Can Erectile Dysfunction Predict Major Cardiovascular Events?

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ABSTRACT

It is estimated that erectile dysfunction (ED) affects more than 150 million people worldwide and this number is expected to double by the year 2025. Vascular component represents the most important etiological cause of erectile dysfunction. ED shares almost all risk factors, such as hypertension, diabetes mellitus, hyperlipidaemia and smoking, with arteriosclerosis. Moderate to severe ED is associated with a considerably increased risk for coronary heart disease (CHD). This review was conducted in May 2016, when the PubMed database was searched using the combination of the terms "erectile dysfunction" and "cardiovascular diseases", "coronary artery diseases", "coronary artery diseases" and "risk factors". In this review, we analyzed the published literature, regarding the predictive role of ED in CVD and the association of ED risk factors with CVD risk factors, aiming to draw particular attention on the role of sexual inquiry of all men to prevent or decrease major cardiovascular events. In conclusion, the early detection of ED can prevent major cardiovascular events with early management of cardiovascular risk and permits to include patients in a risk stratification group. Erectile function should be evaluated using questionnaires in all male patients to prevent and decrease the rates of major cardiovascular events.

Keywords: erectile dysfunction, cardiovascular diseases, coronary artery diseases, risk factors

INTRODUCTION

Erectile dysfunction (ED) is defined as the inability of the male to attain and maintain an erect penis with sufficient rigidity at a sufficient level to permit satisfactory sexual intercourse.1 The vascular component represents the most important etiological cause of erectile dysfunction.2 ED has been associated with many other cardiovascular risk factors, such as hypertension, hyperlipidaemia, diabetes mellitus or smoking.3–7 Any disease located at the level of the systemic vascular bed, affects the penile arteries too, as it affects the blood supply of the genital organs. Consequently, patients with heart diseases show frequent symptoms of ED.8,9 It has been suggested that ED may represent a marker of lack of vascular integrity in general.10 ED could therefore serve as a predictive symptom for potentially life-threatening coronary heart disease.
(CHD) or stroke. Studies have suggested that the role of ED as an independent risk factor for future cardiovascular events is even independent from the classical risk factors, such as diabetes and hypertension. Moderate to severe ED was associated with a considerably increased risk for CHD and stroke. Several studies showed that ED is associated with many CHD risk factors, including diabetes mellitus, hypertension, smoking and abnormal lipids.

It has been suggested that ED may be considered as a clinical manifestation of a functional (endothelial dysfunction) or structural abnormality affecting penile circulation, as part of a more generalized vascular disorder. So far, the predictive role of ED as a marker of subclinical coronary artery disease (CAD) has not been completely elucidated. Pathological calcification in the coronary arteries, which is a common feature of atherosclerosis, is thought to be present even in the early subclinical phases of the atherosclerotic plaque formation.

**SYSTEMATIC REVIEW METHODOLOGY**

This review was conducted in May 2016, when the PubMed database was searched using the combination of the following terms: "erectile dysfunction" and "cardiovascular diseases", "coronary artery diseases" and "risk factors". Additional references were included by cross-referencing the bibliography of selected articles.

We intended to identify published articles discussing the predictive role of erectile dysfunction in the development of cardiovascular diseases and coexisting risk factors in ED and cardiovascular diseases (CVD). The PubMed database search results identified 2528 references. Articles written in other languages than English were excluded.

**DEFINITION AND PREVALENCE OF ERECTILE DYSFUNCTION**

After many years when the term "impotence" was used, the NIH Consensus Development Conference (1992) suggested to use the term "erectile dysfunction" instead, to denote the constant inability of the male to attain and maintain an erect penis with sufficient rigidity to permit satisfactory sexual intercourse. A cross-sectional study on 2126 adult males enrolled in the 2001–2002 National Health and Nutrition Examination Survey indicated the presence of various degrees of erectile dysfunction in over 18 million men in the US, representing 18.4% of the male population aged 20 years or older.

The incidence of erectile dysfunction in Romania has been estimated at 3% in young men aged between 15–25 years and at 7% in those aged between 25–45 years, increasing up to 22% in men aged between 45–55 years. It is estimated that ED affects 150 million people worldwide and this number is expected to more than double by the year 2025.

**ETIOLOGY OF ERECTILE DYSFUNCTION**

For the correct diagnosis it is necessary to identify the cause of ED, and proper evaluation of the psychological, neurological, hormonal, and vascular system is required to identify more severe comorbidities and to treat them properly.

**Vasculogenic ED.** Endothelial dysfunction seems to be the link between vasculogenic ED and macrovascular disease. The severity of ED has been associated with the extent of angiographically confirmed CAD. Patients with ED present high rates of macrovascular atherosclerosis, as well as its main precursor, hyperlipidemia. A recent meta-analysis of 740 patients from 6 clinical trials in 4 countries found that treatments for cardiac risk factors (lifestyle modifications and pharmacotherapy) were associated with a significant increase in the International Index of Erectile Dysfunction (IIEF-5) score and improvements in sexual function, indicating a common pathophysiological process for ED and cardiovascular disease.

**Psychogenic ED.** Psychogenic ED is the form related to stress, performance anxiety, or overt psychological disorders, such as depression or schizophrenia. Several factors such as traumatic or abusive experiences, inadequate sex education or social pressures are likely to contribute to sexual dysfunction.

**Neurogenic ED.** Central nervous system disorders and spinal cord injury can impede initiation and maintenance of an erection. The degree and severity of ED is highly associated with the extent of the neurological lesions and depend also on its nature and location.

**Hormonal ED.** Androgen deficiency is a recognized cause for decreased libido and erectile and ejaculatory function. Testosterone regulates the expression of NO synthase and phosphodiesterase-5, and maintains the integrity of vascular smooth muscle and endothelium. Low testosterone is not only associated with ED, but also with cardiovascular morbidity and mortality. Testicular disorders, such as orchitis and cryptorchidism, hypothalamic-pituitary dysfunction, and generalized chronic diseases are common causes of androgen deficiency. Hyperprolactinemia, often due to antimuscarinic drugs, inhibits the release of GnRH and causes hypogonadotropic hypogonadism.
Drug-induced ED. Many medications used to treat systemic illnesses can lead to ED, including antipsychotic, anti-depressant, and antihypertensive drugs. Risperidone, olanzapine, and serotonin reuptake inhibitors have the highest probability of causing sexual dysfunction. Thiazides, spironolactone, and beta-blockers can also cause ED.30

Lifestyle factors and systemic disorders. Smoking contributes to ED both indirectly though its atherogenic effects and endothelial injury, and directly through the effects on cavernosal smooth muscle. While a small amount of alcohol intake improves libido and erection, larger amounts of alcohol trigger central sedation and transient ED, and chronic alcoholism can cause hypogonadism and penile neuropathy.31 In addition, diabetes mellitus, chronic kidney, liver, and pulmonary disease, as well as a sedentary lifestyle and sleep disorders may cause ED.30

COMMON RISK FACTORS IN ED AND CVD

The prevalence of cardiovascular risk factors is significantly higher in men with erectile dysfunction at all ages, while the lack of physical activity has been identified as a powerful independent risk factor for erectile dysfunction.32–34 The crude prevalence of erectile dysfunction was over 50% among men with diabetes.35 The risk factors of ED include advanced age, hypertension, dyslipidemia, metabolic syndrome, cardiovascular disease, central neuropathologic conditions, psychological factors, diabetes mellitus (DM), radical prostatectomy and the use of certain medications prescribed for the treatment of depression and hypogonadism.36

Onder et al. observed a positive correlation between ED severity and coronary artery calcium (CAC) levels. A retrospective study shows that early perfusion of acute ST elevation myocardial infarction (STEMI) can preserve erectile function and percutaneous coronary intervention (PPCI) is superior to thrombolytic treatment (TT) for reducing the prevalence of ED after STEMI.37

DOES ERECTILE DYSFUNCTION PRECEDE CAD?

Montorsi et al. proposed the artery-size hypothesis, as a common pathophysiologic mechanism is the endothelial dysfunction and flow-limiting stenosis linking ED and CAD.38,39 Larger vessels tolerate better the same amount of endothelial dysfunction and/or atherosclerotic burden. A significant proportion of patients with angiographically documented CAD have ED and this condition may become evident prior to angina symptoms in almost 70% of cases.39 The Princeton III consensus panel defines cardiovascular risk in patients with ED as the risk of cardiovascular morbid events in a 3- to 5-year interval from the onset of ED (American College of Cardiology Foundation/American Heart Association [ACCF/AHA class Ib]).38–40 Erectile dysfunction commonly occurs in the presence of silent CAD,38,41–43 in a time period of 2 to 5 years between the onset of ED and CAD event [ACCF/AHA class Ia].38,39,41,43 ED is far more predictive of CAD in men 40 to 49 years of age than in older men,46 and the incidence of atherosclerotic cardiovascular events in younger men has been proved to be 7 times higher in the general male population in Western Australia.47 The more severe forms of ED have been associated with a significantly greater risk of major cardiovascular events,48 CAD, extent of CAD14,28,42,44 and risk of PAD (ACCF/AHA class Ia).49 The correct treatment of ED will not affect negatively the status of cardiovascular health.30

SEXUAL ACTIVITY AND CV RISK

STRATIFICATION (Princeton III Consensus recommendations)48

Low-risk Patients

The low-risk group is represented by patients for whom sexual activity is not associated with a significant cardiovascular risk (Table 1).

TABLE 1. Princeton Guidelines

<table>
<thead>
<tr>
<th>High risk</th>
<th>Low risk</th>
<th>Intermediate risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>unstable or refractory angina pectoris</td>
<td>controlled hypertension</td>
<td>mild or moderate stable angina pectoris</td>
</tr>
<tr>
<td>uncontrolled hypertension</td>
<td>mild valvular disease</td>
<td>past MI (2-8 wks)</td>
</tr>
<tr>
<td>CHF (NYHA class IV)</td>
<td>recent MI without intervention (&lt;2 weeks)</td>
<td></td>
</tr>
<tr>
<td>high-risk arrhythmia (ventricular tachycardia, implanted cardioverter defibrillator, atrial fibrillation)</td>
<td>post succesful revascularization</td>
<td></td>
</tr>
<tr>
<td>moderate to severe valve diseases, particularly aortic stenosis</td>
<td>(coronary artery by pass, stenting, angioplasty)</td>
<td></td>
</tr>
<tr>
<td>obstructive hypertrophic cardiomyopathy</td>
<td>without ischemia on recent exercise testing</td>
<td></td>
</tr>
</tbody>
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Intermediate-risk Patients

Intermediate risk patients will be classified, according to the results of paraclinical investigations, into the low-risk or high-risk class. When the patient cannot complete a standard cycloergometric test, chemical stress tests (nuclear imaging associated with dipyridamole or adenosine) are appropriate.

High-risk Patients

High-risk patients are patients in whom the cardiac condition is severe or unstable enough to be associated with a significant risk in case of sexual activity.

CONCLUSION

ED has common risk factors with CVD, however this is an independent marker of increased risk for CVD and a marker of significantly increased risk for CVD, CAD, stroke, and all-cause mortality. It is necessary to evaluate erectile function in all men with questionnaires (IIEF-15, IIEF-5) to prevent and decrease the rates of major cardiovascular events in urological, cardiological or primary care practice. The early detection of ED can prevent major cardiovascular events with early management of cardiovascular risk, and permits to include patients in a risk stratification group both for ED and CVD.

CONFLICT OF INTEREST

Nothing to declare.

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