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Erectile dysfunction and lower urinary tract symptoms should trigger a metabolic screen and cardiovascular risk estimation

Mike Kirby, MBBS, LRCP, MRCS, FRCP
Visiting Professor, Faculty of Health and Human Sciences, Centre for Research in Primary and Community Care (CRIPACC), University of Hertfordshire, UK; Visiting Professor, The Prostate Centre, London, UK; Editor in Chief, Primary Care Cardiovascular Journal, Warwickshire, UK; Visiting Professor of Primary Care, Institute of Diabetes for Older People (IDOP), Beds and Herts Postgraduate Medical School, Luton, UK

Correspondence: Professor Mike Kirby, The Cottage, 30 Wedon Way, Bygrave, Baldock, Herts, SG7 5DX, United Kingdom
E-mail: kirbym@globalnet.co.uk

Abstract

The UK has made great strides in reducing death from cardiovascular disease (CVD), but there is still room for improvement compared with other Western European Countries. CVD accounts for approximately one-third of all deaths in men and women in the UK. Half of these deaths are related to coronary heart disease (CHD), which is the most common cause of premature death in those under the age of 75 years. Atherosclerotic changes in the coronary arteries eventually lead to CHD, and nine key risk factors have been well recognized. Erectile dysfunction (ED) is an independent risk factor and provides a window of opportunity to identify early CVD. ED and lower urinary tract symptoms (LUTS) share underlying pathophysiological etiological mechanisms and will often drive men to consult. This provides the opportunity to consider what burden of CVD risk factors the patient carries, and to perform an appropriate metabolic screen. ■ *Heart Metab*. 2015;66:27-31

Keywords: cardiovascular disease; erectile dysfunction; lower urinary tract symptoms; metabolic syndrome; lifestyle

The UK has made great strides in reducing death from cardiovascular disease (CVD), but there is still room for improvement compared with other Western European Countries.[1] CVD accounts for approximately one-third of all deaths in men and women in the UK. Half of these deaths are related to coronary heart disease (CHD), which is the most common cause of premature death in those under the age of 75 years.[2]

Atherosclerotic changes in the coronary arteries eventually lead to CHD, and nine key risk factors have been well recognised.[3] In 2001, we raised the question "Is erectile dysfunction a marker for cardiovascular disease?"[4] and recently highlighted the importance of the co-diagnosis of erectile dysfunction (ED) and lower urinary tract symptoms (LUTS).[5]

The link between ED and LUTS was brought home by the multinational survey of the aging male (MSAM)

Abbreviations

CHD: coronary heart disease; **CVD:** cardiovascular disease; **ED:** erectile dysfunction; **LUTS:** lower urinary tract symptoms; **PDE5:** phosphodiesterase type 5; **PSA:** prostate-specific antigen

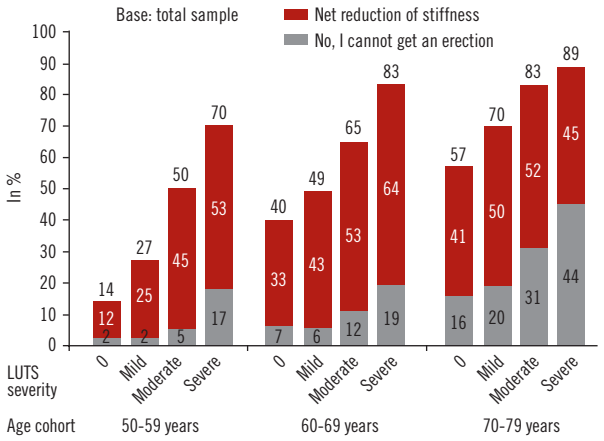

Fig. 1 *Erectile dysfunction according to age and severity of lower urinary tract symptoms (LUTS) using the Danish Prostate Symptom Score Sex (DAN-PSSsex) questionnaire.*
From reference 6: *Rosen R et al.* Eur Urol. *2003;44:637-649. © 2003, Elsevier BV.*

study (*Figure 1*).[6] Many large epidemiological studies using well-powered multivariate analyses consistently provide overwhelming evidence of a link between ED and LUTS.[7,8] The pathogenic mechanisms underlying the relationships between ED and LUTS have been the subject of several recent reviews.[7,9-11] The underlying mechanisms include the alteration of the nitric oxide–cyclic guanosine monophosphate pathway; enhancement of the Rho-kinase (ROCK) signalling; autonomic hyperactivity; and pelvic atherosclerosis, secondary to endothelial dysfunction. Additional contributing factors may include chronic inflammation[12] and sex steroid ratio imbalance.[13]

Two meta-analyses have clearly shown that ED predicts CVD events and all-cause mortality.[14,15] Because ED and LUTS are very common worldwide clinical problems, enquiring about these symptoms in middle-aged men who have no cardiac symptoms provides a window of opportunity to identify those with underlying CVD. This is important, as it has been well demonstrated in two significant studies that ED can precede a cardiac event by between an average of 2 to 5 years.[16,17]

This has also been emphasised in the Princeton III Consensus, showing that ED is a marker of increased CVD risk and the identification of ED may allow the identification of at-risk men who require further cardiovascular evaluation.[18] Therefore, a multidisciplinary collaborative approach is encouraged and the screening net should be cast as widely as possible.

It is important to recognise that ED is an independent marker of increased CVD, over and above the conventional risk factors.[19] It has been well demonstrated in a systematic review and meta-analysis that lifestyle intervention together with cardiovascular risk factor reduction improves erectile function.[20] In addition to this, factors associated with decreased risk of LUTS include increased physical activity, moderate alcohol intake, and increased vegetable consumption,[21] and LUTS can also be improved by means of lifestyle changes.[22,23]

Case history

Initial visit

Background

A 60-year-old scientist and company director attended with some concern regarding perineal discomfort that had been present for two weeks. There had been a past history of prostatitis 15 years previously, but he had been prescribed no treatment for this. He had undertaken a company medical 14 years previously, when it was noted that he had an elevated cholesterol of 6 mmol/L and triglycerides (TG) of 2.61 mmol/L. He was advised to deal with this by means of diet and exercise. He gave a history of ED for the previous 5 years, which had been treated with on-demand Cialis and Viagra, neither of which he had found particularly helpful. His urinary symptoms included frequency, some morning urgency, getting up once at night, and a rather poor flow rate.

On direct questioning, his general health appeared to be good. He had a history of some acid reflux, but no cardiac symptoms. His exercise level was low to moderate, in terms of playing tennis once per week with occasional walks. He was a nonsmoker and consumed 15 to 20 units of alcohol per week. He was not taking any medication. There was a family history of type 2 diabetes in his father and brother. In his personal history, he had experienced pericarditis at the age of 24 and a Bell's palsy in 2009.

Initial clinical examination and investigations

Clinical examination revealed height 181 cm, weight 91 kg, waist circumference 98 cm, and blood pressure 150/92 mm Hg. His heart was normal and all peripheral pulses were present. There were no abdominal bruits and the chest was clear. There were no abnormal swellings in the abdomen. Digital rectal examination revealed a nontender and nodular prostate, which felt to be about 30 g. This was subsequently confirmed to be 31 g on the transrectal ultrasound report (*Table I*). The abdominal ultrasound showed some features suggesting fatty liver infiltration. His urinary investigation findings are summarized in *Table II*.

The electrocardiogram (ECG), renal function, and liver function were normal. His cholesterol profile was: cholesterol 6.6 mmol/L, high-density lipoprotein (HDL) 1.3 mmol/L, low-density lipoprotein (LDL) 4.6mmol/L, TG 1.5 mmol/L. HbA_{1c} 43 mmol/mol (6.1%) and fasting plasma glucose 5.8 mmol/L. Fibrinogen was 4.5 g/L (normal range 1.5 to 4). Testosterone was 17.8 nmol/L, prostate-specific antigen (PSA) 3.09 mcg/L, free PSA 0.52 mcg/L, and free/total PSA ratio 17.8. Occult blood tests were negative

This patient had the features of metabolic syndrome (*Table III*),[24] with an increased waist circumference, raised blood pressure and blood glucose, and dyslipidemia.

Using the Joint British Societies recommendations on the prevention of Cardiovascular Disease (JBS3) risk calculator, his heart age was 74 years. He had a 17% 10-year risk of a cardiovascular event, with a life expectancy of 83 years. The calculator predicted that he would gain 3 extra years of life and his 10-year risk would reduce to 5.3% if his risk factors were suitably adjusted, giving him a life expectancy of 86 years.

At the time the patient was seen, the threshold for intervention with statins was a 20% 10-year risk, but having ED in addition to his current risk factors put this man at high risk of having underlying and future CVD. He was, however, reluctant to take statins due to adverse reports of side effects that he had read in the media.

It was decided that, to further evaluate his potential CVD risk, he would undertake a computed tomography coronary calcium scan, which was duly performed. This showed a total calcium score of 585 (left marginal artery, 0; left anterior descending artery, 319; left circumflex artery, 0; and right coronary artery, 266), putting him in the 80th-centile range for age and gender. There was no abnormality identified in the lungs.

This man therefore had a high burden of coronary artery calcification for his age and an exercise stress echo was performed. On standard Bruce protocol, the patient achieved 89% maximum predicted heart rate (MPHR) and 13.4 metabolic equivalents (METs)

- Prostate measures 31 mL in volume.
- There is periurethral calcification and focal echogenic areas in the central gland, which could be due to previous prostatitis.
- There is very early central benign prostatic hypertrophy change and an early medium lobe enlargement.
- The peripheral zone is relatively uniform in reflectivity.
- The gland vascularity is within normal limits.
- The seminal vesicles are symmetrical and normal in appearance.

Conclusion: There are some areas of prostate that would suggest previous episodes of prostatitis, but no definite current active inflammatory changes seen. The bladder and upper tracts appear normal.

Table I *Transrectal ultrasound results.*

Voided volume	441 mL
Maximum flow rate	14.7 mL/sec
Average flow rate	7.7 mL/sec
Residual urine	190 mL
IPSS	22 (severe symptoms)
IIEF	14 (moderate to severe erectile dysfunction)

Table II *Results of urinary investigations and IPSS/IIEF scores after initial visit.*
Abbreviations: *IIEF, International Index of Erectile Function; IPSS, International Prostate Symptom Score.*

Central obesity	Waist circumference: ≥94 cm for Europid men; ≥80 cm for Europid women; with ethnicity specific values for other groups*
Plus any two of the following:	
Raised blood pressure	Systolic ≥130 or diastolic ≥85 mm Hg, or taking medication for previously diagnosed hypertension
Raised triglyceride level	≥150 mg/dL (1.7 mmol/L) or taking medication for this specific lipid abnormality
Reduced high-density lipoprotein cholesterol	<40 mg/dL (1.03 mmol/L) in men, <50 mg/dL (1.29 mmol/L) in women, or taking medication for this specific lipid abnormality
Raised fasting plasma glucose	≥ 100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes. If >5.6 mmol/L or 100 mg/dL, oral glucose tolerance test is strongly recommended, but is not necessary to define presence of the syndrome

Table III *International Diabetes Federation (IDF) definition of the metabolic syndrome.*
**If body mass index is >30 kg/m², central obesity can be assumed and waist circumference need not be measured.*
Modified from reference 24: *International Diabetes Federation. http://www.idf.org/metabolic-syndrome. © 2006, International Diabetes Federation.*

of workload. He did not have any chest pain and no ischemic ECG changes. Left ventricular wall motion was normal both before and after exercise. He therefore had a negative exercise stress echocardiogram.

Management

He agreed to take statin therapy and was started on atorvastatin 40 mg. He was also recommended a Mediterranean-style diet and provided with a twice-daily exercise programme. Regarding the ED and LUTS, he was started on daily Tadalafil (phosphodiesterase type 5 [PDE5] inhibitor) at a dose of 5 mg.

In summary, this man presented with LUTS, ED, and some perineal discomfort, possibly related to previous prostatitis. Clinical examination and subsequent investigations confirmed that he had the metabolic syndrome and this, combined with a history of ED, gave him a significant risk of having underlying CVD. This was subsequently confirmed on a coronary calcium scan and he was started on statin therapy (atorvastatin 40mg daily), aiming for a reduction of 50% in the lipid profile. He was provided with a diet and exercise programme. He was asked to check his own blood pressure at home.

In addition to the statin therapy, he was prescribed daily Tadalafil 5 mg, which has the benefit of treating both his ED and his LUTS. PSA levels were to be carefully followed up

Three-month review

Repeat clinical examination, investigation, and score results at 3-month review are summarized in *Table IV*.

Parameter	3-month review	*Initial visit*
Weight	85 kg	*91 kg*
Waist circumference	97 cm	*98 cm*
PSA	2.33 mcg/L	*3.09 mcg/L*
HbA_{1c}	6.1% (43 mmol/mol)	*No change*
Cholesterol	3.1 mmol/L	*6.6 mmol/L*
HDL	1.4 mmol/L	*1.3 mmol/L*
LDL	1.3 mmol/L	*4.6 mmol/L*
BP	132/84 mm Hg	*150/92 mm Hg*
IIEF	24	*14*
IPSS	10	*22*
JBS3 heart age	61 years	*74 years*

Table IV *Examination and investigation results at 3-month review compared with initial visit.*
Abbreviations: *BP, blood pressure; HDL, high-density lipoprotein; IIEF, International Index of Erectile Function; IPSS, International Prostate Symptom Score; JBS3, Joint British Societies recommendations on the prevention of Cardiovascular Disease; LDL, low-density lipoprotein; PSA, prostate-specific antigen.*

At this 3-month review, he reported feeling very well, and was eating a Mediterranean-style diet and walking twice daily. Pelvic/perineal discomfort was no longer a problem. He reported walking 10 000 steps per day using a pedometer. He had gained 3.1 life years.

This is a good response to daily PDE5 inhibitor therapy relating to ED and LUTS, with a significantly reduced risk of future CVD as the result of lifestyle changes and statin therapy. ■

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