Erectile dysfunction and the cardiovascular patient: endothelial dysfunction is the common denominator

H Solomon, J W Man, G Jackson

Erectile dysfunction (ED) is a common condition and studies predict that it will become even more common in the future. There is increasing evidence to suggest that it is predominantly a vascular disease and may even be a marker for occult cardiovascular disease. The common pathological process is at the level of the endothelium, and cardiovascular risk factor control may be the key to preventing ED. Many men with established cardiovascular disease have ED. Specific guidelines for the management of ED in these patients have been produced by an expert panel. Cardiovascular risk stratification is an important initial step in managing such patients. In cardiac patients considered to have low cardiovascular risk, the management of ED can be safe and effective.
vascular disorders such as diabetes, hypertension, and hyperlipidaemia tend to be the most common culprits.

**ED AND CARDIOVASCULAR DISEASE**

The MMAS (Massachusetts male aging study), a large population-based random sample, confirmed that ED is highly correlated with vascular diseases such as hypertension, heart disease, and diabetes. Patients who were being treated for hypertension had a 15% probability of complete ED and those who had cardiac disease had a probability of 39%. This probability increased to 20% for hypertensive men who smoked cigarettes and to 56% for cardiac patients who smoked. The association between ED and hypercholesterolaemia has also been documented in a group of healthy men complaining of ED, with over 60% having abnormal cholesterol concentrations and over 90% of these showing evidence of penile arterial disease on Doppler ultrasound testing.

Diabetes has been associated with an increased risk of ED. The prevalence is approximately 50%, with a range of 27.5–59% depending on age and disease severity. Other studies have shown that atherosclerosis is associated with almost 40% of cases of ED in men aged 50 years or more. Recently, Bortolotti and colleagues analysed four studies involving 1476 men with heart disease, myocardial infarction or vascular surgery. They found incidences of ED ranging from 39–64% in each patient group.

ED and vascular disease are thought to be linked at the level of the endothelium. Endothelial dysfunction results in an inability of the smooth muscle cells lining the arterioles to relax, thus preventing vasodilatation. Diabetic men with ED infused with L-arginine were found to have a lower reduction in blood pressure and platelet aggregation response (markers of endothelial function) than that in diabetic men without ED. Hence, the endothelial response was significantly reduced in impotent diabetic men thereby preventing adequate arterial vasodilatation and causing ED. Similar findings have been found in conditions of hypercholesterolaemia. Rabbits were fed a cholesterol enriched diet or normal diet (controls) for three months, after which time cavernous tissue biopsies were taken. Ultramorphological examination of the control group found normal smooth muscle cell architecture. The high cholesterol diet group had significant smooth muscle cell degeneration with loss of intercellular contacts. This study suggests that impaired lipid metabolism causes cavernous smooth muscle cell degeneration and plays a major part in the development of ED.

Insults such as these not only damage the endothelium and hence cause ED but they are also precursors for the development of atherosclerosis and coronary artery disease. Indeed, the presence of vasculogenic ED has been suggested as a risk factor for the presence of occult cardiovascular disease. Pritzker reviewed the results of cardiovascular stress testing, risk profile analysis, and angiography in 50 asymptomatic men with ED of presumed vascular origin aged between 40–60 years. Multiple cardiovascular risk factors were present in 80% and graded exercise testing was electrically positive in 28 of 50 men. Coronary angiography in 20 men found left main stem or severe three vessel disease in six, moderate two vessel disease in seven, and significant single vessel disease in a further seven. In addition, other recent work has suggested that erectile function correlates with the severity of cardiovascular disease. Patients with single vessel ischaemic heart disease had less difficulty obtaining an erection than did patients with two or three vessel ischaemic heart disease.

Pharmacological measures to control these vascular risk factors are also associated with the onset of ED. Many antihypertensive medications (particularly β blockers and thiazide diuretics) have sexual dysfunction as one of their main side effects, which invariably reduces compliance. Statin treatment routinely recommended for cardiovascular disease has been related to worsening erectile function. An association between angiotensin converting enzyme (ACE) inhibitors and
ED has been previously described in a survey of the causes of impotence in 101 men with hypertension, which found a prevalence of 26%. Among those with hypertension, 70% were taking an ACE inhibitor. Furthermore, 12 men in this study identified medication as the cause and over 50% attributed the onset of ED to the ACE inhibitor treatment. The management of ED remains primarily within the domain of urologists, psychologists, and family practitioners. However, the association of ED with vascular disease has led to the need for other medical specialists, including cardiologists, to become involved in the management of ED. In 1999 the Princeton Consensus Panel, an expert panel comprising cardiologists, urologists, pharmacologists, and psychiatrists, evaluated the scientific evidence on sexual activity and its risk in cardiac patients.

**MANAGEMENT OF ED IN PATIENTS WITH CARDIOVASCULAR DISEASE**

The convenience and efficacy of new oral treatments for ED have led to a significant increase in demand for treatment. With the use of these new oral agents has also come a concern about the risks of sexual activity by cardiac patients, so that family practitioners may be reluctant to prescribe these medications to patients considered to be at risk of cardiovascular disease. Thus, the Princeton Consensus Panel produced specific guidelines for the management of ED in the cardiovascular patient.

The rationale of these guidelines lies in the principle that sexual activity poses a small but definite risk of a cardiac event for the patient with cardiac disease during and immediately after sexual activity. A 50 year old healthy man has a baseline annual risk of myocardial infarction of 1%. As a consequence of sexual activity by a healthy man, the risk increases to 1.01% but it increases to 1.1% in a man with previously documented coronary artery disease. In addition, the absolute risk for healthy men to have a cardiac event from normal daily life is one chance in a million. This risk increases to two chances per million following sexual activity and lasts for a two hour period. Hence, a small but definite risk of a cardiac event exists for the patient with a history of cardiovascular disease who is resuming sexual activity.

During sexual intercourse the average maximal heart rate is 120–130 beats/minute with a systolic blood pressure increase to 150–180 mm Hg. This peak lasts for only 3–5 minutes of the average 5–15 minute duration of sexual activity. This equates to 5–6 metabolic equivalents or 4 minutes of the Bruce treadmill protocol (10% grade, 2.7 km/h). To resume sexual activity, patients need to be capable of sustaining this physiological demand without any cardiovascular symptoms. The Princeton guidelines stratify patients into cardiovascular risk groups according to cardiovascular symptoms and physiological reserve (Table 1). The low risk group are those for whom sexual activity is not a significant cardiovascular risk and who meet the requirements of physiological reserve to resume sexual activity. The high risk patient is one in whom cardiovascular symptoms are limiting to the extent that further cardiovascular evaluation and investigation are considered necessary. Sexual activity and the management of ED should be deferred in these patients until the patient’s cardiovascular condition has been fully evaluated, treated, and stabilised. A third group has been identified as being at intermediate risk and these patients must have ED management deferred until further cardiovascular evaluation can reclassify them into either the low or high risk groups.

These guidelines incorporate clinically useful methods for the assessment of cardiac risk associated with sexual activity and for the management of sexual dysfunction among patients with known cardiovascular risk factors or diseases. They are already in use in the clinical setting and are extremely valuable in managing ED in cardiac patients.

**CONCLUSION**

ED is a common condition particularly affecting men with underlying vascular disease. The reluctance of men to discuss this sensitive issue leads to an impaired quality of life. In addition, this reluctance may hinder the opportunity to diagnose occult cardiovascular disease and hence prevent significant morbidity and sometimes mortality. Endothelial dysfunction appears to be the link between these conditions and increasing awareness of this association should encourage men to discuss their ED with medical practitioners.

The Princeton guidelines have addressed the issue of the management of ED in men with established cardiovascular disease. Cardiovascular risk stratification is the mainstay of

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**Table 1 Recommendations for management of erectile dysfunction based on graded cardiovascular risk assessment**

<table>
<thead>
<tr>
<th>Grading of risk</th>
<th>Cardiovascular status on presentation</th>
<th>Management recommendations for the primary care physician</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>Asymptomatic, &lt;3 major risk factors for CAD, excluding age and sex, controlled hypertension, mild stable angina, successful coronary revascularisation, mild valve disease, LVD/CHF (NYHA class I)</td>
<td>Provide primary care management, review treatment options with patient and his partner (where possible)</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>&gt;3 major risk factors for CAD, excluding age and sex, moderate stable angina, recent myocardial infarction or cardiovascular event (≤6 weeks), LVD/CHF (NYHA class II), murmur of unknown cause</td>
<td>Conduct a specialised evaluation (for example, exercise treadmill test for angina, echocardiography for murmur), place patient into high or low risk category, depending on outcome of testing</td>
</tr>
<tr>
<td>High risk</td>
<td>Unstable or refractory angina, uncontrolled hypertension (SBP &gt;180 mm Hg), CHF (NYHA class III, IV), recent myocardial infarction or cardiovascular event (≤2 weeks), high risk arrhythmias, hypertrophic obstructive and other cardiomyopathies, moderate/severe valve disease</td>
<td>Refer for specialised cardiac evaluation and management, defer treatment for erectile dysfunction until cardiac condition stabilised or specialist evaluation completed</td>
</tr>
</tbody>
</table>

Reproduced from Jackson and colleagues with permission. CAD, coronary artery disease; CHF, congestive heart failure; LVD, left ventricular dysfunction; NYHA, New York Heart Association; SBP, systolic blood pressure.
these guidelines and allows the identification of intermediate to high risk patients who may continue to have uncontrolled cardiovascular disease. Cardiovascular disease control must be the priority in these groups over ED management. Low risk patients are also identified and in these patients the management of ED can be safe and effective.

Authors’ affiliations
H Solomon, J W Man, G Jackson, Department of Cardiology, 6th Floor, East Wing, St Thomas’ Hospital, Lambeth Palace Road, London SE1 7EH, UK

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he following electronic only articles are published in conjunction with this issue of Heart.

Takayasu’s arteritis: management of left main stem stenosis
I S Malik, O Harare, A Al-Nahhas, K Beatt, J Mason Takayasu arteritis is a chronic vasculitis involving the aorta and its main branches, the pulmonary arteries, and the coronary tree, and needs to be considered in a young patient with angina, in particular when pulses are absent. This case illustrates the limitations of exercise testing in diagnosing the extent of coronary artery disease and the risks associated with coronary angiography in patients with inflammatory disease in the left main stem coronary artery. It also highlights the novel use of non-invasive scanning with positron emission tomography using 18-fluorodeoxyglucose in assessing remission from this disease. Revascularisation was performed with percutaneous transluminal coronary angioplasty and stenting as an emergency procedure, but treatment of the restenosis with directional atherectomy was based on a review of the available literature. The lymphocytic alveolitis seen in this patient has not been previously described in Takayasu’s disease.

(Art 2003;89:e9) www.heartjnl.com/cgi/content/full/89/3/e9

Artefact mimicking tachycardia during magnetic resonance imaging in a patient with an implantable loop recorder
J R Gimbel, B L Wilkoff An implantable loop recorder (ILR) was implanted in a 45 year old man with recurrent syncope. A subsequent episode of injurious syncope led to performance of a cranial and shoulder magnetic resonance imaging (MRI). An artefact mimicking both wide and narrow complex tachycardias was recorded by the ILR during the shoulder MRI but not the cranial MRI. Caution should be used when interpreting the ECGs of ILRs in patients who have undergone MRI.

(Art 2003;89:e10) www.heartjnl.com/cgi/content/full/89/3/e10

Unexplained recurrent pericardial effusion: a lethal warning?
C H Lee, G S W Chan, W M Chan A case of a 37 year old man with cardiac angiosarcoma causing recurrent pericardial effusion, who eventually died of cardiac rupture, is presented. The diagnosis was not established until the postmortem examination despite echocardiography, pericardiocentesis, and pericardial biopsy investigations. There is neither a specific manifestation that enables early recognition nor well proven effective treatment against this disease. Accordingly, the prognosis of cardiac angiosarcoma remains grave. A high index of suspicion is recommended in patients who present with unexplained pericardial effusion.

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