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CASE STUDY

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Cardiovascular Risk Assessment and Treatment Modality in Erectile Dysfunction

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Abstract

Erectile dysfunction (ED) is an important public health problem due to cardiovascular diseases (CVD), which is very common and associated with aging in men. The fact that the risk factors of CVD and ED are similar and the mechanisms in their pathophysiology are similar explains the coexistence of these two diseases. In this review, we aimed to evaluate cardiovascular risk assessment for ED patients to have a healthy sexual intercourse.

Keywords: Cardiovascular disease, Erectile dysfunction

1 | INTRODUCTION

Erectile dysfunction (ED) is defined as the inability to achieve or maintain an erection at a level that can provide repetitive or continuous sexual intercourse (1). ED is an important health problem that negatively affects the sexual life, psychosocial life, and general quality of life in men. Its prevalence in the general population is variable and has been reported to be between 20-50% (2,3). The relationship between ED and cardiovascular diseases (CVD) has been known for a long time, and this has been demonstrated in many studies (4-6). The presence of similar risk factors in the etiology of both diseases and the similar pathophysiological mechanisms explain this association (7-9). These common risk factors include hypertension, diabetes mellitus, sedentary life, hyperlipidemia, smoking, obesity and metabolic syndrome. About 40% of men diagnosed with ED have hypertension, 42% have hyperlipidemia, and 20% have diabetes mellitus (10). The common pathophysiological basis for ED and CVD are endothelial dysfunction, increased oxidative stress, inflammation, and atherosclerosis. A normal arterial flow is necessary for a healthy erectile function. The mean diameter of the penile arteries that supply blood to the corpus cavernosum

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is 1.5 -2 times less than the mean diameter of the coronary arteries. These differences in artery size may explain why ED symptoms appear many years before coronary artery disease symptomsPenile arterial blood flow is impaired earlier than coronary blood flow in male patients with atherosclerosis. Vascular atherosclerotic infiltration harms erectile function.

2 | DISCUSSION

Aging is an independent risk factor for the development of ED. This is why many men think that sexual dysfunction is an inevitable consequence of aging. Therefore, they hesitate to apply for a professional health service. Social factors also have a place based on this shyness. However, it should not be forgotten that ED is not only a condition related to aging but it should be kept in mind that it may be a reflection of important underlying diseases. For this reason, a physician should perform a thorough health screening to rule out other causes before assuming that incipient erectile dysfunction is merely the result of advancing age.

Studies have shown that the degree of severity of erectile dysfunction experienced by a patient may be associated with cardiovascular disease risk, with erectile dysfunction beginning 3-5 years before a cardiovascular event (11). The presence of ED may therefore provide an opportunity to reduce CVD risk in men with unrecognized CVD and clinically silent CAD plaque burden. The Princeton Consensus Conference in 2012 identified ED as an important independent risk factor for CVD (12). However, the answer to the question of whether ED is a precursor to CVD or whether the underlying CVD first appears as ED remains unclear. The available data come from cross-sectional studies linking ED symptoms and overt CVD, or from very limited prospective cohort studies linking ED incidence or severity to case CV events. Half of the men with sudden CVD events have no previous symptoms of CAD, and between 70% and 90 % of sudden cardiac events occur in men (13). ED may be the only warning of the risk of these sudden CVD events. The severity of ED was associated with the burden of atherosclerotic coronary disease, and the presence of ED was independently associated with CVD events (14).

An exercise capacity of at least 3 to 6 METs is required in men to achieve normal sexual activity (15). Therefore, patients should undergo a cardiovascular evaluation to avoid cardiovascular events such as angina, myocardial infarction, or cardiac death during sexual performance. Patients with ED are divided into three groups when assessing cardiovascular risk. These are low-risk, intermediate-risk and high-risk patient groups (Table 1).

Table 1 : Risk group classification of CVD patients

Low CVD risk patient	Intermediate CVD risk patient	High CVD risk patient
Presence of <3 risk factors for CAD	Presence of =3 risk factors for CAD (excluding age)	Patient describing CCS III or IV angina pectoris
Patient describing CCS I stable angina pectoris	Presence of CCS II stable angina	Presence of acute coronary syndrome
Uncomplicated previous myocardial infarction (>6 weeks)	Myocardial infarction two to six weeks ago	Uncontrolled hypertension (SBP >180 mmHg)
Presence of CHF with class I dyspnea according to NYHA	Presence of CHF with class II dyspnea according to NYHA	Presence of CHF with class III or IV dyspnea according to NYHA
After successful percutaneous coronary artery revascularization		Recent myocardial infarction (<14 days)
Presence of controlled hypertension		Presence of risky arrhythmia
		Presence of moderate and severe heart valve disease

CAD: coronary artery disease, CCS: Canadian Cardiovascular Society, CHF: Congestive Heart Failure, CVD: Cardiovascular dısease, NHYA: New York Heart Association, SBP: Systolic blood pressure

There is no situation requiring restriction of sexual performance in the patient group with a low risk of CVD disease. There is no need for additional cardiovascular testing before sexual activity recommendations or treatment for erectile dysfunction for low-risk patients.

Cardiac evaluation should be performed before sexual activity or erectile dysfunction treatment recommendations for patients included in the intermediate-risk group in the cardiovascular risk classification. In these patients, a treadmill exercise test can be recommended to investigate the presence of coronary ischemia after electrocardiographic and echocardiographic evaluation. Sexual activity restriction is not required for patients with an effort capacity of 6 METs and above without ischemia findings in the

exercise treadmill test. Myocardial perfusion scintigraphy may be recommended for coronary ischemia investigation in patients who are unsuitable for exercise test as a result of the electrocardiographic evaluation (presence of left bundle branch block, preexcitation, left ventricular hypertrophy, presence of a digital effect, presence of ST-T change at baseline) or who cannot exert effort due to orthopedic problems. Patients with no evidence of coronary ischemia in these tests are considered low risk, and sexual activity restriction is not required. Patients with signs of ischemia in cardiological tests are considered high-risk.

High-risk patients have severe and unstable cardiac disease. In this group of patients, sexual activity may worsen existing cardiac disease and lead to adverse cardiovascular events. Therefore, it is recommended to postpone sexual activity and ED treatment in this patient group.

Another important cardiovascular issue in the treatment of erectile dysfunction is the use of phosphodiesterase 5 (PDE5) inhibitors. PDE5 inhibitors increase the concentration of cGMP in the tissue by preventing cyclic guanosine monophosphate (cGMP) degradation in penile erectile tissue. Increasing cGMP reduces the amount of intracellular calcium and provides penile erection by relaxing penile cavernosal smooth muscle cells (16). Many PDE5 inhibitors are available for medical use worldwide. All PDE5 inhibitors are metabolized in the liver. Sildenafil and vardenafil have a shorter half-life, while those of tadalafil and udenafil are longer.

Although PDE5 inhibitors do not have a direct adverse effect on the cardiovascular system, caution should be exercised when using them because of their potential to cause fatal drug interactions and hypotension. In healthy young men, all the aforementioned PDE5 inhibitors reduce mean systolic and diastolic blood pressure by 9 and 7 mmHg, respectively. In Tadalafil, this decrease is less, with decreases of 1.6 and 0.8 mmHg, respectively. . Orthostatic hypotension may occur, especially in case of simultaneous use with other antihypertensives. To prevent this, treatment with a low-dose PDE5 inhibitor should be started. If they need to be used together, care should be taken to ensure that there is at least a 6-hour difference between antihypertensive drugs and PDE5 inhibitor intake.

Current guidelines recommend starting PDE5 inhibitors in those with a blood pressure of 90/60 mmHg and above.

Another issue to be considered with PDE5 inhibitors is a drug interaction. As it is known, PDE5 inhibitors cause peripheral vasodilation via cGMP, and thus blood pressure decrease in varying degrees. Concomitant use of nitrate-derived drugs (such as isosorbide mononitrate, isosorbide dinitrate, nitroglycerin) that use the same pathway with PDE5 inhibitors may result in fatal hypotension. Nitrate-derived drugs are frequently used in cardiology practice for the relief of anginal complaints and the treatment of heart failure. Therefore, it should be questioned whether there is a nitrate-derived drug among the drugs used by the patient who will be started on a PDE5 inhibitor. . If the need to use nitrate-derived drugs arises in a patient using PDE5 inhibitor, it is necessary to wait following the guideline recommendations. This period is 24 hours after sildenafil and vardenafil use, while it is 48 hours for tadalafil, which has a longer half-life (17, 18). In patients receiving nitrate therapy, nitrate should be discontinued for PDE5 inhibitor use, and other antianginal agents (such as ivabradine, trimetazidine, and ranolazine) can be started instead of nitrates. In these patients, however, it is recommended to wait at least 24-48 hours before starting a PDE5 inhibitor to avoid possible interference (19).

Vardenafil, unlike other PDE5 inhibitors, can cause mild QT interval prolongation on electrocardiography. Therefore, it should not be used in patients with congenital long QT syndrome. In addition, it should not be used together with antiarrhythmic drugs such as quinidine, procainamide, amiodarone and sotalol that prolong the QT interval.

3 | CONCLUSION

In conclusion, erectile dysfunction is closely associated with the presence of cardiovascular risk factors. Cardiovascular evaluation should be recommended before sexual activity and erectile dysfunction treatment in these patients. In high-risk patients, sexual activity and ED treatment should be delayed. FDE5

inhibitors are often used in the treatment of ED. However, their possible hypotensive effects should not be ignored, and caution should be exercised in the case of antihypertensive use. In addition, it should never be used with nitrate-derived drugs used in the treatment of coronary artery disease due to its potential to cause fatal drug interactions.

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