Erectile Dysfunction and Coronary Artery Disease: Two manifestations, one same underlying mechanism

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Abstract

Erectile dysfunction (ED) is a common disorder whose prevalence increases with age. Over time a strong correlation between erectile dysfunction and cardiovascular disease has been established as the result of the same pathophysiological process: endothelial dysfunction and atherosclerosis. Because small vessels of the penis can be affected by atherosclerotic plaque earlier than coronary arteries, carotids or femoral arteries, men often have symptoms of ED long before the signs of cardiovascular disease appear. For this reason, ED can act as a marker of early atherosclerosis that predicts the onset of cardiovascular disease at a later time.

Erectile dysfunction (ED) is defined as the inability to achieve and/or sustain an adequate erection to complete a sexual relationship; it may be accompanied by decreased libido and abnormal ejaculation [1]. It is a common disorder and its prevalence increases with age, being more frequent in elderly men. It affects 5-10% of those over 40’s and 40-70% of those over 70’s; it is estimated that there are about 150 million affected men worldwide and that by 2025 it will affect more than 300 million [2-5].

Over time many studies have shown a correlation between ED and cardiovascular risk; both entities share many risk factors such as age, type 2 diabetes mellitus (DM2), hypertension (HT), dyslipidemia, smoking, obesity and sedentary lifestyle [6-9]. Therefore, it is believed that ED and coronary artery disease (CAD) are clinical manifestations of the same pathophysiological process, product of a severe endothelial dysfunction [10-12]. In the study conducted by Demirkol S et al., it was found that erectile function was significantly decreased in patients who presented both microvascular angina (syndrome X) and CAD, thus they conclude that ED and syndrome X are manifestations of a common vascular phenomenon that includes endothelial dysfunction as the mechanism underlying both conditions [4].

The pathophysiology of microvascular angina has not been clearly elucidated, although several abnormalities have been proposed including: alteration in coronary flow reserve, insulin resistance, abnormal autonomic control and microvascular spasm; all these, also associated with endothelial dysfunction, which is another traditional risk factor for cardiovascular disease and occurs before the development of apparent functional or structural systemic vascular disease [6,12]. It is characterized by a decrease in the bioavailability of endogenous nitric oxide (NO) and increase in plasma levels of endothelin-1, promoting in turn an increase in oxidative stress and vasoconstrictor mediators such as angiotensin II, causing generalized damage in the vascular endothelium, being the arteries of the penis more susceptible due to their size and therefore affected earlier1. In this way, both the loss in bioavailability of NO and endothelial dysfunction are phenomena that occur in the earliest stages of atherosclerosis and are also associated with traditional risk factors of cardiovascular disease [13].

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Because small vessels in the penis can be affected by atherosclerotic plaque earlier than coronary arteries, carotids, and femoral arteries, men often have symptoms of ED long before signs of cardiovascular disease appear [12]. The hypothesis of the size of the artery has been proposed to establish this association, probably because the large vessels have the capacity to tolerate the same atherosclerotic load better than the smaller arteries; this explains why the CAD is not clinically manifest in the initial stages of DE. The atherosclerotic load significantly alters circulation in the small arteries of the penis, which may represent an occlusion of 30-40% in vessels of a larger caliber such as the coronary, carotid and/or femoral arteries [5,7]. Thus, ED represents not only an early marker of coronary disease but also of peripheral or cerebral vascular disease, since this dysfunction is carried out in multiple vessels. Consequently, ED can act as a marker of early atherosclerosis, predicting the onset of cardiovascular disease at a later time [1,6].

Several studies support the hypothesis that ED is a silent marker of cardiovascular disease [5,11]. These patients have a known high risk of cardiovascular events. It is estimated that the ED independently predicts the symptoms of CAD in 2-3 years and the appearance of established ischemic events in 3-5 years [7,14].

The predictive value of ED for CAD is higher in young men (40-49 years) compared with the older ones (≥70 years). The prevalence of risk factors for CAD in men with ED was 50 times higher in younger men and 5 times higher in older men, compared with individuals without ED. This predictive value is also high in diabetic men [7,15].

Chronic inflammation and circulation of inflammatory markers affect systemic endothelial function. ED and its severity have been associated with an increase in the expression of markers such as C-reactive protein (CRP), IL-6, IL-10, IL-1B, intercellular adhesion molecule 1 and tumor necrosis factor alpha (TNF-α). Likewise, endothelial and prothrombotic factors such as Von Willebrand factor, tissue plasminogen activator (TPA), plasminogen activator inhibitor 1 (PAI-1) and fibrinogen have been found at high levels in patients with ED [14-16]. Therefore, chronic inflammation may represent an important relationship between ED and cardiovascular disease [5].

High levels of total cholesterol, low density lipoprotein (LDL) and triglycerides as well as low levels of high density lipoprotein (HDL) are associated with an increased risk of developing ED and correlate with its severity. It has also been shown to be associated with smoking, both active and passive, since smoking induces endothelial dysfunction, inflammation, oxidative stress with generation of reactive oxygen species and decreased NO production; therefore suspending tobacco is one of the strategies in the multimodal therapy of ED. Other related factors have been hypertension, obesity, metabolic syndrome and DM2 [2,16].

It is estimated that 38-42% of men with ED have hypertension and that about 35% of patients with hypertension have ED. ED can predict the morbidity and mortality due to cardiovascular disease in patients with DM2, since these may present a silent disease, therefore the early identification of risk factors can be beneficial in terms of prevention. It is estimated that approximately 35-75% of men with DM2 have ED and that they tend to develop the disease 5-10 years earlier than those without DM2 [2,16].

The factors that contribute to the development of ED in patients with DM2 are related to hyperglycemia, which causes alterations in the relaxation of the corpora cavernosa and glycation of the elastic fibers; decreased release of NO, resulting in defective vasodilation; diabetic neuropathy, hypogonadotropic hypogonadism; presence of advanced glycation end products, causing an increase in reactive oxidant substances; dyslipidemia; decreased arterial and arteriolar flow due to peripheral vascular disease and the adverse effects of medications such as thiazide diuretics; beta-blockers, with exception of nebivolol; insulin, statins among others that can affect erectile function; calcium channel blockers and angiotensine converting enzyme inhibitors may have a neutral effect [2,7,8].
Impaired fasting glucose has been associated with the prevalence and severity of ED. Individuals with glycosylated hemoglobin between 5.7-6.4% are also more likely to develop DE. Chronic kidney disease grade 3-5 has also been recognized as a coronary equivalent and has been related with the presence and severity of it [6-8]. Likewise, it increases the risk of developing ED, which can reach a prevalence of up to 80% or even more in patients on hemodialysis [1].

In a study conducted by Canat L et al., it was shown that erectile function after an acute myocardial infarction was significantly lower in patients with 2-3 vessel disease than in patients with only one affected vessel. It was also observed that the glomerular filtration rate was affected in the presence of ED in patients with single-vessel involvement [1].

Patients with ED should be carefully monitored in terms of prevention, early diagnosis and treatment of cardiovascular risk factors. Changes in lifestyle should be promoted aimed at a healthier diet, physical activity, weight reduction and smoking cessation; strategies that contribute to the reduction of morbidity and mortality due to cardiovascular causes [4,7]. The Third Princeton Consensus Conference recommends cardiac risk stratification in patients with ED [17]. A cost analysis carried out by Pastuszak AW et al., showed that cardiovascular screening in patients with ED can be a cost-effective secondary prevention strategy for cardiovascular disease [18].

Conclusion

Since ED is related to endothelial dysfunction, it is considered an early marker of cardiovascular disease that can predict the development of coronary artery disease at a later time and correlates with its severity. Identifying and treating cardiovascular risk factors in these patients would be reasonable for preventing the development of this and others atherosclerotic vascular outcomes.

References

1. Canat L, Canat M, Guner B, Gurbuz C, Caşkurlu T. Association between renal function, erectile function and coronary artery disease: detection with coronary angiography. Korean J Urol. 2015; 56: 76-81. Ref.: https://goo.gl/cDh9rR
2. Menezes A, Artham S, Lavie CJ, Milani RV, O’Keefe J. Erectile dysfunction and cardiovascular disease. Postgrad Med. 2011; 123: 7-16. Ref.: https://goo.gl/EKyVq
3. Gandaglia G, Briganti A, Jackson G, Klener RA, Montorsi F, et al. A Systematic Review of the Association between Erectile Dysfunction and Cardiovascular Disease. European Urology. 2014; 65: 968-978. Ref.: https://goo.gl/AUEj3f
4. Demirkol S, Balta S, Kucuk U, Celik T, Arslan Z, et al. Association between microvascular angina and erectile dysfunction. Int J Impot Res. 2014; 26: 124-127. Ref.: https://goo.gl/hNPHXP
5. Sanchez E, Pastuszak AW, Khera M. Erectile dysfunction, metabolic syndrome, and cardiovascular risks: facts and controversies. Transl Androl Urol. 2017; 6: 28-36. Ref.: https://goo.gl/u9JX3Y
6. Raheem OA, Su JJ, Wilson JR, Hsieh TC. The Association of Erectile Dysfunction and Cardiovascular Disease: A Systematic Critical Review. Am J Mens Health. 2017; 11: 552-563. Ref.: https://goo.gl/DfAPng
7. Katsiki N, Wierzbicki AS, Mikhailidis DP. Erectile dysfunction and coronary heart disease. Curr Opin Cardiol. 2015; 30: 416-421. Ref.: https://goo.gl/xsyUgm
8. Braftett BH, Wessells H, Sarma AV. Urogenital Autonomic Dysfunction in Diabetes. Curr Diab Rep. 2016; 16: 119. Ref.: https://goo.gl/SbbKxzZ
9. Brock G. Diagnosing erectile dysfunction could save your patient’s life. Can Urol Assoc J. 2014; 8: 151-152. Ref.: https://goo.gl/CYS0Bx
10. Tian GX, Liu XP, Zeng XT, Su XJ, Wei WL, et al. Bibliometric analysis on relations between cardiovascular disease and erectile dysfunction. Zhonghua Liu Xing Bing Xue Za Zhi. 2017; 38: 810-813. Ref.: https://goo.gl/B6kFd7
11. Hackett G. The Graham Jackson Memorial Lecture ISSM 2016—“The Man Who Knew Too Much”: Time to Recognize Erectile Dysfunction and Low Testosterone as Independent Risk Factors for Cardiovascular Disease. Sex Med Rev. 2017; 5: 256-265. Ref.: https://goo.gl/u8ByZp

12. Canat L, Cicek G, Atis G, Gurbuz C, Caskurlu T. Is there a relationship between severity of coronary artery disease and severity of erectile dysfunction? Int Braz J Urol. 2013; 39: 465-473. Ref.: https://goo.gl/8Tt1R5

13. Lerman A, Zeiher AM. Endothelial function: cardiac events. Circulation. 2005; 111: 363-368. Ref.: https://goo.gl/FKAj4P

14. Montorsi P, Ravagnani PM, Galli S, Rotatori F, Veglia F, et al. Association between erectile dysfunction and coronary artery disease. Role of coronary clinical presentation and extent of coronary vessels involvement: the COBRA trial. Eur Heart J. 2006; 27: 2632-2639. Ref.: https://goo.gl/SXrCkk

15. Kumar J, Bhatia T, Kapoor A, Ranjan P, Srivastava A, et al. Erectile dysfunction precedes and is associated with severity of coronary artery disease among Asian Indians. J Sex Med. 2013; 10: 1372-1379. Ref.: https://goo.gl/ximYXk

16. Osondu CU, Vo B, Oni ET, Blaha MJ, Veledar E, et al. The relationship of erectile dysfunction and subclinical cardiovascular disease: A systematic review and meta-analysis. Vasc Med. 2017. Ref.: https://goo.gl/FbxggL

17. Nehra A, Jackson G, Miner M, Billups KL, Burnett AL, et al. The Princeton III Consensus recommendations for the management of erectile dysfunction and cardiovascular disease. Mayo Clin Proc. 2012; 87: 766-778. Ref.: https://goo.gl/dMtk7v

18. Pastuszak AW, Hyman DA, Yadav N, Godoy G, Lipshultz LI, et al. Erectile dysfunction as a marker for cardiovascular disease diagnosis and intervention: cost analysis. J Sex Med. 2015; 12: 975-984. Ref.: https://goo.gl/pFKUTX