Management of erectile dysfunction in men with cardiovascular conditions

MICHAEL KIRBY

Abstract

Erectile dysfunction (ED) is reported to coexist with cardiovascular disease. It may be the first clinical manifestation of cardiovascular disease making it a helpful, early marker. Psychogenic causes are also an important component of ED. Around half of all men over the age of 40 years are affected by ED but treatment is often not requested by the patient. ED can be successfully treated pharmacologically. PDE-5 inhibitors are currently the treatment of choice. Physicians should initiate discussion about sexual health and ED in the diagnosed cardiovascular patient.

Key words: erectile dysfunction, cardiovascular risk, PDE-5 inhibitors.

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Michael Kirby

ED: an under-recognised problem

Around half of all men over the age of 40 years are affected by erectile dysfunction (ED)[1] with worldwide prevalence estimated to be as high as 322 million by 2025.[2] While this distressing condition has been shown to have a significant negative impact on quality of life measures,[2] only a small proportion of sufferers currently seek help due to the social stigma attached to the illness.[1]

ED and cardiovascular disease

ED is reported to coexist with cardiovascular disease[3] (including hypertension,[3] recent myocardial infarction (MI),[4] atherosclerosis,[4] hyperlipidaemia,[5] peripheral vascular disease,[3] angina[6] and stroke[3]) at an estimated prevalence of 39–64%.[3]

The critical association between ED and cardiovascular disease lies with endothelial cells.[5] Cavernosal endothelial cells have been shown to contribute to proerectile nitric oxide (NO) production *in vivo*.[7] NO is critical to normal erectile function as it stimulates the formation of cyclic guanosine monophosphate (cGMP), which, in turn, brings about relaxation of smooth muscle.[8] A recent study has suggested that an abnormality in the systemic NO-cGMP vasodilator system may result in ED as the first clinical manifestation of cardiovascular disease.[9] This may occur prior to the development of other demonstrable vascular disease. ED may therefore be a helpful, early marker, being suggestive of oxidative stress, which could eventually progress to atherosclerosis and ischaemic vascular events.[9]

Patients who have a primarily organic cause of ED invariably have a psychogenic component as well. For example, in men who have had an MI or cardiac bypass surgery, the fear that sexual activity may precipitate an MI may contribute to their ED.[5] In addition to organic or psychogenic causes, patients may be taking drugs to treat their condition, some of which are known to cause erection problems (see table 1).[5]

In addition to this correlation, a three-way, holistic, mutually reinforcing relationship between depressive symptoms, cardiovascular disease and ED has been postulated.[8] This theory is based on the repeated observation that these conditions share many of the same risk factors and aetiological associations.[10] Since up to 90% of men with severe depression suffer moderate to complete erectile dysfunction,[11] one important consequence of this model is that patients presenting with any of these three conditions should be routinely evaluated for the other two.[10]

Do men with cardiovascular conditions wish to resume a sex life?

Both patients and their partners may be worried about resuming sexual activity when they know their cardiovascular system is

The Hertfordshire Primary Care Research Network, The Surgery, Nevells Road, Letchworth, Herts, SG6 4TS.
Michael Kirby, Director of Hertnet
Correspondence to: Dr M Kirby
(email: kirbym@globalnet.co.uk)

Table 1. Drugs linked to erectile dysfunction[5]

- Thiazide diuretics
- Calcium antagonists
- Centrally acting agents
  - methyldopa
  - clonidine, reserpine
  - ganglion blockers
- Beta blockers
- Digoxin
- Lipid-lowering agents
- Angiotensin-converting enzyme (ACE) inhibitors

Table 2. Licensed therapies for erectile dysfunction*[23]

Oral	
- dopaminergic agonist	apomorphine hydrochloride
- PDE-5 inhibitors	sildenafil citrate†
	tadalafil†
	vardenafil†
Intracavernosal injections	alprostadil
	papaverine
	phenotolamine
Transurethral	alprostadil
Vacuum constriction devices	
Penile implants	

Key: *Concurrent use of PDE-5 inhibitors with nitrates, either episodic or continuous, is contraindicated; †The majority of ED treatments are also contraindicated in patients for whom sexual activity is inadvisable

compromised in some way. These worries, combined with embarrassment, mean men are often reluctant to request treatment for ED.

It is important to realise that many men with ED do wish to be treated and, furthermore, want their doctor to initiate a discussion on the topic.[12] Sensitive, routine questioning about sexual functioning by a GP or nurse is an important part of the holistic assessment of all men with cardiovascular conditions. With limited time available, the first few questions concerning sexual problems are pivotal in putting patients at ease. One suggested introductory question is: "It is quite common for men with cardiovascular disease to experience problems getting or keeping an erection. Is this a problem you have experienced? If so, are you bothered by it and would you like to do something about it?"[5]

Cardiac risk and sexual activity in men with cardiovascular disease

All currently licensed ED treatments are suitable for managing ED in the cardiovascular patient, provided physicians adhere to the manufacturer's instructions. The advantages and disadvantages of any chosen treatment option are the same for the cardiovascular patient as for any other, and the treatments do not increase the overall cardiovascular risk in patients with diagnosed cardiovascular disease providing they are used correctly. There are two exceptions:

- Patients on warfarin may experience an increase in bruising using injection therapy and urethral bleeding with intraurethral alprostadil; haematomas can occur using a vacuum device.
- For those patients taking nitrate therapy, or nitric oxide donors, all the PDE-5 inhibitors are contraindicated and apomorphine is cautioned.

Sexual intercourse is no more stressful to the heart than many other normal daily activities. The multi-centre Investigation of Limitation of Infarct Size Study found that less than 50% of patients reported a triggering activity for their MI.[13]

It is inevitable that some cardiac events occur simply coincidentally following the commencement of ED therapy, particularly in an age group at risk of ischaemic heart disease. The most extensive published data reviewing efficacy and safety of ED treatments in the cardiovascular patients relate to sildenafil.[14] A comprehensive review confirmed that there is no evidence to support sildenafil as a cause of serious cardiac events. In addition to this, the first phase of prescription event monitoring of cardiovascular events in 5,600 sildenafil users concluded there was no evidence of a higher incidence of fatal MI or ischaemic heart disease among men who take sildenafil.[15] Further studies have also been reassuring – there is no evidence of adverse events in men with severe coronary heart disease[16] and sildenafil is well tolerated and does not change the onset, extent or severity of ischaemia in men with known coronary artery disease.[17,18]

The overall safety database for tadalafil includes more than 4,000 participants from over 60 clinical studies, including more than 1,000 subjects in clinical pharmacology studies and more than 2,700 patients in phase 2, phase 3 and open-label studies. An analysis of all these studies revealed only six reports of MI in tadalafil patients. This was an incidence rate of 0.39 per 100 patient-years in tadalafil-treated patients compared with 1.1 per 100 patient-years in patients who received placebo. The incidence rate of MI in tadalafil-treated patients was lower than the rate reported for a similar age-standardised British male population (0.6 per 100 patient-years). None of the six reported deaths were considered by the investigator as related to tadalafil treatment. Based on the number of patients who received tadalafil and the total number of patients/exposure (1,539.4 total patient-years), the cardiac mortality in tadalafil-treated patients was less than two per 1,000 patient-years. This rate, again, is similar if not lower than the cardiac mortality rates reported in an age standardised general population of British men (2.6 per 1,000 patient-years).[19]

The cardiovascular safety of vardenafil is also reassuring and has been reviewed by Kloner in an analysis of five placebo-controlled trials. The incidence rates of selected cardiovascular adverse events in this review were similar to placebo.[20] Exercise-induced ischaemia has been shown not to be adversely affected

Key messages

- Erectile dysfunction (ED) commonly co-exists with cardiovascular disease[3] although few ED sufferers seek advice[1]
- Treatment of ED in men with cardiovascular disease is likely to have a positive impact on sexual function and lead to a substantial improvement in quality of life[5]
- ED in the diagnosed cardiovascular patient should be identified by routine questioning in general practice[5]

by vardenafil during an exercise stress test in men with known coronary artery disease.[21]

The Princeton and UK consensus panels have both produced specific guidelines for the management of ED in the cardiovascular patient. They incorporate clinically useful methods for the assessment of cardiac risk associated with sexual activity, and for the management of sexual dysfunction among patients with cardiovascular risk factors or cardiac disease. They are now being used widely in the clinical setting and are extremely valuable in managing ED in cardiac patients.[22]

Management options in men with ED and co-morbid cardiovascular disease

Although no peer reviewed papers comparing ED treatments have yet been published, the PDE-5 inhibitors are currently the treatment of choice for erectile dysfunction.[12] All the pharmacological treatments currently licensed for use in men with ED (see table 2) can be used in men with cardiovascular disease according to the manufacturers' instructions. At least seven published consensus statements and practice guidelines make it clear that nearly all cardiovascular patients* (see table 2 footnote) can take sildenafil citrate, which has been proven to be effective and well tolerated in men with cardiovascular conditions.[24,25]

What is the message to men with ED and cardiovascular disease?

In the majority of cases* (see table 2 footnote), men with ED and cardiovascular disease can be reassured that erection problems can be successfully treated.[6,23] These men may need practical advice on issues such as when they can resume sexual activity after a heart attack, or overcoming misconceptions – for example that sex is 'bad for the heart'. Men will also need to have realistic expectations surrounding the resumption of sexual activity. These issues can be dealt with verbally, and may be backed up by leaflets produced by UK support groups, such as The Impotence Association. Physicians should take on board the message that men with erection problems want their doctor to initiate a conversation about sexual health – ED in the diagnosed cardiovascular patient can be easily identified by routine questioning in general practice.[5]

Declared interest

Dr Kirby is an adviser to Pfizer, Lily Icos and GSK.

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