HHS Public Access

Author manuscript

Am J Med. Author manuscript; available in PMC 2021 February 09.

Published in final edited form as:

Am J Med. 2021 February ; 134(2): 282–284. doi:10.1016/j.amjmed.2020.07.015.

Association of Peripheral Neuropathy with Erectile Dysfunction in US Men

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Abstract

Background: Peripheral neuropathy and erectile dysfunction are common conditions that have both been linked to cardiovascular disease and its risk factors, especially diabetes. The aim of this study was to assess the association of large-fiber peripheral neuropathy with erectile dysfunction in adult US males with and without diabetes.

Methods: We included all men aged ≥40 years from the 2001–2002 National Health and Nutrition Examination Survey (NHANES) with data on erectile dysfunction and peripheral neuropathy (n=1213, including n=206 with diabetes). Erectile dysfunction was assessed by a single question during a self-paced, computer-assisted self-interview. Peripheral neuropathy was evaluated using standardized 10g monofilament testing, which assesses lower extremity sensation. We used logistic regression to examine the association of peripheral neuropathy with erectile dysfunction overall and stratified by diabetes status adjusting for demographic and cardiovascular risk factors.

Results: The prevalence of peripheral neuropathy was 26.1% (51.2% in men with diabetes and 22.5% in men without diabetes). There was a significant independent association of peripheral neuropathy with erectile dysfunction overall (OR 1.71, 95%CI 1.20 – 2.43) and among US adult men without diabetes (OR 1.68, 95%CI 1.11 – 2.56). The association in adults with diabetes was not statistically significant (OR 1.29, 95%CI 0.39 – 4.26), possibly owing to limited power in this subgroup.

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Conflicts of Interest: The authors have no conflicts of interest to disclose.

Verification: All authors had access to the data and a role in writing the manuscript.

Conclusions: Our study suggests that decreased lower extremity sensation, even in the absence of diabetes, is common and a novel risk factor for erectile dysfunction.

Keywords

peripheral neuropathy; erectile dysfunction; diabetes

Introduction

Peripheral neuropathy is a common neurologic condition in middle-aged and older adults[1]. Reduced sensation to touch is a feature of large fiber peripheral polyneuropathy that is particularly prevalent among adults with diabetes[1]. We have recently demonstrated an association of large fiber peripheral neuropathy with cardiac and kidney biomarkers[2], suggesting a shared etiology with microvascular cardiac dysfunction and kidney disease.

Erectile dysfunction also has neurologic[3] and microvascular etiologies[4] and is strongly linked to cardiovascular disease and its risk factors, especially diabetes[5, 6]. Adult men with erectile dysfunction and diabetes have previously been shown to have a higher prevalence of cardiovascular autonomic neuropathy[7] and small-fiber neuropathy[8] compared to adult men with diabetes but no erectile dysfunction.

The aim of this study was to assess the association of large-fiber peripheral neuropathy with erectile dysfunction in adult US males with and without diabetes.

Methods

We performed a cross-sectional analysis of 1213 male participants aged ≥40 years (mean age 54.4±0.3 years) in the 2001–2002 National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of the civilian, non-institutionalized population in the US. Erectile dysfunction was assessed by a single question during a self-paced, computer-assisted self-interview[6]. Peripheral neuropathy was assessed using 10g monofilament testing at three sites on each foot and was defined as having at least one insensate site on either foot. Peripheral neuropathy therefore represents reduced sensation to touch. We used logistic regression to examine the association of peripheral neuropathy with erectile dysfunction overall and stratified by diabetes status (self-reported doctor-diagnosis, current glucose-lowering medication use, or HbA1c ≥ 6.5%). Model 1 included age and race. Model 2 additionally included education, body mass index, smoking, drinking, prevalent coronary heart disease, hypertension, and hypercholesterolemia. We performed all analyses using Stata v15.1 (StataCorp). P-values <0.05 were considered statistically significant. We incorporated sampling weights in the Stata *svy* commands to obtain unbiased estimates from the NHANES sampling design and used Taylor series (linearization) to estimate standard errors.

Results

The prevalence of peripheral neuropathy assessed by monofilament testing was 26.1%. The prevalence of peripheral neuropathy was 51.2% in men with diabetes and 22.5% in men

without diabetes. The crude prevalence of erectile dysfunction varied significantly according to peripheral neuropathy and diabetes status (Figure 1). There was a significant association of erectile dysfunction with peripheral neuropathy overall and among US adult men without diabetes (**Model 1**, Table 1). These associations persisted after adjusting for traditional cardiovascular risk factors (**Model 2**, Table 1). The associations of erectile dysfunction with peripheral neuropathy in adults with diabetes were not significant in either model.

Discussion

We found a robust association of erectile dysfunction with peripheral neuropathy in US men ≥40 years of age. This association was pronounced in the absence of diabetes and persisted after adjusting for traditional risk factors. The non-significant association in diabetes may reflect the small number of cases in this subpopulation. Our data suggest a strong link between peripheral neuropathy and erectile dysfunction, possibly due to shared underlying etiologies.

Although the association of peripheral neuropathy with diabetes is well described[1], the prevalence of peripheral neuropathy in adults without diabetes is underappreciated. This may be because the etiology of peripheral neuropathy is frequently attributed to dysregulated metabolic pathways in the setting of long-term hyperglycemia and insulin resistance[1]. However, emerging evidence suggests that peripheral neuropathy (as defined by monofilament testing) is common in older adults in the absence of hyperglycemia and is associated with a high burden of cardiovascular risk factors, kidney function, and markers of cardiac damage[2]. We have also recently demonstrated that peripheral neuropathy in adults without diabetes is independently associated with all-cause and cardiovascular mortality (*Hicks et al., under review*).

Prior studies have also demonstrated that erectile dysfunction is associated with cardiovascular disease. Erectile dysfunction precedes the clinical presentation of coronary heart disease by 2–3 years[9] and is predicative of incident cardiovascular disease independent of cardiovascular risk factors[5]. Similar to peripheral neuropathy, erectile dysfunction is closely associated with diabetes, but can affect adult men without diabetes as well[6].

Despite having possible similar etiologies, the association of peripheral neuropathy with erectile dysfunction is not well characterized. There is one cross-sectional study that reports an association of peripheral neuropathy with erectile dysfunction among 287 Japanese males <65 years of age with type 2 diabetes[10]. That study found the prevalence of peripheral neuropathy and erectile dysfunction to be 47% and 39%, respectively. We report slightly higher prevalences in our study, possibly because NHANES includes older adults. The association of peripheral neuropathy with erectile dysfunction in adult men without diabetes has not previously been reported.

The limitations of our study were the cross-sectional design, which limited our ability to establish temporality, and low power in subgroups. The diabetes group, specifically, had a low number of events, resulting in wide confidence intervals and a lack of significance.

Strengths of our study included the nationally representative sample and standardized measurements of all variables.

Our finding of a strong link between peripheral neuropathy and erectile dysfunction in both adults with and without diabetes is novel and suggests potentially common microvascular and/or neurological etiologies. The underlying mechanism linking erectile dysfunction with cardiovascular disease is thought to be microvascular endothelial dysfunction leading to small arteriole disease[4], which could potentially play a role in peripheral neuropathy as well. Both peripheral neuropathy and erectile dysfunction strongly overlap with cardiovascular risk factors and subclinical vascular disease. Our study suggests that decreased lower extremity sensation, even in the absence of diabetes, is common and a novel risk factor for erectile dysfunction.

Funding Sources:

Dr. Hicks was supported by NIH/NIDDK grant K23 DK124515. Dr. Selvin was supported by NIH/NHLBI grant K24 HL152440.

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Clinical Significance

- Peripheral neuropathy (decreased lower extremity sensation) is common even in the absence of diabetes
- There is a significant independent association of peripheral neuropathy with erectile dysfunction in US men aged ≥40 years
- The association of peripheral neuropathy with erectile function is more pronounced in men without diabetes
- Peripheral neuropathy is a novel risk factor for erectile dysfunction

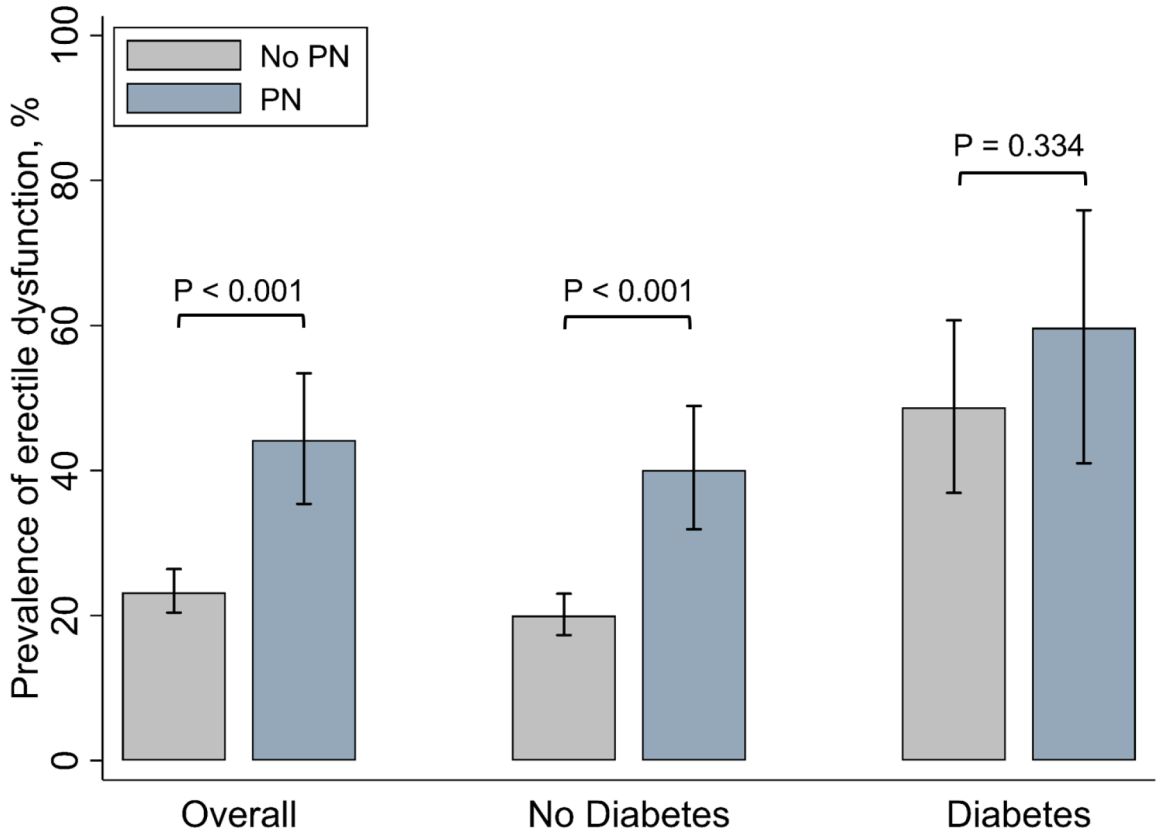

Figure 1. Prevalence (95% confidence intervals) of erectile dysfunction according to peripheral neuropathy (monofilament testing) and diabetes status in US men ≥40 years of age.

Vertical bars are 95% confidence intervals

Table 1.

Associations (OR, 95% CI) of peripheral neuropathy (monofilament testing) with erectile dysfunction overall and stratified by diabetes status among US adult men ≥ 40 years of age, NHANES (2001–2002)

	Erectile Dysfunction Unweighted n / N	Model 1 OR (95% CI)	Model 2 OR (95% CI)
Overall			
No PN	314/1002	1 (ref)	1 (ref)
PN	111/211	1.66 (1.10 – 2.50)	1.71 (1.20 – 2.43)
No Diabetes			
No PN	235/847	1 (ref)	1 (ref)
PN	76/160	1.55 (1.08 – 2.22)	1.68 (1.11 – 2.56)
Diabetes			
No PN	79/155	1 (ref)	1 (ref)
PN	35/51	1.31 (0.47 – 3.68)	1.29 (0.39 – 4.26)

Model 1: age and race

Model 2: variables in Model 1 plus education, body mass index, smoking status, drinking status, prevalent coronary heart disease, hypertension and hypercholesterolemia