

Prevalence and determinants of erectile dysfunction in hemodialysis patients

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Prevalence and determinants of erectile dysfunction in hemodialysis patients.

Background. The prevalence of erectile dysfunction (ED) among patients with end-stage renal disease (ESRD) is not known.

Methods. A cross-sectional study was conducted to determine the prevalence of ED among a community-based hemodialysis (HD) population using a two-stage cluster random sampling design. The presence and severity of ED were assessed among 302 ESRD patients using the self-administered International Index of Erectile Function-5 (IIEF-5). Logistic regression was used to examine and test associations between ED and other medical conditions.

Results. The prevalence of any level of ED was 82% (95% CI, 76 to 87%) for all HD subjects. The prevalence of severe ED was 45% (CI, 36 to 55%). Subjects younger than 50 years had a prevalence of ED of 63% (CI, 53 to 71%), while in subjects 50 years or older, it was 90% (CI, 84 to 94%). A multivariable analysis demonstrated increasing age (50 to 59, OR = 2.04, 95% CI, 1.3 to 3.1; 60 to 69, OR = 5.5, 95% CI, 1.9 to 15.6) and diabetes (OR = 2.0, 95% CI, 1.2 to 3.3) to be independently associated with the presence of any level of ED. However, neither the subjects' age nor history of diabetes predicted the severity of ED among subjects with ED. The use of angiotensin-converting enzyme inhibitors (ACEIs) was inversely associated with ED (OR = 0.41, 95% CI, 0.17 to 0.98). Poor functional status (Karnofsky score or the Index of Physical Impairment) was not associated with ED.

Conclusions. ED is extremely prevalent among HD patients. Increasing age, diabetes, and nonuse of ACEIs were associated with higher prevalence of ED. The high prevalence of ED was seen even among patients with good functional status.

Erectile dysfunction (ED) is estimated to affect between 10- and 30-million men in the United States [1]. However, the prevalence of ED among patients with end-stage renal disease (ESRD) is not known. Several cross-sectional studies in hemodialysis (HD) patients have attempted to measure the prevalence of ED in small convenience samples [2]. Perhaps because of varied definitions of ED, the estimates of its prevalence have ranged from 41 to 93%.

There are many reasons to expect a high prevalence of ED in HD populations. A number of the illnesses, such as atherosclerosis, heart disease, diabetes, and hypertension, that are associated with ED also tend to be common among patients with ESRD. Medications frequently used in the setting of renal disease have also been associated with ED, including several diuretics, antihypertensives, antidepressants, and H₂ antagonists.

Despite the suspected association of ED and ESRD and the impact that ED might have on the quality of life of these patients, the prevalence of ED in those with ESRD has not been well characterized. An accurate measure of the prevalence of ED in ESRD patients using newer, standardized, and validated diagnostic instruments has not been completed. With the availability of newer effective therapies for ED, a better understanding of the prevalence and determinants of ED in HD patients should be a useful guide to medical practice. We report the findings of a population-based study of the prevalence of ED among a representative sample of community-based patients receiving chronic HD.

METHODS

Study design and research population

Men aged 18 years or older in metropolitan Philadelphia who were treated with chronic HD for at least six months were studied. Because it was not feasible to recruit subjects from all outpatient dialysis facilities in

Key words: end-stage renal disease, IIEF-5, diabetes, chronic hemodialysis, men and HD, sexual health in men, quality of life.

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the area, we used a two-stage cluster sampling design to obtain a study sample from which population-based inferences could be made [3]. In the first stage, 16 HD facilities were randomly selected from all 51 facilities in the area, with the probability of each facility's inclusion being set approximately proportional to its size, as measured by its number of dialysis stations. In the second stage, 20 subjects who met the eligibility criteria were randomly selected from each chosen facility. Subjects were excluded if they were cognitively impaired or spoke no English. Refusals were replaced with alternate subjects until 20 individuals from each facility were enrolled. Using this sampling scheme, larger facilities had a higher probability of being selected, but eligible individual patients had an approximately equal probability of selection into the study.

This study was approved by the University of Pennsylvania Institutional Review Board and the review boards of the clinical centers.

Data collection

Sexual function. Each subject completed a self-administered five-item validated questionnaire [4], the IIEF-5, which is an abridged version of the 15-item International Index of Erectile Function [5], which is commonly known as the Sexual Health Inventory for Men (SHIM). The five items included in the abbreviated IIEF-5 address the National Institutes of Health's definition of ED, discriminate well between men with and without ED, and reflect the severity of ED [4]. Subjects' ED was measured and categorized according to severity using a five-level ordinal scale based on their score on the IIEF-5. A cutoff score of 21 (range of scores of 5 to 25) was used to define ED. Subjects with scores of 21 or less were considered to have ED. ED was also classified likewise into five validated severity levels, ranging from none (22–25), mild (17–21), mild/moderate (12–16), moderate (8–11), through severe (5–7). Subjects also rated their ED on a supplemental single-item scale from the Massachusetts Male Aging Study as not impotent, minimally impotent, moderately impotent, and completely impotent, according to the ability to always, usually, sometimes, or never achieve and keep an erection good enough for sexual intercourse [6].

Comorbidity and functional status. Medical and demographic data were obtained for each subject from abstraction of dialysis records. Medical data collected included measures of health status, time on dialysis, comorbid conditions, laboratory studies such as hemoglobin, creatinine, albumin and parathyroid hormone, adequacy of dialysis, compliance with dialysis, prior transplantation, and current medications.

The Karnofsky Performance Status was used to determine the clinicians' assessments of physical function [7]. The Karnofsky Performance Status score is a numeric representation of the patient's functional ability. We re-

quested each patient's primary nurse to evaluate their functional status at the time of data collection. The scale ranges from 0 (dead) in 10-point increments to 100 (normal with no complaints). Each primary nurse was given written instructions on what each 10-point increment meant with regard to functional ability. The nurses were unaware of the patients' response to the IIEF.

The Index of Co-Existing Disease (ICED) is a previously validated instrument that classifies subjects with ESRD on a four-point scale based on the presence and severity of 19 medical conditions and 11 physical impairments (abstract; Greenfield et al, *Clin Sci* 35:346A, 1987). These two components are summarized in the Index of Disease Severity (IDS) and the Index of Physical Impairment (IPI). The IDS reflects the severity of each of a selected list of 19 disease categories. The disease categories are rated using an explicit list of symptoms, signs, and diagnostic tests indicating the presence and increasing severity of each identified condition. Level 1 characterizes a condition with little or no morbidity. Level 2 is a symptomatic controlled disease. Level 3 is an uncontrolled disease with moderate or severe manifestations. Level 4 refers to an uncontrolled life-threatening disease (not appropriate for outpatients). The IPI is intended to act as a snapshot of the impact of all of the conditions on the patients' functional ability where level 0 is normal function, level 1 is mild to moderate impairment, and level 2 is serious to severe impairment. The IDS and IPI are combined to yield a single ICED score. Higher scores reflect greater severity of disease or impairment.

Statistical methods

Our analyses sought to estimate the frequency or prevalence of ED in the HD population in metropolitan Philadelphia and to identify the associations of various conditions with ED in that population. Because of the two-stage sampling design, all prevalence estimates accounted for (1) the somewhat unequal probabilities of selection of individual subjects in facilities of varying size and (2) the clustered sampling, which affected the variability of estimates [3]. To account for unequal selection probabilities, weighted estimation methods were used [3], with each subject's weight inversely proportional to his probability of selection into the study. The probability of selection into the study was the probability of selecting a given dialysis unit times the probability of selection of a given subject from that unit. Continuous variables were described by their means and standard errors and categorical variables by the proportion in each category.

Logistic regression (accounting for sampling design by weighted estimation methods) was used to examine and test associations between ED and other conditions, excluding measures of quality of life [3]. First, the associa-

Table 1. Prevalence and 95% CI of erectile dysfunction (ED) in all subjects and by age

ED severity	Prevalence % (CI)		
	All	<50 Years	≥50 Years
No ED	18 (13–24)	37 (29–47)	10 (6–17)
Mild	21 (16–27)	24 (18–31)	20 (14–27)
Mild/moderate	8 (5–12)	11 (5–23)	7 (5–11)
Moderate	8 (5–13)	7 (3–18)	8 (4–14)
Severe	45 (36–55)	21 (15–30)	56 (44–67)

tions between the presence of ED and demographic variables, prior comorbidities, medications, and laboratory values were examined. Those variables in which the unadjusted rate ratios had an associated *P* value of less than 0.1 were considered for inclusion in multivariable models. Then backward selection strategies were employed to fit the final models. These modeling activities initially considered only baseline characteristics, including demographics and comorbidity. Next, medications, examined individually, were considered conditional on the baseline characteristics included in the previous step. Finally, laboratory values and other physiologic parameters such as mean arterial pressure were added to the model. For adding these variables, the same approach as described previously in this article was used. Analyses were performed using SAS version 6.12 (SAS Institute, Cary, NC, USA) and the survey estimation facilities of STATA, version 5 (Stata Corporation, College Station, TX, USA).

RESULTS

Using the methods described, 482 of 705 potentially eligible men receiving HD in the 16 facilities were selected. Twenty-seven were excluded because of cognitive impairment. Thirty-seven were not available. Twenty-four were not eligible, and four had language barriers, leaving a total of 390 subjects who were asked to participate. Of these, 88 (22.6%) subjects refused or did not complete the questionnaires. The individuals who refused did not differ from study subjects with regard to age. The proportion less than 50 years of age was 23 versus 25.4%, respectively. Because we did not have access to the medical records of patients who refused to participate, we were unable to compare them with subjects with respect to other characteristics, such as race and diabetes.

The final study cohort was made up of 302 subjects. One hundred seventy-two (59%) subjects were African American. Nine patients (2.6%) were Hispanic. The mean \pm SD age was 59.5 ± 15.5 years. Nearly all subjects (97%) were hypertensive, and 39% had diabetes mellitus. The cause of ESRD was diabetes type I (17%), diabetes type II (18%), hypertension (46%), glomerulo-

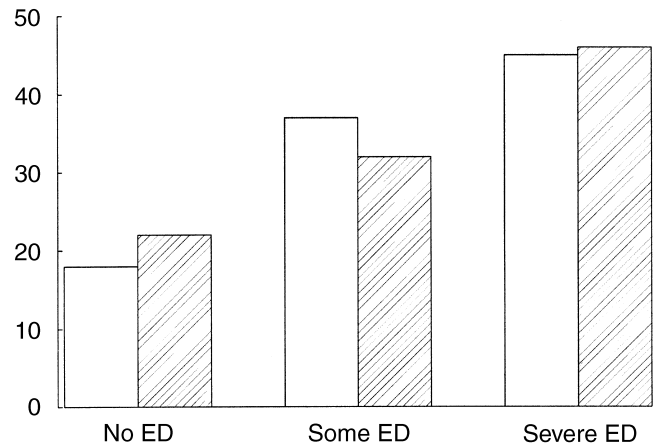


Fig. 1. International Index of Erectile Function-5 (IIEF-5; □) versus the self report of impotence (▨), measured using the Massachusetts Male Aging Self-Report Questionnaire. The abbreviation ED is erectile dysfunction. Kappa = 0.672.

nephritis (2%), cystic disease (4%), and other (12%). A history of cerebral vascular disease was present in 12% of subjects, while peripheral vascular disease was found in 27%. Nineteen percent had a history of lung disease, including emphysema, chronic bronchitis, asthma, sleep apnea, or home oxygen requirement. Ten percent had a history of malignancy (other than basal cell carcinoma of the skin). A history of HIV infection was present in 2.5% of subjects.

Fourteen percent of subjects had been on HD for six months to one year, 26% for one to two years, 33% for two to four years, and 28% for more than four years.

Prevalence of ED

The prevalence and 95% CI for each of the five levels of ED defined by the IIEF-5 for all subjects and stratified by age group are shown in Table 1. The prevalence of any level of ED was 82% (95% CI, 76 to 87%) for all HD subjects. Forty-five percent (CI, 36 to 55%) of men had severe ED. Older subjects (≥ 50 years) were more likely to experience ED [prevalence 90% (CI, 84 to 94%)], but younger patients (<50 years) also demonstrated a high prevalence [63% (CI, 53 to 71%)]. Using the single item self-report supplemental scale, the proportions reporting no ED, mild ED, moderate ED, and severe ED were 22% (CI, 18 to 28%), 15% (CI, 9 to 24%), 17% (CI, 15 to 19%), and 46% (CI, 37 to 54%), respectively, results very similar to those seen with the IIEF-5 self-report. Figure 1 represents the prevalence of ED as measured by the IIEF and by the Massachusetts Male Aging Study single item questionnaire.

Eighteen percent of subjects reported having been treated for ED. Eight percent of subjects who scored higher than 21 on the IIEF-5 had sought treatment for ED compared with 21% of those who scored 21 or less

on the IIEF-5. Nineteen of the 302 subjects reported having been treated with sildenafil. Two of these 19 were not identified as having ED by the IIEF questionnaire.

Comorbidities and physical function

No clear-cut association between functional status and ED was observed. The mean \pm SD ICED score was 2.11 ± 0.83 . The distribution of subjects by score was 0 (0%), 1 (30%), 2 (29%), and 3 (41%). In unadjusted analyses, a higher ICED score was not significantly associated with ED ($P = 0.44$).

The mean of the Karnofsky Index score was 81.3. The Karnofsky Index was marginally associated with ED ($P = 0.074$). Patients with ED had lower scores when compared with patients without ED (81, 95% CI, 76.5 to 85.5, vs. 86.5, 95% CI, 80.7 to 92.2).

Predictors of ED

Table 2 describes the different demographic variables stratified by the presence of ED along with the unadjusted odds ratio. A history of prior kidney transplant was present in 20 men (7.0%), and this history was not statistically associated with ED (OR = 0.55, 95% CI, 0.09 to 3.36, $P = 0.49$). Forty-six (15.3%) subjects reported prostate problems, including history of prostatic cancer, prostatic surgery, or benign prostatic hypertrophy. A history of prostatic disease was a statistically significant predictor of ED in unadjusted analyses (OR = 2.99, 95% CI, 1.07 to 8.4, $P = 0.039$).

Table 3 summarizes the subjects' physiologic parameters stratified by ED. Subjects without ED had higher serum levels of parathyroid hormone (508.9 vs. 324.5, $P \leq 0.001$) and higher creatinine (13.1 vs. 10.9, $P = 0.037$) in unadjusted analyses.

The mean medications per patient were 2.69. No medication or combination of medications was found to increase the probability of ED in our population. The use of angiotensin-converting enzyme inhibitors (ACEIs) was associated with a decreased prevalence of ED. Among those using an ACE inhibitor, 72.5% had ED, while among those not using an ACEI, 86.4% had ED (OR = 0.42, 95% CI, 0.18 to 0.96). There was no evidence for confounding of this association between ACEIs and ED by the presence of diabetes mellitus or by age group. Patients with diabetes had a very similar exposure to ACEIs (27%) as compared with patients without diabetes (33%, $P = 0.38$). The unadjusted associations between all medications and ED are presented in Table 4. When subjects who were using ACE inhibitors were compared to subjects who were on other antihypertensive agents, the odds ratio of ED for ACE inhibitors compared with other antihypertensive drugs was 0.44 (0.20 to 0.94, $P = 0.04$). The result remained significant after adjusting for age and diabetes, OR = 0.42 (0.20 to 0.90, $P = 0.03$).

Table 2. Association with presence of erectile dysfunction (ED)

Variable	% with ED (N)	OR (95% CI) for variable predicting presence of ED
Age group		
<50	61.2 (39)	1.00
50–59	76.0 (50)	2.01 (1.24–3.26)
60–69	90.8 (58)	6.23 (2.06–18.82)
70+ ^b	100.0 (83)	∞
Race ^a		
White	90.5 (97)	1.00
Black	77.1 (130)	0.36 (0.15–0.82)
Other	81.3 (4)	0.46 (0.07–3.08)
Duration on dialysis		
<1 year	89.1 (33)	1.00
1–<2 years	85.1 (61)	0.70 (0.15–3.32)
2–<4 years	83.2 (81)	0.60 (0.10–3.58)
4+ years	75.3 (59)	0.37 (0.07–2.06)
Hypertension		
Yes	81.8 (223)	0.30 (0.03–3.27)
No	93.8 (11)	1.00
Diabetes		
Yes	89.5 (94)	2.45 (1.61–3.72)
No	77.7 (140)	1.00
ACE inhibitors		
Yes	72.5 (61)	0.42 (0.18–0.96)
No	86.4 (173)	1.00
Individual disease severity		
1	91.1 (6)	1.00
2	81.1 (143)	0.42 (0.04–4.89)
3	83.8 (85)	0.51 (0.04–6.93)
Index of physical impairment		
0	76.8 (83)	1.00
1	87.6 (118)	2.13 (0.68–6.73)
2	81.9 (31)	1.37 (0.52–3.58)
Index of coexistent disease		
1	78.2 (65)	1.00
2	85.8 (71)	1.68 (0.71–3.98)
3	82.8 (97)	1.34 (0.61–2.92)
Cause of ESRD		
Diabetes mellitus	89.9 (82)	1.00
Hypertension	78.3 (105)	0.41 (0.23–0.73)
Other	75.9 (41)	0.36 (0.14–0.88)
Smoking status		
Never smoked	84.0 (59)	1.00
Smoked <40 packs	78.5 (75)	0.70 (0.39–1.25)
Smoked \geq 40 packs	89.3 (72)	1.60 (0.51–5.05)
Alcohol use ^c		
Doesn't drink	83.6 (169)	1.00
<6 drinks/week	76.5 (44)	0.64 (0.20–2.05)
6+ drinks/week	83.4 (14)	0.99 (0.31–3.12)
Karnofsky Index	Mean (SE) patients with ED	
(per 10 unit increase)	80.98 (2.1)	0.81 (0.64–1.02)

^a Includes American Indian, Asian, and other/multiracial; there was no difference in estimates between models examining white versus non-white

^b All patients over 70 had ED

^c Quantitation of ETOH consumption was done using the Khavari Alcohol Test (36)

Age, diabetes, and cause of ESRD were statistically significantly associated with the presence of ED (Table 5), while smoking status and alcohol intake were not. Race was not found to be associated with ED after adjusting for age. Subjects 50 to 59 years of age had an odds of ED that was two (95% CI, 1.3 to 3.1) times higher when compared with subjects less than 50 years of age. For subjects between the ages of 60 to 69 years, the odds ratio increased to 5.5 (95% CI, 1.9 to 15.6). All

Table 3. Association of physiologic parameters with presence of erectile dysfunction (ED)

Lab value units	Patients with ED N = 234	Patients without ED N = 47
Hemoglobin mg/dL	11.5 (0.1)	11.3 (0.2)
Hematocrit %	35.5 (0.3)	34.8 (0.6)
Albumin g/dL	3.9 (0.04)	4.0 (0.05)
Kt/V	1.4 (0.03)	1.4 (0.06)
Urea reduction ratio %	69.1 (0.7)	66.6 (1.3)
Parathyroid hormone pg/dL	324.5 (29.8)	508.9 (61.6)
Creatinine mg/dL	10.9 (0.4)	13.1 (0.5)
Mean arterial pressure mm Hg	103.8 (0.9)	110.3 (2.1)

Data are mean (SE). For modeling purposes, each lab value was divided into categories as follows:

Hemoglobin (mg/dL): <10, 10–11, 11–12, 12+

Hematocrit (%): <30, 30–33, 33–36, 36+

Albumin (g/dL): <3.5, 3.5–4, 4+

Kt/V: <1.2, 1.2–1.4, 1.4+

URR (%): <58, 58–65, 65–70, 70+

PTH (pg/dL): <400, 400+

Creatinine (mg/dL): <8, 8–11, 11–13, 13+

MAP (mm Hg): <93, 93–106, 106–120, 120+

Table 4. Unadjusted analysis according to medication class

Medication	ED among patients taking medication % (n)	ED among patients not taking medication % (n)	OR (95% CI) for medication predicting presence of ED
Beta blockers	79.7 (67)	83.3 (167)	0.79 (0.32–1.95)
Diuretics	84.2 (19)	82.1 (215)	1.16 (0.27–5.07)
Central	100.0 (1)	82.2 (233)	—
ACE inhibitors	72.5 (61)	86.4 (173)	0.42 (0.18–0.96)
Anticholinergics	94.0 (12)	81.7 (222)	3.53 (0.30–41.76)
Digoxin	92.8 (36)	80.6 (198)	3.13 (0.76–12.83)
Anxiolytic/antidepressant	92.5 (23)	81.3 (211)	2.85 (0.68–12.00)
Calcium channel blockers	80.5 (114)	84.0 (120)	0.79 (0.29–2.13)
Clonidine	78.2 (40)	83.1 (194)	0.73 (0.19–2.87)
Erythropoietin	81.5 (201)	88.2 (33)	0.59 (0.16–2.22)
Alpha blockers	92.3 (27)	81.3 (207)	2.77 (0.66–11.64)
ARB	72.4 (20)	83.3 (214)	0.53 (0.22–1.24)
Antihypertensives	80.7 (179)	87.6 (55)	0.59 (0.16–2.23)
Total number of medication classes			
0	71.9 (10)		1.00
1	89.0 (37)		3.15 (0.66–15.14)
2	81.4 (62)		1.71 (0.35–8.24)
3	88.7 (68)		3.08 (0.78–12.16)
4	72.3 (35)		1.02 (0.16–6.65)
5+	78.7 (22)		1.45 (0.30–7.10)

Abbreviations are: ARB, angiotensin receptor blocker; ACE, angiotensin-converting enzyme; ED, erectile dysfunction.

Table 5. Final multivariable logistic regression model

Variable	OR (95% CI) for variable predicting presence of ED
Age group ^a	
<50	1.00
50–59	2.04 (1.34–3.13)
60–69	5.49 (1.94–15.58)
70+	∞
Diabetes	
Yes	1.97 (1.18–3.30)
No	1.00
ACE inhibitors	
Yes	0.41 (0.17–0.98)
No	1.00

^a All patients over 70 had ED

subjects over 70 had ED. Subjects with diabetes had twice the odds of having ED when compared with subjects without diabetes (OR = 2.0, 95% CI, 1.2 to 3.3). However, neither the subjects' age nor history of diabetes predicted the severity of ED among those with ED.

Although unadjusted analyses suggested that a history of prostate disease, mean arterial pressure, parathyroid hormone levels, and serum creatinine were significantly associated with ED, none were associated with ED after adjustment for age and diabetes and use of ACEI.

DISCUSSION

Using population survey sampling techniques, we estimated the prevalence of ED among an urban HD popu-

lation and found that over four fifths of male HD patients have some degree of ED. In 45% of the HD patients studied, the ED was severe. Even among younger subjects (<50 years), 63% reported some degree of ED, of which one third was severe. Age and history of diabetes were positively associated with the presence of ED, while the use of ACEIs was associated with a lower risk of ED.

A variety of definitions has been used to evaluate ED in the HD population in 10 prior small studies. Eight of these 10 prior studies included fewer than 34 HD subjects [2, 9–17]. Perhaps because of the varied definitions of ED and small sample size, the estimates of prevalence ranged broadly from 41 to 93%. Levy defined ED as the difficulty in getting or maintaining an erection [14]. Using mail survey responses from 345 subjects, the investigator found that 70% of men had “some problem” with ED. Using a definition of ED that was a “problem with erections which reduced sexual intercourse by 50% or more,” Abram et al found a prevalence of 78% [17].

Hemodialysis patients in our study demonstrated a high prevalence of ED. Diabetes, increasing age, and the non-use of ACEIs were associated with the presence of ED. Age was also correlated with ED in other studies, including the Massachusetts Male Aging Study [6, 18, 19]. Several prior studies have linked diabetes mellitus and ED. The Massachusetts Male Aging Study showed that among patients with treated diabetes, the age-adjusted probability of “complete impotence” was 28% compared with 9.6% in the general population [6]. Another population-based study of men aged 21 and older with 10 or more years of diabetes taking insulin found an overall prevalence of ED of 20%. Among older subjects (over age 43), the prevalence of ED was 47.1% [18].

The prevalence of ED was not associated with the ICED score or functional status as measured by the Karnofsky score. The mean ICED score of 1.9 obtained in some other large multicenter prospective dialysis trials was similar to the results observed in this study [20]. However, in this study, 44% of subjects were women, and 39% were on peritoneal dialysis.

In addition to chronic illnesses and medications, there are numerous reasons why patients with ESRD may suffer from ED. Dialysis patients have lower testosterone levels and have been shown to have suppression of the pituitary testicular axis [21, 22]. Other proposed reasons for the high prevalence of ED among dialysis patients include zinc deficiency [23, 24], hyperprolactinemia [25], hyperparathyroidism [26], and psychological conditions [13]. In an unadjusted analysis, higher mean levels of parathyroid hormone and creatinine were found in patients without ED. These associations disappeared after adjustment for age and diabetes. The increased mean creatinine value in the patients without ED may be a reflection of increased muscle mass in younger patients.

The use of ACEIs was significantly and inversely asso-

ciated with ED, a finding consistent with prior published research. Commonly prescribed medications, particularly diuretics, β blockers, and central α agonists, may cause sexual dysfunction [27, 28]. A double-blind, randomized, cross-over design study comparing lisinopril to atenolol evaluated subjects of 40 to 49 years of age with newly diagnosed essential hypertension and without a history of ED. The subjects in the lisinopril-treated group complained of sexual dysfunction symptoms elicited by the study questionnaire less often than the subjects treated with atenolol (3 vs. 17%, $P < 0.05$) [29]. It is difficult, however, to determine whether the erectile impairment in controlled hypertension is due to the influence of the disease, medications, or both. Therefore, investigators have evaluated penile cavernous pressure in normotensive animal models. Using this model, the penile cavernous pressure response to nerve stimulation is significantly impaired with propranolol and clonidine, while captopril had no significant effect on these parameters [30].

The increased incidence of ED among hypertensive patients in different therapeutic regimens is not a universal finding. In six randomized, blinded, prospective trials in which 1251 men received placebo, 5 mg qd to 20 mg bid enalapril, 2.5 to 10 mg qd amlodipine, and 6.25 to 25 mg of hydrochlorothiazide (HCTZ), bisoprolol 5 mg qd or a combination of 2.5 to 10 mg qd bisoprolol/HCTZ for an average exposure duration of 6 to 14 weeks, adverse effects and symptoms were spontaneously volunteered by each subject. There was no difference between treatment modalities with respect to self-reported ED ($P = 0.69$), decrease in libido ($P = 0.97$), or overall sexual dysfunction ($P = 0.71$) for 1251 men [31]. We may have not been able to find a deleterious effect of the use of β blockers or diuretics due to a small subgroup sample size. There were only 19 patients on diuretics and 67 subjects on β blockers.

The correlation of 0.672 between the IIEF in this study population with the single question was similar to a recent report [32]. Our results provide support for the use of the single question as a practical tool for large population-based studies, where detailed clinical measures of ED are impractical.

Despite having performed a population-based sampling of male HD patients, our study, nonetheless, has several limitations. Because the presence of ED and associated conditions and exposures were assessed simultaneously, it was impossible to determine whether we identified causal associations with ED. All of our measures of ED were based on self-reporting, and no other physical or diagnostic tests were performed. We attempted to standardize self-report of ED by using a questionnaire that has been validated in other settings [4, 5, 33].

When the interactions of race were examined with

the various other predictors, race did not modify the association of any of other variable with ED when age was included in the model. Thus, the associations we found between various predictors with ED should be generalizable to other populations with different race compositions.

Although the 77.4% response rate in our study population is generally considered good, we cannot exclude that patients who refused were systematically different from study subjects. We were able to collect very limited information on patients who refused to participate.

In view of the observed high prevalence of ED in HD patients, we believe that a complete health evaluation of male HD patients should include a discussion about erectile function. Some studies have shown that physician frequency of initiated discussions of ED in high-risk populations such as diabetics, hypertensive, and older patients is poor [34, 35].

In summary, ED is highly prevalent in the HD population. It is strongly associated with increasing age and history of diabetes, and is less common among patients who use ACEIs. Future research activities should include evaluation of the effectiveness of and barriers to treatment of ED and their impact on quality of life in the dialysis population.

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REFERENCES

1. ANONYMOUS NIH CONSENSUS DEVELOPMENT PANEL ON IMPOTENCE: Impotence. *JAMA* 270:83-90, 1993
2. GLASS CA, FIELDING DM, EVANS C, ASHCROFT JB: Factors related to sexual functioning in male patients undergoing hemodialysis and with kidney transplants. *Arch Sex Behav* 16:189-207, 1987
3. KISH L: *Survey Sampling*. New York, John Wiley and Sons Inc., 1995
4. ROSEN R, CAPPELLERI J, SMITH M, et al: Development and evaluation of an abridged, 5-item, version of the IIEF as a diagnostic tool for erectile dysfunction. *Int J Impot Res* 11:319-326, 1999
5. ROSEN RC, RILEY A, WAGNER G, et al: The International Index of Erectile Function (IIEF): A multidimensional scale for assessment of erectile dysfunction. *Urology* 49:822-830, 1997
6. FELDMAN HA, GOLDSTEIN I, HATZICHRISTOU DG, et al: Impotence and its medical and psychosocial correlates: Results of the Massachusetts Male Aging Study. *J Urol* 151:54-61, 1994
7. KARNOFSKY D, BURCHENAL J: The clinical evaluation of chemotherapeutic agents in cancer, in *Evaluation of Chemotherapeutic Agents in Cancer*, edited by MACLEOD C, New York, Columbia University Press, 1999
8. Deleted in proof
9. ALLEYNE S, DILLARD P, MCGREGOR C, HOSTEN A: Sexual function and mental distress status of patients with end-stage renal disease on hemodialysis. *Transplant Proc* 21:3895-3898, 1989
10. PROCCI WR, MARTIN DJ: Effect of maintenance hemodialysis on male sexual performance. *J Nerv Ment Dis* 173:366-372, 1985
11. PROCCI WR: The study of sexual dysfunction in uremic males: Problems for patients and investigators. *Clin Exp Dial Apheresis* 7:289-302, 1983
12. THURM J: Sexual potency of patients on chronic hemodialysis. *Urology* 5:60-62, 1975
13. MILNE JF, GOLDEN JS, FIBUS L: Sexual dysfunction in renal failure: A survey of chronic hemodialysis patients. *Int J Psychiatry Med* 8:335-345, 1977
14. LEVY NB: Sexual dysfunctions of hemodialysis patients. *Clin Exp Dial Apheresis* 7:275-288, 1983
15. STEELE TE, FINKELSTEIN SH, FINKELSTEIN FO: Hemodialysis patients and spouses. *J Nerv Ment Dis* 162:225-237, 1976
16. RODGER RS, FLETCHER K, DEWAR JH, et al: Prevalence and pathogenesis of impotence in one hundred uremic men. *Uremia Invest* 8:89-96, 1984
17. ABRAM HS, HESTER LR, SHERIDAN WF, EPSTEIN GM: Sexual functioning in patients with chronic renal failure. *J Nerv Ment Dis* 160:220-226, 1975
18. KLEIN R, KLEIN BEK, LEE KE, et al: Prevalence of self-reported erectile dysfunction in people with long-term IDDM. *Diabetes Care* 19:135-141, 1996
19. JONLER M, MOON T, BRANNAN W, et al: The effect of age, ethnicity and geographical location on impotence and quality of life. *Br J Urol* 75:651-655, 1995
20. NICOLUCCI A, CUBASSO D, LABBROZZI D, et al: Effect of coexistent diseases on survival of patients undergoing dialysis. *ASAIO J* 38:M291-M295, 1992
21. HOLDSWORTH SR, DE KRETZER DM, ATKINS RC: A comparison of hemodialysis and transplantation in reversing the uremic disturbance of male reproductive function. *Clin Nephrol* 10:146-150, 1978
22. CHOPP RT, MENDEZ R: Sexual function and hormonal abnormalities in uremic men on chronic dialysis and after renal transplantation. *Fertil Steril* 29:661-666, 1978
23. MAHAJAN SK, ABBASI AA, PRASAD AS, et al: Effect of oral zinc therapy on gonadal function in hemodialysis patients: A double blind study. *Ann Intern Med* 97:357-361, 1982
24. ANTONIOU LD, SHALHOUB RJ, SUDHAKAR T, SMITH JC JR: Reversal of uremic impotence by zinc. *Lancet* 2:895-898, 1977
25. BOMMER J, RITZ E, DEL POZO E, BOMMER G: Improved sexual function in male haemodialysis patients on bromocriptine. *Lancet* 2:496-497, 1979
26. MASSRY SG, GOLDSTEIN DA, PROCCI WR, KLETZKY OA: Impotence in patients with uremia: A possible role for parathyroid hormone. *Nephron* 19:305-310, 1977
27. CROOG SH, LEVINE S, SUDILOVSKY A, et al: Sexual symptoms in hypertensive patients: A clinical trial of antihypertensive medications. *Arch Intern Med* 148:788-794, 1988
28. GRIMM RHJ, GRANDITS GA, PRINEAS RJ, et al: Long-term effects on sexual function of five antihypertensive drugs and nutritional hygienic treatment in hypertensive men and women: Treatment of Mild Hypertension Study (TOMHS). *Hypertension* 29:8-14, 1997
29. FOGARI R, ZOPPI A, CORRADI L, et al: Sexual function in hyperten-

- sive males treated with lisinopril or atenolol: A crossover study. *Am J Hypertension* 11:1244–1247, 1998
30. SRILATHA B, ADAIKAN PG, ARULKUMARAN S, NG SC: Sexual dysfunction related to antihypertensive agents: Results from the animal model. *Int J Impot Res* 11:107–113, 1999
 31. PRISANT L, WEIR M, FRISHMAN W, et al: Self-reported sexual dysfunction in men and women treated with bisoprolol, hydrochlorothiazide, enalapril, amlodipine, placebo, or bisoprolol/hydrochlorothiazide. *J Clin Hypertens* 1:22–26, 1999
 32. DERBY CA, ARAUJO AB, JOHANNES CB, et al: Measurement of erectile dysfunction in population-based studies: The use of a single question self-assessment in the Massachusetts Male Aging Study. *Int J Impot Res* 12:1–8, 2000
 33. GOLDSTEIN I, LUE TF, PADMA-NATHAN H, et al: Oral sildenafil in the treatment of erectile dysfunction. *N Engl J Med* 338:1397–1404, 1998
 34. PERTTULA E: Physician attitudes and behaviour regarding erectile dysfunction in at-risk patients from a rural community. *Postgrad Med J* 75:83–85, 1999
 35. MORLEY JE: Impotence. *Am J Med* 80:897–905, 1985
 36. KHAVARI KA, FARBER PD: A profile instrument for the quantification and assessment of alcohol consumption: The Khavari Alcohol Test. *J Stud Alcohol* 39:1525–1539, 1978