strongest of the human bones, it would theoretically be the most active bone with respect to modeling and remodeling. It is possible that the observed negative association between adult height and the risk of diabetes is mainly determined by the altered length of the femur bone. People with a longer femur bone may be more likely to have a higher level of osteocalcin; the longer femur bone may therefore explain their lower risk of developing diabetes.

Using the data from the National Health and Nutrition Examination Survey (NHANES), we examined the diabetes risk association with three different height components: standing height, femur length, and the height without femur length (HWFL) (HWFL = standing height − femur length). We hypothesized that femur length is the key height component contributing to the negative relationship between adult height and the risk of diabetes.

RESEARCH DESIGN AND METHODS

— The NHANESs (1999–2000, 2001–2002, and 2003–2004) are national representative cross-sectional surveys conducted with a stratified multistage probability design of the U.S. population. The details of NHANES regarding design, sampling, and data-collecting procedures have been previously published elsewhere (7). A total of 15,332 people aged 20 to 85 years were involved in the three NHANES time periods. Among them, 6,943 people were assigned to a morning session for physical examinations and laboratory tests at the mobile examination center. After excluding those who fasted <8 h, had a missing standing height or femur length measurement, were identified as pregnant, or had diabetes diagnosed before age 40 years and were currently treated with insulin, we included a total of 6,188 subjects (3,128 men and 3,060 women) in this study. Anthropometric measures followed the survey protocol (8). Standing height was measured using a specially designed stadiometer. Femur length was measured as the length between the proximal and distal ends of the femur while the subject was sitting straight on a specially designed measurement box, with the right knee bent at a 90° angle (8). Measurements were taken to the nearest tenth of a centimeter for both standing height and femur length. The HWFL was calculated by subtracting femur length from standing height. Diabetes in this study was defined by the criteria of the American Diabetes Association (9) as either diabetes diagnosis by a physician before the surveys or overnight fasting (≥8 h) plasma glucose levels >125 mg/dl. Fasting plasma glucose was determined from overnight fasting blood samples and was measured by a modified hexokinase enzymatic method.

Datasets were analyzed with Stata (version 8.2; StataCorp, College Station, TX), which accounted for the weighted and clustered nature of the NHANES sample. Multivariate logistic regression models were used to assess the association

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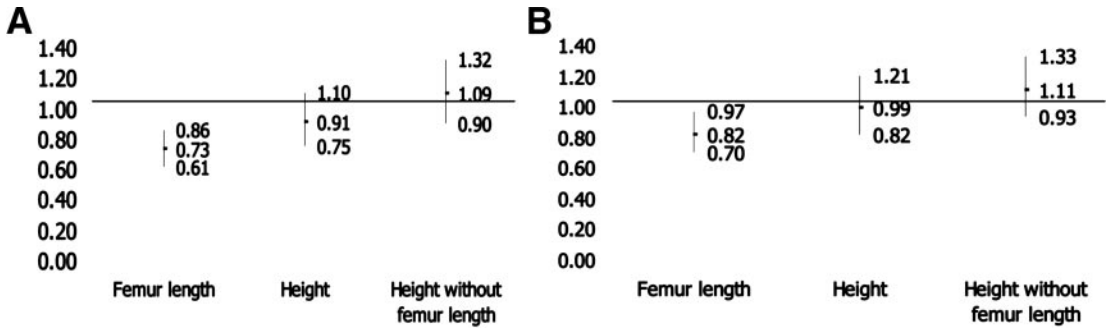

Figure 1—*Adjusted odds ratios of diabetes for different height measurements in 1 SD by sex according to NHANES (1999–2000, 2001–2002, 2003–2004). Adjusted for age, race, current smoking status, family income, and waist circumference.* A*: Men.* B*: Women.*

between each height component (i.e., femur length, standing height, and HWFL) as continuous variables and the prevalence of diabetes with adjustment for age, race, current smoking status, annual family income, and waist circumference. The statistical significance level was set at a two-tailed type I error of 0.05.

RESULTS — Overall, the prevalence of type 2 diabetes among this sample population was 8.9% (men 9.4% and women 8.4%). The adjusted odds ratios of diabetes for different height components by sex are shown in Fig. 1. The odds of diabetes were 0.73 (95% CI 0.61–0.86), 0.91 (0.75–1.10), and 1.09 (0.90–1.32) for every 1-SD increase in femur length, standing height, and HWFL in men, respectively, and 0.82 (0.70–0.97), 0.99 (0.82–1.21), and 1.11 (0.93–1.33) in women. To minimize the possibility of the influence of age-related osteoporosis, additional analyses were also conducted among adults aged <60 years. These analyses yielded similar patterns of results. In this subgroup, after adjusting for the potential confounding variables, 1-SD higher values in femur length, standing height, and HWFL were associated with odds of diabetes of 0.66 (0.52–0.84), 0.78 (0.59–1.04), and 0.97 (0.72–1.32), respectively, for men and 0.84 (0.66–1.07), 1.00 (0.74–1.36), and 1.10 (0.84–1.45) for women.

CONCLUSIONS — Results from this study indicate that femur length may be the key component in height contributing to the negative association between height and the prevalence of type 2 diabetes. It has been suggested that short leg length and low leg-to-height ratio in adults reflect impaired growth during childhood (10). Although every part of height is likely to be influenced by genetic factors, it has been observed that the early childhood environment, in particular infant nutrition, is an important determinant of leg length (10–12). The results from Lee et al. (6) suggest that short leg length might indicate less capacity for the synthesis of osteocalcin in bones. It is possible that the observed correlation between short femur length and diabetic risk might be the outcome of intrauterine or early childhood metabolic alterations that affect femur length. However, the lack of osteocalcin measurement from NHANES precludes direct testing of the hypothesis that osteocalcin mediates the association of femur length and the risk of type 2 diabetes.

Our analysis concludes that femur length could be the key component in height contributing to the risk of diabetes in adults, independently of other known risk factors. However, the novel hypothesis of this association, that the level of osteocalcin produced by the femur bone might be crucial in the development of type 2 diabetes, needs further research.

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