



Prevalence of Cardiovascular Risk Factors in Erectile Dysfunction

Monika K. Walczak, MD, Naaznin Lokhandwala, MD, Mary Beth Hodge, MD, and Andre T. Guay, MD, FACP

OBJECTIVE: Thirty million men in the United States may have erectile dysfunction, and coronary artery disease (CAD) is the major cause of death in men over 55 years old. Several studies have shown a correlation between erectile dysfunction and risk factors for coronary artery disease. Hyperlipidemia plays a pivotal role in CAD, and obesity is now considered an independent risk factor for CAD. Therefore, we attempted to determine the prevalence of obesity and hyperlipidemia, along with other established risk factors such as diabetes, hypertension, and tobacco use, in men with erectile dysfunction.

METHODS: Men who had had symptoms of erectile dysfunction for at least six months were recruited from the Center for Sexual Function. Participants underwent detailed clinical interviews, blood analyses, and physical examinations including calculation of body mass index, and they completed a questionnaire on sexual function.

RESULTS: Of the 154 men evaluated, 44% had hypertension; 23% had diabetes mellitus; 16% used tobacco; 79% had a body mass index of $> 26 \text{ kg/m}^2$; and 74% had a low-density lipoprotein cholesterol level of $> 120 \text{ mg/dL}$.

CONCLUSION: Impotence is an important symptom, and its presence should instigate assessment and aggressive management of coexistent risk factors for CAD. Intervention could restore sexual function and ultimately improve cardiovascular health.

(*J Genit Specif Med* 2002;5[6]:19-24)

Erectile dysfunction (ED)—defined as a persistent inability to achieve and maintain an erection adequate for satisfactory sexual activity—occurs to varying degrees in nearly 30 million men in the United States.¹ According to the Massachusetts Male Aging Study (MMAS), the prevalence of impotence at all degrees is approximately 52% in men aged 40-70 years.² There are many possible etiologies of ED. Historically, impotence was thought to be psychogenic. That theory began to change in the 1970s, when medical factors were recognized. In 1992, the National Institutes of

Health (NIH) Consensus Conference on Impotence reported that approximately 75% of ED cases had physical rather than psychological etiologies.³ Nonetheless, psychological factors, such as performance anxiety, relationship problems, stress, and psychiatric disorders (depression or schizophrenia), are still present in many cases.⁴

Organic ED is often associated with vascular risk factors, including veno-occlusive dysfunction and arterial insufficiency.^{4,5} Neurologic causes include compromised central neural pathways, such as in Parkinson's disease, Alzheimer's disease, multiple sclerosis, stroke, and cerebral trauma, or peripheral neural pathways, as in spinal cord injury, pelvic injury, or neuropathy.^{1,4}

Endocrine causes of ED include hypogonadism, diabetes mellitus, and thyroid dysfunction. Androgens, in addition to stimulating libido centrally, have peripheral effects on the penis as well, and nighttime erections

From the Center for Sexual Function and Section of Endocrinology, Labey Clinic Northshore, Peabody, MA. Address for correspondence: A.T. Guay, MD, Center for Sexual Function, Labey Clinic Northshore, One Essex Center Dr, Peabody, MA 01960. E-mail: andre.t.guay@labey.org.



decrease in the presence of androgen deficiency.^{1,4} Elevated prolactin inhibits central dopaminergic activity, decreasing the secretion of gonadotropin-releasing hormone, which results in hypogonadotropic hypogonadism. Excessive prolactin levels can be caused by medications or by pituitary tumors. ED also can be associated with use of various medications, such as antihypertensive agents and central nervous system agents prescribed for anxiety and depression.⁴

Important risk factors include systemic diseases that accelerate and amplify the progressive decline of sexual function with age.⁴ In the MMAS, results indicated that impotence was strongly associated with age, but after adjustment for age there was a significant correlation of ED with diabetes mellitus, hypertension, heart disease, and low-serum high-density lipoprotein (HDL) cholesterol.² The NIH Consensus Conference found similar risk factors, including diabetes mellitus, hypertension, vascular disease, hyperlipidemia, and low-serum HDL cholesterol.³

Combinations of factors are also very common. Cigarette smoking is associated with a greater probability of complete impotence in men with heart disease and hypertension. Medication side effects are amplified by smoking.² In a recent study of 990 men evaluated for ED, 36.3% had hypogonadism, 35.8% had hypertension, 28.2% used multiple medications, 23.1% had diabetes mellitus, 19.9% had atherosclerotic coronary artery disease (CAD), and 14.1% used tobacco.⁶

In another study of 50 men aged 40-60 years, 56% of those with ED but without apparent symptoms or history of heart disease had positive stress test results, suggesting a link between ED and CAD. A high prevalence of risk factors for CAD, as well as established CAD, was reported in this population of patients with no symptoms other than ED.⁷

Obesity, previously thought to be an indirect factor, is an independent risk factor for endothelial dysfunction that precedes atherosclerosis. The American Heart Association recently recommended reclassification of obesity as a major modifiable risk factor for CAD.⁸ Since ED and cardiovascular (CV) disease may share common risk factors, we examined the medical risks of ED, including lipid metabolism and obesity.

MATERIALS AND METHODS

Men were recruited in consecutive order from new consultations at the Lahey Clinic Center for Sexual Function during a six-month period from October 2000 to March 2001. Referrals to this clinic are mostly from family practitioners and internists and thus reflect a medical bias. Because the clinic is staffed by endocrinologists, a further bias is introduced by the large number of men with endocrine disorders who are seen.

Only candidates who had ED of organic or organic-psychological etiology were enrolled in the study. The symptoms of ED must have been present for at least six months, and the men had to be in stable heterosexual relationships for the same amount of time. The patients underwent detailed clinical interviews that included past medical and surgical history, physical examination, laboratory analysis, and completion of the Sex Health Inventory for Men (SHIM).^{9,10} This survey consists of five questions graded on a scale of 0 to 5. A score of 22 or less indicates the presence of ED that should be evaluated further. The lower the score, the more severe the ED. When the etiology of the ED was uncertain, a nocturnal penile study was performed using the RigiScanTM portable home monitor (Timm Medical, Minneapolis, MN), and/or a consultation with the sex therapist was scheduled. Of the candidates identified as appropriate for the study, 86% agreed to participate.

Minimal laboratory analysis, if not current in the patients' clinical charts, included fasting glucose, analog-free testosterone, prolactin, creatinine, and fasting lipid profiles (12-hour fast minimum with abstinence from alcohol for 48 hours). Men with low testosterone levels were excluded from the study. Current height and weight were measured, and body mass index (BMI) was calculated.

The group selected for study had significant ED, as indicated by a total SHIM score of less than 21 out of a possible 25. Alcohol intake was assessed, with *excessive intake* defined as more than two drinks per day. A *drink* was defined as 12 ounces of beer, 5 ounces of dry wine, or 1.5 ounces of 80-proof hard alcohol.

RESULTS

One hundred fifty-four men participated in the study. The demographic data are shown in Table I. The mean age of



Table I
Patient Demographic Data

n = 154	
Mean age: 53 years	
Median age: 53 years	
Age range: 24-77 years	
SHIM	Question 2 (n = 131): mean 2.18 Distribution: 0 (n = 10), 1 (n = 26), 2 (n = 48), 3 (n = 20), 4 (n = 22), 5 (n = 5)
SHIM	Question 4 (n = 139): mean 2.19 Distribution: 0 (n = 10), 1 (n = 33), 2 (n = 32), 3 (n = 40), 4 (n = 19), 5 (n = 5)

SHIM = Sex Health Inventory for Men.

participants was 53 years. The men had moderate to severe ED, as evidenced by their responses to the SHIM, especially questions 2 and 4 on specific erectile capacities. Question 2, which dealt with erections being sufficiently rigid for penetration, had a mean response of 2.18 on a scale of 0 to 5. Question 4, which addressed the ability to maintain an erection until completion of intercourse, had a mean response of 2.19 on a scale of 0 to 5.

The frequency of the various medical risk factors is shown in Table II. The most common factor associated with ED was *hypertension*, defined as blood pressure > 140/90 mm Hg. Abnormal glucose metabolism was the next most common factor. Type 2 diabetes mellitus was seen in 22% of patients, and *borderline diabetes*, defined as a

fasting glucose of 111-125 mg/dL, was seen in 12% of patients. The normal fasting glucose in our laboratory is 70-110 mg/dL, and the American Diabetes Association defines *diabetes* as a fasting glucose of ≥ 126 mg/dL. Tobacco use was reported by 16% of men, and established CAD was found in 9% of participants.

Medication use was associated with ED in 27% of participants; 14% of the men took multiple medications, and 13% took single medications known to be associated with ED. Neurologic disease was present in 8% of the patients and included history of stroke, alcoholic neuropathy, seizure disorder, or multiple sclerosis. Alcohol abuse was identified in 6% of the study group. Only 3% of the men had histories of pelvic surgery, which included radical prostatectomy and colonic resection; this small percentage reflects a negative referral bias, in that urologists treat their own patients after radical prostatectomy rather than referring them.

Excess weight was defined as a BMI of > 26 kg/m² (Table III). A large number of patients (79%) had high BMIs. *Overweight* was defined as a BMI between 27 and 29 kg/m², and *obesity* was defined as a BMI of > 29 kg/m². Hyperlipidemia, diagnosed on a fasting lipid profile, demonstrated hypertriglyceridemia in 44% of men and HDL fraction below 35 mg/dL in 12% of men. Seventy-four percent of the men had low-density lipoprotein (LDL) cholesterol levels above 120 mg/dL, and 64% of the population had LDL levels above 130 mg/dL.

Table II
Prevalence of Common Risk Factors in Men With Erectile Dysfunction

Risk Factor	%
Hypertension	44
Abnormal glucose	34
Type 2 diabetes mellitus	22
Borderline diabetes mellitus	12
Tobacco use	16
Multiple medications	14
Single medication	13
Coronary artery disease	9
Neurologic disorder	8
Alcohol abuse	6
Pelvic surgery	3

Table III
Risk Factors Related to Weight and Lipid Status

Hyperlipidemia	
LDL cholesterol (> 120 mg/dL)	74%
Total cholesterol (> 200 mg/dL)	71%
Triglycerides (> 150 mg/dL)	44%
HDL cholesterol (< 35 mg/dL)	12%
Overweight and Obesity	
BMI > 26 kg/m ²	79%
BMI 27-29 kg/m ²	39%
BMI > 29 kg/m ²	40%

LDL = low-density lipoprotein; HDL = high-density lipoprotein; BMI = body mass index.

Table IV shows various combinations of risk factors in the study population. Diabetes and hypertension were seen together in 11.0% of the group, diabetes and obesity in 19.4%, and diabetes and elevated LDL cholesterol in 14.9%. Hypertension and obesity were seen in 37.6% and elevated LDL in 30.5% of the group. If we combined three risk factors—hypertension, obesity, and elevated LDL—the incidence was 26.6%. Obesity plus elevated

LDL was the most common combination. When we eliminated the major risk factors (diabetes mellitus, hypertension, CAD, and LDL > 120 mg/dL), only 13 men (8.4%) remained. When obese patients were also eliminated, this left only five men (3.2%) with other risk factors for ED. When smokers were eliminated, only four men (2.6%) remained.

Table V shows the relationship between the severity of ED and the number of CV risk factors. Moderately severe ED scores were seen with one to three risk factors and worsened when more than three risk factors were present.

DISCUSSION

Our study, much like the hallmark results from the MMAS, confirmed the presence of CV risk factors in patients with ED. Adequate arterial supply is critical for an erection, and any disorder that impairs blood flow may be implicated in the etiology of erectile failure. Most medical disorders associated with ED appear to affect the endothelial system.³ The endothelium has emerged as an organ that has functions as complex as any in the body. Endothelial dysfunction plays a pivotal role in the development and progression of atherosclerosis,¹¹ and it is being recognized increasingly as a critical component in

Table IV
Combinations of Cardiovascular Risk Factors in Men With Erectile Dysfunction

Risk Factors	No.	%
DM and HTN	17	11.0
DM + BMI > 26 kg/m ²	30	19.4
DM + LDL > 120 mg/dL	23	14.9
HTN + BMI > 26 kg/m ²	58	37.6
HTN + LDL > 120 mg/dL	47	30.5
HTN + BMI > 26 kg/m ² + LDL > 120 mg/dL	41	26.6
BMI > 26 kg/m ² + LDL > 120 mg/dL	91	59.1

DM = diabetes mellitus; HTN = hypertension; BMI = body mass index; LDL = low-density lipoprotein.

the development of ED. The Princeton Consensus Panel appreciated the frequent coexistence of ED and CAD and outlined safety guidelines for treating sexual dysfunction in patients with CV disease.¹² The fact that ED in a previously asymptomatic man may be a marker for occult CAD was suggested in the MMAS and by Pritzker.^{2,7}

In our cohort, 44% of men with ED had hypertension, which is similar to the 40% found in the

MMAS.¹³ Several studies have shown endothelial dysfunction in patients with hypertension. The nitric oxide–cyclic guanosine monophosphate pathway may be involved in endothelium-impaired vasodilation in patients with hypertension.¹⁴

The prevalence of overweight men in our study was striking. Obesity was seen in 40% of our patient population, which was similar to the MMAS, in which 41% of men were obese. Obesity is associated with insulin resistance and endothelial dysfunction.⁸ An elegant study by Higashi et al¹⁴ demonstrated that the vasodilatory effect of acetylcholine is compromised in obese normotensive individuals, and insulin resistance was postulated as the underlying factor. Although our clinic is medically biased, our

Table V
Results of SHIM (n = 146): Comparison of Total SHIM Score to Number of Major CV Risk Factors (DM, HTN, Tobacco Use, Obesity, Hyperlipidemia)

No. of Risk Factors	No. of Patients	Mean SHIM Score
1	23	11.3
2	62	11.8
3	42	10.5
4	18	7.8
5	1	5.0

SHIM = Sex Health Inventory for Men; CV = cardiovascular; DM = diabetes mellitus; HTN = hypertension.

incidence of obesity and hypertension is similar to that of the MMAS study, which was not biased.

Elevated LDL was found in 74% of our patient population. Several studies have shown that endothelial relaxation is impaired if the blood vessel wall is exposed to oxidized LDL, and these free radicals can inactivate nitric oxide.¹¹ Anecdotal experience in our clinic has indicated that lowering LDL with hepatic hydroxymethylglutaryl coenzyme A reductase inhibitors alone moderated ED, as documented objectively on the RigiScan™ monitor.

Twenty-two percent of our patients had type 2 diabetes mellitus, and 12% had borderline diabetes. Men with diabetes mellitus have a threefold increased risk of developing ED, and the ED usually occurs 10-15 years earlier than in men without diabetes.¹⁵ Insulin in euglycemic men has been shown to produce endothelium-dependent relaxation of isolated arteries, whereas increased glucose results in reduced release of endothelium-derived nitric oxide.¹¹ The development of ED correlates with the level of glycemic control.¹⁵ Similarly, optimal glycemic control reduces CV complications, especially when dyslipidemia is improved.¹⁶

Sixteen percent of our patients used tobacco. In the MMAS, the incidence of ED was higher in smokers who were also exposed to passive inhalation. Cigarette smoking is a well-established risk factor for the development of atherosclerosis and CV disease. One theory suggests that cigarette smoke may induce oxidative stress and cause endothelial damage, which initiates the development of atherosclerotic plaques.¹¹

When all men with one or more of the five major CV risk factors were eliminated from analysis, 5.2% of patients were left in the study pool. This underscores the prevalence of CAD risk factors in men presenting with ED.

Assessment and management of endothelial dysfunction are critical in the prevention of vascular disease. Health care providers, however, do not always initiate or intensify therapy aggressively during patient visits; this behavior is termed *clinical inertia*.¹⁷ There is ample epidemiologic evidence demonstrating clinical inertia in the management of CV risk factors. Pharmacologic treatment is prescribed for only 53% of patients with hypertension, and only 45% of patients treated for hypertension have adequate blood pres-

sure control. Only 33% of treated patients with diabetes achieve a glycosylated hemoglobin of 7% in accordance with goals defined by the American Diabetes Association.¹⁷ The data are even more discouraging for lipid intervention. Only 17-23% of patients with elevated cholesterol are treated pharmacologically. Our experience has corroborated the inertia in treating hyperlipidemia because only 27% of patients with LDL levels of > 120 mg/dL were receiving treatment.

Sexual function is an important component of patients' quality of life and subjective well-being.¹² Therefore, treatment of ED is rewarding because it not only enables the patient to have satisfactory sexual performance, but it also results in increased self-esteem and may help preserve relationships. Perhaps even more importantly, it provides insight into patients' vascular health and can be a powerful impetus to treat vascular risk factors, which are often not addressed aggressively enough. ED is a symptom of underlying vascular disease in the helicine arteries of the penis, just as angina is a symptom of vascular disease in the coronary arteries. Sildenafil citrate has been marketed widely based on its success in restoring erectile function. Working at the endothelium, sildenafil increases levels of cyclic guanosine monophosphate (a nucleotide derived from nitric oxide) by decreasing its breakdown. This drug effect provides indirect proof of impaired endothelial function in patients with impotence. Treating patients with sildenafil citrate is rewarding in that it may allay patients' immediate distress, but aggressive management of organic etiologies will help restore vascular health and ultimately prevent CV disease.

The authors report no conflict of interest.

References

1. Cohan P, Korenman SG. Erectile dysfunction. *J Clin Endocrinol Metab* 2001;86:2391-2394.
2. Feldman HA, Goldstein I, Hatzichristou DG, et al. Impotence and its medical and psychosocial correlates: Results of the Massachusetts Male Aging Study. *J Urol* 1994;151:54-61.
3. NIH Consensus Development Panel on Impotence. NIH Consensus Conference. Impotence. *JAMA* 1993;270:83-90.
4. Lue TF. Erectile dysfunction. *N Engl J Med* 2000;342:1802-1813.
5. Nehra A, Barrett DM, Moreland RB. Pharmacotherapeutic advances in the treatment of erectile dysfunction. *Mayo Clin Proc* 1999;74:709-721.
6. Guay AT, Velasquez E, Perez JB. Characterization of patients in a medical endocrine-based center for male sexual dysfunction. *Endocr Pract* 1999;5:314-321.



7. Pritzker MR. The Penile Stress Test: A window to the hearts of man? [abstract]. *Circulation* 1999;100(suppl 1):I-711;3751. Poster presented at: 72nd Session of the American Heart Association; November 7-10, 2001.
8. al Suwaidi J, Higano ST, Holmes DR Jr, et al. Obesity is independently associated with coronary endothelial dysfunction in patients with normal or mildly diseased coronary arteries. *J Am Coll Cardiol* 2001;37:1523-1528.
9. Rosen RC, Cappelleri JC, Smith MD, et al. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. *Int J Impot Res* 1999;11:319-326.
10. Cappelleri JC, Rosen RC, Smith MD, et al. Diagnostic evaluation of the erectile function domain of the International Index of Erectile Function. *Urology* 1999;54:346-351.
11. Cooke JP. The endothelium: A new target for therapy. *Vasc Med* 2000;5:49-53.
12. Debusk R, Drory Y, Goldstein I, et al. Management of sexual dysfunction in patients with cardiovascular disease: Recommendations of the Princeton Consensus Panel. *Am J Cardiol* 2000;86:175-181.
13. Feldman HA, Johannes CB, Derby CA, et al. Erectile dysfunction and coronary risk factors: Prospective results from the Massachusetts Male Aging Study. *Prev Med* 2000;30:328-338.
14. Higashi Y, Sasaki S, Nakagawa K, et al. Effect of obesity on endothelium-dependent nitric oxide-mediated vasodilation in normotensive individuals and patients with essential hypertension. *Am J Hypertens* 2001;14:1038-1045.
15. Romeo JH, Seftel AD, Madhun ZT, Aron DC. Sexual function in men with diabetes type 2: Association with glycemic control. *J Urol* 2000;163:788-791.
16. Sosenko JM, Breslow JL, Miettinen OS, Gabbay KH. Hyperglycemia and plasma lipid levels: A prospective study of young insulin-dependent diabetic patients. *N Engl J Med* 1980;302:650-654.
17. Phillips LS, Branch WT, Cook CB, et al. Clinical inertia. *Ann Intern Med* 2001;135:825-834.