Is femur length the key height component in risk prediction of type 2 diabetes among adults?

Jian Liu, MD, PhD, Brock University
Hongzhuan Tan, MD, PhD, Central South University
Brian Jeynes, PhD, Brock University

Corresponding author:
Jian Liu,
E-mail: jliu@brocku.ca

Submitted 22 August 2008 and accepted 11 January 2009.

This is an uncopyedited electronic version of an article accepted for publication in Diabetes Care. The American Diabetes Association, publisher of Diabetes Care, is not responsible for any errors or omissions in this version of the manuscript or any version derived from it by third parties. The definitive publisher-authenticated version will be available in a future issue of Diabetes Care in print and online at http://care.diabetesjournals.org.
Objective: To examine the diabetic risk association with femur length (FL), standing height (SH) and the height without femur length (HWFL: SH-FL).

Research design and methods: We used the 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 had fasted ≥8 hours and had no missing values of FL and SH. 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 FL, SH, and HWFL were 0.73 (95% CI: 0.61–0.86), 0.91 (0.75–1.10), 1.09 (0.90–1.32) for men, respectively, and 0.82 (0.70-0.97), 0.99 (0.82–1.21), 1.11 (0.93–1.33) for women, respectively.

Conclusions: Our study supports the hypothesis that the FL may be the key height component in diabetic risk association.
A number of studies have observed that adult height is negatively associated with the risk of glucose intolerance, type 2 diabetes, and gestational diabetes [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 the osteocalcin displayed decreased pancreatic β cell proliferation, glucose intolerance and insulin resistance. Since the femur bone is the longest and the strongest bone of the human bones, theoretically, it would 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 femur bone. People with a longer femur bone may be more likely to have a higher level of osteocalcin, and therefore, explain their lower risk of developing diabetes.

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

METHODS

The NHANES surveys (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 the NHANES regarding design, sampling, and data collecting procedures have been published elsewhere [7]. A total of 15,332 people aged 20 to 85 years were involved in the three time periods NHANES surveys. Among them, 6,943 people were assigned to a morning session for physical examinations and laboratory tests at the mobile examination centre. After excluding those who either fasted less than 8 hours, or had a missing value of the SH or FL measurement, or were identified as pregnant, or had diabetes diagnosed before age 40 and were treated with insulin currently, a total of 6,188 subjects (3,128 men and 3,060 women) were eligible in this study. Anthropometric measures followed the survey protocol [8]. SH was measured using a specially designed stadiometer. FL was measured with the subject sitting straight on a specially designed measurement box, with the right knee bent at a 90 degree angle, as the length between the proximal and distal ends of the femur [8]. Measurements were taken to the nearest tenth of a centimeter for both SH and FL. The HWFL was calculated by subtracting FL from SH. Diabetes in this study was defined on the criteria of the American Diabetes Association (ADA) [9] as either a subject who had been previously diagnosed with diabetes by a physician before the surveys or as an overnight fasting (≥ 8 hours) plasma glucose levels higher than 125 mg/dL. Fasting plasma glucose was
determined from overnight fasting blood samples and was measured by a modified hexokinase enzymatic method.

The datasets were analyzed with Stata version 8.2 (Stata Corp., College Station, Texas), which accounted for the weighted and clustered nature of the NHANES sample. Multivariate logistic regression models were used to assess the association between each height component (i.e., FL, SH, and HWFL) as continuous variables and the prevalence of diabetes with adjustment for age, race, currently smoking, annual family income, and waist circumference. The statistical significant level was set up 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%; women: 8.4%). The adjusted odds ratios of diabetes for different height components by sex are shown in Figure 1. The odds of diabetes were 0.73 (95% CI: 0.61–0.86), 0.91 (0.75–1.10), 1.09 (0.90–1.32) for every one standard deviation increase in FH, SH, and HWFL in men, respectively, and 0.82 (0.70–0.97), 0.99 (0.82–1.21), 1.11 (0.93–1.33) in women, respectively. To minimize the possibility of the influence of age-related osteoporosis, additional analyses were also conducted among adults aged less than 60 years. These analyses yielded similar patterns of results. In this subgroup, after adjusting for the potential confounding variables, one standard deviation higher values in the FL, SH, and HWFL were associated with odds of diabetes of 0.66 (95% CI: 0.52–0.84), 0.78 (0.59–1.04), and 0.97 (0.72–1.32), respectively, for men, and of 0.84 (0.66–1.07), 1.00 (0.74–1.36), and 1.10 (0.84–1.45), respectively, for women.

CONCLUSIONS

Results from this study indicate that FL 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 an 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 [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 the short FL and diabetic risk might be the outcome of intrauterine or early childhood metabolic alterations that affect FL. However, the lack of osteocalcin measurement from the NHANES precludes direct testing of the hypothesis that osteocalcin mediates the association of FL and the risk of type 2 diabetes.

Our analysis concludes that FL could be the key component in height contributing to the risk of diabetes in adults, independently from 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.

ACKNOWLEDGMENTS

Conflict of interest: none.
REFERENCES

1 Brown DC, Byrne CD, Clark PM, Cox BD, Day NE, Hales CN, Shackleton JR, Wang TW, Williams DR: Height and glucose tolerance in adult subjects. Diabetologia 1991;34:531-533.

2 Njolstad I, Arnesen E, Lund-Larsen PG: Sex differences in risk factors for clinical diabetes mellitus in a general population: A 12-year follow-up of the finnmark study. Am J Epidemiol 1998;147:49-58.

3 Sayeed MA, Hussain MZ, Banu A, Rumi MA, Azad Khan AK: Prevalence of diabetes in a suburban population of bangladesh. Diabetes Res Clin Pract 1997;34:149-155.

4 Kousta E, Lawrence NJ, Penny A, Millauer BA, Robinson S, Johnston DG, McCarthy MI: Women with a history of gestational diabetes of european and south asian origin are shorter than women with normal glucose tolerance in pregnancy. Diabet Med 2000;17:792-797.

5 Dangour AD, Schilg S, Hulse JA, Cole TJ: Sitting height and subischial leg length centile curves for boys and girls from southeast england. Ann Hum Biol 2002;29:290-305.

6 Lee NK, Sowa H, Hinoi E, Ferron M, Ahn JD, Confavreux C, Dacquin R, Mee PJ, McKee MD, Jung DY, Zhang Z, Kim JK, Mauvais-Jarvis F, Ducy P, Karsenty G: Endocrine regulation of energy metabolism by the skeleton. Cell 2007;130:456-469.

7 Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS): National health and nutrition examination survey data.

8 Lohman TG, Roche AF, Martorell R: Anthropometric standardization reference manual. Champaign, Ill.; United States, Human Kinetics Books, 1988.

9 The expert committee on the diagnosis and classification of diabetes mellitus.Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 2003;26 Suppl 1:S5-20.

10 Leitch I: Growth and health. Br J Nutr 1951;5:142-151.

11 Mitchell HS: Nutrition in relation to stature. J Am Diet Assoc 1962;40:521-524.

12 Wadsworth ME, Hardy RJ, Paul AA, Marshall SF, Cole TJ: Leg and trunk length at 43 years in relation to childhood health, diet and family circumstances; evidence from the 1946 national birth cohort. Int J Epidemiol 2002;31:383-390.
Figure 1. Adjusted odds ratios\(^*\) of diabetes for different height lengths in one standard deviation by sex the National Health and Nutrition Examination Survey (1999-2000, 2001-2002, 2003-2004)

\(^*\)adjusted for age, race, current smoking, family income, and waist circumference.