Original Contribution

Peripheral Insensate Neuropathy—A Tall Problem for US Adults?

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The relation between height and lower extremity peripheral insensate neuropathy among persons with and without diabetes was examined by use of the 1999–2002 US National Health and Nutrition Examination Survey with 5,229 subjects aged 40 or more years. A monofilament was used to determine whether any of three areas on each foot were insensate. Peripheral insensate neuropathy was defined as the presence of one or more insensate areas. Its prevalence was nearly twice as high among persons with diabetes (21.2%) as among those without diabetes (11.5%; $p < 0.001$). Men (16.2%) had 1.7 times the prevalence of peripheral insensate neuropathy as did women (9.4%), but the difference was not significant after adjustment for height. Greater height was associated with increased peripheral insensate neuropathy prevalence among persons with and without diabetes ($p < 0.001$). This association was characterized by a sharp increase in prevalence among persons who were taller than 175.5 cm. Peripheral insensate neuropathy risk was significantly higher among those taller than 175.5 cm (adjusted odds ratio = 2.3, 95% confidence interval: 1.5, 3.5). The authors conclude that body height is an important correlate of peripheral insensate neuropathy. This association largely accounts for the difference in peripheral insensate neuropathy prevalence between men and women. Height may help health-care providers to identify persons at high risk of peripheral insensate neuropathy.

aging; body composition; data collection; diabetes mellitus; peripheral nervous system diseases

Peripheral insensate neuropathy is common in the middle-aged or older adult US population (1). It is one of the most disabling complications of diabetes because of its high incidence and its potential to lead to lower extremity ulceration, deformation, and amputation (2). Early identification of neuropathy, tight glycemic control among people with diabetes, smoking cessation, and other preventive care are considered key public-health strategies against costly foot complications (3–6). Factors associated with neuropathy include diabetes mellitus, poor glycemic control, male sex, White race, and older age (1, 7, 8).

There is also growing, yet still unappreciated evidence that height may be an important and practical predictor of peripheral insensate neuropathy or lower extremity amputation (7–9). Height may increase the risk of peripheral insensate neuropathy because of increased axon surface exposure to toxins. Most studies that have noted a relation of height with peripheral neuropathy or amputation were conducted among persons with diabetes mellitus (7, 10–15), and few population-based studies have been conducted (13). It is unknown whether there is a threshold in the association between height and risk for peripheral insensate neuropathy in the general population.

As the first nationally representative epidemiologic survey to include an assessment of peripheral insensate neuropathy based on monofilament testing, the 1999–2002 US National Health and Nutrition Examination Survey (NHANES) allowed us to explore the relation between body height and peripheral insensate neuropathy among persons with and without diabetes mellitus, while accounting for various confounders or effect modifiers. In particular, it allowed us to examine whether there are threshold effects in the association between height and peripheral insensate neuropathy and whether any association is modified by the effects of factors such as diabetes status, sex, and race/ethnicity.

MATERIALS AND METHODS

The NHANES is a nationally representative survey of the US civilian noninstitutionalized population conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention (16). Since 1999, NHANES staff have conducted interviews and performed physical examinations on a continuous basis. Participants are interviewed in their homes about their health history, health behaviors, and risk factors and subsequently undergo the physical examination at a mobile examination center. The procedures to select the sample and conduct the interview and examination have been described elsewhere (16). Informed consent is obtained from all participants, and the protocol has been approved by the institutional review board of the National Center for Health Statistics.

This report is based on 4 years of NHANES data (from 1999 to 2002). Of 6,668 persons aged 40 or more years who answered the diabetes questionnaire during this time, 5,848 (87.8 percent) also underwent the health examination, which included anthropometry. Of this sample, 619 (10.6 percent) did not undergo the peripheral insensate neuropathy examination because they refused or had a physical/health limitation, because of technical problems and errors in measurement, or because of some other unspecified reason; 86 more were excluded from our analysis because they had no height measurement. Thus, peripheral insensate neuropathy examination results and height were available for 5,229 subjects aged 40 or more years.

Assessment of peripheral insensate neuropathy

Peripheral insensate neuropathy was assessed by testing subjects' foot sensation with a standardized 5.07-gauge (10-g force) Semmes-Weinstein nylon monofilament according to a standard protocol (1). Health technicians applied pressure with the monofilament at three sites on the bottom of each of the subjects' feet (plantar, first metatarsal head; plantar, fifth metatarsal head; and plantar, hallux) (i.e, a total of six sites). They applied the monofilament until it buckled and then held it for another second. A site was considered insensate if there were 1) two incorrect responses, 2) two ''unable to determine'' responses, or 3) one incorrect and one ''unable to determine'' response for a site. The sites are tested in a nonsequential order to allow for better dis-

crimination of sensation by the examinee. Impaired sensation was quantified by the total number of insensate areas for both feet (range: 0–6), and peripheral insensate neuropathy was defined as one or more insensate area. Previous studies have found the presence of one or more insensate areas to be highly predictive of ulcers and amputation and to have moderately high sensitivity (~85 percent) and specificity (~80 percent) based on vibration testing and ulcer history (17–20).

Diabetes and other measurements

Participants' responses to the questionnaires were used to categorize them by their self-reported physician-diagnosed diabetes status, duration of history of diabetes (no diabetes; diabetes <7 years; diabetes ≥7 years), measured high blood pressure (yes, no), and age (years), race/ethnicity (non-Hispanic White vs. others), education (less than high school vs. high school education or more), current smoking status (yes, no), and current alcohol consumption status (none; mild: <1 drink/week; moderate: 1–7 drinks/week; and heavy: ≥8 drinks/week).

Participants' height (cm) and weight (kg) were measured with a standard protocol, and they were divided into four quartile groups by height (<161, 161–167.9, 168–175.9, and ≥176 cm) and by weight (<67, 67–78.9, 79–91.9, and ≥92 kg). Their body mass index was calculated as weight (kg)/height (m)^2, and they were divided into three groups on the basis of their body mass index: normal (<25), overweight (25–29.9), and obese (≥30).

The glycated hemoglobin A1c (A1c) percentage was used to measure participants' glycemic control. They were divided into two sets of four quartiles on the basis of their A1c percentage levels: ≤6.1, 6.2–7.1, 7.2–8.3, and ≥8.4 percent for those with diabetes and <5.1, 5.1–5.2, 5.3–5.4, and ≥5.5 percent for those without diabetes. Detailed descriptions about blood collection and processing are provided in the *NHANES Laboratory/Medical Technologists Procedures Manual* (21).

The self-reported average level of physical activity, including work, housework if a homemaker, and going to and attending classes if a student, each day had been divided into three levels: mainly sit, walk a lot, and carry loads or climb often.

Participants' blood pressure was measured according to standard protocol involving three and sometimes four systolic and diastolic blood pressure measurements taken with a mercury sphygmomanometer in the mobile examination center on all eligible individuals (21). We defined high blood pressure as an average systolic blood pressure of 140 or more mmHg or an average diastolic blood pressure of 90 or more mmHg.

Statistical analyses

In our primary analyses, we estimated the prevalence of peripheral insensate neuropathy in the overall noninstitutionalized US population aged 40 or more years and within several subgroups. We used SAS, version 9.1, software (SAS Institute, Inc., Cary, North Carolina) for data

TABLE 1.   Characteristics of the estimated 106.7 million noninstitutionalized US residents aged 40 or more years, by self-reported diabetes status, based on projections from data of the National Health and Nutrition Examination Survey, 1999–2002

Variables	With diabetes mellitus (n = 683, estimated US 10.1 million population)		Without diabetes mellitus (n = 4,546, estimated US 96.6 million population)	
	No.	% or mean (SE*)	No.	% or mean (SE)
Height, cm (%)				
<161 (quartile 1)	231	30.2 (2.6)	1,337	24.9 (0.6)
161–167.9 (quartile 2)	158	23.8 (2.6)	1,135	25.3 (0.7)
168–175.9 (quartile 3)	181	26.5 (2.1)	1,136	25.3 (0.7)
≥176 (quartile 4)	113	19.5 (2.5)	938	24.6 (0.7)
Weight, kg (%)				
<67 (quartile 1)	120	18.2 (2.1)	1,222	26.2 (0.9)
67–78.9 (quartile 2)	176	19.5 (2.2)	1,232	25.5 (0.9)
79–91.9 (quartile 3)	176	23.9 (2.1)	1,127	25.2 (0.7)
≥92 (quartile 4)	208	38.4 (2.5)	953	23.2 (1.0)
Body mass index, kg/m^2 (%)				
<25 (normal)	114	17.9 (2.5)	1,353	31.8 (1.2)
25–29.9 (overweight)	258	32.6 (2.2)	1,763	37.8 (0.9)
≥30 (obese)	308	49.5 (3.0)	1,418	30.4 (1.2)
Age, years (mean)	683	61.3 (0.6)	4,546	56.0 (0.3)
Sex, men (%)	351	51.9 (2.4)	2,263	46.9 (0.7)
Race/ethnicity, White (%)	257	63.6 (3.5)	2,549	79.5 (1.5)
Education, less than high school (%)	331	34.8 (2.8)	1,522	20.5 (1.1)
Current smoking, yes (%)	100	17.1 (2.1)	886	20.3 (0.9)
Alcohol, drinks/week (%)				
<1	584	85.0 (2.3)	2,969	62.2 (1.8)
1–7	55	10.1 (2.0)	918	23.1 (1.5)
≥8	32	4.9 (1.3)	574	14.8 (0.8)
Physical activity (%)				
Mainly sit	254	35.9 (3.2)	1,109	25.4 (0.9)
Walk a lot	345	50.2 (3.3)	2,540	52.9 (0.9)
Carry loads or climb often	83	13.9 (1.8)	887	21.8 (1.0)
Glycated hemoglobin A1c (%)				
Lowest quartile	133	21.1 (2.3)	580	17.3 (1.7)
Second quartile	172	26.8 (1.9)	788	21.0 (0.7)
Third quartile	174	25.8 (2.2)	1,029	22.9 (0.6)
Highest quartile	179	26.3 (2.1)	2,016	38.8 (1.9)
High blood pressure (%)	265	36.4 (2.3)	1,479	27.2 (1.1)
Duration of diabetes mellitus, years (%)				
0.1–6.9	301	46.4 (3.2)		
≥7	382	53.6 (3.2)		
Peripheral insensate neuropathy (%)	185	25.0 (2.0)	668	11.2 (0.6)

* SE, standard error.

management and manipulation. Analyses were conducted with SUDAAN, version 9.0.1, software (SUDAAN Statistical Software Center, Research Triangle Park, North Carolina) to take into account the complex sampling design and to obtain representative estimates. For each of the primary outcomes, we used the largest sample size available to estimate prevalence. We computed 95 percent confidence intervals using the critical value for a *t* distribution with
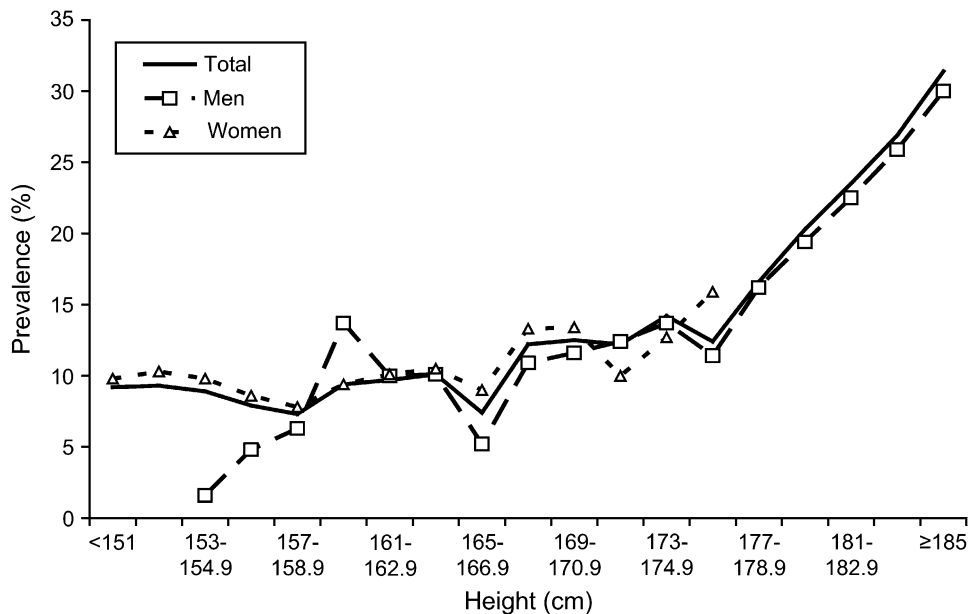
FIGURE 1. Age- and race-adjusted population prevalence of peripheral insensate neuropathy by 2-cm height increments among non-institutionalized US residents aged 40 or more years, National Health and Nutrition Examination Survey, 1999–2002.

the appropriate number of degrees of freedom for each subgroup, and we used logistic regression to calculate age- and race-adjusted and other multivariate-adjusted prevalence estimators (predictive marginals), as well as the odds ratio with 95 percent confidence interval. We applied a joinpoint regression model and used the permutation test to determine whether there was a change of linear trend for age- and race-adjusted prevalences of peripheral insensate neuropathy by height (22). The joinpoint and 95 percent confidence interval were calculated by Joinpoint, version 3.0, freeware (23). We also assessed the significance of interaction terms between height and other variables and tested statistical hypotheses at the 0.05 level.

RESULTS

Persons with diabetes are older than persons without diabetes ($p < 0.001$). The means of height and weight were 167.0 cm (standard error (SE): 0.6) and 87.8 kg (SE: 1.3) for persons with diabetes and 168.5 cm (SE: 1.3) and 79.9 kg (SE: 0.5) for persons without diabetes. Table 1 shows characteristics of the sample by diabetes status weighted to the US population. Among the 5,229 persons representing a US population of 107 million (90.5 percent) noninstitutionalized civilians aged 40 or more years, 12.5 percent had peripheral insensate neuropathy (15.5 percent among men and 9.9 percent among women; $p < 0.001$). The age- and race-adjusted prevalence of peripheral insensate neuropathy was 21.2 percent among persons with diabetes and 11.5 percent among persons without diabetes ($p < 0.001$). Compared with persons without diabetes, those with diabetes were,

on average, shorter, heavier, and less likely to be non-Hispanic White, not to have finished high school, or to smoke or drink. Persons with diabetes also had a higher prevalence of high blood pressure than did persons without diabetes. The mean duration of diabetes among persons with diabetes was 11.8 years; the median duration was 7 years with an interquartile range of 2–15 years.

Peripheral insensate neuropathy prevalence increased with age and was higher among men than women in all age groups. The prevalence of peripheral insensate neuropathy among persons aged 40–44 years was 7.9 percent for men and 3.0 percent for women, and it increased linearly to 22.2 percent and 12.6 percent among those aged 65–69 years, reaching 45.5 percent and 32.9 percent, respectively, among those aged 85 or more years.

The mean height was 176 cm among men and 161 cm among women. The median and interquartile range of body height for men and women were 176 (171–181) and 162 (157–166) cm, respectively; 78 percent of men had height greater than 170 cm, while only 10 percent of women had height greater than 170 cm. For our analyses of both sexes together, we chose the second quartile of body height as the referent quartile, because it provided the greatest amount of overlap of the height distributions among men and women.

As shown in figure 1, the age- and race-adjusted prevalence of peripheral insensate neuropathy was fairly constant among men 175.5 cm (5 feet, 9 inches) or shorter and among women 171.5 cm (5 feet, 8 inches) or shorter but increased sharply with height. The joinpoint regression detected a linear threshold for men of 175.5 cm (95 percent confidence interval (CI): 161.5, 181.5); however, it did not find any statistically significant threshold for women, probably

TABLE 2. Multivariate-adjusted peripheral insensate neuropathy prevalence among noninstitutionalized US residents aged 40 or more years, with and without diabetes, based on data from the National Health and Nutrition Examination Survey, 1999–2002*

	With diabetes mellitus			Without diabetes mellitus		
	Peripheral insensate neuropathy (% (SE†) for categorical variable)	Odds ratio	95% confidence interval	Peripheral insensate neuropathy (% (SE) for categorical variable)	Odds ratio	95% confidence interval
Height, cm						
<161 (quartile 1)	25.2 (5.6)	1.7	0.7, 4.2	8.0 (1.0)	0.8	0.6, 1.1
161–167.9 (quartile 2)	17.4 (3.9)	1.0	Referent	9.3 (1.1)	1.0	Referent
168–175.9 (quartile 3)	22.8 (4.2)	1.5	0.6, 3.6	9.8 (1.2)	1.1	0.7, 1.7
≥176 (quartile 4)	36.3 (6.5)	3.1	1.1, 8.8	17.5 (1.9)	2.2	1.5, 3.3
Weight, kg						
<67 (quartile 1)	24.2 (5.0)	1.0	Referent	7.6 (0.7)	1.0	Referent
67–78.9 (quartile 2)	19.3 (3.8)	0.7	0.3, 1.6	10.3 (1.1)	1.4	1.1, 1.9
79–91.9 (quartile 3)	22.3 (3.3)	0.9	0.4, 1.8	10.9 (1.0)	1.5	1.1, 2.0
≥92 (quartile 4)	29.5 (4.2)	1.4	0.6, 3.2	15.6 (1.5)	2.4	1.8, 3.1
Sex						
Men	25.2 (3.5)	1.1	0.5, 2.2	11.1 (0.8)	1.0	0.8, 1.4
Women	24.1 (3.4)	1.0	Referent	10.8 (1.0)	1.0	Referent
Race/ethnicity						
White	23.7 (3.1)	1.0	Referent	10.4 (0.7)	1.0	Referent
Non-White	26.5 (2.5)	1.2	0.7, 2.1	14.1 (1.3)	1.5	1.1, 1.9
Education						
Less than high school	26.2 (4.0)	1.2	0.6, 2.2	13.9 (1.6)	1.5	1.1, 2.1
High school or more	23.8 (2.7)	1.0	Referent	10.2 (0.7)	1.0	Referent
Smoking						
Yes	22.2 (5.8)	0.8	0.4, 1.8	12.3 (1.7)	1.2	0.8, 1.8
No	25.1 (1.9)	1.0	Referent	10.7 (0.7)	1.0	Referent
Alcohol (drinks/week)						
<1	25.1 (1.9)	1.3	0.5, 3.0	11.6 (0.8)	1.3	0.9, 1.8
1–7	21.6 (6.4)	1.0	Referent	9.3 (1.2)	1.0	Referent
≥8	24.2 (9.0)	1.2	0.3, 5.4	11.3 (1.3)	1.3	0.9, 1.9
Physical activity						
Mainly sit	25.7 (3.1)	1.0	Referent	10.8 (0.9)	1.0	Referent
Walk a lot	21.6 (2.3)	0.8	0.5, 1.2	11.0 (0.7)	1.0	0.8, 1.3
Carry loads or climb often	33.6 (8.4)	1.5	0.6, 4.2	11.3 (1.1)	1.1	0.8, 1.3
Glycated hemoglobin A1c						
Lowest quartile	19.8 (5.1)	1.0	Referent	11.5 (2.3)	1.0	Referent
Second quartile	21.7 (3.3)	1.1	0.5, 2.7	11.5 (1.5)	1.0	0.6, 1.8
Third quartile	23.6 (3.9)	1.3	0.5, 3.2	11.1 (1.1)	1.0	0.5, 1.8
Highest quartile	32.5 (4.4)	2.1	0.9, 5.2	10.6 (0.7)	0.9	0.5, 1.6
Duration of diabetes mellitus, years						
0.1–6.9	16.3 (2.6)	1.0	Referent			
≥7	31.4 (3.0)	2.5	1.4, 4.5			
High blood pressure						
Yes	24.5 (3.9)	1.0	0.5, 1.9	10.9 (1.0)	1.0	0.8, 1.3
No	24.8 (2.7)	1.0	Referent	11.0 (0.8)	1.0	Referent
Age, years (β)	0.047 (0.012)	1.0	1.0, 1.1	0.063 (0.006)	1.1	1.1, 1.2

  * Variables included in full models: height, weight, sex, race/ethnicity, education, smoking, alcohol, average level of physical activity, glycated hemoglobin A1c, duration of diabetes, high blood pressure, and age.
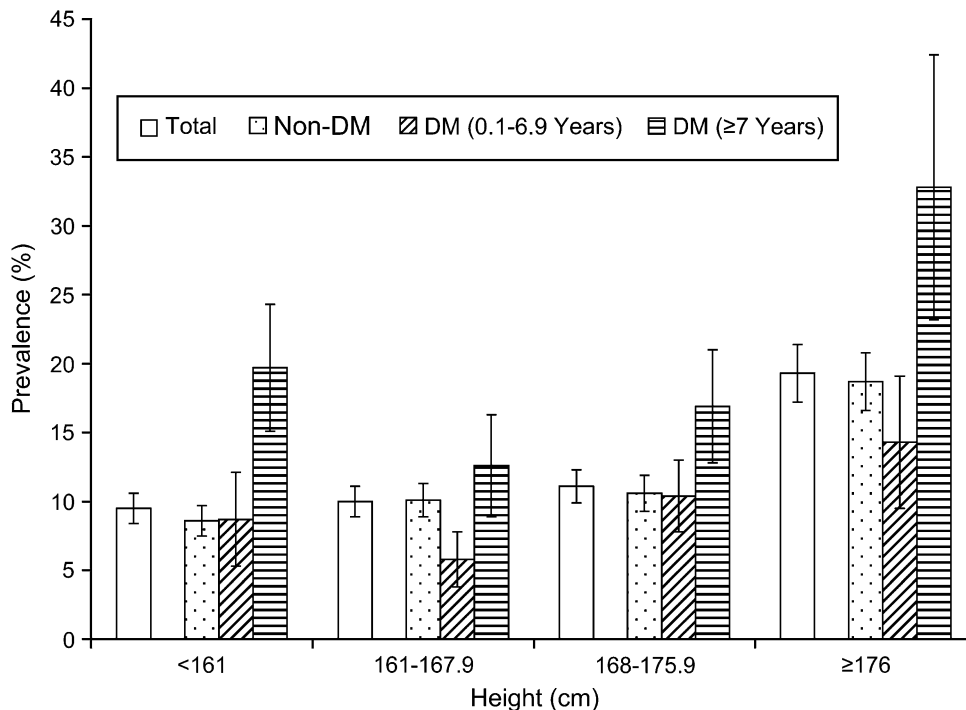 † SE, standard error.

FIGURE 2. Adjusted estimated population prevalence of peripheral insensate neuropathy among US residents aged 40 or more years, by diabetes status and height quartiles, based on data from the National Health and Nutrition Examination Survey, 1999–2002. T-shaped bars, 95% confidence intervals; non-DM, persons without diabetes; DM, persons with diabetes.

because there were not enough women 170 cm tall or taller in the study sample. The threshold of peripheral insensate neuropathy prevalence by height for the entire study population was also 175.5 cm (95 percent CI: 163, 177), similar to that for men. The age- and race-adjusted prevalence of peripheral insensate neuropathy was 11.4 percent among men 175.5 cm or shorter and 20.5 percent among men 176 cm or taller ($p < 0.001$), while the adjusted prevalence of peripheral insensate neuropathy among women was 9.8 percent among those 171.5 cm or shorter and 11.9 percent among those taller than 171.5 cm ($p = 0.500$ for only 136 women).

As shown in table 2, we found similar associations between height and peripheral insensate neuropathy across strata of diabetes status. Those 176 cm or taller had almost twice the age- and race-adjusted peripheral insensate neuropathy prevalence (19.1 percent) as those between 161 and 168 cm in height (10.3 percent). Among persons with diabetes, duration of diabetes was a strong predictor of peripheral insensate neuropathy risk, while among persons without diabetes, heavy weight, non-White race, and not having finished high school were each associated with higher risk for peripheral insensate neuropathy. In a separated multivariate logistic model without height and weight, the odds ratios of peripheral insensate neuropathy among persons with diabetes were 1.0 (referent), 1.2 (95 percent CI: 0.6, 2.3), and 1.5 (95 percent CI: 0.8, 2.9) for normal, overweight, and obese persons, respectively, while the odds ratios of peripheral insensate neuropathy among persons

without diabetes were 1.0 (referent), 1.4 (95 percent CI: 1.1, 1.9), and 1.8 (95 percent CI: 1.3, 1.5) by the same three body mass index groups.

Adjusted total prevalences by height or adjusted prevalences by height and diabetes status adjusted for height, weight, age, sex, race/ethnicity, education, smoking, alcohol consumption, average level of physical activity each day, diabetes and duration of diabetes, and blood pressure status are displayed in figure 2. For the entire population, peripheral insensate neuropathy risk was significantly higher among persons 176 cm or taller (odds ratio = 2.3, 95 percent CI: 1.5, 3.5) than among persons 161–167.9 cm. Adjusted peripheral insensate neuropathy prevalence rates were higher among persons with diabetes than among those without diabetes (odds ratio = 1.8, 95 percent CI: 1.3, 2.5) from another multivariate logistic model. Among persons with diabetes, the likelihood of peripheral insensate neuropathy was increased among persons who were either taller than 175.5 cm or had been diagnosed with diabetes for at least 7 years.

We found no statistically significant interactions between subjects' height and any of the other potential risk factors we examined, including weight, age, sex, race/ethnicity, educational level, smoking status, alcohol consumption status, A1c percentage, and diabetes status and duration. In addition, among persons with diabetes, p values of the interaction terms of height and diabetes duration, as well as height and A1c percentage, were 0.428 and 0.450, respectively.

When we compared the characteristics of potential study subjects who were excluded from analysis because of missing peripheral insensate neuropathy or height data with those of the study subjects with peripheral insensate neuropathy and height data, we found that those who were excluded were, on average, older (60 vs. 57 years), had a higher prevalence of diabetes (14.5 percent vs. 9.4 percent), had a higher mean A1c level (5.8 vs. 5.6 percent), and were less likely to be male (41.3 percent vs. 47.4 percent) or non-Hispanic White (63.8 percent vs. 78.0 percent).

DISCUSSION

In this nationally representative study, we confirmed earlier findings that peripheral insensate neuropathy is common and that it is associated with diabetes, age, and male sex. We also found that being tall was a similarly important risk factor and that this association between height and peripheral insensate neuropathy prevalence probably explains the difference in prevalence between men and women. Our analysis of both sexes together found that the age- and race-adjusted peripheral insensate neuropathy prevalence among persons in the highest quartile of height was 2.3 times higher than that among those in the second quartile (the quartile of height distribution that included adequate numbers of both men and women). Of note, this association was stronger than the association between A1c percentage levels and peripheral insensate neuropathy prevalence among persons with diabetes. Our findings suggest that height, particularly when considered in combination with current recommendations for screening among persons with diabetes, may help to identify persons at relatively high risk for peripheral insensate neuropathy. We estimated that 65.6 percent of noninstitutionalized US adults aged 40 or more years (about 6.6 million people) were at high risk for peripheral insensate neuropathy because they were taller than 175.5 cm or had diagnosed diabetes for more than 7 years. These findings may be useful in the development of risk-stratification algorithms to focus peripheral insensate neuropathy screening on persons at high risk for the condition.

The pathogenesis of the relation between height and the prevalence of peripheral insensate neuropathy remains unclear. It seems unlikely that increased stature has a generalized adverse effect on peripheral nerve function since sensorineural hearing loss, another form of peripheral deficit, by contrast, is associated with reduced stature (24). Instead, the association of height with peripheral insensate neuropathy may be specific to long nerves of the body. Increased nerve length is associated with greater axon surface area, and any localized injury to an axon may impair the overall conduction properties of the nerve. Therefore, persons with longer nerves (and thus a larger total axon surface area) may be at greater risk for neurologic impairment when exposed to otherwise equivalent hazards (e.g., constant concentration of advanced glycation end products). Greater leg length might also be associated with a prolonged time requirement for the complete regeneration of any injured nerve (25); this would tend to increase the duration of pe-

ripheral insensate neuropathy, thus increasing the prevalence of peripheral insensate neuropathy in the population. Alternatively, the association of height with peripheral insensate neuropathy might be related to the increased hydrostatic pressure experienced in the feet of tall persons when they stand up. Peripheral insensate neuropathy would occur more often if aging or prolonged diabetes is linked to a loss of compensatory responses to large pressure changes in small blood vessels. Yet another alternative explanation could be related to greater skin thickness or other protective characteristics on the soles of tall people. This would be consistent with our finding that peripheral insensate neuropathy prevalence is related to weight among nondiabetic persons even after adjustment for height and other covariates (table 2).

In addition, Harris et al. (26) showed that height was not associated with extremity symptomatic neuropathy. Sorensen et al. (7) demonstrated that only 11.7 percent of persons with lower extremity insensate neuropathy defined by vibration perception threshold had lower foot painful neuropathy. In this latter study, height was related to insensate neuropathy but not related to painful neuropathy. These data suggest that sensate neuropathy may be different from insensate neuropathy and perhaps less associated with structural nerve damage.

There were limitations to our study. First, because NHANES does not collect information from people in nursing homes or other similar institutions, our subjects were not representative of the entire older US population. Second, "duration of diabetes" as measured in this study did not reflect the true duration of the disease but the time since diagnosis, and actual diabetes onset might precede its diagnosis by several years (27). Third, there were not enough women taller than 170 cm to reliably determine the peripheral insensate neuropathy prevalence among them. Fourth, because this was a cross-sectional study, we could not determine whether the association between modifiable risk factors and the risk of peripheral insensate neuropathy was a cause-effect association. This may explain why we did not find smoking to be associated with an increased risk of peripheral insensate neuropathy as the authors of a previous study did (8). Fifth, although persons with significant calluses had been excluded from the study, NHANES did not have detailed information about calluses. Finally, we used monofilament testing to determine the peripheral insensate neuropathy status of study subjects when electrophysiologic, nerve conduction, or skin biopsy studies could have produced more accurate diagnostic data; however, in epidemiologic studies, monofilament testing is still an improvement over the use of symptom questionnaires in terms of sensitivity, specificity, and capacity to predict adverse outcomes (17–19, 28).

In conclusion, we found that body height is a risk factor of peripheral insensate neuropathy, that the difference in height between men and women may explain much of the difference in peripheral insensate neuropathy prevalence between them, and that peripheral insensate neuropathy prevalence increases sharply with height at a height threshold of around 175.5 cm. Height may help health-care providers identify persons who require more intensive neuropathic

screening because of their higher risk for peripheral insensate neuropathy.

REFERENCES

1. Gregg EW, Sorlie P, Paulose-Ram R, et al. Prevalence of lower-extremity disease in the US adult population ≥40 years of age with and without diabetes: 1999–2000 National Health and Nutrition Examination Survey. Diabetes Care 2004;27: 1591–7.
2. Vinik AI, Park TS, Stansberry KB, et al. Diabetic neuropathies. Diabetologia 2000;43:957–73.
3. Mason J, O'Keeffe C, McIntosh A, et al. A systematic review of foot ulcer in patients with type 2 diabetes mellitus. I. Prevention. Diabet Med 1999;16:801–12.
4. Ragnarson TG, Apelqvist J. Prevention of diabetes-related foot ulcers and amputations: a cost-utility analysis based on Markov model simulations. Diabetologia 2001;44:2077–87.
5. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA 2005;293:217–28.
6. Sullivan KA, Feldman EL. New developments in diabetic neuropathy. Curr Opin Neurol 2005;18:586–90.
7. Sorensen L, Molyneaux L, Yue DK. Insensate versus painful diabetic neuropathy: the effects of height, gender, ethnicity and glycaemic control. Diabetes Res Clin Pract 2002;57: 45–51.
8. Tesfaye S, Stevens LK, Stephenson JM, et al. Prevalence of diabetic peripheral neuropathy and its relation to glycaemic control and potential risk factors: the EURODIAB IDDM Complications Study. Diabetologia 1996;39:1377–84.
9. Tseng CH. Prevalence of lower-extremity amputation among patients with diabetes mellitus: is height a factor? CMAJ 2006;174:319–23.
10. Gadia MT, Natori N, Ramos LB, et al. Influence of height on quantitative sensory, nerve-conduction, and clinical indices of diabetic peripheral neuropathy. Diabetes Care 1987;10: 613–16.
11. Sosenko JM, Gadia MT, Fournier AM, et al. Body stature as a risk factor for diabetic sensory neuropathy. Am J Med 1986;80:1031–4.
12. Shaw JE, Hodge AM, de Courten M, et al. Diabetic neuropathy in Mauritius: prevalence and risk factors. Diabetes Res Clin Pract 1998;42:131–9.
13. Tapp RJ, Shaw JE, de Courten MP, et al. Foot complications in type 2 diabetes: an Australian population-based study. Diabet Med 2003;20:105–13.
14. Robinson LR, Stolov WC, Rubner DE, et al. Height is an independent risk factor for neuropathy in diabetic men. Diabetes Res Clin Pract 1992;16:97–102.
15. Herman WH, Kennedy L. Underdiagnosis of peripheral neuropathy in type 2 diabetes. Diabetes Care 2005;28:1480–1.
16. National Center for Health Statistics. National Health and Nutrition Examination Survey. NHANES 1999–2004. Hyattsville, MD: National Center for Health Statistics, 2005. (http://www.cdc.gov/nchs/about/major/nhanes/nhanes99-02.htm).
17. Mayfield JA, Reiber GE, Sanders LJ, et al. Preventive foot care in people with diabetes. Diabetes Care 1998;21:2161–77.
18. Mayfield JA, Sugarman JR. The use of the Semmes-Weinstein monofilament and other threshold tests for preventing foot ulceration and amputation in persons with diabetes. J Fam Pract 2000;49(suppl):S17–29.
19. McGill M, Molyneaux L, Spencer R, et al. Possible sources of discrepancies in the use of the Semmes-Weinstein monofilament. Impact on prevalence of insensate foot and workload requirements. Diabetes Care 1999;22:598–602.
20. Abbott CA, Carrington AL, Ashe H, et al. The North-West Diabetes Foot Care Study: incidence of, and risk factors for, new diabetic foot ulceration in a community-based patient cohort. Diabet Med 2002;19:377–84.
21. NHANES laboratory/medical technologists procedures manual. Hyattsville, MD: National Center for Health Statistics, 2005.
22. Kim HJ, Fay MP, Feuer EJ, et al. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med 2000;19:335–51.
23. Statistical Research and Applications Branch, Division of Cancer Control and Population Sciences, National Cancer Institute. Joinpoint freeware, version 3.0. Bethesda, MD: National Cancer Institute, 2005.
24. Barrenas ML, Jonsson B, Tuvemo T, et al. High risk of sensorineural hearing loss in men born small for gestational age with and without obesity or height catch-up growth: a prospective longitudinal register study on birth size in 245,000 Swedish conscripts. J Clin Endocrinol Metab 2005; 90:4452–6.
25. Polydefkis M, Hauer P, Sheth S, et al. The time course of epidermal nerve fibre regeneration: studies in normal controls and in people with diabetes, with and without neuropathy. Brain 2004;127:1606–15.
26. Harris M, Eastman R, Cowie C. Symptoms of sensory neuropathy in adults with NIDDM in the U.S. population. Diabetes Care 1993;16:1446–52.
27. Harris MI, Klein R, Welborn TA, et al. Onset of NIDDM occurs at least 4–7 yr before clinical diagnosis. Diabetes Care 1992;15:815–19.
28. Sosenko JM, Kato M, Soto R, et al. Comparison of quantitative sensory-threshold measures for their association with foot ulceration in diabetic patients. Diabetes Care 1990;13:1057–61.