Factors Affecting the Increased Prevalence of Erectile Dysfunction in Greek Hypertensive Compared With Normotensive Subjects

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ABSTRACT: Arterial hypertension is considered a risk factor for erectile dysfunction. The aim of the study was to evaluate the prevalence of erectile dysfunction in hypertensive compared with normotensive individuals of similar demographic characteristics in Greece. Furthermore, the effect of age, hypertension severity, hypertension duration, and antihypertension medication on erectile function of these subjects was investigated. The study population consisted of 634 consecutive young and middle-aged men (31–65 years) that visited our outpatient clinic. From them, 358 patients had arterial hypertension and 276 were normotensive. Erectile dysfunction was evaluated with the International Index for Erectile Function questionnaire. Erectile dysfunction was found in 35.2% of patients with essential hypertension compared with 14.1% of normotensive subjects ($\chi^2 = 35.92$, $P < .001$). Patients with essential hypertension had more severe erectile dysfunction than their normotensive counterparts ($\chi^2 = 17.1$, $P < .001$). Hypertension duration, hypertension severity, antihypertension medication, and age were positively correlated with erectile dysfunction. The prevalence of erectile dysfunction is higher in patients with essential hypertension compared with normotensive subjects of similar demographic characteristics. Erectile dysfunction is related to age in both groups, whereas duration and severity of hypertension as well as antihypertension drugs affect erectile function of hypertensive patients. Erectile dysfunction affects patient quality of life, underlining the need for vigorous research of this condition and appropriate management.

Key words: Erectile function, hypertension, hypertension severity, hypertension treatment, age.

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Erectile dysfunction is defined as the persistent inability to attain or maintain penile erection sufficient for sexual intercourse. Approximately 10–20 million American men have some degree of erectile dysfunction (National Institutes of Health, 1993; Feldman et al, 1994). Erectile dysfunction has a major effect on patients' and their sexual partners' quality of life. Current advances in treatment options have generated great public interest among men and their sexual partners.

Arterial hypertension affects more than 20% of the general population with its incidence rising with age. Arterial hypertension and aging are considered, among others, major risk factors for erectile dysfunction.

The prevalence of erectile dysfunction in the general population varies widely among countries, from 15% to 34% (Martin-Morales et al, 2001; Giuliano et al, 2002; Moreira et al, 2003; Nicolosi et al, 2003). This large variation could be because of ethnic differences, different study populations, and different assessment methods, underlying the need for accurate data in each country obtained with an established method. The International Index of Erectile Function (IIEF) has proven to be a cross-cultural and psychometrically valid measure of male erectile dysfunction (Rosen et al, 1997).

Several studies have reported a higher prevalence of erectile dysfunction in hypertensive compared with normotensive subjects (Moreira et al, 2002; Aranda et al, 2004). Contrary to common belief, a similar prevalence of impotence in hypertensive and normotensive individuals has been reported (Newman and Marcus, 1985), and the presence of hypertension did not affect the prevalence of erectile dysfunction in other studies (Virag et al, 1985; Shabsigh et al, 1991).

The aim of the study was to evaluate the prevalence of erectile dysfunction in a sample of white Greek hypertensive and normotensive individuals of similar demographic characteristics and to investigate the effect of age, hypertension severity, hypertension duration, and antihypertension medication on erectile function of these subjects.

Materials and Methods

The study was conducted in accordance with the principles of the Helsinki declaration and was approved by the Hospital Ethics Committee. All subjects gave informed consent, and the procedures followed were in accordance with institutional guidelines. The study population consisted of 634 consecutive young and middle-aged men (31–65 years) that visited the outpatient clinic of the 4th Department of Internal Medicine, University of Athens. From them, 358 patients had arterial hypertension and 276 were normotensive. Essential hypertension was defined as blood pressure higher than 140/90 mm Hg according to guidelines used at that time (which were not changed by Joint National Committee VII [JNC VII, 2003] and European Society of Hypertension–European Society of Cardiology [ESH-ESC, 2003] guidelines) or current use of antihypertension drugs. Secondary hypertension was excluded by clinical and, if appropriate, laboratory examination.

Individuals with diabetes mellitus, heart disease, renal failure, or liver or vascular disease were not included in the study because these conditions have been associated with increased prevalence of erectile dysfunction.

A thorough history was taken, and subjects with a history of the above-mentioned chronic diseases were excluded from the study (19 patients with diabetes mellitus, 6 patients with heart disease, 5 patients with renal failure, 3 patients with liver disease, and 6 patients with vascular disease). The number of patients with the these diseases was considerably low because such patients are attended to in the specialized departments at our hospital. Patient demographic data (age, body weight), cigarette consumption, and alcohol intake were recorded. Detailed information regarding hypertension severity, hypertension duration, and medication administration was extracted from patient histories and files.

Blood pressure was measured with a mercury sphygmomanometer according to standard methodology. Three blood pressure recordings were obtained consecutively, and blood pressure was determined as the mean of the second and the third recording. Systolic blood pressure was defined at the point of appearance of the sounds (Korotkoff phase I), and diastolic blood pressure at the point of disappearance of the sounds (Korotkoff phase V).

Genital examination assessed for local abnormalities, such as phimosis, hypospadias, signs of hypogonadism, and prostate hyperplasia. Individuals with such conditions (2 patients with phimosis, 1 with crypsorchia, and 12 with prostate hyperplasia) were excluded from the study and referred to our Urologic outpatient clinic.

Erectile dysfunction evaluation was performed by a standardized questionnaire, with ''inform-then-probe'' types of questions. First, the question: ''Many people experience sexual problems. Has this ever appeared to you?'' was asked of the individuals to reassure them that their symptoms (if present) are not uncommon or embarrassing.

Then the patient was asked to fill a questionnaire regarding erectile dysfunction. The IIEF was chosen because it is considered an accurate, widely used test for defining the area of sexual dysfunction. Moreover, it provides information on several domains of sexual function, such as erectile function (questions 1–5,15), intercourse satisfaction (questions 6–8), orgasmic function (questions 9, 10), sexual desire (questions 11, 12), and overall satisfaction (questions 13, 14). Erectile dysfunction is classified according to IIEF questionnaire scoring of 6 questions as severe (6–10 points), moderate (11–16 points), mild (17–25 points), or none (26–30 points).

Statistical Analysis

Data are reported as mean ± standard deviation ($\bar{x}$ ± SD). Statistical analyses were carried out with the chi-square test to compare proportions and to evaluate the association between existence and severity of erectile dysfunction in hypertensive and normotensive individuals, as well as the association of different degrees of hypertension severity and duration with erectile dysfunction. Multiple regression analysis was used to evaluate the independent associations of erectile dysfunction with different variables. Associations were considered to be statistically significant at $P < .05$. Data were processed with the STATISTICA (Version 5.0; Statsoft Inc, Tulsa, Okla) statistical program for Windows.

Results

Patient demographic characteristics are described in the Table. There were no statistically significant differences between hypertensive and normotensive subjects with regard to age, body weight, body mass index, and alcohol and cigarette consumption. Only 2% of our study participants mentioned sexual problems when usual history was taken, and 96% agreed to fill out the questionnaire.

Baseline characteristics of hypertensive patients and normotensive individuals

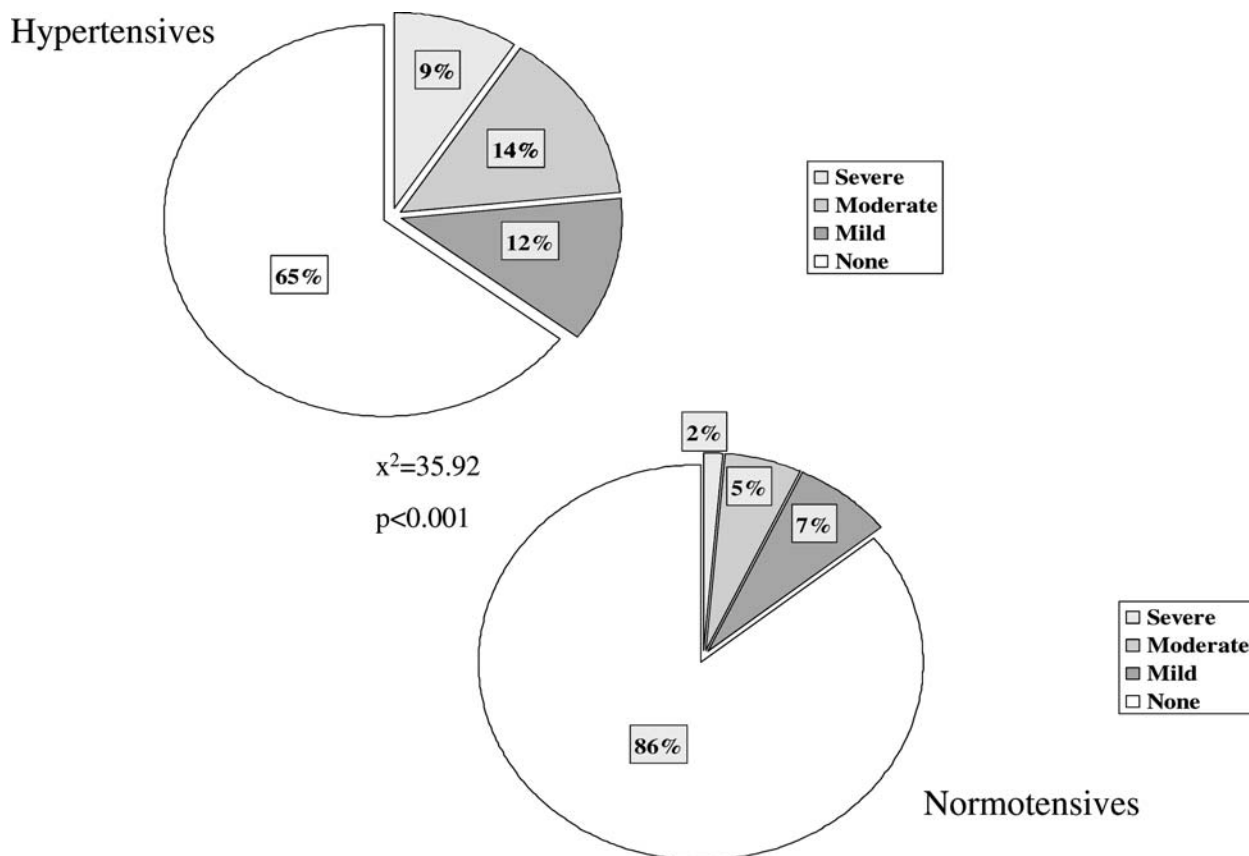|	Hypertensive Patients (n = 358)	Normotensive Subjects (n = 276)
Age, y	49.1 + 5.2	49.8 ± 5.6
Systolic blood pressure, mmHg	155.4 ± 16.9	112.1 ± 7.9
Diastolic blood pressure, mmHg	90.9 ± 5.1	77.3 ± 5.0
Body weight, kg	76.2 ± 8.1	75.9 ± 7.9
Smoking status		
Never	31%	29%
Former	32%	33%
Current	37%	38%
Cigarettes/d		
None	63%	62%
1–20	15%	18%
>20	22%	20%
Alcohol units/wk		
None	17%	16%
1–7	51%	53%
>7	32%	31%

Hypertensives

Figure 1. Prevalence of erectile dysfunction (severe, moderate, mild, none) in hypertensive patients compared with normotensive subjects.

Overall, erectile dysfunction of any degree was found in 35.2% of patients with essential hypertension compared with 14.1% of normotensive subjects with similar demographic characteristics, and the difference was statistically significant ($\chi^2 = 35.92$, $P < .001$).

Severe erectile dysfunction was found in 33 of 358 (9.2%) patients with essential hypertension and in 4 of 276 (1.5%) normotensive subjects ($\chi^2 = 17.11$, $P < .001$), moderate erectile dysfunction in 50 of 358 (14%) hypertensive and 15 of 276 (5.4%) normotensive individuals ($\chi^2 = 11.93$, $P < .001$), and mild erectile dysfunction in 43 of 358 (12%) hypertensives and 20 of 276 (7.2%) normotensives ($\chi^2 = 3.95$, $P < .05$), as shown in Figure 1.

Erectile dysfunction was more frequent in older hypertensive patients: 102 of 236 (43.2%) hypertensive patients more than 50 years of age presented with erectile dysfunction, whereas it was found in only 24 of 122 (19.7%) hypertensive subjects less than 50 years of age ($\chi^2 = 22.0$, $P < .001$). Normotensive individuals exhibited the same pattern (older than 50, 31/181 [17.1%]; younger than 50, 8/95 [8.4%]), and the difference was statistically significant ($\chi^2 = 3.89$, $P < .05$).

Hypertension duration significantly affected erectile function in our patients. Only 11 of 81 (14%) patients with essential hypertension for less than 3 years presented with symptoms of erectile dysfunction, whereas it was found in 45 of 161 (28%) patients with hypertension for 3–6 years and 70 of 116 (60%) patients with hypertension duration of more than 6 years ($\chi^2 = 21.37$, $P < .001$; Figure 2).

Severity of hypertension affected sexual function in our study population as well according to either JNC VII or ESH-ESC guidelines. According to JNC VII staging of hypertension, 86 of 193 (44.6%) patients with stage 2 hypertension exhibited erectile dysfunction, whereas only 40 of 165 (24%) patients with stage 1 hypertension presented such a dysfunction ($\chi^2 = 19.4$, $P < .001$). According to ESH-ESC, the percentage of patients with erectile dysfunction with grade 1, grade 2, and grade 3 hypertension was 24%, 37.5%, and 70%, respectively ($\chi^2 = 56.8$, $P < .001$). In addition, subjects with prehypertension or high normal blood pressure (according to JNC VII and ESH-ESC guidelines) exhibited erectile dysfunction more frequently than subjects with normal blood pressure (Figure 3).
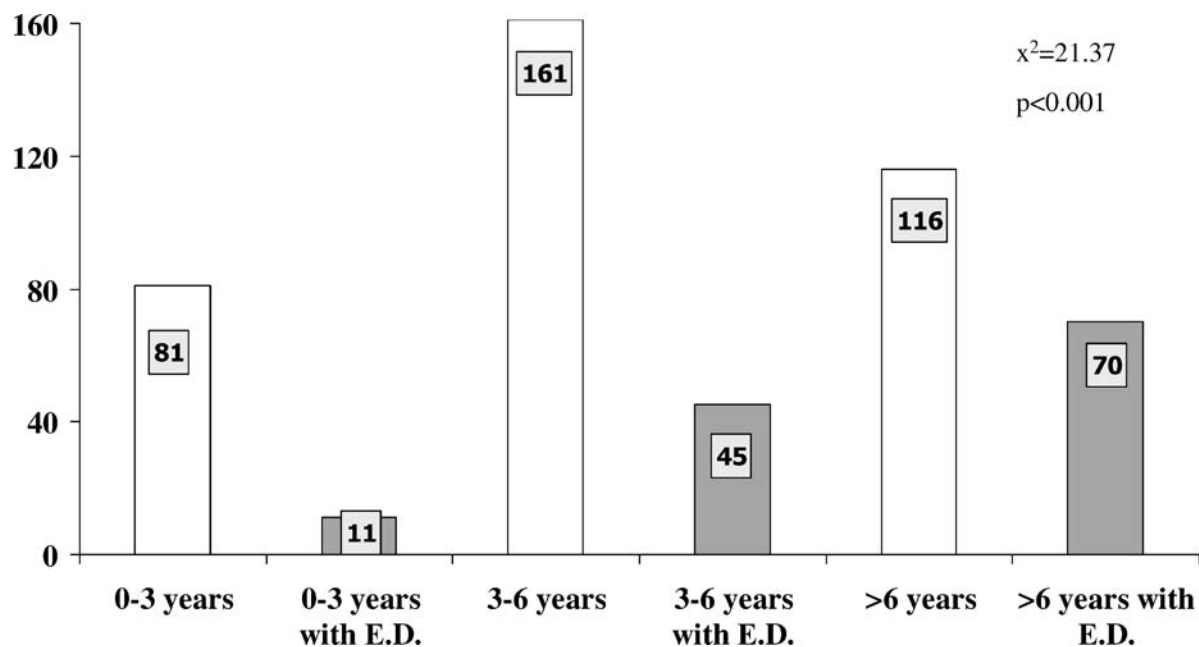
Figure 2. Relationship between hypertension duration (white bars: total number of patients with hypertension for <3 years, 3–6 years, and >6 years) and erectile dysfunction (ED; shaded bars, number of patients with erectile dysfunction in each category).
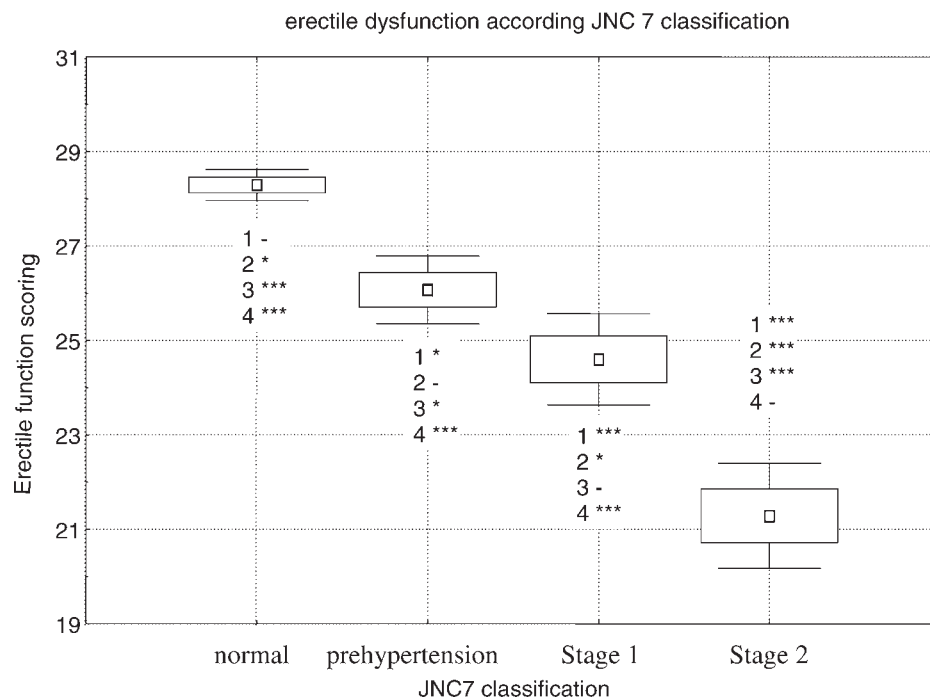

Figure 3. Correlation of erectile dysfunction score (International Index for Erectile Function: severe, 6–10 points; moderate, 11–16 points; mild, 17–25 points; and none, 26–30 points) with blood pressure levels according to Joint National Committee VII guidelines. **(1)** Normal blood pressure <120/80 mm Hg, **(2)** prehypertension 120–139/80–89 mm Hg, **(3)** stage 1 hypertension 140–159 mm Hg, and **(4)** stage 2 hypertension >160/>100 mm Hg. * $P < .05$, **= $P < .01$, *** $P < .001$.
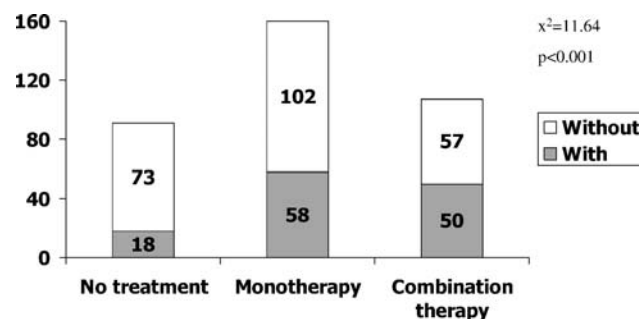
Figure 4. Prevalence of erectile dysfunction (ED) in patients with essential hypertension not taking any antihypertension drug (no treatment), taking 1 drug (monotherapy), and taking 2 or more drugs (combination therapy). White bars, number of patients without erectile dysfunction; shaded bars, number of patients with erectile dysfunction.

Multiple regression analysis revealed that systolic blood pressure and age were independently associated with erectile dysfunction (systolic blood pressure: $\beta = -0.5034$, $\chi^2 = -15.67$, $P < .00001$; age: $\beta = -2.6678$, $\chi^2 = -8.31$, $P < .00001$).

Treatment with antihypertension drugs has influenced the appearance of erectile dysfunction in our patients. Of 267 patients on treatment, 108 exhibited erectile dysfunction (40.4%), whereas only 18 of 91 patients (19.8%) without treatment presented with symptoms of erectile dysfunction ($\chi^2 = 11.64$, $P < .001$). Of 267 patients that were on therapy, 160 were on monotherapy and 107 were on combination therapy. Of patients on monotherapy, 44 were on b-blockers, 5 on diuretics, 44 on ACE inhibitors, 19 on angiotensin II receptor blockers, and 48 on calcium antagonists. Of patients on combination therapy, 77 were on diuretics. Patients on combination therapy exhibited erectile dysfunction more frequently (46.7%) than patients on monotherapy (36.3%), and the difference was statistically significant ($P < .001$; Figure 4).

Although our patient population is not large enough to permit for definite conclusions, patients on older drugs (b-blockers, diuretics) presented erectile dysfunction more frequent than patients on newer drugs (calcium antagonists, ACE inhibitors, angiotensin II receptor blockers), and the difference was statistically significant (Figure 5).

Discussion

Problems with erectile function have been a long-standing concern in the treatment of hypertension and could influence the choice of treatment drugs and the decision to discontinue antihypertension medication. Our study results, in addition to the observation that erectile dysfunction is more prevalent in patients with essential hypertension compared with age-matched normotensive individuals, indicate that 1) the severity of erectile dysfunction is greater in hypertensive than
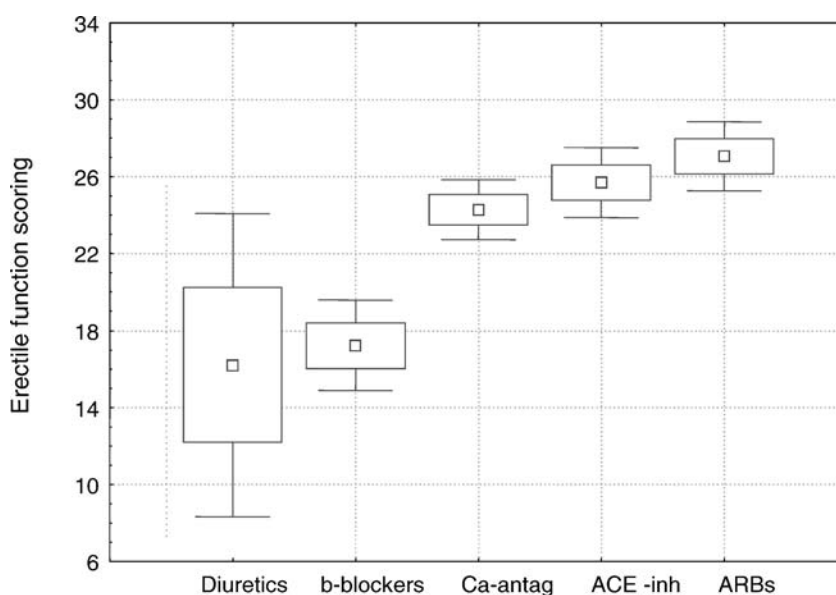

Figure 5. Correlation of erectile dysfunction score (International Index for Erectile Function; severe, 6–10 points; moderate, 11–16 points; mild, 17–25 points; and none, 26–30 points) with different classes of antihypertension medication (diuretics, b-blockers, calcium antagonists, ACE inhibitors, and angiotensin II receptor blockers). Ca-antag, calcium antagonists; ACE-inh, ACE inhibitors; ARBs, angiotensin II receptor blockers.

normotensive individuals; 2) erectile dysfunction depends on the severity of hypertension; 3) longer duration of hypertension results in increased prevalence of erectile dysfunction; 4) antihypertension drug administration is related to erectile dysfunction, with older drugs possessing the worse profile; and 5) age is the main determinant of erectile function.

Our study demonstrated a higher prevalence of erectile dysfunction in hypertensive than normotensive individuals (35% vs 14%), a finding that is in line with previous reports. In a recently published study, essential hypertension tripled the risk of erectile dysfunction (Moreira et al, 2002). The prevalence of erectile dysfunction in male hypertensives is lower than that observed in Spain (46%); however, patients with diabetes mellitus were not included in our study in contrast with the Spanish study (Aranda et al, 2004). If patients with diabetes mellitus were included in our study, the anticipated percentage of erectile dysfunction would have been much higher. The observed prevalence is much higher than that observed in the TOMHS study (Grimm et al, 1997); however, sexual dysfunction in that study was based on only one question. Specifically, hypertensive males were asked: "During the past 12 months, have you had a problem with sexual activity?" Thus, the different methodology and the lack of specific questioning and time dedicated could have accounted for the difference in prevalence of erectile dysfunction.

One of the most surprising and interesting findings of our study was the extremely low percentage (2%) of individuals that reported sexual problems. The vast majority of subjects with erectile dysfunction expressed their relief when the sexual function topic was raised, perhaps because of local perceptions, because erectile function in a Mediterranean country represents a matter of honor, and patients are reluctant at the beginning to discuss such issues even with a doctor. Although historically erectile dysfunction was a problem identified and treated by urologists, today general practitioners and other specialists subscribe 80% of the phosphodiesterase type-5 inhibitors (Mulcachy, 2000). The annual incidence of erectile dysfunction in the United Kingdom increased almost threefold during the last decade because of the introduction of sildenafil (Kaye and Jick, 2003). More than 70% of erectile dysfunction remains undiagnosed (Chun and Carson, 2001), mainly because of physicians' reluctance to ask about such abnormalities. Inadequate training and misperceptions of medical practitioners represent the major causes of this lack of communication. In a survey of primary care physicians, almost 2 of 3 admitted a lack of knowledge or skills in dealing with erection problems (Broekman et al, 1994). Moreover, more than half of them hesitated to

discuss such subjects because of incapacity or lack of time.

Erectile dysfunction is often found in hypertensive men, and several mechanisms could be implicated in its pathogenesis. Erectile dysfunction and cardiovascular disease might have some shared pathways on the basis of animal and human models (Sullivan et al, 2001). Erectile dysfunction can be considered a symptom of damage to the vascular endothelium (Sasayama et al, 2003). Nitric oxide synthesis is necessary to stimulate smooth muscle relaxation and to increase blood flow to levels appropriate for an erection; however, it is inhibited through several age-, disease-, and behavior-related pathways. Severe hypertension is related to endothelial dysfunction with reduced nitric oxide production by the endothelium (Schifrin, 2001). Thus, severity of hypertension might negatively affect erectile function through reduced nitric oxide production. Impotence was related to the severity of hypertension in a previous study; however, only 27 hypertensive patients with impotence were included in the study (Jensen et al, 1999). In our study, severity of hypertension was positively related to erectile dysfunction in a larger number of patients.

Erectile function is impaired in men with essential hypertension not by the increased blood pressure but by the associated stenotic lesions (Hsieh et al, 1989). The primary pathogenetic mechanism seems to be atherosclerosis compromising penile arterial flow, whereas blood pressure reduction by antihypertension drugs might worsen the situation. The atherosclerotic process in penile arteries might result in decreased blood flow, whereas endothelial dysfunction secondary to hypertension and other related diseases could lead to neurovegetative changes and contribute to erectile dysfunction. These mechanisms could be responsible for the effect of duration of hypertension on erectile function found in our study.

Although hypertension seems to be related to erectile dysfunction, oftentimes the onset of erectile dysfunction is related to the initiation of antihypertension therapy (Korenman, 1998). In everyday practice, medical practitioners often attribute sexual problems to the antihypertension drugs and modify or even discontinue treatment to address this problem. As many as 25% of cases of erectile dysfunction are related to medication side effects, with antihypertension drugs being the most implicated class (Feldman et al, 1994). However, scientific data that links antihypertension medication to erectile dysfunction in placebo-controlled trials is very limited (Prisant et al, 1994). In our study, patients taking antihypertension medication exhibited erectile dysfunction more frequently than patients that were not

taking drugs, with patients on combination therapy showing the highest percentage of erectile dysfunction.

Erection involves a coordinated action of the autonomic nervous system, wherein certain drugs (β-blockers, centrally acting sympatholytics) might interfere and cause erectile dysfunction. β-Blockers could cause erectile dysfunction by reducing testosterone levels and potentiating α_1-adrenergic activity in the penis. Thiazide diuretics are essentially devoid of central or autonomic nervous system activity, yet they are associated with erectile dysfunction, possibly because of fluid and zinc depletion (Khedum et al, 1995), although the definitive pathogenetic role of zinc in erectile dysfunction remains unclarified. Spironolactone can cause erectile dysfunction as well as gynecomastia and a decrease in libido. Moreover, higher blood pressure is required to achieve erection in atherosclerotic patients taking vasodilators and diuretics. Recent evidence suggests that drugs inhibiting the renin-angiotensin system exert favorable actions on erectile function (Fogari et al, 1998, 2001, 2002; Llisteri et al, 2001; Dusing, 2003). In our study, patients on older drugs (β-blockers, diuretics) presented with erectile dysfunction more frequent than patients on newer drugs (calcium antagonists, ACE inhibitors, angiotensin II receptor blockers).

Sexual function progressively declines with age, which could cause erectile dysfunction through several mechanisms. In about 40% of men over 50 years old, the primary cause of erectile dysfunction is related to atherosclerosis (Kaiser et al, 1988). Diabetes mellitus, hypertension, heart disease, and medication use are more frequent in aged people and have been directly associated to erectile dysfunction; however, erectile dysfunction occurs in healthy older people as well. The period between sexual stimulation and erection increases, erections are less turgid, ejaculation is less forceful, and the period between erections lengthens (Masters, 1977). Penile hemodynamic changes occurring in aging might account for erectile dysfunction because cavernous arterial flow is decreased, the response time of the cavernous artery is increased, and peak systolic velocity occurs much later in subjects after the fifth decade of life (Chung et al, 1997). Moreover, a decrease in smooth muscle cells has been observed in the corporeal tissue of aged impotent individuals (Jevtich et al, 1990; Wespes, 2000), and experimental data indicate that aging results in more collagen fibers and fewer elastic fibers in the corpora cavernosa (Shen et al, 2001). In our study, increased age was found to correlate with erectile dysfunction in both hypertensive and normotensive individuals.

The role of smoking in erectile dysfunction remains controversial. A recently published study from Spain showed a 2.5-fold increase in the risk of erectile dysfunction among smokers (Martin-Morales et al, 2001), in contrast with the Massachusetts Male Aging Study, in which smoking and alcohol consumption were not found to be causally associated with the incidence of erectile dysfunction (Johannes et al, 2000; Kleinman et al, 2000). A recent consensus group analysis failed to document a direct link between cigarette consumption and erectile dysfunction; however, smoking seems to amplify other risk factors, such as coronary artery disease and hypertension (McVary et al, 2001). Moreover, smoking can induce vasoconstriction and penile venous leakage because of its contractile effect on cavernous smooth muscle (Juenemann et al, 1987). In our study, no association was found between smoking and erectile dysfunction.

Alcohol in small amounts improves erection and increases libido because of its vasodilatory effect and anxiety suppression; however, large amounts can result in central sedation, decreased libido, and transient erectile dysfunction. Chronic alcoholism can cause hypogonadism and polyneuropathy, which can affect penile nerve function (Miller and Gold, 1988). In the Health Professionals Follow-up Study, moderate drinkers (1 or 2 drinks per day) had a lower prevalence of erectile dysfunction, compared with either heavy drinkers or nondrinkers (Rimm et al, 2000). In the Massachusetts Male Aging Study, a change in heavy drinking status was not associated with reduced risk of erectile dysfunction (Derby et al, 2000), suggesting that chronic heavy alcohol consumption might have an irreversible effect on erectile function because of neurological damage (Lemere and Smith, 1973). In our study, no association was found between alcohol consumption and erectile dysfunction.

Patients with essential hypertension present with erectile dysfunction more frequently than matched normotensive individuals, a condition with a major effect on their quality of life. Because erectile dysfunction is a topic of potential embarrassment, doctors must be motivated to discuss such issues. Antihypertension treatment seems to increase the prevalence of erectile dysfunction, with older drugs (diuretics, b-blockers) showing a worse profile than newer drugs (calcium antagonists, ACE inhibitors, angiotensin II receptor blockers). Larger studies are needed to confirm this observation and affect the choice of antihypertension medication.

Acknowledgments

References

Aranda P, Ruilope L, Calvo C, Luque M, Coca A, De Miguel A. Erectile dysfunction in essential arterial hypertension and effects of sildenafil: results of a Spanish national study. *Am J Hypertens.* 2004;17:139–145.

Broekman CPM, van der Werff ten Bosch JJ, Slob AK. An investigation into the management of patients with erection problems in general practice. *Int J Impot Res.* 1994;6:67–72.

Chun J, Carson CCIII. Physician-patient dialogue and clinical evaluation of erectile dysfunction. *Urol Clin North Am.* 2001;28:249–258.

Chung WS, Park YY, Know SW. The impact of aging on penile hemodynamics in normal responders to pharmacological injection: a doppler sonographic study. *J Urol.* 1997;157:229–231.

Derby CA, Mohr BA, Goldstein I, Feldman HA, Johannes CB, McKinlay JB. Modifiable risk factors and erectile dysfunction: can lifestyle changes modify risk? *Urology.* 2000;56:302–306.

Dusing R. Effect of the angiotensin II antagonist valsartan on sexual function in hypertensive men. *Blood Pressure.* 2003;12(suppl 2):29–34.

European Society of Hypertension–European Society of Cardiology (ESH-ESC). 2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. *J Hypertens.* 2003;21:1011–1053.

Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and phychosocial correlates: results of the Massachusetts Male Aging Study. *J Urol.* 1994;151:54–61.

Fogari R, Preti P, Derosa G, Marasi G, Zoppi A, Rinaldi A, Mugellini A. Effect of antihypertensive treatment with valsartan or atenolol on sexual activity and plasma testosterone in hypertensive men. *Eur J Clin Pharmacol.* 2002;58:177–180.

Fogari R, Zoppi A, Corradi L, Mugellini A, Poletti L, Lusardi P. Sexual function in hypertensive males treated with lisinopril or atenolol. *Am J Hypertens.* 1998;11:1244–1247.

Fogari R, Zoppi A, Poletti L, Marasi G, Mugellini A, Corradi L. Sexual activity in hypertensive men treated with valsartan or carvedilol: a crossover study. *Am J Hypertens.* 2001;14:27–31.

Giuliano F, Chevret-Measson M, Tsatsaris A, Reitz C, Murino M, Thonneau P. Prevalence of erectile dysfunction in France: results of an epidemiological survey of a representative sample of 1004 men. *Eur Urol.* 2002;42:382–389.

Grimm R, Grandits G, Prineas R, McDonald R, Lewis C, Flack J, Yunis C, Svendsen K, Liebson P, Elmer P. Long-term effects on sexual function of five antihypertensive drugs and nutrititional hygienic treatment in hypertensive men and women. *Hypertension.* 1997;29:8–17.

Hsieh JT, Lue TF, Muller SC. The influence of blood flow and blood pressure on penile erection. *Int J Impot Res.* 1989;1:35–42.

Jensen J, Lendorf A, Stimpel H, Frost J, Ibsen H, Rosenkilde P. The prevalence and etiology of impotence in 101 male hypertensive outpatients. *Am J Hypertens.* 1999;12:271–275.

Jevtich MJ, Khawand NY, Vidic B. Clinical significance of ultrastructural findings in the corpora cavernosa of normal and impotent men. *J Urol.* 1990;143:289–293.

Johannes CB, Araujo AB, Feldman HA, Derby CA, Kleinman KP, McKinlay JB. Incidence of erectile dysfunction in men 40 to 69 years old: longitudinal results from the Massachusetts Male Aging Study. *J Urol.* 2000;163:460–463.

Joint National Committee (JNC) VII. Seventh Report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension.* 2003;42:1206–1252.

Juenemann KP, Lue TF, Luo JA, Benowitz NL, Abozeid M, Tanagho EA. The effect of cigarette smoking on penile erection. *J Urol.* 1987;138:438–441.

Kaiser FE, Viosca SP, Morley J, Mooradian AD, Davis SS, Korenman SG. Impotence and aging: clinical and hormonal factors. *J Am Geriatr Soc.* 1988;36:511–519.

Kaye JA, Jick H. Incidence of erectile dysfunction and characteristics of patients before and after introduction of sildenafil in the United Kingdom: cross sectional study with comparison patients. *BMJ.* 2003;326:424–425.

Khedum SM, Naicker T, Makarey B. Zinc, hydrochlorothiazide and sexual function. *Cent Alp J Med.* 1995;41:312–315.

Kleinman KP, Feldman HA, Johannes CB, Derby CA, McKinlay JB. A new surrogate variable for erectile dysfunction status in the Massachusetts Male Aging Study. *J Clin Epidemiol.* 2000;53:71–78.

Korenman SG. Sexual function and dysfunction. In: Wilson JD ed. *Williams Textbook of Endocrinology,* 9th ed. Philadelphia, Pa: WB Saunders Co; 1998:927–938.

Lemere F, Smith JW. Alcohol-induced sexual impotence. *Am J Psychiatry.* 1973;130:212–213.

Llisterri Caro JL, Vidal JL, Vicente JA, Roca MA, Bravo CP, Sanchez Zamorano MA, Ferrario CM. Sexual dysfunction in hypertensive patients treated with losartan. *Am J Med Sci.* 2001;321:336–341.

Martin-Morales A, Sanchez-Cruz JJ, Saenz de Tejada I, Rodriguez-Vela L, Jimenez-Cruz JF, Burgos-Rodriguez R. Prevalence and independent risk factors for erectile dysfunction in Spain: results of the Epidemiologia de la Disfunction Erectil Masculina Study. *J Urol.* 2001;166:569–575.

Masters WH, Johnson VE. Sex after sixty-five. *Reflections.* 1977;12:31–43.

McVary KT, Carrier S, Wessels H. Subcommittee on smoking and erectile dysfunction socioeconomic committee, Sexual Medicine Society of North America. Smoking and erectile dysfunction: evidence based analysis. *J Urol.* 2001;166:1624–1632.

Miller NS, Gold MS. The human sexual response and alcohol and drugs. *J Subst Abuse Treat.* 1988;5:171–177.

Moreira E, Bestane W, Bartolo E, Fittipaldi J. Prevalence and determinants of erectile dysfunction in Santos, southeastern Brazil. *Sao Paulo Med J.* 2002;120:131–139.

Moreira E, Lobo C, Diament A, Nicolosi A, Glasser D. Incidence of erectile dysfunction in men 40–69 years old: results from a population-based cohort study in Brazil. *Urology.* 2003;61:431–436.

Mulcachy JJ. Erectile dysfunction—is the incidence increasing? *J Urol.* 2000;163:471–473.

National Institutes of Health. NIH consensus conference on impotence. *JAMA.* 1993;270:83–90.

Newman HF, Marcus H. Erectile dysfunction in diabetes and hypertension. *Urology.* 1985;26:135–137.

Nicolosi A, Moreira E, Shirai M, Tambi M, Glasser D. Epidemiology of erectile dysfunction in four countries: cross-national study of the prevalence and correlates of erectile dysfunction. *Urology.* 2003;61:201–206.

Prisant LM, Carr AA, Bottinni PB, Solursh DS, Solursh LP. Sexual dysfunction with antihypertensive drugs. *Arch Intern Med.* 1994;154:730–736.

Rimm EB, Bacon CG, Giovanucci EL, Kawachi I. Body weight, physical activity, and alcohol consumption in relation to erectile dysfunction among US male health professionals free of major chronic diseases. *J Urol.* 2000;163(suppl):15.

Rosen R, Riley A, Wagner G. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology.* 1997;49:822–830.

Sasayama S, Ishii N, Ishikura F, Kamijima G, Ogawa S, Kanmatsuse K, Kimoto Y, Sakuma I, Nonogi H, Matsumori A, Yamamoto Y. Men's health study. Epidemiology of erectile dysfunction and cardiovascular disease. *Circ J*. 2003;67:656–659.

Schifrin E. Role of endothelin-1 in hypertension and vascular disease. *Am J Hypertens*. 2001;14:83S–89S.

Shabsigh R, Fishman IJ, Schum C, Dunn JK. Cigarette smoking and other vascular risk factors in vasculogenic impotence. *Urology*. 1991;38:227–231.

Shen ZJ, Jin XD, Chen ZD, Shi YH. Effect of aging on penile ultrastructure. *Asian J Androl*. 2001;3:281–284.

Sullivan ME, Keoghane SR, Miller MA. Vascular risk factors and erectile dysfunction. *BJU Int*. 2001;87:838–845.

Virag R, Bouilly P, Frydman D. Is impotence an arterial disorder? A study of arterial risk factors in 440 impotent men. *Lancet*. 1985;1:181–184.

Wespes E. Erectile dysfunction in the aging men. *Curr Opin Urol*. 2000;10:625–628.