

Erectile dysfunction: Cardiology at the epicenter

Michael Doumas *, Kostas Stavropoulos, Kostas Imprialos, Chrysoula Boutari

Aristotle University, Thessaloniki, Greece

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Introduction

Erectile dysfunction (ED) is the most common sexual problem among men. It is defined as the persistent inability to attain and/or maintain penile erection sufficient for successful sexual intercourse [1]. The normal erection requires the involvement and coordination of psychological, neurological, hormonal, vascular, and cavernosal factors. Traditionally, ED was considered of psychological origin and was managed by psychiatrists and psychologists. Then, the contribution of urological disorders was widely recognized and urologists came along. During the last two decades however, advances in the understanding of physiology and pathophysiology of erection combined with the revolutionary introduction of phosphodiesterase-5 (PDE-5) inhibitors for the management of ED rendered cardiologists at the epicenter of sexual health. Several reasons dictate the inquiry of erectile dysfunction in patients with cardiovascular problems, including the increased prevalence,

the impact on life quality and adherence to drug therapy, the effects of cardiovascular drugs on erectile function and the interactions with PDE-5 inhibitors, the unique opportunity to identify asymptomatic coronary artery disease, and the necessity to provide appropriate sexual counseling.

Prevalence

Erectile dysfunction is currently considered of vascular origin in the vast majority of patients. Atherosclerotic lesions in the penile arteries limit the blood supply to the penile tissue, while endothelial dysfunction and subclinical inflammation are associated with reduced nitric oxide bioavailability [2]. These structural and functional alterations are usually observed in patients with coronary artery disease as well as in patients with cardiovascular (CV) risk factors, such as arterial hypertension, diabetes mellitus, dyslipidemia, obesity and smoking. Therefore, the pathophysiological resemblance between ED and cardiovascular disease (CVD) provides the basis for an increased prevalence of ED in patients with CVD. Indeed, ED occurs in 15-20% of the general adult population [3], while its prevalence in patients with heart disease is significantly higher. In

* Correspondence to: Prof. Michael DOUMAS
49, Konstantinoupoleos street
54643 Thessaloniki, Greece
e-mail: michalisdoumas@yahoo.co.uk

particular, patients with acute coronary artery disease (CAD) or heart failure usually suffer from ED, with prevalence rates between 50% and 90% [4].

Likewise, ED is frequently encountered in patients with traditional CV risk factors. Several lines of evidence demonstrate that hypertensive patients have a 2-fold increased prevalence of ED compared to normotensive subjects. Furthermore, ED tends to be more severe in hypertensive patients and is affected by the severity and duration of hypertension [5]. Similarly, ED is 3-fold more prevalent in diabetic patients, tends to be more severe, and resistant to therapy compared to non-diabetic patients [6]. The association between dyslipidemia, obesity and smoking with ED seems somehow weaker; however it is evident and further exacerbates erectile function when these conditions coexist with coronary artery disease, hypertension or diabetes mellitus [7-9].

Adherence to therapy - Quality of life

Poor adherence to drug therapy represents one of the main problems in the CV field. Accumulating evidence indicates that almost half of hypertensive patients discontinue antihypertensive drugs within 5 years. Poor adherence to antihypertensive medications is multifactorial, with drug side effects being among the main contributors, especially because hypertension is usually an asymptomatic disease. ED greatly affects the quality of life of affected patients and their sexual partners and is currently considered the “prima ballerina” of impaired life quality in hypertensive patients [10]. Patients who develop ED tend to discontinue antihypertensive medications due to the unbearable impact on life quality. It is therefore of no surprise that the proper management of ED greatly improves adherence to antihypertensive therapy [11].

Another very important and clinically meaningful aspect regards the effects of antihypertensive drugs on erectile function. A wealth of evidence strongly indicates that not all antihypertensive medications affect erectile function in the same way. In fact, some antihypertensive drug categories exert detrimental effects on erectile function, while other categories have neutral or even beneficial effects on erectile function [12]. Centrally acting antihypertensive drugs, diuretics, beta blockers and aldosterone antagonists are associated

with significant deterioration of erectile function and are considered among the most common agents causing ED. Nebivolol is the only beta blocker that does not seem to share the deleterious effects of the whole class on erectile function, possibly due to its unique way of action through enhancing nitric oxide bioavailability [13]. The remaining first choice antihypertensive drugs are either neutral (calcium antagonists, ACE-inhibitors) or potentially beneficial (angiotensin receptor blockers) when it comes to erectile function. Based on the above, patients using drugs respecting erectile function are more likely to adhere to and less likely to withdraw antihypertensive therapy, without compromising their quality of life.

Drug interactions

PDE-5 inhibitors represent the therapeutic cornerstone and are considered as first line agents for the management of ED. Since the introduction of sildenafil in 1999, several other agents are now available (vardenafil, tadalafil, avanafil) with different pharmacokinetic and pharmacodynamic characteristics, thus allowing for tailoring of therapy according to the needs and preferences of affected individuals [14].

PDE-5 inhibitors enhance nitric oxide bioavailability by attenuating its degradation and thus possess vasodilatory properties. The hemodynamic effects of PDE-5 inhibitors are, most of the times, weak and the mean blood pressure reduction is usually small and clinically insignificant. However, clinically significant hypotension might occur in some patients requiring dose reduction or adjustment of concomitant antihypertensive therapy. PDE-5 inhibitors are absolutely contra-indicated in patients on nitrate therapy, since the concomitant administration of these two drugs might result in symptomatic hypotension and fainting. In the case of an acute coronary syndrome or an acute pulmonary edema requiring intravenous nitrate therapy, a time-interval of 6 to 24 hours post PDE-5 inhibitor administration has to be inserted, in order to avoid excessive hypotension and its sequelae. The co-administration of PDE-5 inhibitors and alpha blockers is no longer contra-indicated but requires precautions, including dose adjustments, use of selective alpha blockers and different time dosing. The administration of PDE-5 inhibitors in patients taking every other antihy-

pertensive drug has proven safe, even in patients taking multiple antihypertensive agents [15].

Identification of asymptomatic CAD

Atheromatic lesions in the penile arteries are implicated in the pathogenesis of ED. The diameter of the penile arteries is significantly smaller than the diameter of coronary and carotid arteries; therefore, occlusive symptoms are more likely to develop first in the penis, well before the heart and the brain. Indeed, several lines of evidence, clearly suggests that ED precedes CV events by 3 to 5 years [16]. Accumulating evidence suggests that ED is an independent CV risk factor. A recent meta-analysis revealed that ED is associated with increased risk for myocardial infarction, cerebrovascular events and even all-cause mortality. Moreover, ED is useful in risk classification, permitting for more accurate risk prediction by re-classification of low- and moderate-risk individuals [17]. Therefore, ED offers a unique opportunity to identify asymptomatic CAD. There is no consensus as to who, when and how to screen for asymptomatic CAD. It seems clinically wise however, to guide the inquiry for asymptomatic CAD according to the CV risk of the patient and the probability to identify coronary disease [18].

Sexual counseling

Sexual intercourse is a form of physical exercise and it might be very demanding, depending on the intensity, the type and position, the duration and the in- or extra- relationship nature. As every other form of vigorous exercise, sexual intercourse might be associated with an acute cardiovascular event or sudden cardiac death. Several lines of evidence suggest that the risk of CV events or death during sex is evident but low. However, in patients with overt CV disease or in high-risk patients it seems clinically wise to perform a cardiologic evaluation and a treadmill exercise test before engaging to sexual intercourse [19]. Likewise, sexual counseling is essential in patients after an acute CV event i.e. acute myocardial infarction, unstable angina, acute stroke, angioplasty, and coronary artery by-pass grafting. Such patients need to be carefully evaluated, a stress test needs to be performed and detailed instructions need

to be provided by specialized healthcare personnel (physician or dedicated nurse) as to when to restart sex, the type, the positions and the intensity permitted for the individual patient. Moreover, advice regarding the potential use of PDE-5 inhibitors and relevant precautions should be part of detailed sexual counseling. Unfortunately, sexual counseling is an extremely under-recognized and under-appreciated field and intense efforts are needed to find its place in everyday clinical practice.

The ESH initiative

The European Society of Hypertension is the only Medical Association in the cardiovascular field that acknowledged the significance of ED and made significant steps towards the identification and the appropriate management of ED in hypertensive patients. Lectures regarding sexual dysfunction are incorporated into the program of each annual European meeting during the last decade, for the proper education of physicians managing hypertensive patients. Then, a Working Group was founded specifically addressing the association between arterial hypertension and ED and has up to now been very vivid with many activities. Moreover, a book regarding ED and CVD was published by the members of the Working Group [20]. Finally, a position paper was published at the official journal of the European Society of Hypertension, describing what has been done and what needs to be done [21].

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