



Erectile dysfunction in the elderly male

Yaşlanan erkekte erektil disfonksiyon

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ABSTRACT

Erectile dysfunction (ED) is a health problem which mainly effects elderly men and this problem has become a more important health problem with the increased life expectancy. The basic risk factors of ED are hypertension, dyslipidemia, diabetes mellitus, and atherosclerotic heart disease which also have a higher incidence in the elderly men. The aim of this review article is to highlight the age- related changes in ED together with recommendations for patient evaluation and treatment

Keywords: Atherosclerosis; diabetes mellitus; erectile dysfunction; hypogonadism.

ÖZ

Erektil disfonksiyon (ED) özellikle yaşlanan erkekleri ilgilendiren bir sağlık problemidir ve artan yaşam beklentisi ile daha da önemli bir sağlık problem haline gelmektedir. ED için temel risk faktörleri olan hipertansiyon, dislipidemi, diabetes mellitus ve aterosklerotik kalp hastalığı aynı zamanda yaşlanan popülasyonda da daha sık görülmektedir. Bu derlemede ED’de yaşa bağlı meydana gelen değişiklikleri vurgulamak ve hasta değerlendirmesi ve tedavisi için bazı önerilerde bulunmak amaçlanmıştır.

Anahtar Kelimeler: Ateroskleroz; diabetes mellitus; erektil disfonksiyon; hipogonadizm.

Introduction

Inability to maintain a penile erection for successful sexual intercourse permanently is defined as erectile dysfunction (ED). ED mainly effects elderly men and this problem has become a more important health problem with the increased life expectancy.^[1-3] According to the Massachusetts Male Aging Study, aging increases the risk of ED from 1.2% per year for men aged between 40-49 years to 4.6% for men aged between 60 - 69 years.^[4]

The common risk factors of ED, ie. hypertension, dyslipidemia, diabetes mellitus, and atherosclerotic heart disease, also have a higher incidence in the elderly men. Besides vascular, neuroendocrine, and pelvic surgery- related causes of ED, these conditions also have a role in increased incidence of ED in the elderly population. Therefore, aging is one of the most

important risk factors for ED. The aim of this review article is to highlight the age- related changes in erectile function with special emphasis on the erectile physiology and other clinical entities that are associated with aging process and ED.

Testosterone deficiency in the aging male

Testosterone deficiency in association with decreased testicular function is commonly seen in the elderly men.^[5,6] Significant reduction in the number and volume of Leydig cells has been shown at histological studies in aging men. Testosterone levels in the aged population of 50-70 years of age were shown to be lower compared to men of 20-40 years of age in about 50% of the cases.^[7]

Although the direct cause and effect relationship between testosterone deficiency and severity of ED has not been shown, a decrease in testoster-

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one level in patients with erectile dysfunction has been observed in a study with 4 years of follow up.^[8] Although we clearly know that testosterone is needed to maintain erectile functions, testosterone level was shown to correlate with normal libido and nocturnal erections but not with presence of ED. Additionally, testosterone replacement therapy was shown to be effective only in case of testosterone deficiency without being efficient in men with normal testosterone levels. Effect of testosterone deficiency on the penile ultrastructure and morphology is another important factor to be considered. Androgens were shown to play a pivotal role in maintaining the function of the peripheral penile nerve network, the structural integrity of the corpora cavernosa, the tunica albuginea, and the endothelium of the cavernous spaces.^[9]

Vascular and penile morphological alterations in the aging male

Proper vascular endothelial functioning is crucial for maintenance of erections. Therefore, any vascular alteration related to aging process has the potential to cause endothelial damage and effect the erectile functions. Organic causes are the underlying pathology in about 80% of the ED cases and vascular insufficiency is the most common type among organic causes.^[10] Risk factors for endothelial dysfunction such as hypertension, diabetes mellitus, atherosclerosis, and hyperlipidemia are observed more commonly in the aging male and therefore increase the risk of ED in this population as well.^[10]

Relaxation of the smooth muscle cells located in the corpus cavernosum and the small arteries is essential for erection and vascular endothelial dysfunction has the potential to disrupt this process. Atherosclerotic occlusion of the cavernosal arteries and impaired release of nitric oxide due to endothelial dysfunction is the underlying pathogenesis of ED.^[10] Testosterone deficiency in the elderly male also contributes to the vascular endothelial dysfunction. As a peripheral mechanism testosterone was shown to have a role in the production of nitric oxide by the vascular endothelium.^[11] In a study conducted with castrated rats, testosterone replacement was shown to be effective in compensating reduced nitric oxide synthase activity and therefore testosterone aids in vasodilation of the penis.^[12] Endothelial cell activation is one of the key events in the process of atherosclerosis. This occurs mainly due to the oxidation of low density lipoproteins.^[13] This process can take place earlier in the smaller arteries, like the cavernosal arteries, before being effective in larger ones, like coronary arteries. Therefore, ED can manifest as the first sign of systemic atherosclerosis.^[14]

Normal erectile function also depends on the venous system and corporal venous occlusion is one of the key steps in this process. Corporal venous occlusion occurs through relaxation of trabecular smooth muscle cells and return of the blood is prevented by compression of the venules with tunica albuginea.^[15] Testosterone was shown to have a role in mediating the alpha adrenergic activity in vascular smooth cells and therefore it maintains re-

laxation of the corporal veins.^[16] Decrease in testosterone activity also results in increased fibrosis in the corpus cavernosum and decreases vascular tissue and nitric oxide activity in the cavernosal arteries further diminishes.^[17]

Risk factors for ED in the elderly men

Metabolic syndrome is observed more commonly in the aging male and it is associated with ED through induction of hormonal changes and inflammatory effects.^[18] The diagnosis of metabolic syndrome depends on at least three of the following five components: 1) central obesity, 2) hypertension, 3) increased fasting glucose levels, 4) elevated triglycerides, and 5) reduced high-density lipoprotein cholesterol levels.^[18] Lifestyle modifications, testosterone replacement and pharmacotherapy are the essentials of management of metabolic syndrome-related ED in the elderly male.

Hypertension

Hypertension is another condition associated with ED and it is observed more commonly in the elderly population. The RhoA-ROCK pathway contributes to the ED physiopathology and it is associated with decreased relaxation of the corporal vessels and increased level of collagen accumulation and fibrosis.^[19] Hypertension is also associated with endothelial dysfunction, atherosclerosis and therefore further contributes to the development of ED. Besides medications prescribed for hypertension such as first generation beta-blockers and thiazide diuretics can have detrimental effects on erectile functions as well.^[20]

Diabetes mellitus

Type 2 diabetes mellitus is also more commonly seen in the elderly population. Diabetes was shown to interfere with the erectile functions and patients with diabetes have an earlier onset of ED more severely.^[21,22] Hyperglycemia provokes production of reactive oxygen species and these interfere with erectile physiology. Vascular and neuronal changes together with endothelial dysfunction further contribute to the development and severity of the ED in the diabetic males. Another important problem is the resistance of diabetes-associated ED to oral phosphodiesterase type 5 inhibitor treatment.^[23]

Smoking and tobacco

Cumulative effects of smoking can also show up in the elderly and a commonly observed consequence is severe ED.^[24] Smoking was shown to alter penile neuronal NOS expression, endothelial integrity, and smooth muscle content within the corporal tissue.^[25] Testosterone levels may also be effected in addition to vascular alterations as well.^[26] Cessation of smoking may help in restoring erectile functions. Nocturnal penile tumescence test results were shown to improve following 24 hours of cessation of smoking.^[27] In a prospective study, smokers were shown to have a higher risk of ED compared to men who have never smoked.^[28]

Hyperlipidemia

Hyperlipidemia, which is also a component of the metabolic syndrome is also observed commonly in the elderly male. Hyperlipidemia causes endothelial dysfunction and inflammation. Statins are the primary treatment of hyperlipidemia and were shown to have protective effects on endothelium and can improve erectile functions.^[29] Although, effects of statins on erectile functions are still under debate, a recent meta-analysis reported an increase in the IIEF score of patients under statin treatment.^[30] Statin treatment was also shown to increase the response to sildenafil as well.^[31]

Depression and physical activity

Besides the organic causes, there are other issues associated with ED in the elderly males. Depression is an important risk factor for ED. Elderly men have the propensity to develop depression and may be more importantly this group of men can be effected severely from the effects of medications such as selective serotonin reuptake inhibitors on erectile functions.^[32] Physical activity is commonly diminished in the elderly males. In the The Massachusetts Male Aging Study, physical activity was shown to be associated with decreased level of ED.^[33] In a study by Esposito et al. with life style modification, erectile function scores improved compared to the control group.^[34] In a recent meta-analysis physical activity was shown to have protective effects on erectile functions.^[35]

ED and coronary artery disease in the elderly male

Endothelial dysfunction leads to decreased blood flow and this is the main underlying mechanism for both ED and coronary artery disease.^[36,37] The above- mentioned risk factors for ED, i.e. hypertension, diabetes mellitus, smoking, hyperlipidemia and lack of physical activity, also have effect on the development of coronary artery disease.^[38] In an evidence- based consensus report, Jackson et al.^[38] focused on the association of ED and coronary artery disease and mentioned that coronary artery disease and cardiovascular events develop after 2-3 and 3-5 years after the onset of ED respectively. Moreover, the increased all-cause mortality rates in ED patients is mainly linked to the association of coronary artery disease.^[39]

Jackson et al.^[38] also suggested that all elderly men with diagnosis of ED should undergo a medical evaluation and risk stratification for future cardiovascular events. Further management of the two conditions should be based on the risk group. While treating ED the clinician should keep in mind the cardiovascular status of the patient and exercise tolerance should be established before treatment of ED as sexual activity have the potential to trigger cardiac events.^[40]

Treatment of ED in the elderly patient

The first step in the management of an elderly patient with ED should be modification of his lifestyle. Changes in dietary habits, cessation of smoking, regular physical exercise, and reduc-

tion of body weight should be offered to the patients. These advices, though debatable, also have a potential to exert benefit on the cardiovascular health status as well.^[41]

Medical management of ED mainly relies on the use of phosphodiesterase type 5 inhibitors (PDE5Is) for over a decade and these drugs are also commonly prescribed for the elderly patients. The use of these drugs has been shown to be safe in patients with cardiovascular diseases, with the sole definitive contraindication in patients under nitrate treatment.^[42] The PDE5Is have also been shown to have a potentially protective effect on the cardiovascular system as well. In a systemic review of studies on the association of ED with cardiovascular diseases, PDE5i drugs have been shown to diminish the risk of future cardiac events in diabetic patients.^[43] Therefore, the clinicians should not avoid prescription of PDE5i for ED in the elderly population, unless the patient is under nitrate treatment or has a high risk of cardiovascular disease that needs restriction of physical activity.

In case of testosterone deficiency, testosterone replacement therapy should be considered as a treatment option in the elderly male with ED. Testosterone replacement has the potential to have an effect on insulin resistance and therefore serum glucose levels together with lipid profile.^[44] Testosterone replacement to normalize testosterone levels was shown to diminish the risk of myocardial infarction and stroke.^[45] On the other hand, there are studies reporting increased rate of vascular events due to increased red cell production and hematocrit levels with testosterone replacement and a recent systemic review on this topic showed no obvious effect of testosterone replacement on the cardiovascular mortality rates.^[46]

Another important point that should be kept in mind with testosterone replacement is the alterations in prostate histology. The androgen dependency of prostate cancer reminds the risk of prostate cancer development with testosterone replacement therapy. However, it was shown that androgen receptors are already saturated and exogenous addition of testosterone does not provoke development of adenocarcinoma of prostate.^[47] Under the light of these data, we suggest use of testosterone replacement in symptomatic hypogonadal elderly men with ED.

ED in the elderly population should be treated carefully and treatment should be individualized. We suggest a careful history taking involving the partner and physical examination prior to any treatment. As the next step the risk stratification for cardiovascular disease should be prompted. In case of a high risk status the patient should be directed to a cardiologist with restriction of sexual activity to restore the stable cardiac condition. The low risk patients should undergo evaluation for comorbid conditions including hypogonadism, hypertension, diabetes mellitus, smoking, hyperlipidemia, and depression. Recommendations about modification of lifestyle should be the first step of treatment. In case of hypogonadism, testosterone replacement

should be offered. The mainstay of the medical treatment should be PDE5i unless the patient is under nitrate treatment. Further treatment options of intra-cavernosal injection, vacuum erection device and penile prosthesis surgery should also be considered in case of failed medical treatment. A flowchart summarizing these recommendations is provided in Figure 1.

In conclusion, ED is a common health problem in the elderly men and effects the quality of life of both the patients and their partners adversely. Most of the risk factors for ED inevitably appear by aging and even aging process itself is a risk factor for the development of ED. Endothelial dysfunction, penile morphological alterations, and testosterone deficiency are the key mechanisms associated with development of ED in the elderly men and these mechanisms are also interrelated. Besides, ED can be the sentinel complaint of a life-threatening condition, and atherosclerosis as well and the patients should be questioned carefully as for the presence of a systemic disorder. This condition should be evaluated as a systemic disease, and Proper life-style recommendations together with medical and/or surgical management should be offered to this population.

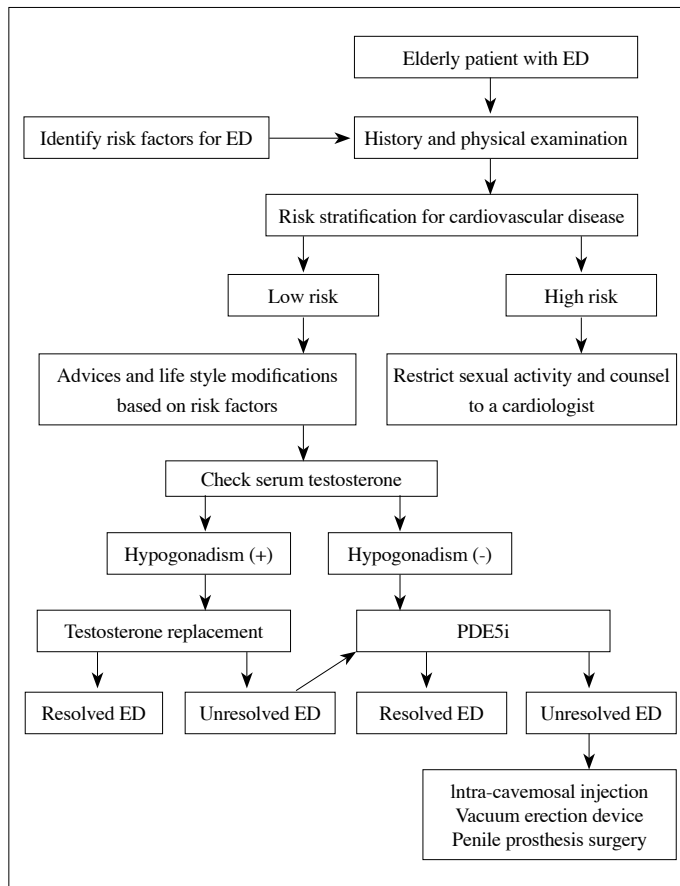


Figure 1. Recommendations for evaluation and treatment of erectile dysfunction in the elderly male
ED: erectile dysfunction

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