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Associations between Body Height and Drinking Status with Diabetes in a Rural, Non-Overweight, Elderly, Japanese Male Population: The Nagasaki Islands Study

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Abstract

Aim: A previous study of ours reported finding a positive association between height and hyperuricemia among non-overweight men (BMI<25kg/m²). Although hyperuricemia is known to be also associated with diabetes, no published study has examined possible associations. Furthermore, while alcohol consumption is also reportedly associated with insulin resistance and risk of diabetes, there have been no reports on associations between height and diabetes which take drinking status into account.

Objective: We conducted a cross-sectional study to investigate the associations between height and diabetes in relation to drinking status among 787 non-overweight men aged 60-89 years undergoing a general health check-up.

Results: Of the study population consisting of 402 non-drinkers and 385 drinkers, 83 men (46 non-drinkers and 37 drinkers) were diagnosed with diabetes. Independent from classical cardiovascular risk factors, a significant positive association between height and diabetes was established for non-drinkers, whereas drinkers did not show any significant association. The cardiovascular risk factors-adjusted odds ratio (OR) and 95% confidence interval (CI) for diabetes for an increment of 1 SD in height (6.36cm) was 1.44 (CI: 1.03-2.02) for non-drinkers and 1.01 (CI: 0.67-1.53) for drinkers.

Conclusions: We were able to establish a significant positive association between height and diabetes for nonoverweight, elderly, Japanese, non-drinking men undergoing a health check-up. Since height indicates the influence of childhood social and physical condition childhood social and physical condition may contribute to the development of diabetes later in life.

Keywords: Height; Drinking status; Diabetes; Non-overweight; Elderly men

Abbreviations: AST: Aspartate Transaminase; GGT:γ-Glutamyltranspeptidase; HbA_{1c}: Hemoglobin A_{1c}; JDS: Japanese Diabetes Society; NGSP: National Glycohemoglobin Standardization Program; TG: Triglyceride

Introduction

A previous study of ours reported observing a significant positive association between height and hyperuricemia for non-overweight (BMI<25kg/m²) men [1]. The reason for this association may be based on the assumption that height can be regarded as a surrogate marker of childhood social and physical condition while BMI may reflect primarily current physical condition [1-3], analysis of non-overweight subjects may elucidate a potential effect of height [1,2]. Furthermore, a Chinese study reported a positive association between plasma uric acid concentration and incidence of type2 diabetes [4]. The Rancho Bernardo Study reported uric acid may be a useful predictor for diabetes in older adults with impaired fasting plasma glucose [5]. In another case, a control study, with 50 normal healthy individuals and 50 diabetes patients, reported that serum uric acid levels linearly increased with serum insulin levels in newly diagnosed diabetic patients [6]. A study investigating the association between height and diabetes among non-overweight subjects might indicate the influence of childhood social and physical condition on diabetes. However, no study has reported any association on those topics. Because women might not be suitable subjects for such an investigation since their height is negatively affected by vertebral compression fractures, which are mainly caused by postmenopausal osteoporosis [7], we limited our investigation to Japanese men. Other Japanese studies have reported that there may be a complicated association between drinking status and insulin resistance [8] as well as incidence of diabetes among Japanese men [9]. Since it is known that Japanese men are characterized by a high prevalence of drinking [10,11], studies to investigate the association between height and diabetes should take drinking status into account. We therefore based our study on the hypothesis that height is positively associated

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with risk of diabetes for non-overweight, elderly, Japanese men, especially non-drinkers.

To validate this hypothesis, we conducted across-sectional study of a rural population of elderly, non-overweight, Japanese men who underwent general health check-ups between 2005 and 2012.

Methods

Participants

Written consent forms were available in Japanese to ensure comprehensive understanding of the study objectives, and informed consent was signed off on by the participants. This study was approved by the Ethics Committee for Use of Humans of Nagasaki University (Project Registration No.: 0501120073). The survey population covered 1,175 men aged 60 to 89 years, all residents of the western rural community of the Goto Islands, who participated in this study between 2005 and 2012. A total of 22 individuals with missing data and 366 overweight (BMI ≥ 25 kg/m²) individuals were excluded because analysis among non-overweight subjects may elucidate a potential effect of height [1,2] which is regarded as a surrogate marker of childhood social and physical condition [1-3,12,13], leaving 787 men for enrollment in this study (participation rate=67.0%). The mean age of the study population was 70.5 years (± 6.8 SD; range 60-89). In our study, the mean height values (161.7 cm, SD:6.36) were almost the same as found by the Japan Public Health Center-based Prospective Study (JPHC Study) (162.8 cm, SD:6.43cm) of 15,564 Japanese men [12], and also the height quartiles (<157.9 cm, 157.9-161.7 cm, 161.8-165.7 cm, >165.7 cm) in our present study were similar to the CIRCS study (<159 cm, 159-162 cm, 163-166 cm, >166 cm) of 4,567 Japanese men [2]. Another JPHC Study of 35,365 men reported that the prevalence of overweight participants (BMI ≥ 25 kg/m²) was 28.4 % in their study [14], which is also similar to the prevalence in the present study (31.7%). We therefore believed that our study included sufficient representativeness of the larger community, which might also be representative of the general Japanese population.

Data collection and laboratory measurements

Briefly, height in stocking feet and weight in light clothing were measured with an automatic body composition analyzer (BF-220; Tanita, Tokyo, Japan) when blood was drawn.

Systolic and diastolic blood pressures at rest were recorded using a blood pressure measuring device (HEM-907; Omron, Kyoto, Japan).

Fasting blood samples were obtained and the serum was separated and centrifuged after blood coagulation. Serum samples were also obtained in individual siliconized tubes. Serum triglycerides (TG), serum uric acid, and serum creatinine were measured using the enzyme method, serum HDL-cholesterol using the direct method, HbA_{1c} using the latex agglutination method, while serum Aspartate Aminotransferase (AST) was measured using the JASCC standardized method.

Trained interviewers obtained information on smoking status, drinking status, medical history, use of antihypertensive agents, lipid-lowering medication use, and use of medication for diabetes mellitus. HemoglobinA_{1c} (HbA_{1c}), as defined by the National Glycohemoglobin Standardization Program (NGSP), was calculated with the following equation, which was recently proposed by a working group of the Japanese Diabetes Society (JDS): HbA_{1c} (NGSP) = HbA_{1c} (JDS) + 0.4%. Presence of diabetes was defined as HbA_{1c} (NGSP) \geq 6.5%, and/or initiation of glucose-lowering medication or insulin therapy.

Statistical analysis

We established height categories according to the quartiles of height for all non-overweight subjects.

Differences in age-adjusted mean values or prevalence of potential confounding factors were calculated per height quartile among all subjects using covariance or general linear models, and simple linear regression analysis was also performed between height and other variables. Logistic regression models were used for calculating odds ratios (OR) and 95% confidence intervals (CI) to determine associations of diabetes with height.

Three different approaches were used to adjust for confounding factors. The first adjustment was only for age (Model 1), and the second used other possible confounding factors, namely: body mass index (kg/m²), smoking status (never been a smoker, former smoker, current smoker), alcohol intake (non-drinker, current light-to-moderate drinker (1-6 times/week) and current heavy drinker (every day)), systolic blood pressure (mmHg), antihypertensive medication use (no, yes), history of cardiovascular disease (no, yes) (Model2). Model3 also included lipid lowering medication use (no, yes), HDL-cholesterol (mg/ dL), TG (mg/dL), AST (IU/L), serum creatinine (mg/dL) and serum uric acid (mg/dL). In addition, subjects were stratified by drinking status (non-drinker, drinker (current light-to-moderate drinker (1-6 times/week) and current heavy drinker (every day)) because alcohol consumption reportedly not only influences insulin resistance [8] but also incidence of diabetes in non-overweight men [9]. Furthermore, height may also be associated with drinking status [1-3,12,13], which might have a strong influence on height category and act as a confounding factor, and therefore we used the same height categories as for all subjects for both drinkers and non-drinkers.

All statistical analyses were performed with the SAS system for Windows (version 9.3; SAS Inc., Cary, NC). All p-values for statistical tests were two-tailed, and values of <0.05 were regarded as statistically significant.

Results

Of the 787 men taking part in the general health check-up program, 83 men were diagnosed with diabetes. The prevalence of current drinkers was 48.9%.

Table 1 lists the characteristics of the total study population. The age-adjusted characteristics for this study population in relation to body height show that HbA_{1c} (NGSP), serum uric acid, and serum creatinine showed a significant positive association with body height. Also, whilst not significant, a positive association was observed between the prevalence of current drinkers and height (p=0.057). Simple correlation analysis of height revealed that there was a significant inverse association between age and height.

As shown in Table 2, even though a positive association was observed between height and diabetes for all subjects, it was not statistically significant.

To clarify the association between HbA_{1c} (NGSP) and drinking status, we performed additional analysis of participants who were not taking diabetic medication using the general linear model. In this analysis, we found a significant association between HbA_{1c} (NGSP) and drinking status. The age-adjusted HbA_{1c} (NGSP) values (minimum mean square (minimum mean square error)) were: 5.6% (0.03%) for non-drinkers, 5.5% (0.04%) for current light-to-moderate drinkers (1-6 times/week), and 5.5% (0.04%) for current heavy drinkers (every day) (P for trend=0.007).

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	A	ge adjusted mea	Simple correlation analysis of				
	Height Quartile					height and other variables	
	Q1 (low)	Q2	Q3	Q4 (High)	P for trend	r	р
Median Height level, cm	154.6	159.7	163.9	169.0			
Number	197	196	197	197		2587	
Age, years	73.1 ± 6.9	71.5 ± 7.0	69.4 ± 6.2	68.0 ± 6.2	<0.001	-0.296	<0.001
Systolic blood pressure, mmHg	144	142	140	142	0.229	-0.065	0.068
Diastolic blood pressure, mmHg	83	83	82	84	0.254	0.086	0.015
Antihypertensive medication use, %	29.1	35.7	29.0	34.7	0.312	-0.025	0.488
Antidiabetic medication use, %	5.3	5.5	8.7	8.9	0.367	0.047	0.187
Lipid lowering medication use, %	5.4	6.1	3.6	7.3	0.462	0.017	0.634
History of cardiovascular disease, %	9.0	14.0	13.1	11.2	0.436	-0.016	0.649
Body mass Index, Kg/m ²	22.0	21.9	21.8	21.9	0.836	-0.016	0.363
Current drinkers, %	42.2	46.2	51.9	55.3	0.057	0.140	<0.001
Current smokers, %	22	25	19	22	0.635	0.009	0.791
HbA _{1c} (NGSP), %	5.7	5.9	5.9	6.2	0.012	0.012	0.730
Serum HDL-Cholesterol, mg/dL	56	56	58	55	0.093	0.009	0.795
Serum triglycerides (TG), mg/dL	112	105	107	112	0.707	0.038	0.278
Serum aspartate aminotranferase (AST) IU/L	25	25	25	24	0.384	-0.071	0.045
Serum uric acid, mg/dL	5.7	5.9	5.9	6.2	0.012	0.128	<0.001
Serum creatinine, mg/dL	0.87	0.89	0.91	0.97	0.002	0.119	<0.001

Age: Mean ± Standard Deviation, P: P value, NGSP: National Glycohemoglobin Standardization Program, Height quartile: <157.9cm, 157.9-161.7cm, 161.8-165.7 cm and >165.7 cm.

	Height Quartile					Per 1 SD increment	
	Q1 (low)	Q2	Q3	Q4 (High)	P for trend	in height (6.36 cm)	
All subjects							
Number	197	196	197	197			
No. of cases (percentage)	19 (9.6)	17 (8.7)	23 (11.7)	24 (12.2)			
Model 1	1.00	0.91 (0.46-1.81)	1.29 (0.67-2.49)	1.38 (0.71-2.68)	0.223	1.14 (0.90-1.44)	
Model 2	1.00	0.89 (0.44-1.78)	1.31 (0.68-2.55)	1.41 (0.72-2.77)	0.193	1.15 (0.90-1.47)	
Model 3	1.00	0.92 (0.46-1.84)	1.35 (0.69-2.64)	1.62 (0.82-3.20)	0.102	1.22 (0.95-1.57)	

Model 1: Adjusted for age, Model 2: Age + other CVD risk factors (systolic blood pressure, antihypertensive medication use, body mass index, smoking, alcohol intake, and history of cardiovascular disease), Model 3: Model 2+serum HDL-cholesterol, serum triglycerides (TG) lipid-lowering medication use, serum aspartate aminotranferase (AST), serum uric acid, and serum creatinine, High quartiles: <157.9cm, 157.9-161.7cm, 161.8-165.7 cm and >165.7 cm.

Table 2: Odds Ratios (OR) and 95% confidence Intervals (CI) for Diabetes in relation to height for all subjects.

We conducted further investigations to evaluate height in relation to drinking status using the general linear model. Furthermore, we found that height was also significantly associated with drinking status. The age-adjusted values of height (minimum mean square (minimum mean square error)) were: 161.0 cm (0.3 cm) for non-drinkers, 162.0 cm (0.4 cm) for current light-to-moderate drinkers (1-6 times/week), and 162.6 cm (0.4 cm) for current heavy drinkers (every day) (P for trend=0.009). Since drinking status was established after childhood and we also found height was significantly associated with drinking status, this significant association is not caused by alcohol consumption, although height might affect drinking status in later life. This means height might partly indicate a capacity for alcohol tolerance. Therefore, drinking status-specific height values (mean: 160.9 cm, SD: 6.6 cm for non-drinkers, and mean: 162.6 cm, SD:5.9 cm for drinkers) might have a confounding effect on the influence of height on diabetes. Thus, we used the same height categories, which were categorized among all subjects, to investigate the association between height and diabetes in relation to drinking status.

Table 3 lists associations between height and diabetes stratified by drinking status, showing a significant association between height and diabetes for non-drinkers but no such significant association for drinkers. The fully-adjusted odds ratio (OR) and 95% confidence interval (CI) for diabetes for an increment of 1 SD in height (6.36 cm) were 1.44 (1.03-2.02) for non-drinkers and 1.01 (0.67-1.53) for drinkers.

Discussion

The main finding of the present study was that height is associated with diabetes for non-overweight, elderly, non-drinking Japanese men undergoing health check-ups in the Goto Islands. Since height indicates the influence of childhood social and physical condition, childhood social and physical condition may contribute to the development of diabetes later in life.

The impairment of glucose tolerance with age was first recognized by Spence [15] in subjects over 60-years old. More recent studies have indicated that muscle is the principal site of development of a significant impairment with age of peripheral glucose uptake [16-19]. Aging is

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	Height Quartile					
	Q1 (low)	Q2	Q3	Q4 (High)	P for trend	Per 1 SD incremen in height 6.36cm
Non-drinkers						
Number	118	107	93	84		
No. of cases (percentage)	10 (8.5)	12 (11.2)	10 (10.8)	14 (16.7)		
Model 1	1.00	1.43 (0.59-3.49)	1.56 (0.60-4.01)	2.82 (1.13-7.05)	0.032	1.40 (1.01-1.93)
Model 2	1.00	1.33 (0.54-3.29)	1.44 (0.54-3.79)	2.76 (1.08-7.01)	0.041	1.38 (1.00-1.93)
Model 3	1.00	1.34 (0.53-3.34)	1.39 (0.52-3.73)	3.02 (1.17-7.82)	0.032	1.44 (1.03-2.02)
Drinkers						
Number	79	89	104	113		
No. of cases (percentage)	9 (11.4)	5 (5.6)	13 (12.5)	10 (8.8)		
Model 1	1.00	0.43 (0.14-1.34)	0.98 (0.39-2.47)	0.64 (0.24-1.71)	0.736	0.91 (0.63-1.34)
Model 2	1.00	0.43 (0.14-1.38)	0.98 (0.38-2.50)	0.65 (0.24-1.76)	0.750	0.92 (0.63-1.36)
Model 3	1.00	0.41 (0.13-1.37)	1.05 (0.40-2.75)	0.74 (0.26-2.12)	0.977	1.01 (0.67-1.53)

Model 1: Adjusted for age, Model 2: Age + other CVD risk factors (systolic blood pressure, antihypertensive medication use, body mass index, smoking, alcohol intake, and history of cardiovascular disease), Model 3: Model 2+serum HDL-cholesterol, serum triglycerides (TG) lipid-lowering medication use, serum aspartate aminotranferase (AST), serum uric acid, and serum creatinine, High quartiles: <157.9cm, 157.9-161.7cm, 161.8-165.7 cm and >165.7 cm.

Table 3: Odds Ratios (OR) and 95% confidence Intervals (CI) for Diabetes in relation to height stratified by drinking status.

associated with reduced neuromuscular function [20]; in particular, it has been suggested that changes in the number of cells and levels of neuromuscular systems occur with advancing age [21-25]. Moreover, in present study taller people may suffer a much greater reduction in total muscle mass with advancing age than do shorter people. In fact, previous cross-sectional studies in North America and Europe have described the sarcopenic index, which is used to diagnose the age-associated loss of skeletal muscle mass and function, as: muscle mass \div (height)² [26,27]. In the present study, concentration of serum creatinine, which is a well-known factor that is positively associated with muscle volume, also showed a significant positive association with height. As far as non-overweight, elderly men are concerned, taller individuals may therefore be at a higher risk of impaired glucose tolerance than their shorter counter parts. To prevent incidence of diabetes, taller elderly individuals should make more active lifestyle changes to adapt to aging than their shorter counterparts.

Since previous studies had reported a positive association between blood concentration of uric acid and diabetes [4-6], and a previous study of ours had reported a positive association between height and hyperuricemia (serum uric acid>7.0mg/dL) [1], we conducted further investigations. As a result, we found no significant associations between diabetes and hyperuricemia (serum uric acid>7.0mg/dL). The age-adjusted ORs of diabetes for hyperuricemia were: 0.84(0.48-1.47, P=0.544) for all subjects, 1.05 (0.48-2.28, P=0.911) for nondrinkers and 0.70 (0.31-1.58, P=0.386) for drinkers. We also observed a significant association between serum uric acid and serum creatinine; the simple linear regression analysis showed; r=0.35 (P=<0.001) for all subjects, r=0.37 (P<0.001) for non-drinkers, and r=0.34 (P<0.001) for drinkers. Both serum concentration of uric acid and serum creatinine are well-known factors that are strongly influenced by renal function, and short stature maybe correlated with renal dysfunction [28,29]. The association of hyperuricemia with diabetes might be confounded by renal impairment that could potentially be more frequent among participants of shorter stature. Further investigation using data on precise renal function is necessary.

However, it is not yet clear why no positive association between height and diabetes was observed among drinkers. A previous cross-sectional study of 1,902 asymptomatic Japanese men reported detecting an inverse association between alcohol consumption and insulin resistance, independent of central obesity, metabolic profiles, or fatty liver disease [8]. On the other hand, another previous Japanese prospective study of 12,913 men showed moderate-to-high alcohol consumption was positively associated with incidence of diabetes for BMI \leq 22 kg/m² while no significant association was observed for 22 kg/m²<BMI \leq 25 kg/m² [9]. These studies clearly point to the influence of alcohol consumption on risk of diabetes. Our follow-up study, which excluded potential participants who were taking anti-diabetic medication, showed a significant inverse association between HbA_{1c} (NGSP) and drinking status. Even though we were able to conclude that HbA_{1c} (NGSP) was influenced by drinking status, a larger BMIstratified study is necessary to clarify the influence of drinking status on HbA1. (NGSP). In addition to those complicated reports, height may also be associated with prevalence of drinking status, since in our study, height showed a non-significant positive association with current drinking status, as was also reported by previous studies [1-3,12,13], and in the follow-up study, a significant association between height and drinking status (non-drinker, drinker current light-to-moderate drinker (1-6 times/week) and current heavy drinker (every day)) was observed. Therefore, alcohol may act as a confounding factor for the association between height and diabetes.

Potential limitations of this study warrant consideration. Since we did not have access to data regarding quantities of alcohol consumption, we classified current drinking status only in terms of frequency of drinking per week, which may have also confounded the association between height and diabetes among current drinkers. Also, because we did not have enough data to conduct a stratified analysis by alcohol consumption for current drinkers, we could not determine the exact influence of alcohol consumption. However, we observed a significant positive association between height and diabetes among non-drinkers. Since drinking status is a known factor that is determined after childhood when the height has already been determined, we therefore thought the association between height and diabetes among drinkers is only due to the confounding effect of drinking status. Even though we did not observe a significant association between height and diabetes among drinkers, such associations may be exhibited by drinkers in addition to non-drinkers. Further studies with larger numbers of participants will therefore be necessary. Since data on exercise and food intake was not available, we could not make adjustments for the influence of those factors as in our previous study [30,31]. However, in our present

study, the multivariable adjusted model including BMI values showed a significant association. As in previous studies [1-3,10,11,30,31], our survey population consisted of men undergoing a general health checkup. The influence of selection bias was underlying. Since a previous study reported that the mean height for the age range 30-39was lower for men born between 1936 and 1945 (163.8 cm) than for those born between 1961 to 1970 (170.6cm) [13], this difference might be due to a change in diet and food consumption from the period during World War II to the post-war period. Since Q1 was the oldest age group, it was not unexpected that diabetes was most prevalent in Q1 and less prevalent in Q4, which was the youngest age group. However, our present study showed height is positively associated with diabetes among nondrinking, non-overweight men. Furthermore, the associations between height and diabetes were the same even when we limited the analysis to older subjects who were born in or before 1945; the fully-adjusted ORs of diabetes for an increment of 1SD in height were: 1.27 (0.98-1.66) for all subjects, 1.52 (1.06-2.16) for non-drinkers and 0.98 (0.62-1.53) for drinkers. Furthermore, because we do not have data on distinct diabetes duration and progression, type of diabetes and duration of medication, we could not take account of those factors in the present study. Finally, we could not establish any causal relationships because this study was cross-sectional. However, since height was regarded as a surrogate marker of childhood social and physical condition [1-3,12,13] and the target population in the present study was elderly men, we believe this investigation has the characteristics of a prospective study to a certain degree. Further prospective population based studies are needed to eliminate the possibility of a causal relationship between height and diabetes.

In conclusion, we determined that height is independently and positively associated with diabetes for non-overweight, elderly, Japanese non-drinking men undergoing health check-ups in the Goto Islands. Since height indicates the influence of childhood social and physical condition, childhood social and physical condition may contribute to the development of diabetes later in life.

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