Original Article
Epidemiology

Diabetes Metab J 2019;43:794-803
https://doi.org/10.4093/dmj.2018.0184
pISSN 2233-6079 · eISSN 2233-6087

dmj
DIABETES & METABOLISM JOURNAL

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Relation between Baseline Height and New Diabetes Development: A Nationwide Population-Based Study

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Background: Short stature and leg length are associated with risk of diabetes and obesity. However, it remains unclear whether this association is observed in Asians. We evaluated the association between short stature and increased risk for diabetes using the Korean National Health Screening (KNHS) dataset.
Methods: We assessed diabetes development in 2015 in 21,122,422 non-diabetic Koreans (mean age 43 years) enrolled in KNHS from 2009 to 2012 using International Classification of Diseases 10th (ICD-10) code and anti-diabetic medication prescription. Risk was measured in age- and sex-dependent quintile groups of baseline height (20 to 39, 40 to 59, ≥60 years).
Results: During median 5.6-year follow-up, 532,918 cases (2.5%) of diabetes occurred. The hazard ratio (HR) for diabetes development gradually increased from the 5th (reference) to 1st quintile group of baseline height after adjustment for confounding factors (1.000, 1.076 [1.067 to 1.085], 1.097 [1.088 to 1.107], 1.141 [1.132 to 1.151], 1.234 [1.224 to 1.244]), with similar results in analysis by sex. The HR per 5 cm height increase was lower than 1.00 only in those with fasting blood glucose (FBG) below 100 mg/dL (0.979 [0.975 to 0.983]), and in lean individuals (body mass index [BMI] 18.5 to 23 kg/m^2: 0.993 [0.988 to 0.998]; BMI <18.5 kg/m^2: 0.918 [0.9 to 0.935]).
Conclusion: Height was inversely associated with diabetes risk in this nationwide study of Korean adults. This association did not differ by sex, and was significant in lean individuals and those with normal FBG levels.

Keywords: Body height; Diabetes mellitus; Public health; Risk

INTRODUCTION

The prevalence of diabetes is markedly increasing in Asia-Pacific region [1,2]. This increased prevalence is in part due to the genetic vulnerability to insulin secretory dysfunction at a given body size of people born in this region compared to that of Caucasians [2,3]. Furthermore, the increasing prevalence of obesity in this region suggests an increase in Western-type diabetes, that is, "obese" and "insulin-resistant" diabetes [4,5].

The striking increase in the prevalence of diabetes may be explained by the global increase in the obese population [4]. Excessive body fat and abdominal obesity are important risk factors for the development of diabetes, and numerous studies have reported significant associations between obesity parameters such as body mass index (BMI), waist circumference (WC), waist-hip ratio, and waist-to-height ratio and risk for diabetes [6-8]. However, controversy remains regarding which parameter shows the greatest correlation with risk for diabetes.

For the past decades, numerous studies have suggested a significant association between short stature and increased risk

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Received: Sep. 16, 2018; Accepted: Dec. 1, 2018

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for diabetes [9]. However, this association remains controversial [10]. In a recent study performed in Iranian first-degree relatives of patients with type 2 diabetes mellitus, height was inversely correlated with diabetes incidence in 5.5 years of follow-up, after adjustment for confounding variables [11]. However, in 1,730 participants in San Antonio Heart Study, addition of height to adjust WC did not increase the ability of WC to predict diabetes [10]. In another meta-analysis that included 17 cross-sectional and longitudinal studies, height was inversely associated with type 2 diabetes mellitus only in female [12]. Although there are sufficient numbers of studies published for meta-analyses, most of the studies were performed in Caucasians or South Asians, but not in East Asians.

Therefore, in this study, we analyzed the association between baseline height and future risk for diabetes development in 21,123,022 Korean adults, using data from the Korean National Health Screening (KNHS) dataset.

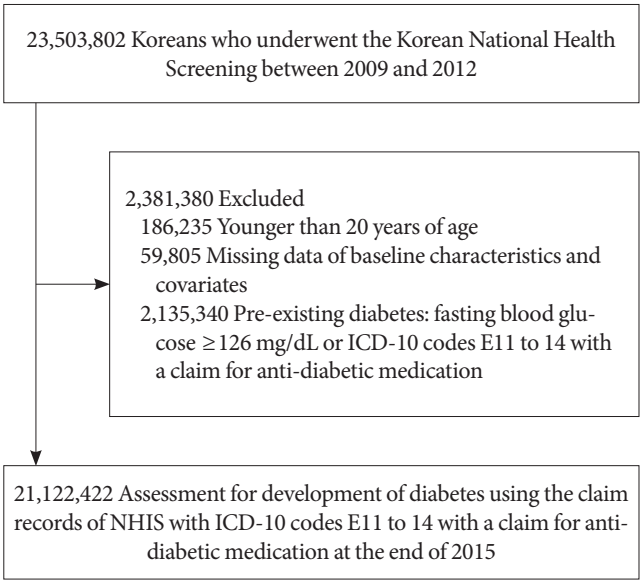

Fig. 1. Selection of the study population. ICD-10, International Classification of Diseases 10th; NHIS, National Health Insurance Service.

METHODS

Database of the National Health Insurance Service

Nearly all Koreans (97.2% of the Korean population, approximately 50 million) are covered by the National Health Insurance Service (NHIS), which is a nonprofit, single-payer health care organization administered by the Korean government. The NHIS maintains patients' demographic information, claims for disease diagnosis codes of the International Classification of Diseases 10th (ICD-10), and examination and treatment data that can be used to construct population-based cohorts [13]. Insured Korean adults over the age of 40 and employees over the age of 20 undergo regular health checkups provided by the NHIS every 1 or 2 years. The KNHS databases obtained through these checkups provide a variety of information including anthropometric measurements, health questionnaire data, and laboratory findings. These databases and the aforementioned nationwide medical records were combined with the aim of constructing a cohort for our study analysis, following NHIS approval of the use of its database for the research (research number NHIS-2017-1-201).

Study design and population

All participants who underwent KNHS during the 4 years from 2009 to 2012 (n=23,503,802) were initially enrolled in the study. Participants younger than 20 years of age (n=186,235) and those with missing data for baseline characteristics and covariates (n=59,805) were subsequently excluded. Participants who had pre-existing diabetes at baseline (n=2,135,340) were also excluded from the study, leaving a total of 21,122,422 participants (Fig. 1).

The diagnosis of diabetes at baseline was made based on fasting blood glucose (FBG) ≥126 mg/dL or ICD-10 code E11 to 14 with a claim for anti-diabetic medication [14]. The diagnosis of hypertension or hyperlipidemia was confirmed using laboratory data (systolic blood pressure ≥140 mm Hg and diastolic blood pressure ≥90 mm Hg; total cholesterol levels ≥240 mg/dL) or ICD code (ICD-10 code I10 to I15; or E78) with a claim for medication for the individual disease. Ischemic heart disease (IHD) was defined by claims of ICD-10 codes I21-25. Cancer was defined as patient registration in the NHIS with ICD-10 code C, and chronic obstructive pulmonary disease (COPD) was defined as ICD-10 codes J41 to J44. Chronic kidney disease (CKD) was defined by estimated glomerular filtration rate <60 mL/min/1.73 m^2 by the Modification of Diet in Renal Disease method [15].

Ethic statement

Our study protocol was approved by the Institutional Review Board (IRB) of the Kangbuk Samsung Hospital (KBSMC2018-07-011). The requirement for informed consent was waived by the IRB as the data released to the researchers were de-identified.

Anthropometric measurement and baseline characteristics

All baseline parameters were measured at the time of NNHS examinations. Body weight (kg) and height (cm) were measured using an electronic scale, and WC (cm) was measured at the middle point between the rib cage and iliac crest by trained examiners. BMI was calculated with body weight (kg) divided by height (m) squared. All blood samples were collected after fasting, and blood pressure was measured using a sphygmomanometer after 5 minutes of rest. Baseline health behaviors such as income, smoking, alcohol drinking, and exercise were confirmed through standardized questionnaires. Participants were divided into three groups according to smoking status (never smoker, ex-smoker, and current smoker), and three groups according to drinking status (none, drinking less than 30 g/day, and drinking equal to or more than 30 g/day). Physical activity was defined as engaging in regular exercise (either of the next intensity levels): physical activity with high intensity of more than 20 minutes per session ≥3 days a week, and physical activity with moderate intensity for more than 30 minutes per session ≥5 days a week.

Study outcomes

We recorded newly diagnosed diabetes using the claim records of the NHIS until the end of 2015. Participants were divided into five groups according to "age-dependent (20 to 39, 40 to 59, and ≥60 years) and sex-dependent" categorization of height, and the hazard ratios (HRs) for development of diabetes per 1-standard deviation (SD) increase in height was analyzed. The cutoffs for each quintile groups were as follows: males (20 to 39 years: <168, 168–172, 172.1–174, 174.1–178, >178 cm; 40 to 59 years: <164, 164–168, 168.1–171, 171.1–174, >174 cm; ≥60 years: <160, 160–163, 163.1–166, 166.1–169, >169 cm); females (20 to 39 years: <156, 156–160, 160.1–162, 162.1–165, >165 cm; 40 to 59 years: <152, 152–155, 155.1–158, 158.1–161, >161 cm; ≥60 years: <146, 146–149, 149.1–152, 152.1–155, >155 cm).

The HRs for diabetes development per 1-SD increase in height were analyzed in seven groups divided by SD of height: <−3, −3 to −2, −2 to −1, −1 to 1, 1 to 2, 2 to 3, >3 SD. The HRs for diabetes were analyzed in five groups divided according to BMI: <18.5, 18.5 to 23, 23.1 to 25, 25.1 to 30, >30 kg/m^2.

In addition, the HRs for diabetes development per 1-SD increase in height were analyzed in two groups divided by FBG <100 or 100 to 125 mg/dL.

Statistical analyses

Comparisons of the continuous variables among the groups divided by quintiles of height were performed using one-way analysis of variance. Comparisons of the categorical variables among the groups were performed with the chi-square test.

HRs were assessed using the Cox proportional hazards model with a 95% confidence interval (CI) by analyzing the risk of diabetes development. We conducted multivariable adjustments of age, sex, health behaviors, and underlying diseases (hypertension, dyslipidemia, IHD, COPD, CKD, and cancer) that could affect the outcome, and further included BMI or WC levels as a calibration variable in the analyses of WC or BMI to demonstrate independent relationships not affected by another anthropometric marker. Various obesity indices such as, body weight, WC, BMI, and abdominal obesity defined by different WC cutoffs according to sex were separately included in the model and the HRs for diabetes were analyzed to observe the effects of individual index on the association between height and diabetes risk, resulting in total of six models.

SAS version 9.3 (SAS Institute Inc., Cary, NC, USA) was used for all statistical analyses. *P* values less than 0.05 were considered significant.

RESULTS

The mean age of participants was 47 years, and 50.1% were male (Table 1). The mean body weight and height of the study population were 63 kg and 163 cm, respectively. Mean values for FBG, lipid profiles, and blood pressure were significantly different among the five groups divided by quintiles of height; however, the differences were small.

During a median follow-up period of 5.6 years, 532,918 cases (2.5%) of diabetes occurred. The incidence rate was shown to decrease from the 1st quintile of height to the 5th quintile (Table 2). When the 5th quintile group, the tallest group, was designated as the reference group, the risk for diabetes development gradually increased from the 5th quintile to the 1st quintile group after adjustment for confounding variables (Table 2). These trends were consistent even when BMI, WC, or abdominal obesity was included in the analyses. When the analyses were performed with height as the continuous variable, a 1-SD increase of height resulted in a 2% decreased risk for diabetes development (Table 2).

When the analyses were performed in groups divided according to sex, similar results were observed (Table 2). When

Table 1. Baseline characteristics of the participants according to age- and sex-dependent quintiles[a] of height

Characteristic	Total	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
Number	21,122,422	4,385,064	4,038,552	4,054,072	4,772,708	3,872,026
Age, yr	46.6±14.1	48.6±14.4	48.2±14.6	46.0±14.5	45.5±13.1	44.6±13.7
Male sex	10,577,336 (50.1)	2,170,664 (49.5)	1,927,488 (47.7)	2,178,411 (53.7)	2,364,968 (49.6)	1,935,805 (50.0)
Body weight, kg	63.3±11.7	57.7±9.7	60.7±10.2	63.5±10.9	65.5±11.4	69.2±12.6
Height, cm	163.6±9.2	155.8±7.5	160.2±7.1	164.1±7.2	166.6±7.5	171.6±8.0
Waist circumference, cm	79.5 ±9.2	78.1±8.7	78.9±8.9	79.6±9.1	80.0±9.2	81.0±9.7
BMI, kg/m^2	23.6±3.2	23.7±3.2	23.6±3.2	23.5±3.2	23.5±3.2	23.4±3.3
Proportion of participants with BMI ≥25 kg/m^2	6,423,973 (30.4)	1,399,744 (31.9)	1,229,699 (30.5)	1,246,410 (30.7)	1,429,971 (30.0)	1,118,149 (28.9)
SBP, mm Hg	121.5±14.9	122.2±15.5	121.8±15.3	121.5±14.9	121.1±14.6	121.1±14.4
DBP, mm Hg	75.8±10.1	76.1±10.2	75.9±10.1	75.8±10.0	75.7±10.0	75.6±9.9
Fasting blood glucose, mg/dL	92.7±11.4	92.8±11.6	92.8±11.4	92.7±11.4	92.7±11.2	92.6±11.2
Total cholesterol, mg/dL	194.7±36.3	197.1±37.1	195.9±36.6	194.1±36.2	194.2±35.9	191.7±35.3
HDL-C, mg/dL	55.9±16.5	56.0±16.8	56.0±16.7	55.7±16.6	55.9±16.3	55.9±16.3
LDL-C, mg/dL	113.7±33.2	115.6±34.1	114.8±33.5	113.2±33.1	113.4±32.8	111.4±32.2
Triglyceride, mg/dL	108.5 (35.9–327.6)	111.2 (37.1–333.1)	109.3 (36.5–327.4)	109.1 (35.8–332.4)	107.6 (35.6–325.0)	105.2 (34.7–318.9)
Proportion of participants with hypertension	4,854,026 (23.0)	1,135,269 (25.9)	1,006,190 (24.9)	925,330 (22.8)	1,003,075 (21.0)	784,162 (20.3)
Proportion of participants with dyslipidemia	3,534,940 (16.7)	832,197 (19.0)	730,843 (18.1)	665,271 (16.4)	754,696 (15.8)	551,933 (14.3)
Proportion of participants with IHD	571,222 (2.7)	131,836 (3.0)	123,277 (3.1)	111,092 (2.7)	112,769 (2.4)	92,248 (2.4)
Proportion of participants with COPD	1,155,182 (5.5)	263,648 (6.0)	238,106 (5.9)	218,717 (5.4)	239,122 (5.0)	195,589 (5.1)
Proportion of participants with history of cancer	365,220 (1.7)	71,352 (1.6)	72,990 (1.8)	67,255 (1.7)	83,637 (1.8)	69,986 (1.8)
Proportion of participants with CKD	1,017,703 (4.8)	207,192 (4.7)	208,944 (5.2)	197,136 (4.9)	216,212 (4.5)	188,219 (4.9)
Tertiles of income						
1	6,882,519 (32.6)	1,625,109 (37.1)	1,347,305 (33.4)	1,289,776 (31.8)	1,473,319 (30.87)	1,147,010 (29.6)
2	8,734,095 (41.4)	1,813,727 (41.4)	1,668,931 (41.3)	1,712,645 (42.3)	1,953,896 (40.9)	1,584,896 (40.9)
3	5,505,808 (26.1)	946,228 (21.6)	1,022,316 (25.3)	1,051,651 (25.9)	1,345,493 (28.2)	1,140,120 (29.5)
Smoking						
Never smoker	13,152,963 (62.3)	2,852,804 (65.1)	2,605,932 (64.5)	2,414,374 (59.6)	2,937,103 (61.5)	2,342,750 (60.5)
Ex-smoker	2,768,679 (13.1)	515,802 (11.8)	507,310 (12.6)	577,399 (14.2)	634,675 (13.3)	533,493 (13.9)
Current smoker	5,200,780 (24.6)	1,016,458 (23.2)	925,310 (22.9)	1,062,299 (26.2)	1,200,930 (25.2)	995,783 (25.7)
Levels of drinking						
Not drinking alcohol	11,164,853 (52.9)	2,497,108 (57.0)	2,238,531 (55.4)	2,045,772 (50.5)	2,456,010 (51.5)	1,927,432 (49.8)
Drinking less than 30 g/day	8,593,386 (40.7)	1,646,310 (37.5)	1,565,403 (38.8)	1,730,863 (42.7)	1,991,976 (41.7)	1,658,834 (42.8)
Drinking equal to or more than 30 g/day	1,364,183 (6.5)	241,646 (5.5)	234,618 (5.8)	277,437 (6.8)	324,722 (6.8)	285,760 (7.4)
Proportion of participants with regular physical activity	10,549,886 (50.0)	1,970,740 (44.9)	1,946,087 (48.2)	2,059,534 (50.8)	2,498,300 (52.4)	2,075,225 (53.6)

Values are presented as mean±standard deviation, number (%), or median (range).

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; IHD, ischemic heart disease; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease.

[a]The cutoffs of age- and sex-dependent quintile groups of height were as follows: in males (20 to 39 years, <168, 168–172, 172.1–174, 174.1–178, >178 cm; 40 to 59 years, <164, 164–168, 168.1–171, 171.1–174, >174 cm; ≥60 years, <160, 160–163, 163.1–166, 166.1–169, >169 cm), in females (20–39 years, <156, 156–160, 160.1–162, 162.1–165, 165 cm; 40–59 years, <152, 152–155, 155.1–158, 158.1–161, >161 cm; ≥60 years: <146, 146–149, 149.1–152, 152.1–155, >155 cm).

Table 2. Hazard ratio for development of diabetes according to age- and sex-dependent quintiles of baseline height

Quintiles of height[a]	No.	No. of participants with event	Incidence duration, person-years	Incidence rate	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Total population										
1	4,385,064	150,352	23,333,538.73	6.4	1.073 (1.064–1.081)	1.055 (1.046–1.063)	2.108 (2.09–2.127)	1.04 (1.031–1.048)	1.345 (1.335–1.356)	1.234 (1.224–1.244)
2	4,038,552	131,661	21,488,387.42	6.1	1.029 (1.02–1.037)	1.016 (1.007–1.024)	1.67 (1.656–1.685)	1.006 (0.998–1.015)	1.213 (1.203–1.224)	1.141 (1.132–1.151)
3	4,054,072	120,743	21,556,903.78	5.6	1.021 (1.013–1.03)	1.007 (0.998–1.015)	1.459 (1.446–1.471)	0.997 (0.989–1.006)	1.147 (1.137–1.157)	1.097 (1.088–1.107)
4	4,772,708	130,162	25,300,006.39	5.1	1.026 (1.018–1.035)	1.019 (1.011–1.028)	1.279 (1.268–1.29)	1.011 (1.003–1.02)	1.106 (1.097–1.115)	1.076 (1.067–1.085)
5	3,872,026	100,907	20,340,528.52	5.0	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
P for trend	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001				
Continuous HR per 1 SD					0.989 (0.987–0.991)	1.012 (1.009–1.015)	0.855 (0.853–0.858)	1.026 (1.023–1.029)	0.966 (0.963–0.969)	0.983 (0.98–0.986)
Males										
1	2,170,664	78,080	11,576,632.29	6.7	1.048 (1.037–1.06)	1.039 (1.028–1.051)	2.234 (2.206–2.261)	1.049 (1.037–1.06)	1.442 (1.426–1.458)	1.27 (1.256–1.285)
2	1,927,488	67,984	10,300,140.31	6.6	1.018 (1.006–1.029)	1.009 (0.998–1.02)	1.749 (1.728–1.77)	1.011 (0.999–1.022)	1.276 (1.262–1.291)	1.172 (1.159–1.185)
3	2,178,411	70,442	11,648,480.25	6.0	1.022 (1.01–1.033)	1.014 (1.002–1.025)	1.524 (1.506–1.541)	1.018 (1.007–1.029)	1.205 (1.191–1.218)	1.134 (1.122–1.147)
4	2,364,968	69,600	12,628,162.87	5.5	1.016 (1.005–1.028)	1.011 (1–1.023)	1.299 (1.285–1.314)	1.008 (0.997–1.019)	1.124 (1.111–1.136)	1.084 (1.072–1.096)
5	1,935,805	55,989	10,254,702.21	5.5	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
P for trend	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001				
Continuous HR per 1 SD					0.987 (0.983–0.99)	0.988 (0.985–0.992)	0.733 (0.73–0.736)	0.984 (0.98–0.987)	0.873 (0.87–0.876)	0.917 (0.914–0.921)
Females										
1	2,214,400	72,272	11,756,906.44	6.1	1.096 (1.083–1.109)	1.072 (1.059–1.085)	1.972 (1.947–1.996)	1.024 (1.012–1.037)	1.257 (1.242–1.272)	1.182 (1.168–1.196)
2	2,111,064	63,677	11,188,247.12	5.7	1.041 (1.029–1.054)	1.024 (1.011–1.036)	1.577 (1.557–1.597)	0.998 (0.986–1.01)	1.152 (1.138–1.166)	1.099 (1.085–1.112)
3	1,875,661	50,301	9,908,423.54	5.1	1.011 (0.998–1.024)	0.994 (0.981–1.007)	1.38 (1.362–1.398)	0.97 (0.958–0.983)	1.089 (1.075–1.103)	1.048 (1.035–1.061)
4	2,407,740	60,562	12,671,843.52	4.8	1.035 (1.023–1.048)	1.028 (1.015–1.041)	1.246 (1.231–1.261)	1.014 (1.002–1.026)	1.087 (1.074–1.1)	1.061 (1.048–1.074)
5	1,936,221	44,918	10,085,826.31	4.5	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
P for trend	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001				
Continuous HR per 1 SD					1.043 (1.04–1.047)	1.041 (1.038–1.045)	0.855 (0.851–0.858)	1.047 (1.044–1.051)	0.988 (0.985–0.991)	1.007 (1.003–1.01)

Model 1: adjusted for age and sex; Model 2: adjusted for age, sex, smoking, drinking, exercise, income, hypertension, dyslipidemia, ischemic heart disease, history of cancer, chronic obstructive pulmonary disease, and chronic kidney disease; Model 3: adjusted for age, sex, smoking, drinking, exercise, income, hypertension, dyslipidemia, ischemic heart disease, history of cancer, chronic obstructive pulmonary disease, chronic kidney disease, and body weight; Model 4: adjusted for age, sex, smoking, drinking, exercise, income, hypertension, dyslipidemia, ischemic heart disease, history of cancer, chronic obstructive pulmonary disease, chronic kidney disease, and body mass index; Model 5: adjusted for age, sex, smoking, drinking, exercise, income, hypertension, dyslipidemia, ischemic heart disease, history of cancer, chronic obstructive pulmonary disease, chronic kidney disease, and waist circumference; Model 6: adjusted for age, sex, smoking, drinking, exercise, income, hypertension, dyslipidemia, ischemic heart disease, history of cancer, chronic obstructive pulmonary disease, chronic kidney disease, and abdominal obesity (waist circumference ≥90 cm in males, ≥85 cm in females).
HR, hazard ratio; SD, standard deviation.
[a]The cutoffs of age- and sex-dependent quintile groups of height were as follows: in males (20–39 years, <168, 168–172, 172.1–174, 174.1–178, >178 cm; 40–59 years, <164, 164–168, 168.1–171, 171.1–174, >174 cm; ≥60 years, <160, 160–163, 163.1–166, 166.1–169, >169 cm); in females (20–39 years, <156, 156–160, 160.1–162, 162.1–165, 165 cm; 40–59 years, <152, 152–155, 155.1–158, 158.1–161, >161 cm; ≥60 years, <146, 146–149, 149.1–152, 152.1–155, >155 cm).

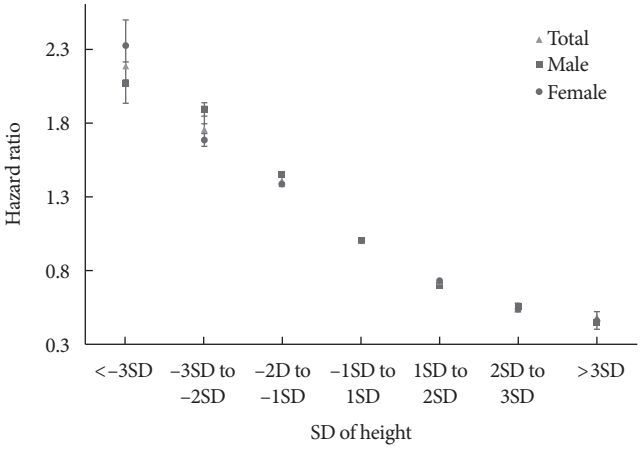

Fig. 2. Hazard ratio for development of diabetes according to seven groups divided by standard deviations of height. SD, standard deviation.

similar analyses were performed in seven groups divided by 1-SD increase in height, the risk for diabetes development significantly decreased from the <−3 SD group to the >3 SD group, a result that was significant even after adjustment for multiple confounding variables including baseline body weight (Fig. 2).

When similar analyses were performed according to the subgroups of various diseases, 1-SD increase in height showed significantly decreased risk for diabetes development in various disease groups, a result that was significant even after adjustment for multiple confounding factors (Fig. 3).

When the risk for diabetes development with 1-SD increase of height was analyzed according to baseline fasting glucose, the decreased HR for diabetes development was significant only in individuals with FBG within normal limits (<100 mg/dL) (HR, 0.979; 95% CI, 0.975 to 0.983). However, in those with FBG 100 to 125 mg/dL, the HR for diabetes development was greater than 1, suggesting that the inverse association between height and diabetes development was only significant in individuals with normal FBG (HR, 1.023; 95% CI, 1.019 to 1.026).

When the risk for diabetes development per 1-SD increase of height was analyzed according to baseline BMI, the HR for diabetes development was lower than 1 only in individuals with BMI lower than 23 kg/m^2, and began to be higher than 1 in those with BMI equal to or greater than 23 kg/m^2, suggesting that the inverse correlation between height and diabetes development was only significant when the participant was lean (Fig. 4). These results were significant even after adjustment for confounding factors.

DISCUSSION

In this study performed in a large study population derived from a nationwide population-based database, an inverse association was observed between height and the risk for diabetes development. Compared to individuals in the highest quintile of height, those in the lowest quintile groups showed a 1.2-fold increased risk for diabetes, and these results were significant even after rigorous adjustment for multiple confounding factors, including common obesity indexes, such as WC and BMI. Interestingly, similar findings were observed in groups analyzed by sex, as well as in numerous subgroups. When the association was separately analyzed in groups divided by baseline FBG, only the group with normoglycemia showed a similar inverse association between height and diabetes development as our main result, and only lean individuals showed a similar inverse association between height and diabetes development.

In the present study, we found that height was inversely associated with diabetes risk. There have been many studies performed regarding the association between height and diabetes in various ethnic groups. The oldest study, which was performed in 11,654 Norwegians followed up for 12 years, showed a 29% decreased risk for diabetes per 5 cm increase of height only in females [9]. In a cross-sectional study performed in over 12,000 Dutch individuals, male in the lowest tertile group of height showed a 4.4-fold increased risk for type 2 diabetes mellitus compared to those in the highest tertile group [16]. In the Tehran Lipid and Glucose Study performed in 5,018 non-diabetic Iranians followed up for 6 years, a 1-SD increase in height was associated with a 38% decrease in diabetes risk only in females [17]. In a recent meta-analysis that included 250,497 participants and 7,765 cases of type 2 diabetes mellitus gathered from 17 studies, individuals in the highest category of height showed a 15% lower risk for type 2 diabetes mellitus compared to those in the lowest category, a finding that was only significant in females [12]. The present study showed a 23% increased risk of diabetes in the lowest quintile group compared with the highest quintile group, after adjustment for multiple factors. Our study results are meaningful in that the analyses were performed in an elaborate manner and this was the first study performed in an East Asian population.

The mechanism by which greater height is associated with a lower risk of type 2 diabetes mellitus is unclear. Height is considered as a marker of superior intrauterine and childhood nu-

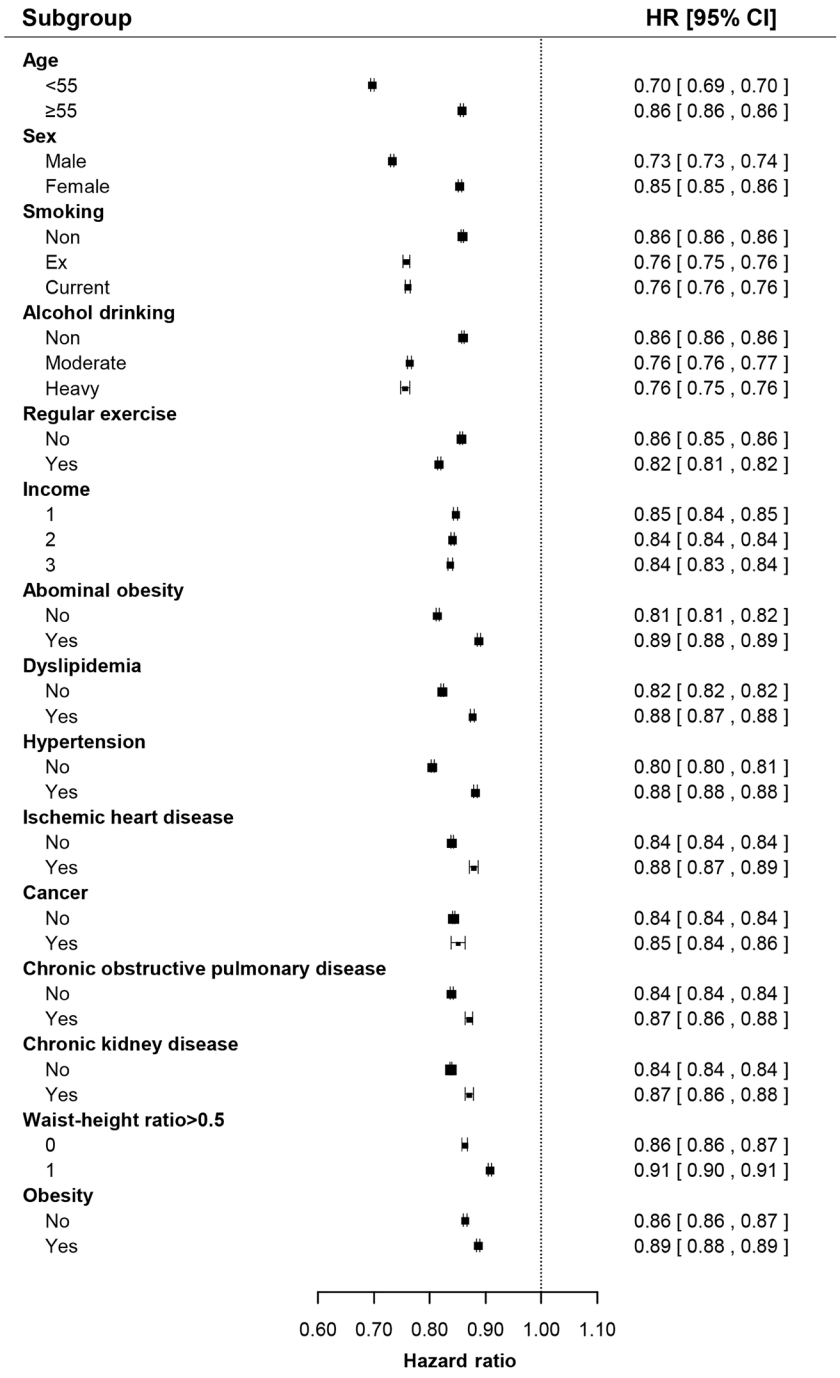

Fig. 3. Hazard ratio for development of diabetes according to subgroups of various diseases. Adjusted for age, sex, smoking, alcohol drinking, regular exercise, income status, hypertension, dyslipidemia, ischemic heart disease, cancer, chronic obstructive pulmonary disease, chronic kidney disease, and baseline body weight. HR, hazard ratio; CI, confidence interval.

trition and growth, and inversely associated with cardiovascular disease risk [18-20]. The risk factors for glucose dysregulation such as obesity are also known to be determined by genetic and early environmental factors [21-23]. In other studies, short leg length and femur length, which reflect disturbed growth during puberty and childhood, were shown to be associated with type 2 diabetes mellitus risk [24,25]. Other factors that might influence these relationships are the hormonal fac-

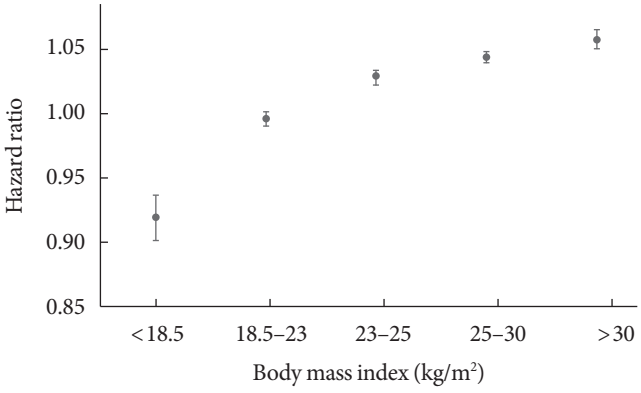

Fig. 4. Hazard ratio for development of diabetes according to 1-standard deviation increase of height in five groups divided by baseline body mass index.

tors relevant to growth, intrauterine environment and childhood nutrition, and vitamin D deficiency [26-28]. Especially in girls, increases in body fat in the prepubertal period can affect the initiation of menarche and the menstrual cycle, which influence final height in females [26]. This process may explain the sex difference observed in the effect of height on diabetes risk [12]. In summary, one's height reflects the degree of appropriate nutrition and environment during one's intrauterine period and childhood, affecting future development of diabetes in association with genetic factors. However, more has to be clarified regarding the mechanism between height and diabetes risk in various ethnic groups.

In our study, the decreased risk for diabetes development was significant only in individuals with FBG within normal limits (<100 mg/dL) with an HR of 0.979, while in those with impaired fasting glucose, the HR for diabetes development was 1.023, suggesting that the inverse association between height and diabetes development was only significant in those with normal FBG. This result is a novel finding that could be interpreted to indicate that in participants who already have prediabetes, the effect of high FBG overwhelms the effect of short stature, suggesting that baseline FBG has a stronger influence than height on diabetes development. Similarly, the inverse correlation between height and diabetes risk was only evident in lean participants (BMI ≤23 kg/m^2), and the HR began to increase in individuals with BMI >23 kg/m^2. This finding indicates that the effect of obesity overwhelms the effect of short stature when the participant is obese. In summary, there is a possibility that the inverse association between height and diabetes risk is only evident in those with normal glucose levels and those who are lean. As obesity and prediabetes are the two predominant strong risk factors for diabetes development, being obese and having high baseline glucose cannot be overwhelmed by the effect of short stature.

Our study has certain limitations. First, the diagnosis of future diabetes was defined only by the ICD-10 code and claims for anti-diabetic medication. Furthermore, those who satisfy postprandial diagnostic criteria for diabetes could not be identified. Therefore, some participants with diabetes could have been missed. Second, other obesity indices known to affect diabetes, such as waist-hip ratio, fat mass, or muscle mass could not be included in the analyses due to lack of data in our nationwide dataset. Third, the outcome determination was based on claim data and the analysis did not include the various biochemical parameters of the subjects. Fourth, the Korean NHIS data include different characteristic data profile according to age, that is, the data in those younger and older 40 years are very different in nature. Our data analyses did not satisfactorily consider these differences. Fifth, the follow-up period of our data was 5.6 years, which is relatively short to observe the full spectrum of the associations between height and diabetes development. Sixth, the measurement method of height was not standardized nor was according to a single protocol. Despite these limitations, the strength of our study is that it was the first performed on this topic in a large nationwide East Asian population of over 21 million.

In conclusion, an inverse association was observed between height and the risk for diabetes development in a large Korean population. In addition, these associations were evident only in those with normoglycemia and those who were lean, suggesting that the effects of fasting hyperglycemia and obesity on the development of diabetes could not be overwhelmed by the effect of short stature. Further analyses should be performed in multiple ethnic groups to determine whether the same results are observed in different races.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Conception or design: E.J.R., W.Y.L.
Acquisition, analysis, or interpretation of data: E.J.R., J.H.J.,

K.D.H., Y.G.P., W.Y.L.
Drafting the work or revising: E.J.R, W.Y.L.
Final approval of the manuscript: J.H.C., H.K., S.E.P., Y.H.K.

ACKNOWLEDGMENTS

None

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