EAU GUIDELINES ON MALE SEXUAL DYSFUNCTION: Erectile Dysfunction and Premature Ejaculation

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ERECTILE DYSFUNCTION

Introduction

Erectile dysfunction (ED) is defined as the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance. Erectile dysfunction may affect physical and psychosocial health and may have a significant impact on the quality of life (QoL) of sufferers and their partners. There is increasing evidence that ED can also be an early manifestation of coronary artery and peripheral vascular disease; therefore, ED should not be regarded only as a QoL issue, but also as a potential warning sign of cardiovascular disease (CVD).

Table 1: Pathophysiology of erectile dysfunction

Vasculogenic
Recreational habits (e.g. cigarette smoking)
Lack of regular physical exercise
Obesity
Cardiovascular diseases (e.g. hypertension, coronary artery disease; peripheral vasculopathy, etc.)
Type 1 and 2 diabetes mellitus; hyperlipidaemia; metabolic syndrome; hyperhomocysteinemia, etc.
Major pelvic surgery (radical prostatectomy) or radiotherapy (pelvis or retroperitoneum)
Neurogenic
Central causes
Degenerative disorders (e.g., multiple sclerosis, Parkinson's disease, multiple atrophy, etc.)
Spinal cord trauma or diseases
Stroke
Central nervous system tumours
Peripheral causes
Type 1 and 2 diabetes mellitus
Chronic renal failure; chronic liver failure
Polyneuropathy
Surgery (major surgery of pelvis/retroperitoneum) or radiotherapy (pelvis or retroperitoneum)
Surgery of the urethra (urethral stricture, urethroplasty, etc.)
Anatomical or structural
Hypospadias; epispadias; micropenis
Phimosis
Peyronie's disease
Penile cancer (other tumors of the external genitalia)

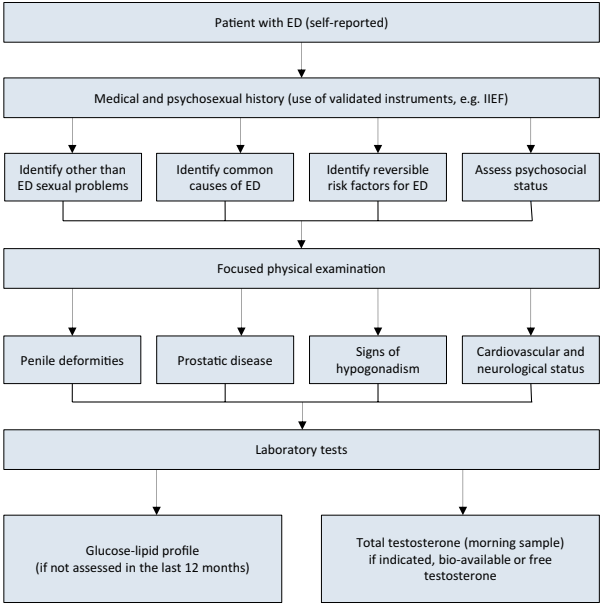
Hormonal
Diabetes Mellitus; Metabolic Syndrome;
Hypogonadism (any type)
Hyperprolactinaemia
Hyper- and hypothyroidism
Hyper- and hypocortisolism (Cushing's disease, etc.)
Panhypopituitarism and multiple endocrine disorders
Mixed pathophysiology pathways
Chronic systemic diseases (e.g., diabetes mellitus; hypertension; metabolic syndrome; chronic renal failure; chronic liver disorders; hyperhomocysteinemia; obstructive sleep apnoea; etc.)
Psoriasis; gouty arthritis; ankylosing spondylitis; non-alcoholic fatty liver; chronic periodontitis; open-angle glaucoma; inflammatory bowel disease
Iatrogenic causes (e.g. transrectal ultrasonography-guided prostate biopsy, etc.)
Drug-induced
Antihypertensives (e.g., thiazide diuretics, beta-blockers, etc.)
Antidepressants (selective serotonin re-uptake inhibitors, tricyclics)
Antipsychotics (e.g., neuroleptics, etc.)
Antiandrogens (GnRH analogues and antagonists; 5-ARIs)
Recreational drugs (e.g., alcohol, heroin, cocaine, marijuana, methadone, synthetic drugs, anabolic steroids, etc.)
Psychogenic
Generalised type (e.g., lack of arousability and disorders of sexual intimacy)
Situational type (e.g., partner-related, performance-related issues or due to distress)

Trauma
Penile fracture
Pelvic fractures

GnRH = Gonadotropin-releasing hormone;
5-ARIs = 5α-Reductase inhibitors

Diagnostic evaluation

Figure 1: Minimal diagnostic evaluation (basic work-up) in patients with erectile dysfunction



ED = erectile dysfunction; IIEF = International Index of Erectile Function.

Table 2: Cardiac risk stratification (based on 2nd Princeton Consensus)

Low-risk category	Intermediate-risk category	High-risk category
Asymptomatic, < 3 risk factors for CAD (excluding sex)	≥ 3 risk factors for CAD (excluding sex)	High-risk arrhythmias
Mild, stable angina (evaluated and/or being treated)	Moderate, stable angina	Unstable or refractory angina
Uncomplicated previous MI	Recent MI (> 2, < 6 weeks)	Recent MI (< 2 weeks)
LVD/CHF (NYHA class I or II)	LVD/CHF (NYHA class III)	LVD/CHF (NYHA class IV)
Post-successful coronary revascularisation	Non-cardiac sequelae of atherosclerotic disease (e.g., stroke, peripheral vascular disease)	Hypertrophic obstructive and other cardiomyopathies
Controlled hypertension		Uncontrolled hypertension
Mild valvular disease		Moderate-to-severe valvular disease

CAD = coronary artery disease; CHF = congestive heart failure; LVD = left ventricular dysfunction; MI = myocardial infarction; NYHA = New York Heart Association.

Table 3: Indications for specific diagnostic tests

Primary ED (not caused by organic disease or psychogenic disorder).
Young patients with a history of pelvic or perineal trauma, who could benefit from potentially curative revascularisation surgery or angioplasty.
Patients with penile deformities which might require surgical correction (e.g., Peyronie's disease, congenital penile curvature).
Patients with complex psychiatric or psychosexual disorders.
Patients with complex endocrine disorders.
Specific tests may be indicated at the request of the patient or his partner.
Medico-legal reasons (e.g., implantation of penile prosthesis to document end stage ED, sexual abuse).

Table 4: Specific diagnostic tests

Nocturnal Penile Tumescence and Rigidity using Rigiscan®.
Vascular studies: - Intracavernous vasoactive drug injection. - Penile Dynamic Duplex Ultrasonography. - Penile Dynamic Infusion Cavernosometry and Cavernosography. - Internal pudendal arteriography.
Neurological studies (e.g., bulbocavernosus reflex latency, nerve conduction studies).
Endocrinological studies.
Specialised psychodiagnostic evaluation.

Recommendations for the diagnosis of erectile dysfunction	Strength rating
Take a comprehensive medical and sexual history in every patient.	Strong
Use a validated questionnaire related to erectile dysfunction to assess all sexual function domains and the effect of a specific treatment modality.	Strong
Include a physical examination in the initial assessment of men with erectile dysfunction (ED) to identify underlying medical conditions and comorbid genital disorders that may be associated with ED.	Strong
Assess routine laboratory tests, including glucose-lipid profile and total testosterone, to identify and treat any reversible risk factors and lifestyle factors that can be modified.	Strong
Include specific diagnostic tests in the initial evaluation only in the presence of the conditions presented in Table 3.	Strong

Figure 2: Management algorithm for erectile dysfunction

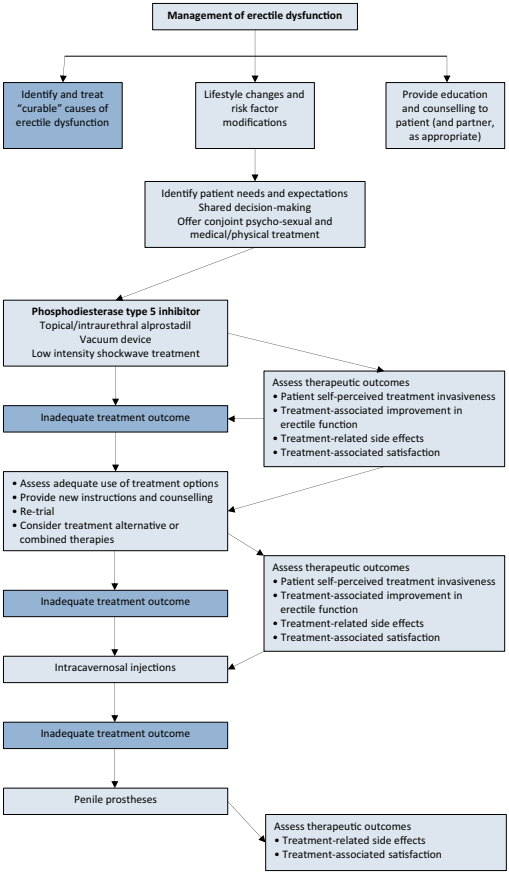


Table 5: Summary of the key pharmacokinetic data for the four PDE5 inhibitors currently EMA-approved to treat erectile dysfunction*

Parameter	Sildenafil, 100 mg	Tadalafil, 20 mg	Vardenafil, 20 mg	Avanafil 200mg
C_{max}	560 µg/L	378 µg/L	18.7 µg/L	5.2 µg/L
T_{max} (median)	0.8-1 hours	2 hours	0.9 hours	0.5-0.75 hours
T1/2	2.6-3.7 hours	17.5 hours	3.9 hours	6-17 hours
AUC	1,685 µg.h/L	8,066 µg.h/L	56.8 µg.h/L	11.6 µg.h/L
Protein binding	96%	94%	94%	99%
Bioavailability	41%	NA	15%	8-10%

** Fasted state, higher recommended dose. Data adapted from EMA statements on product characteristics.*
C_{max}: maximal concentration, T_{max}: time-to-maximum plasma concentration; T1/2: plasma elimination half-time; AUC: area under curve or serum concentration time curve.

Table 6: Common adverse events of the four PDE5 inhibitors currently EMA-approved to treat erectile dysfunction*

Adverse event	Sildenafil	Tadalafil	Vardenafil	Avanafil 200mg
Headache	12.8%	14.5%	16%	9.3%
Flushing	10.4%	4.1%	12%	3.7%
Dyspepsia	4.6%	12.3%	4%	uncommon
Nasal congestion	1.1%	4.3%	10%	1.9%
Dizziness	1.2%	2.3%	2%	0.6%
Abnormal vision	1.9%		< 2%	none
Back pain		6.5%		< 2%
Myalgia		5.7%		< 2%

** Adapted from EMA statements on product characteristics.*

Table 7: Penile prostheses models available on the market

Semi-rigid prostheses	Inflatable prostheses	
	Two-piece	Three piece
Spectra ™ [AMS]	Ambicor™ [AMS]	Titan OTR ™ (One Touch Release) [Coloplast]
Genesis ™ [Mentor]		Titan OTR NB ™ (Narrow base) [Coloplast]
		Titan Zero Degree ™
Tube ™ [Promedon]		AMS 700 CX ™ [Boston Scientific]
ZSI 100 ™ [Zephyr]		AMS 700 LGX ™ [Boston Scientific]
Virilis II ™ [Subrini]		AMS 700 CXR ™ [Boston Scientific]
		ZSI 475 ™ [Zephyr]

Recommendations for the treatment of erectile dysfunction	Strength rating
Enact lifestyle changes and risk factor modification prior to or accompanying erectile dysfunction (ED) treatment.	Strong
Support the resumption of sexual activity through pro-erectile treatments at the earliest opportunity after radical prostatectomy.	Strong
Treat a curable cause of ED first, when found.	Weak
Use phosphodiesterase type 5 inhibitors (PDE5Is) as first-line therapy.	Strong

Assess all patients for inadequate/incorrect information about the mechanism of action and the ways in which drugs should be taken, since they are the main causes of a lack of response to PDE5Is.	Weak
Use vacuum erection devices as a first-line therapy in well-informed older patients with infrequent sexual intercourse and comorbidity requiring non-invasive, drug-free management of ED.	Weak
Use low intensity shockwave therapy in mild organic ED patients or poor responders to PDE5Is.	Weak
Use topical/intraurethral Alprostadil as an alternative to intracavernous injections in patients who prefer a less-invasive therapy.	Weak
Use intracavernous injections as second-line therapy.	Strong
Use implantation of a penile prosthesis as third-line therapy.	Strong

PREMATURE EJACULATION (PE)

Introduction

Although PE is a common male sexual dysfunction, it is poorly understood. Patients are often unwilling to discuss their symptoms and many physicians do not know about effective treatments. As a result, patients may be misdiagnosed or mistreated.

PE (lifelong and acquired) is a male sexual dysfunction characterised by the following:

1. Ejaculation that always or nearly always occurs prior to or within about 1 minute of vaginal penetration (lifelong PE) or

a clinically significant and bothersome reduction in latency time, often to about 3 minutes or less (acquired PE);
2. The inability to delay ejaculation on all or nearly all vaginal penetrations;
3. Negative personal consequences, such as distress, bother, frustration and/or the avoidance of sexual intimacy.

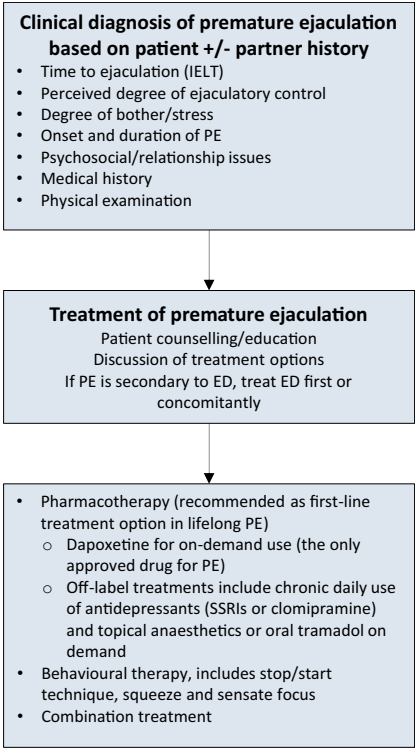
Diagnostic evaluation

Recommendations for the diagnostic evaluation of premature ejaculation	Strength rating
Perform the diagnosis and classification of premature ejaculation (PE) based on medical and sexual history, which should include assessment of intravaginal ejaculatory latency time (IELT) (self-estimated), perceived control, distress and interpersonal difficulty due to the ejaculatory dysfunction.	Strong
Do not use stopwatch-measured IELT in clinical practice.	Weak
Use patient-reported outcomes in daily clinical practice.	Weak
Include physical examination in the initial assessment of PE to identify anatomical, abnormalities that may be associated with PE or other sexual dysfunctions, particularly erectile dysfunction.	Strong
Do not perform routine laboratory or neurophysiological tests. They should only be directed by specific findings from history or physical examination.	Strong

Disease management

Recommendations for the treatment of premature ejaculation	Strength rating
Treat ED, other sexual dysfunction or genitourinary infection (e.g. prostatitis) first.	Strong
Use pharmacotherapy as first-line treatment of lifelong premature ejaculation (PE).	Strong
Use off-label topical anaesthetic agents as a viable alternative to oral treatment with selective serotonin re-uptake inhibitors (SSRIs).	Strong
Use tramadol on demand as a weak alternative to SSRIs.	Strong
Use PDE5Is alone or in combination with other therapies in patients with PE (without ED).	Strong
Use psychological/behavioural therapies in combination with pharmacological treatment in the management of acquired PE.	Weak

Figure 3: Management of premature ejaculation*



** Adapted from Lue et al. 2004.*
ED = erectile dysfunction; PE = premature ejaculation; IELT = intravaginal ejaculatory latency time; SSRI = selective serotonin receptor inhibitor.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-04-2), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.