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Cardiovascular Risk Stratification and Cardiovascular Risk Factors Associated with Erectile Dysfunction: Assessing Cardiovascular Risk in Men with Erectile Dysfunction

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Summary: Cardiovascular risk factors are known to be associated with the presence of erectile dysfunction (ED), and ED is more common in men with cardiovascular disease (CVD). The Princeton Guidelines provide a strategy for assessing cardiac risk and planning a safe return to sexual activity. Men at low risk, who have fewer than three cardiac risk factors, can resume intercourse with very little concern for an untoward cardiac event. Men at high risk need to have their primary disease controlled, and should be stabilized before planning to resume sexual activity. Prior to resuming intercourse, men in the indeterminate category are candidates for restratification as either low or high risk. Certain cardiovascular risk factors may be predictors of ED: most notably, hyperlipidemia, hypertension, and diabetes. Advancing age is also a strong predictor of ED. The close correlation between ED and CVD is a signal to evaluate the sexual histories of all men who present for cardiovascular evaluation and, perhaps, of all men in general. Early detection of ED may allow for early diagnosis and management of CVD and diabetes.

Key words: cardiovascular risk factors, erectile dysfunction, Princeton Guidelines

Introduction

Approximately 30 million men in the United States, 40 to 70 years of age, have some form of erectile dysfunction, known commonly as ED.[1, 2] Some men cannot have an erection at all, whereas others are unable to sustain their erections long enough to complete satisfactory intercourse.

The broad scope of ED means that this disorder is relevant to both primary care physicians and specialists. There are several reasons why cardiologists, in particular, should be concerned about ED. For one, cardiovascular disease (CVD) and ED share common risk factors, including smoking, hyperlipidemia, diabetes, obesity, and hypertension.[1–5] Furthermore, ED is more common in men with CVD.[4] Also, questions abound concerning the relative safety of sexual exertion for men with CVD. Restoring the ability to achieve an erection—through use of a phosphodiesterase type 5 (PDE5) inhibitor—raises this issue in many men with heart disease, as well as their partners and physicians.

The Princeton Guidelines were developed to address specifically the issue of sexual activity and overall management of men with ED and cardiovascular risk factors and/or disease.[6] Those guidelines are reviewed in this article, focusing particularly on how their proposed risk stratification system can be applied clinically to men with ED. In addition, data from selected studies are presented showing the link between cardiovascular risk factors and ED.

Erectile Dysfunction and Cardiovascular Risk Assessment

Baseline Patient Evaluation

A targeted medical, psychosocial, and sexual history, along with a physical examination and appropriate laboratory tests, provides a solid foundation on which to base the approach to care for men with CVD and ED. Sometimes it is a good idea to invite the patient's partner to participate in the sexual history. Questionnaires such as the Sexual Health Inventory for Men (SHIM) and the International Index of Erectile Function (IIEF) can provide insight into the quality, quantity, duration, and functionality of the patient's erections, as well as his satisfaction with sexual activities and intercourse.[7, 8] These tools

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are useful for helping introduce discussion on an uncomfortable topic.[9]

Exercise testing may or may not be of use for predicting a patient's risk of future coronary events.[9] It does provide insight into functional capacity, as well as into heart rate, blood pressure, and workload at which the patient will experience dyspnea, angina, and fatigue. Generally speaking, patients with coronary disease experience a higher heart rate during exercise testing than during sex. Patients who have ischemia during intercourse also demonstrate ischemia during exercise testing.[10]

Sexual Activity and Cardiac Risk

The physical demands of intercourse are moderate, being roughly equivalent to those of walking up a flight of stairs, dancing, or taking a brisk walk. During intercourse with a familiar partner in comfortable surroundings, heart rate and blood pressure seldom exceed 130 beats/min and 170 mmHg, respectively.[6]

Physical exertion is typically measured by the metabolic equivalent task (MET) of energy expenditure at the resting state. One MET is associated with an energy demand involving oxygen consumption of about 3.5 ml/kg/min. To provide some perspective, walking at an average pace of 2 miles/h expends about 2 METs of energy. Sexual activity is associated with a workload of about 2 to 3 METs until the orgasmic phase, during which energy expenditure can increase to 3 or 4 METs. There is one caveat, although not a major one: the sympathetic activation that occurs during sex can cause heart rate and blood pressure to increase more than it does during regular exercise of the same MET intensity.[6]

The risk of cardiac events during intercourse or other types of sexual activity is very low, but is increased over that which occurs at rest. Among the general population, < 1% of myocardial infarctions (MIs) occur during intercourse, and the baseline annual risk of MI for a 50-year-old man living in the United States is about 1%. Participation in sexual activity increases this annual risk to 1.01% in men considered to be at low cardiovascular risk and to 1.1% in men with a previous MI.[6]

Major cardiovascular risk factors are listed in Table I.[6] Patients with three or more of these risk factors (excluding gender) are considered to be at increased cardiac risk during sexual activity.

Categories of Graded Cardiac Risk

The developers of the Princeton Guidelines suggest placing patients into one of three major categories, based on cardiovascular status at the time of initial evaluation:[6]

- Low risk: Men in this category have fewer than three cardiac risk factors and are not at significant risk during sexual activity (Table II)
- High risk: Patients in this category have CVD requiring cardiac consultation, evaluation, and priority management (Table III). The cardiac condition is so sufficiently severe and/or unstable that sexual activity is risky. For example, patients with untreated or uncontrolled hypertension are at risk for an acute cardiovascular event, including stroke, during sex. Patients with refractory angina have a functional cardiac reserve less than the demands of intercourse and are at risk for an acute MI
- Indeterminate risk: Patients in this group have three or more major cardiac risk factors (Table IV). Their cardiac condition is uncertain enough that further testing or evaluation, and possible recategorization as either high or low risk, is recommended before they resume sexual activity.

TABLE I Major risk factors for cardiovascular disease

- Age
- Male or postmenopausal female
- Hypertension
- Diabetes mellitus
- Obesity
- Cigarette smoking
- Dyslipidemia
- Sedentary lifestyle

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TABLE II Princeton Guidelines: Low-risk patient

- Asymptomatic, < 3 coronary risk factors (excluding gender)
- Controlled hypertension
- Mild, stable angina
- Post-successful coronary revascularization
- Uncomplicated previous MI (> 6–8 weeks)
- Mild valvular disease
- LVD/CHF (NYHA class I)

Abbreviations: MI = myocardial infarction, LVD = left ventricular dysfunction, CHF = congestive heart failure, NYHA = New York Heart Association.
Adapted from Ref. No. 6 with permission.

TABLE III Princeton Guidelines: High-risk patient

- Unstable or refractory angina
- Uncontrolled hypertension
- LVD/CHF (NYHA class III/IV)
- Recent MI (< 2 weeks), CVA
- High-risk arrhythmias
- Hypertrophic obstructive and other cardiomyopathies
- Moderate/severe valvular disease

Abbreviation: CVA = cerebrovascular accident. Other abbreviations as in Table II.
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TABLE IV Princeton Guidelines: Indeterminate-risk patient

- ≥ 3 major coronary risk factors (excluding gender)
- Moderate, stable angina
- Recent MI (> 2, < 6 weeks)
- LVD/CHF (NYHA class II)
- Noncardiac atherosclerotic diseases, such as CVA, PVD

Abbreviation: PVD = peripheral vascular disease. Other abbreviations as in Tables II and III.
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Management Recommendations

The Princeton Guidelines' patient management recommendations are summarized in Table V.[6] Patients at low risk can generally have intercourse without the need for additional cardiovascular evaluation or care and can be treated for ED without significant concern. There are a few things to keep in mind when managing low-risk patients. Certain antihypertensive medications—primarily beta blockers and thiazide diuretics—can contribute to sexual dysfunction. Since changing medications or dosages may not resolve the problem, men with controlled hypertension may need to be treated directly for their ED. Men taking nitrates for mild, stable angina need to have their treatment regimen modified when taking a drug for ED. Nitrates are an absolute contraindication to phosphodiesterase (PDE5) inhibitor use. For men who have had revascularization procedures, an exercise stress test may be useful for assessing the extent and severity of residual ischemia. Absence of significant residual ischemia is a "green light" for resuming sexual activity. Patients with a previous MI who are asymptomatic are at low risk for a repeat MI during sex, as long as ischemia is not ongoing and the post-MI stress test is negative. Patients with a recent MI may be at risk for arrhythmias during intercourse, particularly during the first 2 weeks after the MI. The completion of a successful exercise test to 4 or 5 METs offers reassurance that the risk of MI during sex is low.[6]

Men at high risk should not participate in sex or be treated for ED until their cardiac condition has been fully evaluated and treated and their condition is stable. Men who have had an MI should be especially diligent about avoiding sex during the first 2 weeks after the event. Men with high-risk arrhythmias may benefit from wearing a Holter monitor during intercourse. Vasoactive drugs must be given very carefully to men with significant aortic stenosis, since they may not tolerate systemic vasodilation.

Men in the indeterminate-risk group should not be treated for ED or advised to engage in sex until they have been reevaluated and determined to be at either low or high coronary risk. Since these men have cardiac risk factors, consideration should be given to reducing those risks through diet, exercise, and medication as needed. Exercise stress testing can help these patients with moderate, stable angina or a history of MI determine their risk for cardiac events during sexual activity.[6]

Algorithm for Risk Stratification and Patient Management

A strategy for clinically applying the Princeton Guidelines is summarized in Figure 1. According to this plan, assessment and management of intercourse-related cardiac risk, and the treatment of sexual dysfunction, can be approached as a two-step process.[6]

During the first step, all patients with cardiac disease should have an assessment of sexual function. Further evaluation is based on the results of a medical history, physical examination, and laboratory testing. Patients are categorized as being at low, high, or indeterminate risk according to the results of this evaluation. Patients in the indeterminate category have specialized testing to see whether they can be reclassified as high or low risk.[6]

During the second step, most patients at low risk are encouraged to resume sexual activity or be treated for ED. Patients at high risk are stabilized before resuming sex or receiving treatment for ED. Regular reevaluation approximately every 6 months is recommended for all cardiac patients with ED.[6]

TABLE V Princeton Guidelines: Management recommendations based on graded cardiovascular risk assessment

Grade of risk	Management recommendations
Low	Primary care management Consider all first-line therapies Reassess regularly (every 6–12 months)
High	Priority referral for specialized cardiovascular management Treatment for sexual dysfunction deferred until cardiac condition is stable and depends on specialist recommendations
Indeterminate	Specialized cardiovascular testing (echocardiography, exercise tolerance test) Restratification into high or low risk based on results of cardiovascular assessment

Adapted from Ref. No. 6 with permission.

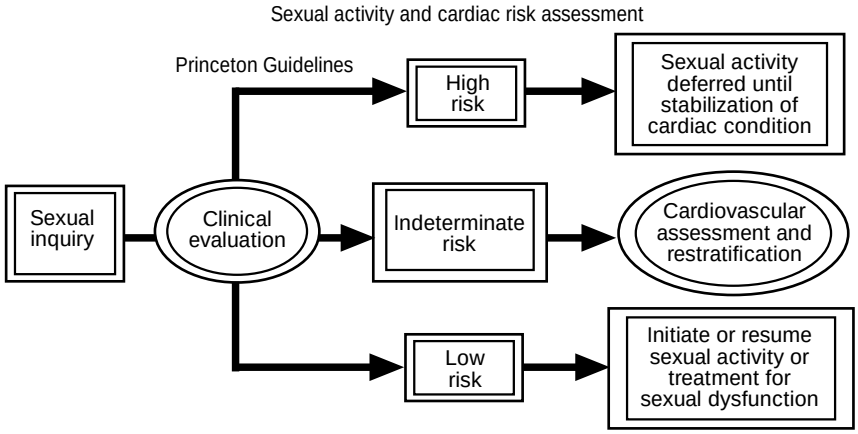

FIG. 1 The Princeton Guidelines strategy for planning sexual activity in men with cardiovascular disease. Men at low risk can engage in intercourse with little concern for cardiovascular events. Men at high risk need to have their underlying disease managed and stabilized before resuming sex. Data from Ref. No. 6.

Predictors of Erectile Dysfunction

Age

Aging is a leading risk factor for ED. The Massachusetts Male Aging Study, a community-based, random-sample observational survey of more than 1,000 men 40 to 70 years of age, found age to be the variable that correlated most strongly with ED.[1] In this study, the incidence of complete ED tripled from 5% at age 40 years to 15% at age 70. The incidence of moderate ED doubled from 17 to 34% over this same age span, whereas minimal ED averaged 17% across all age groups.

A community-based Rancho Bernardo study determined the prevalence of ED based on response to a 5-item version of the IIEF and the use of sildenafil in men with ED.[11] Based on data from a total of 976 men, sexual inactivity or dysfunction correlated strongly with advancing age: 89% of men < 50 years of age versus 37% of men ≥ 80 years of age reported being sexually active. The incidence of severe or complete ED increased from < 1% in men < 50 years of age (n = 3) to 7.5% in men 50 to 64 years of age. More than a third (36%) of men aged 75 to 79 years reported severe or complete ED (Fig. 2). Rates of sildenafil use were much lower than the prevalence of ED, suggesting that this condition is undertreated and under-

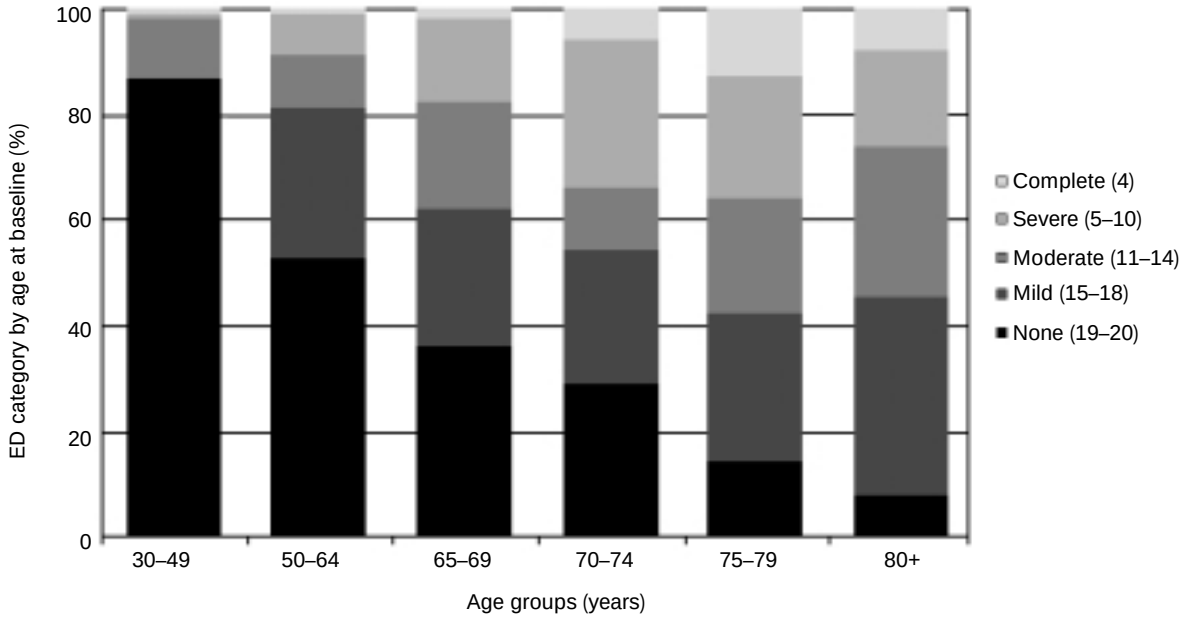

FIG. 2 Domain of erectile function by age among sexually active men in the Rancho Bernardo study. The prevalence of erectile dysfunction (ED) increased with age. Complete and severe ED was most common in men ≥ 80 years of age, whereas moderate ED was most common in men 75 to 79 years of age. Adapted from Ref. No. 11 (Fig. 1) with permission.

diagnosed. For evaluation of ED, this community-based study used the IIEF as a validated assessment tool. An important limitation to use of this questionnaire is the inability to assess sexually inactive men. It is not clear whether the men in this study, who reported no sexual activity, did so because of ED, lack of libido, or unavailability of a partner. A longitudinal study of the Rancho Bernardo men and how their cardiovascular risk factors (e.g., obesity, smoking, hypertension, diabetes, and lipids) predict future ED is pending.

Cardiovascular Risk Factors

Coronary heart disease, MI, hypertension, hyperlipidemia, obesity, smoking, and peripheral vascular disease all correlate with ED. The correlation is so direct that presence of any of these cardiovascular problems should alert the clinician to the possibility of ED.

Sullivan *et al.*[4] explored the connection between cardiovascular risk factors and ED (using fibrinogen and lipoprotein-a levels, two risk factors for coronary disease) in a group of men with ED (48 smokers, 48 nonsmokers) 45 to 70 years of age, who were compared with a control group (21 smokers, 21 nonsmokers). Serum total cholesterol (TC) was significantly higher in nonsmokers with ED than in control nonsmokers or smokers with ED. Plasma fibrinogen levels were significantly higher in smokers with ED than in control smokers and in nonsmokers with ED than in controls, regardless of smoking status. Lipoprotein-a levels were similar among all of the groups. These findings support the concept that cardiovascular risk factors such as smoking, cholesterol, and fibrinogen are predictors of ED.

Walczak *et al.*[3] agree that the presence of ED is strongly linked with CVD risk factors. They examined the prevalence of cardiovascular risk factors in a group of 154 men with ED and found that 44% of the men were hypertensive, 23% had diabetes, 16% used tobacco, 79% were overweight (body mass index > 26 kg/m^2), and 74% had low-density lipoprotein cholesterol (LDL-C) levels > 120 mg/dl.

Hyperlipidemia as a Predictor of Erectile Dysfunction

The connection between hyperlipidemia and ED used to be ambiguous, but data have emerged suggesting that lipid levels are strong predictors of ED. Wei *et al.*[12] followed a group of 3,250 healthy men, aged 26 to 83 years, during clinic visits over a period of 6 to 48 months. The men had no ED at their first visit; over the course of the study, sexual dysfunction developed in 71 of the men (2.2%). The investigators examined the correlation between ED and lipid levels and noted the following trends:

- For each mmol/l increase in total cholesterol (TC), the risk of ED increased 1.32 times
- For each mmol/l increase in high-density lipoprotein cholesterol (HDL-C), the risk of ED increased 0.38 times
- Men with HDL-C levels > 60 mg/dl had 0.3 times the risk of ED as did men with HDL-C levels < 30 mg/dl
- Men with TC levels > 240 mg/dl had 1.83 times the risk of ED as did men having TC levels < 180 mg/dl.

In this study, there was a clear trend associating high levels of TC and low levels of HDL-C with ED.

A more recent study further supports the link between elevated lipid levels and ED. Roumeguere *et al.*[13] examined undiagnosed hyperlipidemia and cardiac risk in patients with ED compared with matched patients with no ED. Parameters examined included risk factors for ED and coronary disease, as well as TC, triglyceride, HDL-C, LDL-C levels, and TC/HDL-C ratio. The investigators reported that the prevalence of hypercholesterolemia was 70.6 versus 52% in the men with and without ED, respectively. Logistic regression analysis indicated that HDL-C level and TC/HDL-C ratio were significantly associated with ED. Also, 10-year coronary heart disease risk was significantly higher in the ED group than in the non-ED group, 56.6 versus 32.6% ($p < 0.05$). Thus, hyperlipidemia was common in men with ED, and patients with ED had a higher risk of developing coronary disease within 10 years.

Diabetes and Hypertension as Predictors of Erectile Dysfunction

Erectile dysfunction is also linked with diabetes and hypertension, and it may be that onset of ED is an indication to check for these conditions if they have not been diagnosed. The converse is true as well: patients presenting to the office with diabetes or hypertension should be queried about any problems with sexual function.

A group of 150 primary care physicians who had patients with known diabetes and/or hypertension collectively conducted a survey asking their patients to complete a full IIEF questionnaire.[14] A total of 1,412 men participated, 37% of whom had diabetes, 38% of whom were hypertensive, and 25% of whom had both diseases. Depending on age, between 46 and 67% had some degree of ED. In this study, the prevalence of ED increased with age and disease (hypertension/diabetes) duration and was more common in men with diabetes than in those with hypertension, especially as the men aged. In addition, poor control of blood sugar was linked to earlier onset of ED.

Conclusions

Common cardiovascular risk factors, including diabetes, hypertension, high lipids, and smoking, are associated with ED, particularly as men age. Erectile dysfunction can serve as a valuable indicator of the need for cardiovascular assessment, especially in men with coronary risk factors. Physicians, regardless of specialty, need to remain alert to this association and to obtain a sexual history from men who present with heart disease or heart disease risk factors. The discovery of a patient's sexual dysfunction could potentially lead to early diagnosis and management of CVD or diabetes. In men with ED and known cardiac risk factors or disease, the Princeton Guidelines can be helpful in planning a strategy for treatment of ED and subsequent resumption of sexual activity.

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