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Brief Correspondence

Diagnostic and Therapeutic Implications of Erectile Dysfunction in Patients with Cardiovascular Disease

Giorgio Gandaglia [a,b], *Alberto Briganti* [a,b], *Piero Montorsi* [c], *Alexandre Mottrie* [d], *Andrea Salonia* [a,b], *Francesco Montorsi* [a,b,*]

[a] *Division of Oncology/Unit of Urology, URI, IRCCS Ospedale San Raffaele, Milan, Italy;* [b] *Vita-Salute San Raffaele University, Milan, Italy;* [c] *Department of Clinical Sciences and Community Health, Cardiovascular Section, University of Milan, Centro Cardiologico Monzino, IRCCS, Milan, Italy;* [d] *Olv Vattikuti Robotic Surgery Institute, Melle, Belgium*

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Abstract

Erectile dysfunction (ED) and cardiovascular disease (CVD) share many common pathophysiologic pathways and might be regarded as two different clinical manifestations of the same systemic disease. Consequently, ED and CVD are pathologic conditions that often coexist in the same patient. The urologist plays an important role in the management of ED in patients with a history of cardiovascular events. Therapeutic measures aimed at improving sexual function in CVD patients should be considered only after careful evaluation of the underlying cardiologic condition and assessment of ability to exercise. Sexual activity and treatment of ED might trigger cardiac events in selected patients with preexisting CVD; therefore, proerectile therapies should be administered only to low-risk patients for whom subsequent risk of cardiac events would not be increased. Conversely, men at high risk of CVD should receive cardiologic reassessment and stabilization before attempting sexual activity and receiving ED treatment. Risk reduction and lifestyle changes, administration of phosphodiesterase type 5 inhibitors, and testosterone replacement therapy, as indicated, might provide benefits not only in terms of improving sexual function but also for reducing the risk of future cardiac events.
Patient summary: Erectile dysfunction (ED) and cardiovascular disease (CVD) share many pathophysiologic mechanisms and often coexist in the same patient. We evaluated the role of the urologist in the management of ED in patients with preexisting CVD and the impact of measures aimed at improving sexual function on the subsequent risk of cardiac events.

* Corresponding author. Division of Oncology/Unit of Urology, URI, IRCCS Ospedale San Raffaele, Vita Salute San Raffaele University, Via Olgettina 60, 20132 Milan, Italy. Tel. +39 0226437286; Fax: +39 0226437298.
E-mail address: montorsi.francesco@hsr.it (F. Montorsi).

The relationship between vasculogenic erectile dysfunction (ED) and cardiovascular disease (CVD) has been investigated extensively in recent years. The presence of shared risk factors and the identification of common pathophysiologic pathways that include inflammation, endothelial dysfunction, and atherosclerosis led to the hypothesis that ED and CVD might represent different manifestations of the same systemic disease [1]. ED typically precedes CVD in up to 70% of cases and should be considered a risk factor for cardiac events [1,2]. Moreover, CVD increases the risk of ED, and 40% of patients with normal sexual activity before experiencing a cardiac event report some form of sexual

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dysfunction during follow-up [3]. This might be related to physiologic factors, side effects of cardiovascular drugs, reduced exercise tolerance, or atherosclerosis progression [3]. The association between ED and CVD in patients with preexisting cardiac conditions is complex and requires the interaction of urologists and cardiologists. We focused on the role of the urologist in the initial diagnostic evaluation of CVD patients presenting with ED and on the possible effect of treatments aimed at improving sexual function on the risk of cardiovascular events.

1. Assessment of patients with cardiovascular disease who present with erectile dysfunction

The Princeton III consensus recommendations comprehensively address the management of ED in the context of CVD [4]. Baseline investigations should include the assessment of ED using validated questionnaires such as the International Index of Erectile Function [1,4]. Because episodic sexual activity might trigger acute cardiac events in selected patients with preexisting CVD [5], exercise assessment represents a critical step in the management of ED in these men. The stress of sexual activity on the heart would correspond to a medium level of physical activity averaging up to 4–5 metabolic equivalents of task (METs). This workload corresponds to walking 1.5 km on the flat in 20 min or climbing two flights of stairs at a brisk pace [6]. The assessment of exercise tolerance is thus a critical step before a patient can be counseled regarding the safety of sexual intercourse and the use of proerectile medications (Fig. 1) [4]. In general, if a cardiac patient can exercise to this level without symptoms, he should be able to have sexual activity without problems. Nevertheless, patients should be further stratified according to their likelihood of CVD events or mortality during or shortly after sexual activity [4].

Low-risk patients can safely perform sexual activity and should receive ED treatment. Men considered at low risk of CVD events are those successfully revascularized, namely, men with asymptomatic controlled hypertension, mild valvular disease, and class I and II heart failure according to the New York Heart Association (NYHA) classification. Sexual activity substantially increases the risk of novel events in high-risk patients due to the severity of the underlying CVD [4,6]. This category includes men with unstable angina, uncontrolled hypertension, NYHA class IV heart failure, myocardial infarction within 2 wk without intervention, high-risk arrhythmia, symptomatic hypertrophic cardiomyopathy, and moderate to severe valve disease. These men should defer sexual activity until the cardiac condition has been stabilized, receive intensive risk-factor correction, and be referred to a cardiologist [4]. Men not included in the low- or high-risk category (eg, men with mild or moderate stable angina, NYHA class III heart failure, or sequelae of atherosclerotic disease) are considered to be at *indeterminate* risk of CVD events [7]. Indeterminate-risk patients should be reassessed using the stress test and, in turn, be reassigned to a low- or high-risk category. The ability to complete 4 min of the standard Bruce treadmill test, up to 4–5 METs, without developing angina or ischemic electrocardiographic changes would help physicians reassign indeterminate-risk patients to a low- or high-risk category [4].

2. Erectile dysfunction treatment and its potential effects on cardiovascular disease risk

The observation that ED and CVD share common risk factors led to the hypothesis that their correction and related lifestyle changes might have a beneficial impact on both conditions. Although dietary patterns, smoking cessation, and physical activity have beneficial effects on lipid profile, blood pressure, and other risk factors [8], the actual impact of lifestyle change on the reduction of cardiovascular events in men at risk is still debated [7]. Nonetheless, recent studies demonstrated that body weight reduction, diet, and physical activity improve erectile function in men with heart failure or a history of ischemic heart disease [9]. Consequently, physicians should counsel their patients regarding the beneficial effects of intensive lifestyle changes on sexual function.

Phosphodiesterase type 5 inhibitors (PDE5-Is) currently represent the most commonly prescribed drugs for ED treatment. These molecules have an excellent safety profile and can be administered to CVD patients except for an absolute contraindication in the simultaneous use of nitrates [4]. In addition to beneficial effects on sexual function, PDE5-Is are also active on systemic circulation, and preclinical studies support a cardioprotective role for these drugs [1]. In particular, the administration of PDE5-Is would reduce infarct size, apoptosis, and cardiac hypertrophy and increase the expression of nitric oxide synthase [1]. When considering clinical data, the administration of PDE5-Is has been shown to reduce the subsequent risk of cardiac events in diabetic patients with asymptomatic coronary artery disease [1]. Moreover, a recent study demonstrated that the acute administration of sildenafil substantially decreases levels of proinflammatory markers, where chronic inflammation might play a major role in the pathogenesis of both ED and CVD [10]. Although this evidence supports a cardioprotective effect of PDE5-Is in CVD patients, further prospective studies specifically evaluating this issue in the clinical setting are needed to comprehensively clarify the role of these molecules.

Testosterone replacement therapy (TRT) might represent a therapeutic option for men with low androgen levels. Of note, low testosterone levels are associated with increased risk of cardiovascular mortality, and the degree of testosterone deficiency might correlate with coronary artery disease severity [11]. TRT might have a beneficial effect on CVD risk factors such as insulin resistance, glycemic control, and cholesterol levels in hypogonadal men [12]. In addition, a recent study demonstrated that men who receive therapies aimed at the normalization of androgen levels might be at reduced risk of myocardial infarction and stroke [13]. This therapeutic approach has also been shown to have a beneficial effect on sexual function in hypogonadal men with vasculogenic ED