Association of Type and Duration of Diabetes With Erectile Dysfunction in a Large Cohort of Men

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OBJECTIVE — Differences in risk of erectile dysfunction (ED) by characteristics of diabetes among older men are not well understood. We examined the association of type and duration of diabetes with erectile function in men >50 years of age in a large prospective cohort study.

RESEARCH DESIGN AND METHODS — Subjects included 31,027 men aged 53–90 years in the Health Professionals Follow-Up Study cohort. On a questionnaire mailed in 2000, participants rated their ability (without treatment) in the past 5 years to have and maintain an erection sufficient for intercourse. Men who reported poor or very poor function were considered to have ED. Diabetes information was ascertained via self-report and documented with supplementary medical data.

RESULTS — Men with diabetes had an age-adjusted relative risk (RR) of 1.32 (95% CI 1.3–1.4) for having ED compared with men without diabetes. In multivariable regression analyses, men with type 1 and type 2 diabetes were at a significantly higher risk for ED (type 1 diabetes RR = 3.0, 95% CI 1.5–5.9; type 2 diabetes RR = 1.3, 1.1–1.5) than nondiabetic men. Men with type 2 diabetes had an increasingly greater risk of ED with increased duration since diagnosis (trend test *P* value <0.0001) (RR = 1.7, 95% CI 1.1–2.7, for men diagnosed >20 years previously).

CONCLUSIONS — For men over age 50 years, increasing duration of diabetes was positively associated with increased risk of ED relative to nondiabetic subjects. This association persisted despite the higher prevalence of other comorbid conditions. ED prevention and diabetes management efforts are likely to go hand-in-hand.

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Erectile dysfunction (ED) is a commonly reported condition among men with diabetes (1–7), and it is associated with reduced quality of life among these men (8). Prevalence estimates of ED among diabetic men range from 27 to 75% (9–29). Much of this variability is due to differences in definitions of ED as well as to various distributions of severity and duration of diabetes between samples. Estimates for the general population are similarly wide-ranging, largely because of differences in study population characteristics and definitions of ED (1,5).

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Abbreviations: ED, erectile dysfunction; HPFS, Health Professionals Follow-Up Study; RR, relative risk.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Several studies have examined ED by diabetes type and duration (14,17,23,24,30), but few have directly compared the prevalence of this condition in men with and without diabetes. Our aim was to examine the effects of type and duration of diabetes on erectile function in men >50 years of age compared with men of similar age in a large well-defined sample of men.

RESEARCH DESIGN AND METHODS

— The Health Professionals Follow-Up Study (HPFS) is a cohort of 51,529 male dentists, optometrists, osteopaths, podiatrists, pharmacists, and veterinarians in the U.S. who initially responded to a mailed questionnaire in 1986 (31,32). Follow-up questionnaires have been mailed every 2 years with an overall average response rate of 94%. Incident and prevalent cases of diabetes have been monitored since baseline.

At the time of the 2000 questionnaire, men participating in the HPFS ranged in age from 53 to 90 years. The HPFS cohort includes 94.7% who reported their major ancestry as Caucasian, 1.8% as Asian, 1.1% as African-American, and 2.5% as other ancestry (33). Among the 43,235 men still alive and actively participating in the study in 2000, we inquired about sexual function and other health and lifestyle characteristics such as obesity, physical activity, and chronic disease. We mailed the four-page questionnaire (long version) up to four times to nonresponders and received 34,282 responses. For persistent nonresponders, we mailed a shorter questionnaire containing only questions regarding health status and did not further query on sexual function. Men with missing responses to the primary outcome variable (n = 2,936) or unspecified type of diabetes (n = 329) were excluded from the analysis.

On the questionnaire, men were asked to rate their ability in the past 5 years (without treatment) to have and maintain an erection good enough for intercourse. Response options included very poor, poor, fair, good, and very

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good. Men who stated that their ability to have and maintain an erection sufficient for intercourse was poor or very poor in the past 5 years were considered to have ED.

Self-reported cases of type 1 (juvenile-onset) and type 2 (adult-onset) diabetes diagnosed before the start of the study in 1986, as well as cases diagnosed since that time, were included in this study. On each mailed questionnaire, we asked HPFS participants to self-report recent physician diagnoses of diabetes (either insulin-dependent or non–insulin-dependent). Men who answered positively were sent a supplementary questionnaire regarding date of diagnosis and other questions specific to their diabetes. Diagnoses before 1996 were based on the following criteria of the National Diabetes Data Group (34): *1*) one or more classic symptoms (thirst, polyuria, weight loss, hunger, or pruritus) of diabetes plus elevated plasma glucose (fasting glucose of at least 7.8 mmol/l [140 mg/dl], nonfasting glucose of at least 11.1 mmol/l [200 mg/dl], or 2-h glucose levels of ≥11.1 mmol/l on a glucose tolerance test), 2) elevated plasma glucose levels on two different occasions, or 3) receiving treatment with insulin or an oral hypoglycemic agent. The threshold of fasting plasma glucose for diagnosis after 1996 was reduced to 7 mmol/l (126 mg/dl) to reflect new diagnostic guidelines (35). Men with confirmed diabetes but missing information on type were assigned to the type 2 diabetes group if diagnosed after age 30 years.

Validity of self-reported diabetes was tested in a subsample of 71 men self-reporting new diagnoses of diabetes between 1996 and 1998. A physician blinded to the questionnaire data reviewed medical records according to the diagnostic criteria noted above. Among 59 men who provided complete records, the self-reported diagnosis of diabetes was confirmed via medical record in 97% of cases.

Based on prior literature (9–17,19–29), there are multiple factors that may confound the relationship between type or duration of diabetes and ED. Binomial regression with the log link function (36) was used to model ED in relation to type of diabetes and duration since diabetes diagnosis. Covariates in the multiple regression models of ED included 5-year categories of age, marital status (married versus not married), smoking status (current smokers versus nonsmokers), alcohol consumption (0, 0.1–4.9, 5.0–14.9, 15.0–29.9, and ≥30.0 g/day), obesity quintiles (BMI [kg/m^2]), physical activity quintiles (MET hours per week), and history of comorbid conditions (heart disease [myocardial infarction, angina, angioplasty, cardiac bypass arterial graft surgery, and other heart conditions], hypertension, hypercholesterolemia, prostate cancer, other cancer, and stroke). All covariates except alcohol consumption were measured at the time erectile function was assessed. Alcohol consumption (assessed in 1998) is measured every 4 years as part of the complete dietary questionnaire. The comparison group for all regression models is men without self-reported physician-diagnosed diabetes.

Table 1—*Age-standardized demographic characteristics by diabetes status*

Demographic characteristic/behavior	No diabetes	Diabetes	
		Type 1	Type 2
n	28,919	51	2,057
Age (mean years)	65.8	63.1	69.5
Marital status			
Married (%)	89.0	86.8	87.6
Divorced/separated (%)	5.8	5.7	6.6
Widow (%)	3.8	6.0	4.1
Never married (%)	1.4	1.5	1.7
Current smoker (%)	4.1	0.0	4.7
Alcohol use (mean g/week)	11.3	10.8	8.3
Obesity (mean BMI)	26.0	25.3	28.1
Physical activity (mean MET h/week)	32.0	38.5	24.8
Comorbid conditions			
Heart disease (%)	14.9	28.5	27.4
Hypertension (%)	39.6	48.9	66.3
Hypercholesterolemia (%)	50.8	47.2	65.8
Prostate cancer (%)	6.7	4.9	5.8
Other cancer (%)	7.1	8.8	7.9
Stroke (%)	1.8	1.8	3.8

Age-standardized in 5-year categories (except mean age).

RESULTS — Among men from the HPFS cohort, 7.8% had a self-reported diagnosis of diabetes by year 2000. As shown in Table 1, the men included in this study tended to be married nonsmokers who engaged in light-to-moderate alcohol consumption and some regular physical activity. Men with type 2 diabetes were more likely to smoke, had a higher average BMI, and were less physically active than men without diabetes. Men with both types of diabetes had a history of more heart disease and hypertension, whereas men with type 2 diabetes also had higher rates of hypercholesterolemia and stroke than men without diabetes.

The prevalence of ED among men with diabetes (45.8%) was nearly double that of men without diabetes (24.1%). Table 2 shows the distribution of erectile function for men with diabetes by type and duration since diagnosis. Standardizing for age, the majority of men with type 1 diabetes reported poor or very poor erectile function (61.8%), whereas the distribution for men with type 2 diabetes was less skewed toward very poor function. Men with more recent diabetes diagnoses reported better erectile function than men diagnosed >5 years in the past. Nearly half (47.7%) of the men with type 2 diabetes reporting very good erectile function were diagnosed with diabetes in the past 5 years, whereas only a quarter (24.6%) of men who reported very poor erectile function were diagnosed in the past 5 years.

In age-adjusted regression models (Table 3), men with type 1 or type 2 diabetes had a similar likelihood of reporting ED than men without diabetes (type 1 diabetes relative risk [RR] = 1.4, 95% CI 1.3–1.6; type 2 diabetes RR = 1.3, 1.3–1.4). However, the point estimate of ED risk for type 1 diabetes more than doubled in the multivariable model (RR =

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Table 2—*Age-standardized erectile function in the past 5 years by diabetes type and duration*

Characteristics of diabetes	*n*	Ability (without treatment) in the last 5 years to have and maintain erections sufficient for intercourse				
		Very good	Good	Fair	Poor	Very poor
n	2,108	312	392	439	422	543
Diabetes type						
Type 1	51	6.0%	10.6%	21.6%	21.7%	40.1%
Type 2	2,057	15.2%	18.7%	20.8%	19.9%	25.3%
Duration of diabetes (years)						
0–5	861	18.1%	22.1%	21.9%	18.3%	19.7%
6–10	535	13.9%	17.8%	23.9%	17.7%	26.8%
11–15	371	11.3%	17.0%	15.5%	25.9%	30.3%
16–20	126	12.5%	13.8%	19.3%	22.4%	32.1%
>20	215	8.3%	13.3%	20.1%	21.3%	37.1%

Age-standardized in 5-year categories.

3.0, 1.5–5.9). When comorbid conditions were not included in the multivariable model, the RR of ED was 2.0 (1.6–2.5) for men with type 1 diabetes compared with men without diabetes.

Because duration of diabetes is associated with an increase in severe chronic health conditions and neurovascular damage, we examined the impact of time since diagnosis on ED (Table 3). The HPFS is a cohort of older men among whom type 1 diabetes cases were diagnosed >20 years before our assessment of ED. We therefore excluded men with type 1 diabetes from the models of diabetes duration. Among type 2 diabetic patients, diagnosis within the past 10 years was not significantly associated with an elevated risk of ED compared with men without diabetes after controlling for potential confounders. After 10 years, the risk of ED was significantly greater for men with diabetes than for men not diagnosed with the disease. Gradually increasing with longer duration of diabetes (multivariable logistic trend test *P* value <0.0001), the risk for ED was 70% greater than that in men without diabetes for men diagnosed more than 20 years ago (RR = 1.7, 95% CI 1.1–2.7).

Figure 1 shows the age-specific prevalences of ED in men with type 2 diabetes compared with men without diabetes. We further stratified the data by heart disease/hypertension status. Men with diabetes and heart disease or hypertension had the highest levels of ED with a prevalence of 50% across age-groups. Men without diabetes and heart disease had the lowest rates of ED (17%). Men who had either type 2 diabetes or heart disease/hypertension had similar rates of ED (33 and 32%, respectively). Within the subgroup of men with heart disease or hypertension, we found that the association between duration of type 2 diabetes and ED was slightly stronger than that among men without heart disease and hypertension (multivariable RR of ED = 1.1, 95% CI 0.8–1.5, for duration of 0–5 years; 1.5, 1.1–2.1, for duration of 6–10 years; 1.6, 1.1–2.1, for duration of 11–15 years; 1.9, 1.1–3.4, for duration of 16–20 years; and 1.9, 1.2–3.2, for duration >20 years).

CONCLUSIONS — In this large cohort of men aged 53–90 years, we found that the risk of ED steadily increased with duration of type 2 diabetes to a nearly twofold greater risk compared with men without diabetes. For middle-aged and older men with type 1 diabetes, the risk of

Table 3—*ED in the past 5 years by type of diabetes and duration of type 2 diabetes*

Diabetes variables	ED by diabetes type (*n* = 31,027)		ED by type 2 diabetes duration† (*n* = 30,976)	
	Age-adjusted	Multivariable*	Age-adjusted	Multivariable*
Type				
Type 1	1.4 (1.3–1.6)	3.0 (1.5–5.9)	—	—
Type 2	1.3 (1.3–1.4)	1.3 (1.1–1.5)	—	—
Duration (years)				
0–5	—	—	1.2 (1.1–1.3)	1.0 (0.8–1.3)
6–10	—	—	1.3 (1.2–1.4)	1.2 (0.9–1.7)
11–15	—	—	1.5 (1.4–1.6)	1.5 (1.2–1.9)
16–20	—	—	1.4 (1.3–1.6)	1.6 (0.9–2.7)
>20	—	—	1.5 (1.4–1.6)	1.7 (1.1–2.7)

Data are RRs (95% CI). Men without diabetes are the reference group. *Adjusted for age, marital status, current smoking status, comorbid conditions (heart disease, hypertension, hypercholesterolemia, stroke, prostate cancer, and other cancers), alcohol use, obesity (BMI), physical activity, and missing independent variables. †Type 1 diabetic subjects excluded from duration models. ED = "Poor" and "very poor" ability (without treatment) to have and maintain erections sufficient for intercourse.

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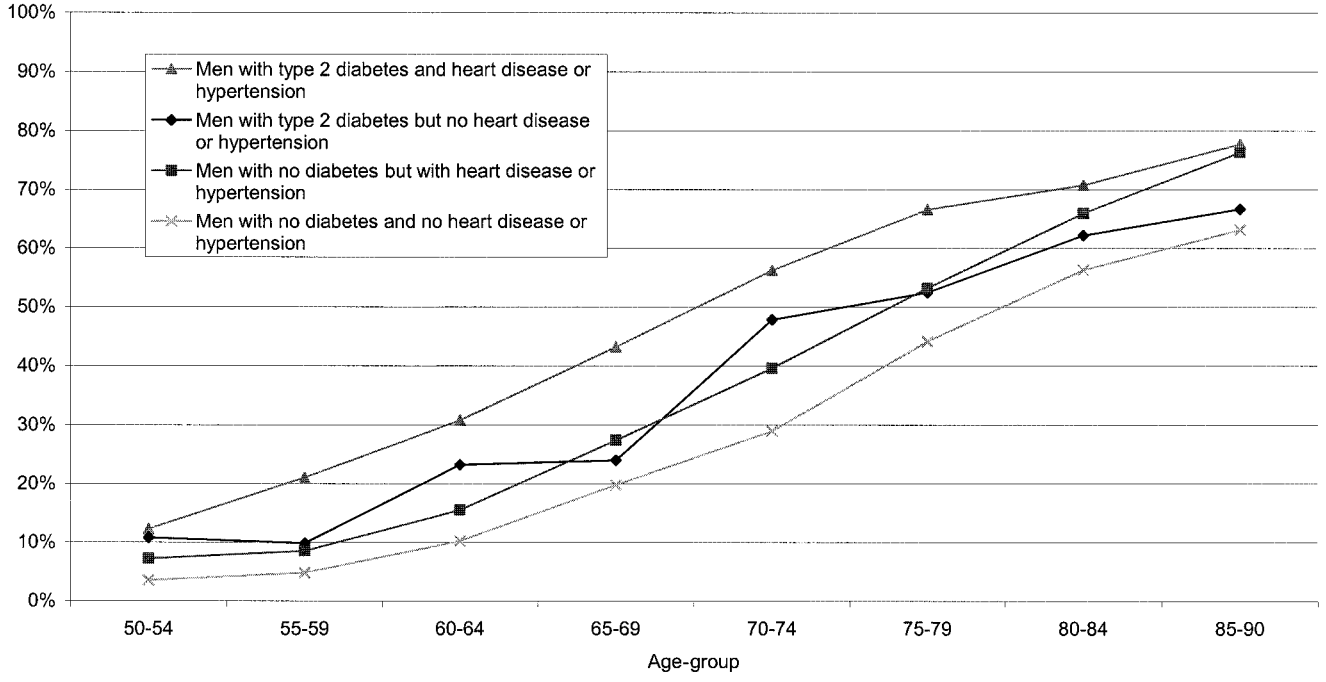

Figure 1—*Prevalence of ED in the past 5 years among men with type 2 diabetes versus men with no diabetes.*

ED was approximately three times higher than that for men of similar age without diabetes. Diabetes and cardiovascular disease appear to have an additive relationship in their contribution to the prevalence of ED across age groups.

Despite multiple aspects of this study that contribute to the current literature on this topic—including the age range of the subjects, the large number of diabetes cases from across the country, and the ability to compare men with diabetes to a similar group of men without diabetes and stratify by heart disease status—there are limitations as well. There was a greater percentage of men with diabetes in the entire HPFS cohort (8.4%) than was included in our analyses (6.4%). We may have slightly underestimated the association between diabetes and ED if the men with diabetes and ED were less likely than men with diabetes and no ED to respond to the ED outcome measure.

We were not able to include glycosylated hemoglobin as a measure of glycemic control in our models because of the unavailability of such data among men in this cohort. It is known that a longer duration of diabetes is strongly related to poor glycemic control (37,38). Therefore, the increased risk of ED associated with increasing diabetes duration is likely to reflect some of the effects of glycemic control. The possibility that a stronger measure of glycemic control would explain the entire effect of diabetes duration after controlling for demographic factors, health behaviors, and comorbid conditions cannot be ruled out.

The HPFS is a longitudinal cohort, but our examination of ED was cross-sectional in nature. Furthermore, the detailed information we assessed on aspects of diagnosis and treatment for diabetes was collected only after the first self-report of diabetes. Thus, change in treatment regimens, which could be used as a proxy measure for severity of diabetes, was not included in the analysis. To confirm the finding of increasing risk of ED associated with duration of diabetes, a study with repeated measures of erectile function before and after diabetes diagnosis is necessary.

There are a small number of type 1 diabetic case subjects still alive and noninstitutionalized within our 50- to 90-year-old population. In a younger cohort, it is likely that there would be more type 1 diabetic case subjects. More than 15% of type 1 diabetic case subjects die before the age of 40 years (39)—well before the prevalence of ED increases among healthy men. However, with a larger number of patients, a more precise estimate of risk could be calculated for older men with type 1 diabetes.

Previous studies have found either no effect of duration (10,13,21,40) or a dose-response relationship (14,16,23,30) after controlling for age. With a larger sample size and broader age distribution than earlier studies, we observed an increased risk of severe ED with increased diabetes duration. The effect sizes of duration we observed are consistent with previous research, although few other studies were able to account for a similar range of potential confounders.

Our results concerning type of diabetes are also consistent with prior research (23,30,41) showing that men with type 1 diabetes are more likely than men with type 2 diabetes to have ED. However, when we controlled for multiple confounders in addition to age, the RR of ED doubled, and the CIs got much wider (RR = 3.0, 95% CI 1.5–5.9) compared with the model adjusted for age only (1.4, 1.3–1.6). This effect is primarily due to the inclusion of comorbid conditions (2.0, 1.6–2.5, in the multiple regression model excluding comorbid conditions). Colinearity between type 1 diabetes and comorbid conditions likely explains the substantially wider CIs around the multiple regression effect estimate. We did not have the same problem for the RR of type

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2 diabetic patients because of the larger sample size and greater variability of risk factors, as well as the reduced overall likelihood of accumulated long-term negative health effects related to this late age-at-onset condition.

The biological mechanisms that link increased risk of ED to diabetes have been posited to be hormonal, vascular, and neural. However, evidence for the hormonal pathway is much weaker than evidence for vascular and neural pathways (2,3,7,19,42). When we examined the effect of diabetes duration on the occurrence of fatal and nonfatal myocardial infarction among the men in this study, the odds increased gradually with increasing diabetes duration (odds ratio = 1.3, 95% CI 0.9–1.7, for 0–5 years; 1.9, 1.3–2.6, for 6–10 years; 2.9, 2.0–4.2, for 11–15 years; 3.6, 2.3–5.5, for 16–20 years; and 3.6, 2.6–5.0, for >20 years). Because the pattern of increased myocardial infarctions associated with increased diabetes duration is similar (although the relative effect is stronger) to the pattern for ED, these outcomes may have similar etiologies.

In a complete review of potential mechanisms for diabetic ED, Hakim and Goldstein (3) concluded that microangiopathy of the cavernosal artery, corporal veno-occlusive dysfunction, and autonomic neuropathy are the primary pathophysiological pathways for ED. Advanced glycation end products, caused by insufficient glycemic control, are elevated in the collagen of the penile tunica and corpus cavernosum of diabetic penile tissue and inhibit nitric oxide production (43). Corporal smooth muscle contraction and relaxation may then be disturbed by reduced nitric oxide action (44). Our results suggest that there may be increasing nitric oxide disturbance related to severe ED among older diabetic men, especially among those with heart disease or hypertension.

We found a significant association between diabetes (and diabetes duration) and ED when comparing diabetic men with nondiabetic men of similar age. Although these results should be confirmed in a longitudinal analysis of men with newly diagnosed diabetes, intervention and prevention efforts aimed at ED among diabetic patients may be most effective early after diabetes diagnosis. Our results are consistent with the hypothesis that health care providers who address sexual function issues with diabetic patients early may be able to reduce severity or delay onset of ED in their patients. It also appears that heart disease and hypertension increase the prevalence of ED among men with diabetes beyond that of men with diabetes only or men with heart disease or hypertension only.

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