

Erectile dysfunction

Cardiovascular risk factors and erectile dysfunction



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Diabetes and cardiovascular disease remain the commonest causes of erectile dysfunction in middle-aged men, and our understanding of the importance of this link and implications for treatment remains of prime importance in the management of ED.

The paper by Walczak and colleagues further confirms the relevance of cardiovascular risk factors in men with ED. There has been much recent mention of the inadequate achievement of clinical targets. This is not necessarily due to the targets being unrealistic, but could be a result of clinical inertia. Diagnosis with ED may provide insight into patients' vascular health and be an impetus to treat vascular risk factors earlier and more aggressively.

A further updated consensus statement regarding treatment in men with overt coronary artery disease is an important read and well structured and presented by Jackson et al. It employs a particularly useful question and answer format, and contains a helpful discussion

on men who desire treatment for ED but are taking concomitant 'nitrate' drugs. This paper is essential reading for professionals running an ED service, and useful for education and reassurance for those who continue to be concerned about treating ED in the cardiovascular patient. It is also essential reading for healthcare professionals running cardiovascular risk factor clinics, who may not be giving ED the attention it deserves.

There is a lot of new research on the role of phosphodiesterase type 5 inhibitors in cardiovascular disease. The review by Gillies et al summarises the study data on sildenafil and its effects on the cardiovascular system. Sildenafil produces a reduction in pulmonary artery pressure and pulmonary vascular resistance with no untoward effects on the heart and systemic circulation, and could be an ideal agent. It will be interesting to see what the future holds regarding both symptomatic and mortality perspectives.

Finally, Francken and colleagues attempt to answer a much-asked question on penis size. The title is self-explanatory and I leave it to the individual to decide on the validity of the results!

JOURNAL OF GENDER SPECIFIC MEDICINE



Cardiovascular risk factors common in patients with ED

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

- 1 The correlation between erectile dysfunction and risk factors for coronary artery disease is well established.
- 2 This study set out to determine the prevalence of obesity, hyperlipidaemia, diabetes, hypertension and tobacco use in men with erectile dysfunction.
- 3 A total of 154 men who had symptoms of erectile dysfunction for at least 6 months were recruited to the study.
- 4 Participants underwent detailed clinical interviews, blood analyses and physical examinations, including BMI, and were given a questionnaire on sexual function to complete.

5 The most common factor associated with erectile dysfunction was hypertension (blood pressure >140/90 mmHg); this was present in 44% of participants. Abnormal glucose metabolism was the second most common factor (34%). Type 2 diabetes was seen in 22% of men.

6 Tobacco use was reported by 16% of men; 79% of participants had a body mass index >26; and 74% had a low-density lipoprotein cholesterol level >120 mg/dL.

7 Impotence is an important symptom, and its presence should prompt assessment and aggressive management of coexistent risk factors for coronary artery disease. Intervention could restore sexual function and ultimately improve cardiovascular health.

Walczak MK, Lokhandwala N, Hodge MB, Guay AT (2002) Prevalence of cardiovascular risk factors in erectile dysfunction. *Journal of Gender Specific Medicine* 5(6): 19–24

INTERNATIONAL JOURNAL OF CLINICAL PRACTICE



2002 consensus statement for management of ED

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

- 1 The original consensus statement in 1999 provided practical advice on the management of ED, specifically in patients with cardiovascular disease.
- 2 This statement aims to ensure that healthcare professionals have access to current advice, supported by clinical evidence and experience.
- 3 Commonly asked questions about the management of ED in patients with diagnosed cardiovascular disease are reviewed.

4 Men with cardiovascular disease should be routinely and sensitively asked about their erectile function.

5 All currently licensed ED treatments are suitable for managing ED in patients with cardiovascular disease according to the manufacturer's instructions.

6 When ED treatments are used correctly, they do not increase the overall cardiovascular risk in patients with diagnosed cardiovascular disease.

7 There should be regular review of cardiovascular status and ED response.

8 The proactive management of ED in patients with cardiovascular disease provides an ideal and effective opportunity to address other cardiovascular risk factors and improve treatment outcomes.

Jackson G, Betteridge J, Dean J et al (2002) A systematic approach to erectile dysfunction in the cardiovascular system – update 2002. *International Journal of Clinical Practice* 56(9): 663–71

‘Sildenafil has been shown to improve the vasomotor aspect of endothelial dysfunction in patients with heart failure and diabetes.’

INTERNATIONAL JOURNAL OF CARDIOLOGY



Sildenafil appears to have modest vasodilatory activity

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓✓

1 Sildenafil citrate is the first oral phosphodiesterase type 5 inhibitor approved for the treatment of erectile dysfunction.

2 The use of sildenafil for the treatment of erectile dysfunction in patients with cardiovascular disease has led to interest in the cardiovascular properties of the drug.

3 This article reviews studies that have investigated the

cardiovascular safety and functional role of the phosphodiesterase type 5–cyclic guanosine monophosphate–nitric oxide pathway in the cardiovascular system.

4 A reduction in the bioavailability of nitric oxide, which is known as endothelial dysfunction, is associated with many of the common risk factors for cardiovascular disease and erectile dysfunction.

5 Sildenafil has been shown to improve the vasomotor aspect of endothelial dysfunction in patients with heart failure and diabetes.

6 Data from haemodynamic studies suggest that sildenafil is a modest vasodilator with effects on coronary blood flow and coronary flow reserve.

7 Sildenafil has been shown to lower mean arterial and pulmonary pressure in patients with ischaemic heart disease. There was

little effect on heart rate, cardiac output, and systemic or pulmonary vascular resistance after treatment with sildenafil. These properties suggest that sildenafil could be an ideal vasodilator for pulmonary hypertension.

8 The absence of an effect on cardiac output supports the lack of an inotropic effect of sildenafil. Sildenafil has no effect on cyclic adenosine monophosphate levels in the vasculature.

9 The use of phosphodiesterase type 5 inhibitors in cardiovascular conditions needs to be investigated further, particularly as treatment for pulmonary hypertension because of the paucity of therapeutic options for this condition.

Gillies HC, Roblin D, Jackson G (2002) Coronary and systemic hemodynamic effects of sildenafil citrate: from basic science to clinical studies in patients with cardiovascular disease. *International Journal of Cardiology* **86**: 131–41

‘Implantation of a penile prosthesis is a feasible option for almost all men with erectile dysfunction.’

UROLOGIA INTERNATIONALIS



Satisfaction rates for penile prostheses are high

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓✓

1 When treatment with sildenafil citrate for erectile dysfunction is unsuccessful, other treatment options need to be considered. One option is penile prosthesis implantation.

2 This paper reviews the contemporary role of penile prosthesis implantation in the treatment of erectile dysfunction.

3 The results of a MEDLINE search on penile prostheses and implants were reviewed with regard to types of penile implants, issues related to prosthesis implantation, results, and patient/partner satisfaction.

4 Contemporary penile prostheses consist of two types: solid and hydraulic. Hydraulic or fluid-filled implants are often known as inflatable prostheses.

5 Penile prostheses should, ideally, allow the implant recipient to have a penis that resembles as closely as possible normal erect and flaccid states. Three-piece inflatable devices are closest to meeting this ideal.

6 Recipients should be free of bacteriuria and skin infections in the region of the external genitalia. Broad-spectrum antibiotics are often used before the skin incision is made.

7 Many surgeons use regional or general anaesthesia for the procedure.

8 There is a relative lack of reports on solid penile prostheses. In one study, no mechanical failure was reported by 196 men followed up for about 13 months. Overall satisfaction rate was 91% at 2 years.

9 Mechanical failure rates for early penile prostheses were reported for the inflatable type. In one study,

there was a 61% failure rate with 116 devices implanted before 1981. However, improvements in devices and implantation techniques have resulted in a fall in complication rates. Five-year actuarial survival rates free of mechanical failure range from 86.2% to 93.6%.

10 In one review, where patients were followed up for a mean of 42 months, 85% of implant recipients were satisfied and 76% of their partners were also satisfied.

11 Contemporary penile prostheses, especially the three-piece inflatable devices, offer men penile flaccidity and nearly normal erection.

12 Advances in penile prosthesis design include length expanding cylinders and antibiotic-coated devices.

13 Penile prosthesis implantation is a feasible option for almost all men with erectile dysfunction.

Montague DK, Angermeier KW (2003) Contemporary aspects of penile prosthesis implantation. *Urologia Internationalis* **70**: 141–6

‘A considerable percentage of the women respondents – although still a minority – attached substantial importance to the size of the male sexual organ.’



Does penis size really matter?

Readability	✓	✓	✓	✓	✓
Applicability to practice	✓	✓	✓	✓	✓
WOW! factor	✓	✓	✓	✓	✓

- 1 Many men worry about the size of their penis, and associate size with sexual power.
- 2 It is not known exactly how many men apply for surgical lengthening and/or thickening procedures, but it is estimated that 10 000 men in the US underwent such procedures from 1990–97.
- 3 The main reason most men give for wanting an operation is women. But there is little evidence

about how much importance women attribute to penis size.

- 4 The aim of this study was to determine how important penis size is to women from a sexual point of view, and to what extent they think that size is related to sexual function.
- 5 A total of 375 sexually active women who had recently given birth were asked questions about sexual functioning and the importance they attach to the size of their partner's penis.
- 6 Only 170 of the 375 questionnaires were returned. Thirty-four (20%) of women said that penis length was important and 1 (0.6%) said it was very important.
- 7 Ninety-four (55%) and 38 (22%) of the women reported that penis length was unimportant and totally unimportant, respectively.
- 8 Opinions on penis girth were similar, with 52 (31%) of women stating that girth was important.

9 Length was considered less important than girth; 21% and 32%, respectively.

- 10 Correlation analysis did not reveal any significant correlation between sexual functioning and opinions about penis girth.
- 11 A considerable percentage of women respondents – although still a minority – attached substantial importance to the size of the male sexual organ.
- 12 The low response rate to the questionnaire and the fact that the population was highly selected means that these results should be interpreted with caution.
- 13 Further research on the motivation to seek surgical intervention is required.

Francken AB, van de Wiel HBM, van Driel MF, Schultz W (2002) What importance do women attribute to the size of the penis? *European Urology* **42**: 426–31

‘Treatment with tadalafil significantly enhanced erectile function and was well tolerated by men with diabetes and erectile dysfunction.’



Tadalafil enhances erectile function and is well tolerated

Readability	✓	✓	✓	✓
Applicability to practice	✓	✓	✓	✓
WOW! factor	✓	✓	✓	✓

- 1 Erectile dysfunction and diabetes each affect more than 150 million people worldwide, and this value is projected to double by the year 2025.
- 2 The oral phosphodiesterase type 5 inhibitor sildenafil citrate has been shown to be effective and well tolerated in men with diabetes and erectile dysfunction.
- 3 Tadalafil is a potent reversible and selective inhibitor of phosphodiesterase type 5 in development for the treatment of mild to severe erectile dysfunction of psychogenic, organic, or mixed aetiology.

4 This study assessed the efficacy and safety of tadalafil as a treatment for men with diabetes and mild-to-severe erectile dysfunction.

- 5 A total of 216 men with a clinical diagnosis of type 1 or type 2 diabetes and erectile dysfunction were recruited to this multicentre, randomised, double-blind, placebo-controlled, parallel group trial.
- 6 Participants were randomly allocated to placebo (71), 10 mg tadalafil (73), or 20 mg tadalafil (72) for 12 weeks.
- 7 Changes from baseline in mean scores on the erectile function domain of the International Index of Erectile Function (IIEF) were measured. The change from baseline in the proportion of ‘yes’ responses to the questions ‘Were you able to penetrate?’ and ‘Were you able to complete intercourse?’ were also determined.
- 8 After 12 weeks of treatment taken whenever patients anticipated sexual activity, nearly two-thirds (64%) of patients in the 20mg tadalafil group and more than half (56%) of those in

the 10mg tadalafil group reported improved erections.

- 9 Treatment with tadalafil significantly enhanced erectile function, according to IIEF erectile function domain, erection vaginal penetration rates and successful intercourse rates.
- 10 Tadalafil (both 10 mg and 20 mg) improved erectile function irrespective of the type of diabetes, presence of microvascular complications, or type of diabetes treatment.
- 11 Tadalafil treatment did not significantly change HbA_{1c} levels from baseline to endpoint.
- 12 Tadalafil was well tolerated, with headache and dyspepsia being the most frequent adverse events with active treatment.
- 13 Tadalafil significantly enhanced erectile function, and was well tolerated in men with diabetes and erectile dysfunction.

de Tejada IS, Knight JR, Anglin G, Emmick JT (2002) Effects of tadalafil on erectile dysfunction in men with diabetes. *Diabetes Care* **25**: 2159–64

JOURNAL OF AMERICAN COLLEGE OF CARDIOLOGY



Vardenafil does not alter response to exercise testing

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The use of phosphodiesterase-5 (PDE5) inhibitors is increasing as a treatment for erectile dysfunction. But the effects of PDE5 inhibition on exercise-induced ischaemia in patients with coronary artery disease have not been examined in detail.

2 This paper assesses the effects of vardenafil, a potent and highly selective PDE5 inhibitor, on symptom-limited exercise time, time to first awareness of angina, and time to ischaemic threshold during exercise tolerance testing in

patients with stable coronary artery disease.

3 Forty-one men with reproducible stable exertional angina due to ischaemic coronary artery disease were recruited to a double-blind, crossover, single-dose multicentre study.

4 Patients received either 10mg vardenafil or placebo, with an exercise tolerance test 1 hour after the dose. Sublingual nitrate use was prohibited for 24 hours or more on the days before and after the exercise tolerance test.

5 Vardenafil did not significantly alter patients' response to exercise testing and delayed the onset of ST-segment changes relative to placebo in 41 patients with stable coronary artery disease with or without exertional angina pectoris.

6 Physicians should consider the cardiovascular status of their patients as recommended by the ACC/AHA guidelines, when they are considering vardenafil for the treatment of cardiac patients with erectile dysfunction.

Thadani U, Smith W, Nash S et al (2002) The effect of vardenafil, a potent and highly selective phosphodiesterase-5 inhibitor for the treatment of erectile dysfunction, on the cardiovascular response to exercise in patients with coronary artery disease *Journal of the American College of Cardiology* **40**(11): 2006–12

CURRENT UROLOGY REPORTS



Future treatment options for erectile dysfunction

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 This paper describes the different types of treatments available for erectile dysfunction and the rationale for using combination therapy.

2 Penile smooth muscle relaxation and erection are regulated by indirect and direct acting smooth muscle relaxing agents. These agents act by increasing the synthesis of secondary messengers cyclic adenosine monophosphate by smooth muscle.

3 Phosphodiesterase (PDE) inhibitors, such as sildenafil citrate, act indirectly and require sexual stimulation and endogenous nitric oxide production for efficacy through activation of the cyclic guanosine monophosphate pathway.

4 There is a lot of documented evidence on the safety and efficacy of sildenafil. But outcomes determined in general urology practice may not compare with that obtained from clinical trials on healthy volunteers, and subsequently patients with minimal and moderate erectile dysfunction.

5 Combination pharmacotherapy has been used to treat erectile dysfunction in an experimental fashion for 25 years, using combinations of cyclic adenosine phosphate synthesis augmentors, smooth muscle relaxants and PDE inhibitors, and α -blockers injected intracavernosally.

6 In one study, there was a bigger improvement in questionnaire scores for erectile function with combination therapy of oral sildenafil and intraurethral alprostadil than with either therapy alone.

7 In another study, there was a nearly 100% satisfaction rate for treatment with the Medical Urethral System for Erection and sildenafil.

8 A single agent may not be ideal to sustain penile rigidity, especially when comorbidity and severity of erectile dysfunction are taken into account.

9 These studies suggest the potential for a convenient, non-invasive treatment for patients with erectile dysfunction who do not respond to PDE inhibition.

Nehra A and Kulaksizoglu H (2002) Combination therapy for erectile dysfunction: where we are and what's in the future. *Current Urology Reports* **3**: 467–70