



12° Congresso Nazionale AME
Associazione Medici Endocrinologi
6th Joint Meeting with AACE American
Association of Clinical Endocrinologists



Bari,
7-10 novembre 2013

MEET THE EXPERT

Il Deficit Erettile

Francesco Romanelli

Dipartimento di Medicina Sperimentale

Sezione di Fisiopatologia Medica,

Endocrinologia e Scienza dell'Alimentazione

Università di Roma "Sapienza"



Una richiesta di aiuto



Buongiorno! Sono il Dott. Romanelli, come posso aiutarla? Mi racconti con calma....



Buongiorno dottore... è un po' difficile parlarne... sono circa due anni che ho difficoltà a letto... capisco che non sono più un ragazzino...in fondo l'erezione c'è... ho un di difficoltà ad averla ma soprattutto a mantenerla... dopo poco PUFF! Sparisce...è un problema serio...

Una richiesta di aiuto



Quindi ha difficoltà a mantenerla? il desiderio c'è? L'eiaculazione è normale? Masturbazione?



Si...non duro, scusi la parola....il desiderio non è piu' come una volta anche se ora sto con una donna giovane...e spesso anche l'eiaculazione viene un po' presto...ma non mi fa male....masturbazione? non ho l'età....insomma un disastro.



Una richiesta di aiuto



*Ha fatto degli esami per questo problema?
Ha già provato dei farmaci?*



*No..non ho fatto nulla...i soliti esami del sangue...sa ho un po' di diabete...
...ho provato un farmaco...mi è sembrato poco "naturale".. pasticcia e via! con quello che costa... l'effetto un po' c'è stato! secondo lei cosa può essere? Lo devo prendere tutta la vita?*



Una richiesta di aiuto



Beh, intanto mi racconti che malattie ha avuto e ha ora, se e quali farmaci prende, qual è la sua situazione familiare, poi la visito e qualora necessario le prescrivo degli accertamenti da fare...ne parliamo insieme



D'accordo dottore, sono nelle sue mani, la ringrazio...non è finita no?



Il Nostro Paziente - I



Bari,
7-10 novembre 2013

- Nome: C. S., di anni 55
- Professione: Idraulico
- Anamnesi Familiare:
 - Negativa per ipertensione
 - Positiva per diabete (nonno) e tireopatia (madre)
- Anamnesi Fisiologica:
 - Abitudine tabagica (circa 10 sigarette/die)
 - Non fa uso di alcolici né di droghe
 - Separato, due figli, attualmente convivente

- Anamnesi Patologica Remota:
 - Varicocelelectomia sinistra a 20 aa
 - Emorroidi
 - Ipercolesterolemia lieve (209)
 - Diabete Mellito (2011)
 - In terapia con Ipoglicemizzante orale (Metformina 2500/die)





Il Nostro Paziente



Bari,
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- **Esame obiettivo:**
 - Lucido, vigile, orientato
 - Altezza 178 cm, peso 84 kg
 - P.A.: 135/85 mmHg, 76 bpm, ritmico
 - Pilifero nella norma, asta nella norma
 - Testicoli di consistenza normale, di volume lievemente ridotto il sinistro, presenza di ectasia del plesso pampiniforme a sinistra con assenza di reflusso al Valsalva

- Al paziente viene somministrato il questionario **IIEF-15** (International Index of Erectile Function)
 - ottenendo il punteggio di **12**

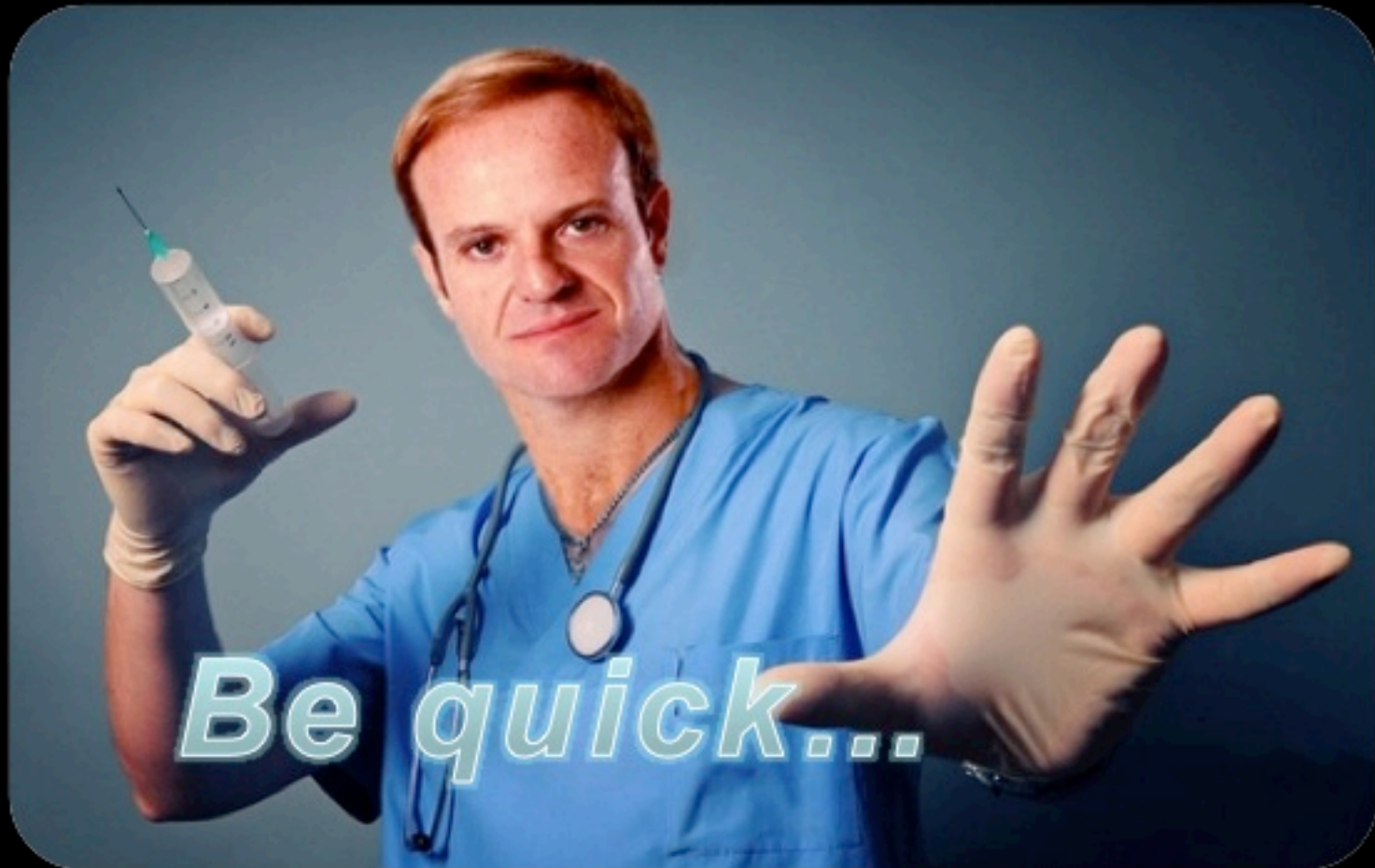
Classificazione della disfunzione erettile

Punteggio (domande da 1 a 5, 15)	Classificazione
1 - 10	Grave
11 - 16	Moderata
17 - 25	Lieve
26 - 30	Assente



Mettersi in gioco - I

- Domanda: che analisi prescrivereste?



INTERVALLO



Quante erezioni ha avuto, in media,
un individuo di sesso maschile
arrivato all'età di 60 anni?

Più di 400000

In media un uomo ha circa 20 erezioni al giorno,
quindi circa 7300 all'anno. A 60 anni avrà avuto
più di 400000 erezioni nel corso della sua vita.

IMPREVISTO!

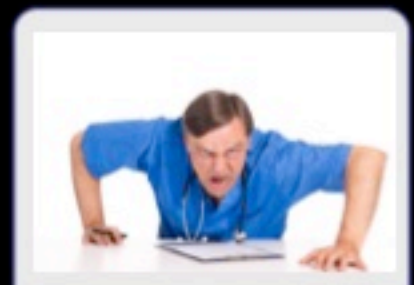


- Il paziente dimentica di prenotare la visita!
- Si presenta in ambulatorio chiedendo un **appuntamento extra!**

LO ACCONTENTATE?



SI



NO





Le analisi del sangue



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- Emocromo [Hb 14,8 gr/dL; Ht 43%]
- PSA 0,947 ng/mL
- HbA1c 6.5% – 48 nmol/mol
- Colesterolo
 - [Totale 194 mg/dL, HDL 52 mg/dL, LDL 124 mg/dL]
- TSH 2,91 mU/L
- Prolattina 12,3 ng/mL
- LH 2,3 U/L
- Testosterone Totale 217 ng/dL



Le analisi del sangue



Bari,
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- Testosterone Totale 226 ng/dL
- SHBG
- Albuminemia
- Testosterone libero
- Testosterone libero calcolato



Ecografia peniena basale e dinamica



Bari,
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ECOCOLORDOPPLER PENIENO DINAMICO

Esame eseguito con apparecchiatura *real-time* con sonda lineare multifrequenza da 10 e 13 MHz.

L'esame ecotomografico ha evidenziato una normale conformazione del pene con aspetto ecograficamente fisiologico delle diverse strutture anatomiche.

I piani di scansione sia longitudinali che trasversali in condizioni di base documentano la normalità morfo-strutturale della fascia di Buck, dei corpi cavernosi e del corpo spongioso uretrale.

Il setto intercavernoso appare di spessore e costituzione normale in tutto il suo decorso.

Le arterie cavernose mostrano normali echi parietali e buona pulsatilità. L'arteria cavernosa destra ha un diametro di mm 1.1 prossimalmente (regione crurale) e di mm 0.8 distalmente (terzo medio); l'arteria cavernosa sinistra mm 1.2 prossimalmente e mm 0.8 distalmente.

FASE DINAMICA

Iniezione intracavernosa di PGE₁ 10 µg (nel corpo cavernoso destro).

Diametro arterie cavernose:

art. cavernosa destra mm 2.3

art. cavernosa sinistra mm 2.3

Normale incremento dei diametri arteriosi con buona pulsatilità.



Ecografia peniena basale e dinamica



Bari,
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Valutazioni flussimetriche:

Arteria cavernosa destra

V.P.S. = 29.8 cm/s

V.T.D. = 10.4 cm/s

I.R. = 0.65

S.R.T. = 108 msec

Arteria cavernosa sinistra

V.P.S. = 30.2 cm/s

V.T.D. = 10.1 cm/s

I.R. = 0.66

S.R.T. = 108 msec



Ecografia peniena basale e dinamica



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Valutazioni flussimetriche:

Arteria cavernosa destra

V.P.S.= 29.8 cm/s

V.T.D.= 10.4 cm/s

I.R.= 0.65

S.R.T.= 108 msec

Arteria cavernosa sinistra

V.P.S.= 30.2 cm/s

V.T.D.= 10.1 cm/s

I.R.= 0.66

S.R.T.= 108 msec

V.P.S.(velocità di picco sistolico) v.n. > 30 cm/s

V.T.D.(velocità telediastolica) v.n. < 5 cm/s

I.R. (indice di resistenza) v.n. 1.0-0.80

S.R.T. (tempo di innalzamento sistolico) v.n. < 110 msec

A.E. (angolo erettile) v.n. > 90°

COMMENTO ALLA FASE DINAMICA

Nella prima fase (fase di tumescenza precoce) si rileva un normale e progressivo aumento sia della componente sistolica della curva spettrale, sia di quella diastolica. Nella seconda fase (fase di tumescenza tardiva) si evidenziano normali valori di V.P.S. con lieve persistenza e mancato azzeramento dell'onda diastolica delle arterie cavernose. Nella norma la fase di accelerazione della curva spettrale con inclinazione superiore a 70°, buona la pulsatilità arteriosa. A.E. > 90°.

CONCLUSIONI

Nella norma lo studio morfo-strutturale penieno.

La valutazione color power doppler, e il tipo di risposta al test farmacologico depongono per funzionamento nei limiti della norma in merito al distretto arterioso penieno associato ad una lieve insufficienza del sistema veno-occlusivo cavernoso.



Considerazioni diagnostico-terapeutiche



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- La disfunzione vascolare è probabilmente correlata a diabete e flebopatie anamnestiche.
- La terapia di primo livello, essendo tra l'altro presente una vasculopatia mista è l'uso di inibitori della fosfodiesterasi 5 (PDE5i).
- Inoltre la terapia ormonale sostitutiva per l'ipogonadismo può fornire ulteriori benefici, soprattutto in caso di franca carenza di testosterone.
- Quale prima? PDE5i? Testosterone?

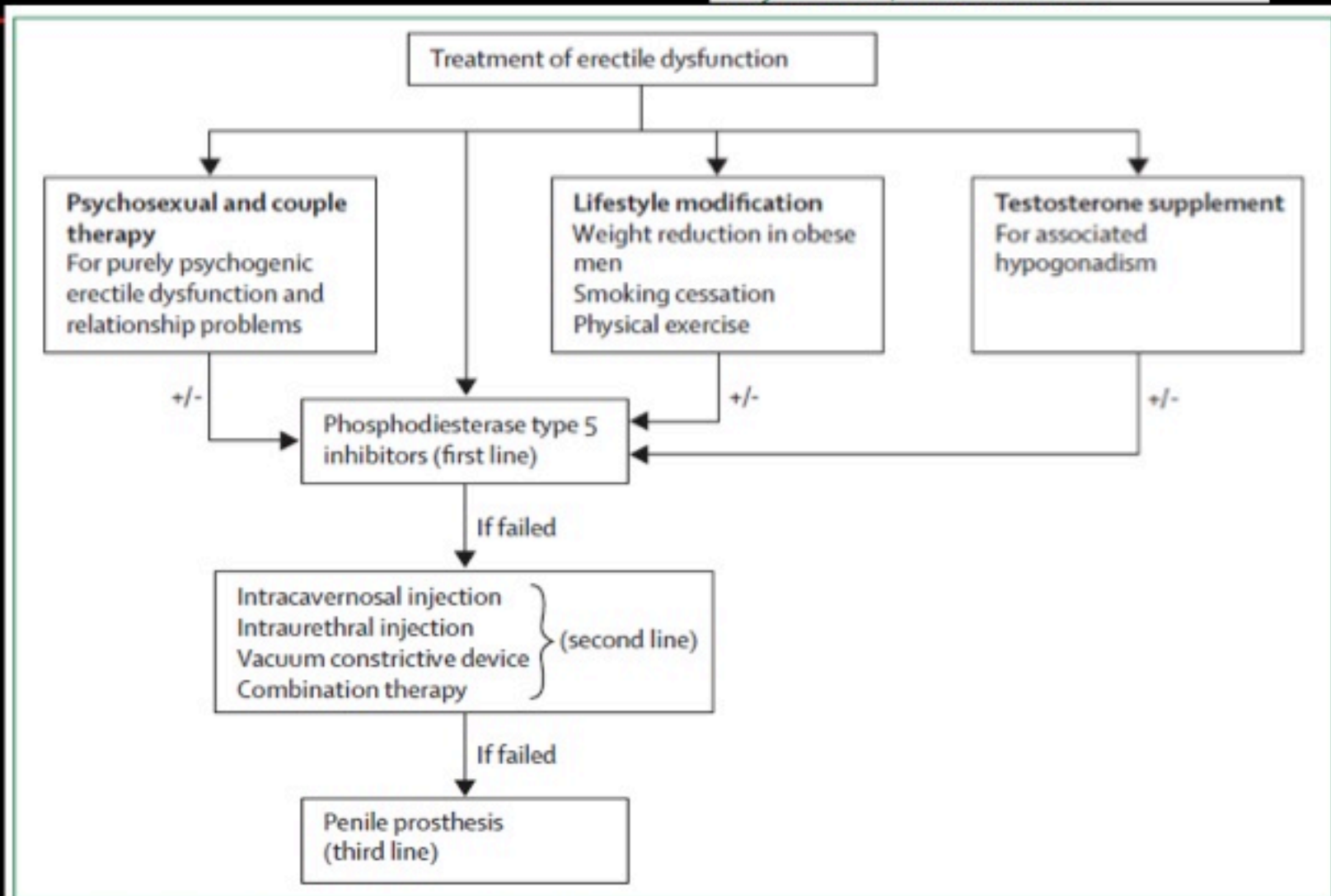


Figure 4: Algorithm for the treatment of erectile dysfunction

Lifestyle modification, testosterone supplementation, and psychosexual therapy can all be associated with medical treatment for erectile dysfunction.



La letteratura



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Wang et al • *Late-Onset Hypogonadism*

Journal of Andrology, Vol. 30, No. 1, January/February 2009
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Investigation, Treatment, and Monitoring of Late-Onset Hypogonadism in Males: ISA, ISSAM, EAU, EAA, and ASA Recommendations

C. WANG*, E. NIESCHLAG,† R. SWERDLOFF*,
H. M. BEHRE,‡ W. J. HELLSTROM,§ L. J. GOOREN,||
J. M. KAUFMAN,¶ J.-J. LEGROS,#
B. LUNENFELD,** A. MORALES,†† J. E.
MORLEY,‡‡ C. SCHULMAN,§§ I. M. THOMPSON,||||
W. WEIDNER¶¶, AND F. C. W. WU###

Testosterone totale (ng/dl)



> 350

12.0 nmol/L



230 - 350

8.0 nmol/L – 12.0 nmol/L



< 230

8.0 nmol/L

2008 European Academy of Andrology • *International Journal of Andrology* **32**, 1–10

Investigation, treatment and monitoring of late-onset hypogonadism in males C. Wang



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7-10 novembre 2013

Journal of Andrology, Vol. 30, No. 1, January/February 2009
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Prior to therapy with testosterone, a man's risk of prostate cancer must be assessed using, as a minimum, digital rectal examination (DRE) and determination of serum prostate-specific antigen (PSA). However, the pretreatment assessment can be improved by incorporating other risk predictors such as age, family history, and ethnicity/race.

Erythrocytosis can develop during testosterone treatment, especially in older men treated by injectable testosterone preparations. Periodic hematologic assessment is indicated



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Testosterone treatment is contraindicated in men with prostate or breast cancer (level 3, grade A). Testosterone treatment is relatively contraindicated in men at high risk of developing prostate cancer. It is unclear whether localized low-grade (Gleason score < 7) prostate cancer represents a relative or absolute contraindication for treatment. (See Sec-



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Men with significant erythrocytosis (hematocrit $> 52\%$; level 3, grade A), untreated obstructive sleep apnea (level 3, grade B), untreated severe congestive heart failure (level 3, grade B) should not be started on treatment with testosterone without prior resolution of the comorbid condition (Calof et al, 2005; Drinka et al, 1995).



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In the presence of a clinical picture of testosterone deficiency and borderline serum testosterone levels, a short (eg, 3 months) therapeutic trial may be justified. An absence of response calls for discontinuation of testosterone administration. A satisfactory response might be placebo generated so that continued assessment is advisable before long-term treatment is recommended (level 2a, grade B; Black et al, 2004).



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Journal of Andrology, Vol. 30, No. 1, January/February 2009
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There is evidence suggesting therapeutic synergism with combined use of testosterone and phosphodiesterase-5 inhibitors in hypogonadal or borderline eugonadal men (level 1b, grade B; Shabsigh et al, 2004; Greenstein et al, 2005). These observations are still preliminary and require additional study. However, the combination treatment should be considered in hypogonadal patients with ED failing to respond to either treatment alone. It is unclear whether men with hypogonadism and ED should be treated initially with phosphodiesterase-5-inhibitor, testosterone, or the combination of the two.

Association of Testosterone Therapy With Mortality, Myocardial Infarction, and Stroke in Men With Low Testosterone Levels

Rebecca Vigen, MD, MSCS; C
Thomas M. Maddox, MD, MS
Margaret E. Wierman, MD; M

EDITORIAL

JAMA November 6, 2013 Volume 310, Number 17 1805

Testosterone Therapy and Risk of Cardiovascular Disease in Men

Anne R. Cappola, MD, ScM

The clinical question about which men should receive testosterone therapy is controversial, with data from short-term clinical trials suggesting benefits for improving sexual function, strength, and well-being. What is missing from the literature are data from randomized trials that include a sufficient number of men for an adequate amount of time to assess the long-term benefits and risks of testosterone therapy. There is no study involving men that is equivalent to the Women's Health Initiative, nor is it likely that there will be a trial of equal scale. Because testosterone therapy is available and prescribed for an estimated 2.9% of US men aged 40 years or older,¹ observational data from existing cohorts of men can contribute meaningfully to assessment of therapeutic risk.

In this issue of *JAMA*,² Vigen and colleagues present retrospective analyses from the Veterans Affairs system of men who had undergone coronary angiography, had subsequent total testosterone assessment, and were found to have a testosterone level of less than 300 ng/dL. Through linkage with pharmacy data, 1223 men, mean age 60.6 years, who initiated testosterone therapy were compared with 7486

sured advantageous health variables. Furthermore, it appears that the 2 study groups were so similar that sophisticated modeling may not have been necessary; the ratio of the unadjusted event rates at 3 years of follow up was 1.30 (25.8% vs 19.9%), nearly identical to the adjusted hazard ratio of 1.29.

The most important issue raised by these findings is determining to which population of men they would apply. The men studied represent a real-world population of men with a sizable burden of comorbidities who have more health problems than do the men enrolled in most randomized clinical trials. The findings are concordant with a trial of testosterone therapy that involved older men with comorbidities.³ Frustratingly little information is available in this VA database analysis about whether testosterone was appropriately prescribed according to accepted guidelines,⁴ which call for morning collection of testosterone on 2 occasions, demonstration of a clinical problem that could be related to testosterone deficiency, and appropriate monitoring. In addition, 35.7% of men were using testosterone injections, which have the advantage of low cost but have the disadvantage of nonphysiologic peak and trough levels over



Related article 1829



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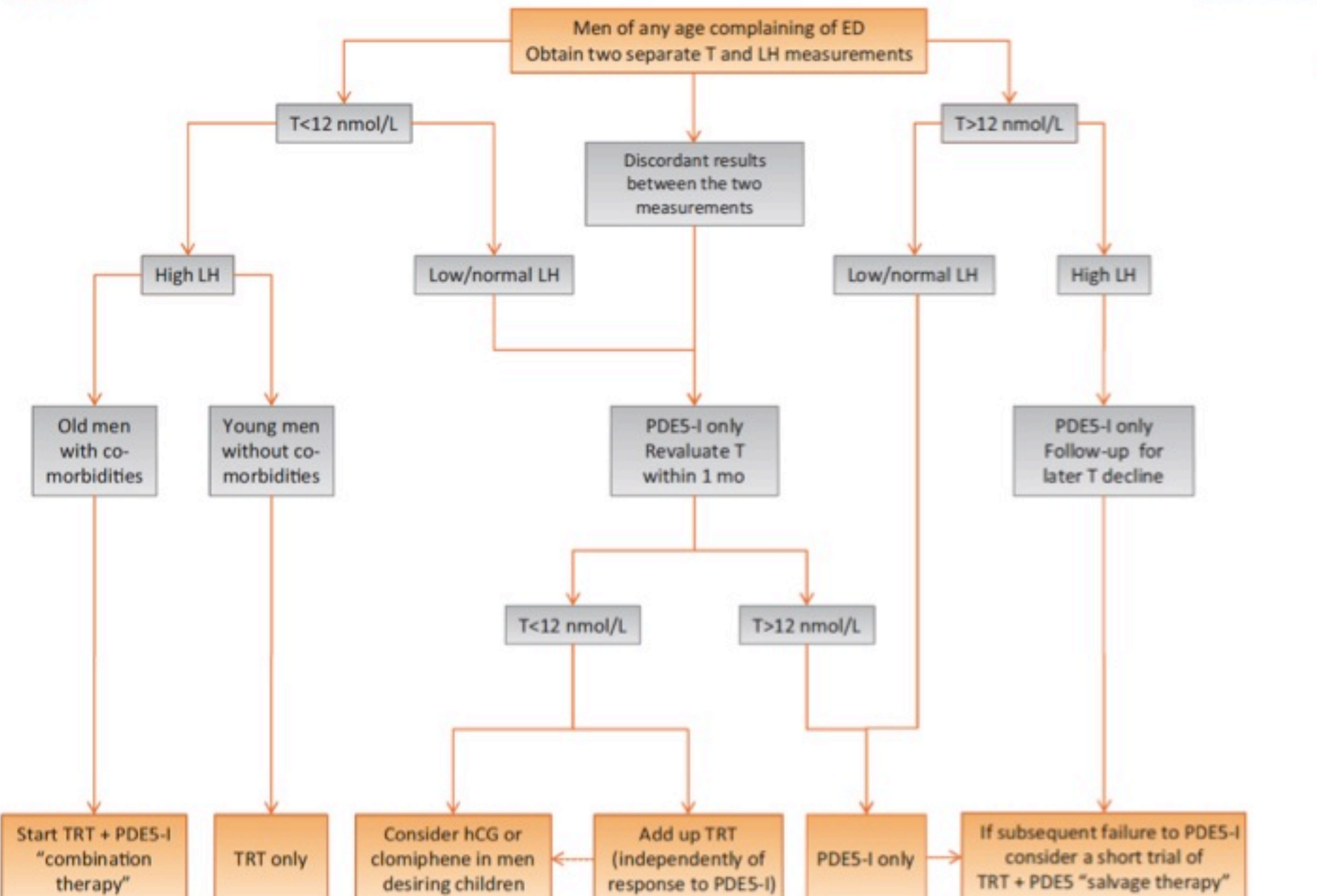
A Critical Analysis of the Role of Testosterone in Erectile Function: From Pathophysiology to Treatment—A Systematic Review

EUROPEAN UROLOGY XXX (2013) XXX-XXX

Andrea M. Isidori^a, Jacques Buvat^b, Giovanni Corona^c, Irwin Goldstein^d, Emmanule A. Jannini^e, Andrea Lenzi^a, Hartmut Porst^f, Andrea Salonia^g, Abdulmaged M. Traish^h, Mario Maggi^{i,*}

All subjects with an organic cause of primary or secondary hypogonadism, especially if young and with a significant drop in T levels, should receive TRT as first-line treatment.

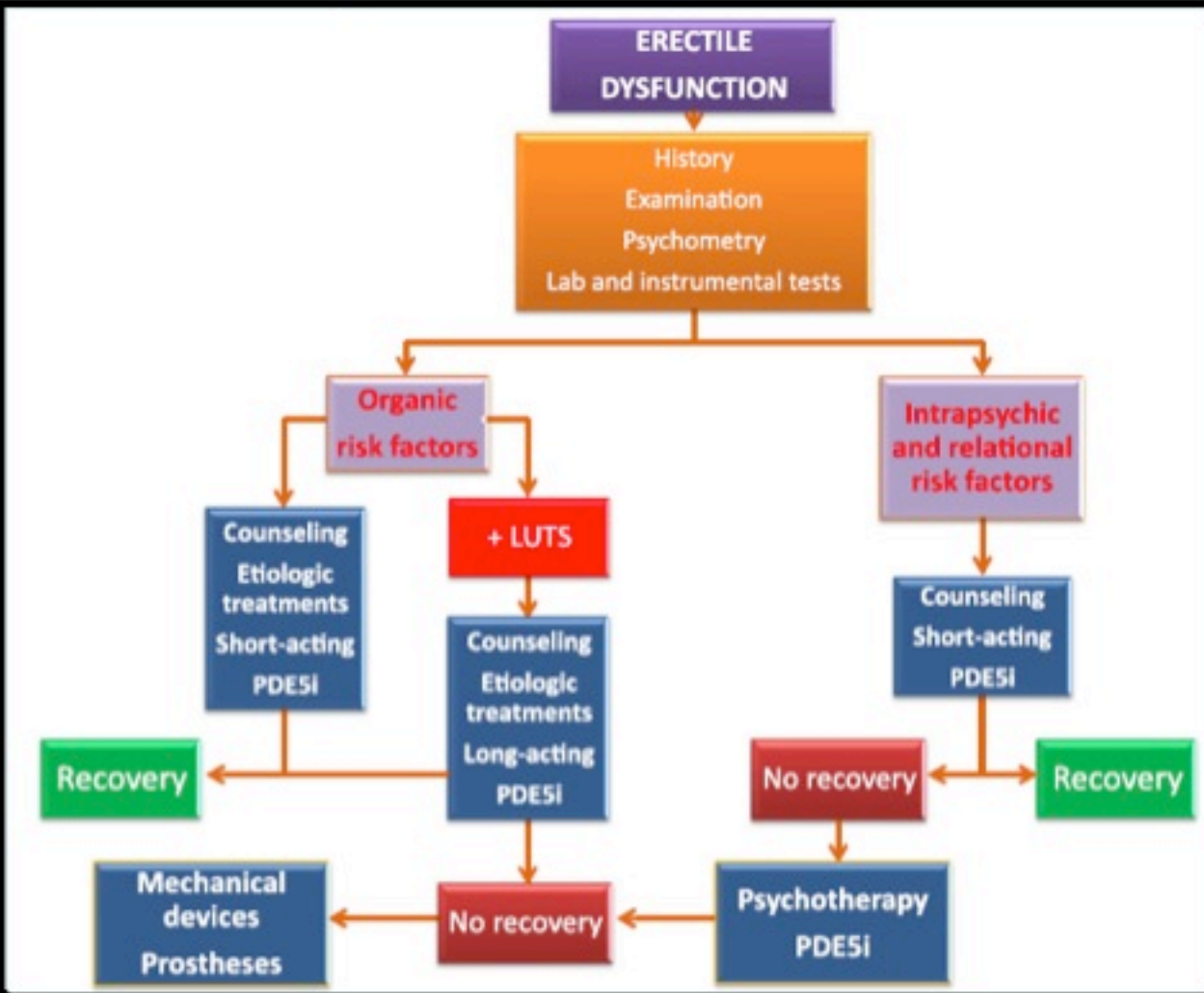
In adults with LOH or any psychological distress, comorbidity, or drug-related marginally reduced T level, a PDE5-I should be administered first in the attempt to restore sexual function, medications affecting sexuality should be discontinued where possible, and finally, but most importantly, any underlying conditions should be treated. Only then, if androgens remain low, should TRT be used in combination therapy (Fig. 3).



Which Is First? The Controversial Issue of Precedence in the Treatment of Male Sexual Dysfunctions

J Sex Med 2013;10:2359-2369

Emmanuele A. Jannini, MD,* Andrea M. Isidori, MD, PhD,† Antonio Aversa, MD, PhD,†
Andrea Lenzi, MD,† and Stanley E. Althof, PhD‡



Which Is First? The Controversial Issue of Precedence in the Treatment of Male Sexual Dysfunctions

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Emmanuele A. Jannini, MD,* Andrea M. Isidori, MD, PhD,† Antonio Aversa, MD, PhD,†
Andrea Lenzi, MD,† and Stanley E. Althof, PhD‡

In conclusion, the answer to the question “which first” is controversial in almost all MSD and even more so in female sexual dysfunctions, which are both less studied and have fewer therapeutic options. Intuition, experience, and available evidence should guide the choice of which treatment to use first. This decision is highly critical in influencing the therapeutic outcome as well the patient’s and couple’s adherence.

Emmanuele A. Jannini, MD



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European
Association
of Urology

Guidelines on Male Sexual Dysfunction:

Erectile dysfunction and premature ejaculation

E. Wespes (chair), I. Eardley, F. Giuliano, D. Hatzichristou,
K. Hatzimouratidis (vice-chair), I. Moncada, A. Salonia, Y. Vardi

MALE SEXUAL DYSFUNCTION - UPDATE MARCH 2013

2.2.5 Guidelines for the diagnostic evaluation of ED

	LE	GR
Clinical use of validated questionnaire related to ED may help to assess all sexual function domains and the effect of a specific treatment modality.	3	B
Physical examination is needed in the initial assessment of men with ED to identify underlying medical conditions that may be associated with ED.	4	B
Routine laboratory tests, including glucose-lipid profile and total testosterone, are required to identify and treat any reversible risk factors and lifestyle factors that can be modified.	4	B
Specific diagnostic tests are indicated by only a few conditions.	4	B

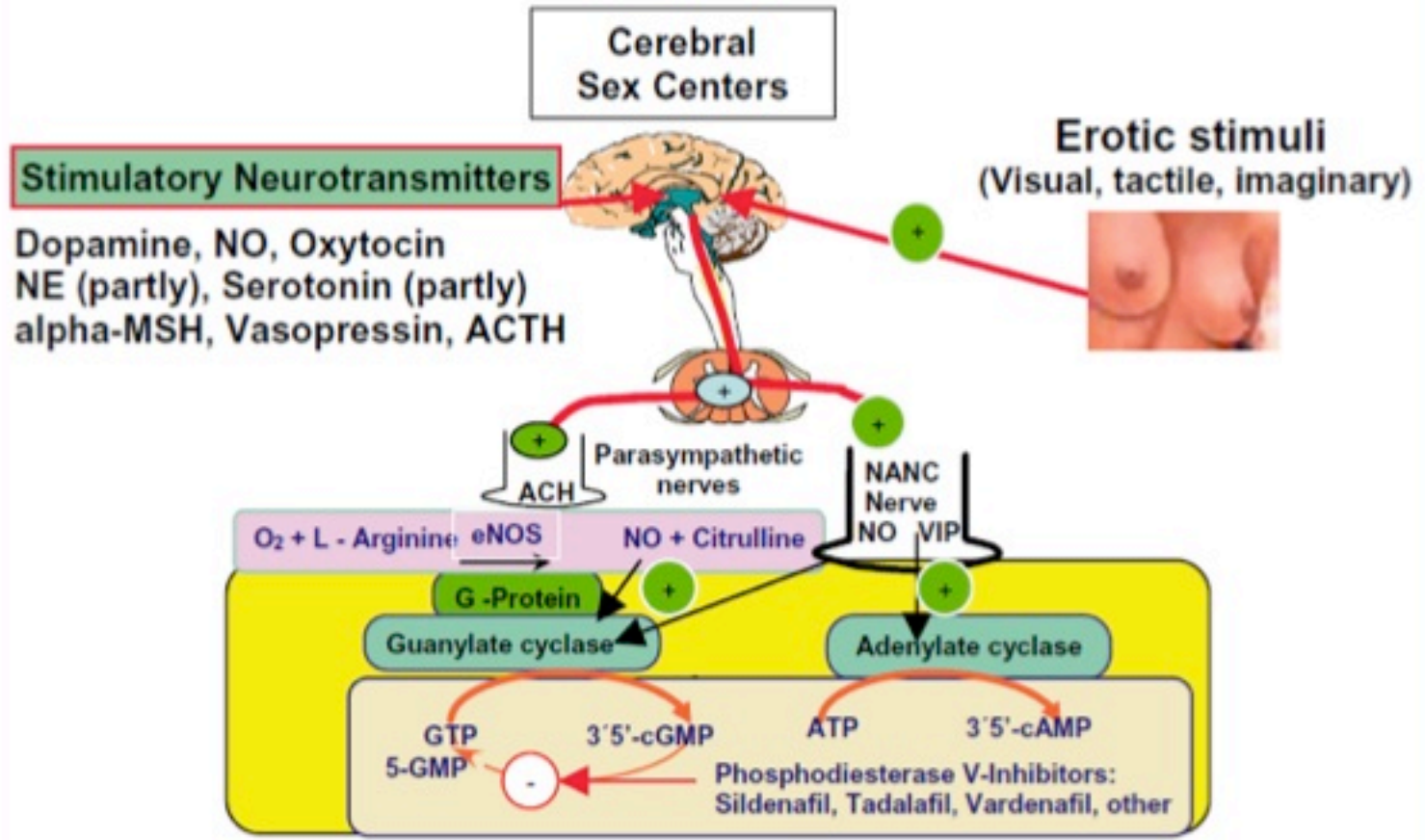
3.8 Guidelines for the treatment of ED

	LE	GR
Lifestyle changes and risk factor modification must precede or accompany ED treatment.	1a	A
Pro-erectile treatments have to be given at the earliest opportunity after RP.	1b	A
When a curable cause of ED is found, it must be treated first.	1b	B
PDE5Is are first-line therapy.	1a	A
Inadequate/incorrect prescription and poor patient education are the main causes of a lack of response to PDE5Is.	3	B
A VED can be used in patients with a stable relationship.	4	C
Intracavernous injection is second-line therapy.	1b	B
Penile implant is third-line therapy.	4	C

SOP Conservative (Medical and Mechanical) Treatment of Erectile Dysfunction

J Sex Med 2013;10:130-171

Hartmut Porst, MD,* Arthur Burnett, MD, MBA, FACS,† Gerald Brock, MD, FRCSC,‡ Hussein Ghanem, MD,§ Francois Giuliano, MD,¶ Sidney Glina, MD,** Wayne Hellstrom, MD, FACS,†† Antonio Martin-Morales, MD,‡‡ Andrea Salonia, MD,§§ Ira Sharlip, MD,¶¶ and the ISSM Standards Committee for Sexual Medicine



Management of Erectile Dysfunction

JOEL J. HEIDELBAUGH, MD, *University of Michigan, Ann Arbor, Michigan*

American Family Physician

www.aafp.org/afp

Volume 81, Number 3 • February 1, 2010

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Diagnostic testing for erectile dysfunction should usually be limited to obtaining a fasting serum glucose level and lipid panel, thyroid-stimulating hormone test, and morning total testosterone level.	C	8
First-line therapy for erectile dysfunction should consist of oral phosphodiesterase type 5 inhibitors.	A	8, 14, 17
Phosphodiesterase type 5 inhibitors are most effective in the treatment of erectile dysfunction associated with diabetes mellitus and spinal cord injury, and of sexual dysfunction associated with antidepressants.	A	9, 12, 17, 19-21
Additional therapy for erectile dysfunction may consist of psychosocial therapy and testosterone supplementation in men with hypogonadism.	B	8, 13, 36
Testosterone supplementation in men with hypogonadism improves erectile dysfunction and libido.	B	13, 29
Screening for cardiovascular risk factors should be considered in men with erectile dysfunction.	C	39

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort.xml>.

First-line therapy for ED consists of lifestyle changes, modifying drug therapy that may cause ED, and pharmacotherapy with phosphodiesterase type 5 inhibitors.

I PDE5i, quale scegliere?





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SOP Conservative (Medical and Mechanical) Treatment of Erectile Dysfunction

J Sex Med 2013;10:130–171

Hartmut Porst, MD,* Arthur Burnett, MD, MBA, FACS,[†] Gerald Brock, MD, FRCSC,[‡] Hussein Ghanem, MD,[§] Francois Giuliano, MD,[¶] Sidney Glina, MD,** Wayne Hellstrom, MD, FACS,^{††} Antonio Martin-Morales, MD,^{‡‡} Andrea Salonia, MD,^{§§} Ira Sharlip, MD,^{¶¶} and the ISSM Standards Committee for Sexual Medicine

Table 5 Pharmacokinetics of the three phosphodiesterase type 5 inhibitors: sildenafil, tadalafil, and vardenafil (Levitra®, and Viagra® labels)

Drug	T_{Max} (minutes)	Onset of action (minutes)		$T_{1/2}$ (hour)	Duration of efficacy (hour) (% succesf. coitus)
		Earliest	>50% patient response		
Sildenafil 100 mg	70 (30–120)	14	20	3.82 ± 0.84	8 (85%)
Tadalafil 20 mg	120 (30–720)	16	30	17.5	36 (59% and 62%)
Vardenafil 20 mg	40 (15–180)	11	25	3.94 ± 1.31	8 ± 2 (69%)



La letteratura



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SOP Conservative (Medical and Mechanical) Treatment of Erectile Dysfunction

Hartmut Porst, MD,* Arthur Burnett, MD, MBA, FACS,[†] Gerald Brock, MD, FRCSC,[‡] Hussein Ghanem, MD,[§] Francois Giuliano, MD,[¶] Sidney Glina, MD,** Wayne Hellstrom, MD, FACS,^{††} Antonio Martin-Morales, MD,^{‡‡} Andrea Salonia, MD,^{§§} Ira Sharlip, MD,^{¶¶} and the ISSM Standards Committee for Sexual Medicine

Table 8 Efficacy of the three PDE5 inhibitors in a variety of ED populations

ED population	Sildenafil/placebo (50/100 mg)		Tadalafil/placebo (10/20 mg)			Vardenafil/placebo (10/20 mg)		
	GAQ (%)	SEP 2/3 (%)	GAQ (%)	SEP 2 (%)	SEP 3 (%)	GAQ (%)	SEP 2 (%)	SEP 3 (%)
Mixed	82/24 (N = 1,600–1,787)*	66/20	81/35 (N = 1,112) [†]	Not reported	75/32	80/30 (N = 601) [‡] 85/28 (N = 804) [§]	Not reported 81/52	75/39 67/33
Diabetes	56/10 (N = 268)*, [¶]	48/12	64/25 (N = 216)**	57/30	48/20	72/13 (N = 452) ^{††}	64/36	54/23
BNSP RRP	No controlled multicenter studies		62/23 (N = 303) ^{‡‡}	54/32	41/19	65/13 (N = 427) ^{§§}	48/22	37/10

BNSP RRP = bilateral nerve sparing retropubic radical prostatectomy; ED = erectile dysfunction; GAQ = General Assessment Question; PDE5 = phosphodiesterase type 5; SEP 2/3 = Sexual Encounter Profile 2/3



Korean Society for Sexual Medicine and Andrology (KSSMA) Guideline on Erectile Dysfunction

World J Mens Health Vol. 31, No. 2, August 2013

Ji Kan Ryu¹, Kang Su Cho², Su Jin Kim³, Kyung Jin Oh⁴, Sung Chul Kam⁵, Kyung Keun Seo⁶, Hong Seok Shin⁷,
Soo Woong Kim⁸

Table 2. Pharmacokinetic data for the five PDE5 inhibitors used to treat erectile dysfunction in Korea

Parameter	PDE5 inhibitors					
	Sildenafil (100 mg)	Tadalafil (20 mg)	Vardenafil (20 mg)	Udenafil (200 mg)	Mirodenafil (100 mg)	Avanafil (200 mg)
T _{max} (h)	0.8~1	2	0.9	1.5	1	0.5
T _{1/2} (h)	2.6~3.7	17.5	3.9	9.88	2.5	10.6
Action duration (h)	0.5~4	1~36	0.5~5	0.5~12	0.5~4	6
C _{max} (μg/L)	560	378	18.7	1,138	NA	5,161
AUC (μg/h/L)	1,685	8,066	56.8	7,898	NA	10,867
Protein binding (%)	96	94	94	NA	NA	99
Bioavailability (%)	41	NA	15	NA	24~43	NA

PDE5: phosphodiesterase type 5, T_{max}: time to maximum plasma concentration, T_{1/2}: terminal half-life, C_{max}: maximum plasma concentration, AUC: area under the curve, NA: not available.



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Comparative Effectiveness and Safety of Oral Phosphodiesterase Type 5 Inhibitors for Erectile Dysfunction: A Systematic Review and Network Meta-analysis

EUROPEAN UROLOGY 63 (2013) 902–912

JinQiu Yuan^a, Renjie Zhang^a, ZuYao Yang^{a,b}, Jack Lee^c, YaLi Liu^d, JinHui Tian^d, XiWen Qin^a, Zhengjia Ren^a, Hong Ding^e, Qing Chen^e, Chen Mao^{a,b,*}, JinLing Tang^{a,b,*}

Table 3 – The absolute treatment effects and the rank of efficacy of phosphodiesterase type 5 inhibitors for erectile dysfunction

PDE5-I	GAQ-1		IIEF-EF		SEP 2		SEP 3	
	Absolute effect, mean (95% CI)	Rank, mean, (95% CI)	Absolute effect, mean (95% CI)	Rank, mean (95% CI)	Absolute effect, mean (95% CI)	Rank, mean (95% CI)	Absolute effect, mean (95% CI)	Rank, mean, (95% CI)
Sildenafil	0.73 (0.59–0.84)	2.96 (1–5)	7.68 (6.81–8.53)	3.30 (2–4)	10.48 (2.44–18.40)	4.92 (4–5)	29.10 (17.53–40.61)	4.94 (4–5)
Tadalafil	0.75 (0.62–0.86)	1.72 (1–4)	9.21 (8.17–10.21)	1.15 (1–2)	29.70 (25.61–33.81)	1.80 (1–3)	48.07 (43.84–51.73)	1.99 (1–3)
Vardenafil	0.73 (0.60–0.84)	2.67 (1–5)	8.39 (7.20–9.58)	2.15 (1–4)	29.22 (24.57–33.73)	1.95 (1–4)	48.13 (42.99–53.23)	1.98 (1–3)
Udenafil	0.69 (0.52–0.83)	4.12 (1–5)	7.53 (6.21–8.86)	3.40 (2–4)	28.09 (22.88–33.21)	2.44 (1–4)	40.23 (33.84–46.59)	3.85 (3–5)
Mirodenafil	0.70 (0.49–0.86)	3.59 (1–6)	NA	NA	19.54 (7.74–31.17)	3.89 (1–5)	47.48 (35.38–59.38)	2.24 (1–4)
Avanafil	0.46 (0.23–0.71)	5.94 (5–6)	NA	NA	NA	NA	NA	NA
Placebo	0.24 (0.14–0.36)	6.99 (7–7)	1.64 (1.20–2.07)	5 (5–5)	1.86 (1.42–2.30)	5.99 (6–6)	11.92 (11.48–12.36)	6 (6–6)

CI = confidence interval; GAQ-1 = Global Assessment Questionnaire question 1: "While using the study medication, did you feel that your erections improved?"; IIEF-EF = International Index of Erectile Function-Erectile Function domain; NA = not applicable; PDE5-I = phosphodiesterase type 5 inhibitor; SEP-2 = Sexual Encounter Profile question 2: "Were you able to insert your penis into your partner's vagina?"; SEP-3 = Sexual Encounter Profile question 3: "Did your erection last long enough for you to have successful completion of intercourse?"



PDE5 inhibitors: considerations for preference and long-term adherence

W. B. Smith II, I. R. McCaslin, A. Gokce, S. H. Mandava, L. Trost, W. J. Hellstrom
Int J Clin Pract, August 2013, **67**, 8, 768–780.

adherence. **Conclusions:** PDE5i represent first line therapy for ED with excellent overall efficacy and satisfactory side effect profiles. Enhanced communication, coupled with increased knowledge of drug characteristics, comparative treatment regimens and optimal prescribing patterns, offer compelling tools to improve long-term treatment success.

British Society for Sexual Medicine Guidelines on the Management of Erectile Dysfunction

J Sex Med 2008;5:1841–1865

Table 8 Adverse events reported with PDE5 inhibitor use

Adverse event	Incidence (%)		
	Sildenafil (N = 5,918) [84]	Vardenafil (N = 2,203) [85]	Tadalafil (N = 804) [10]
Headache	14.6	14.5	14
Flushing	14.1	11.1	4
Dyspepsia	6.2	3.7	10
Rhinitis	2.6	9.2	5
Back pain	0	0	6
Visual disturbance	5.2	0	0

The role of pharmacokinetics and pharmacodynamics in phosphodiesterase-5 inhibitor therapy

International Journal of Impotence Research (2007) 19, 253–264

Table 3 Contraindications and dose adjustments for PDE5 inhibitors^{15,42}

Pharmacodynamic interactions

Contraindications

- *Nitrates*: concomitant use of PDE5 inhibitors with nitrates is absolutely contraindicated as they potentiate the hypotensive effects of nitrates

The role of pharmacokinetics and pharmacodynamics in phosphodiesterase-5 inhibitor therapy

International Journal of Impotence Research (2007) 19, 253–264

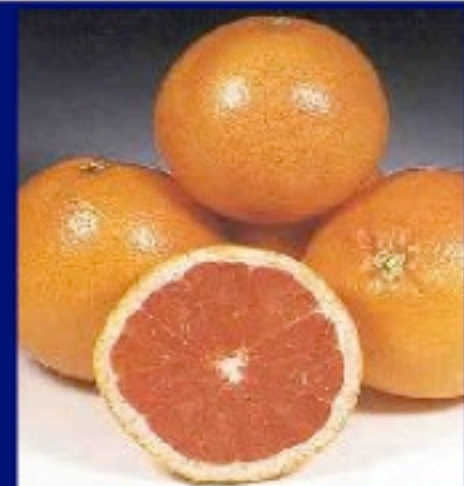
Pharmacokinetic interactions

Concomitant medications potentially requiring lower doses of PDE5 inhibitors or administering them with caution

- Ketoconazole
- Itraconazole
- Erythromycin
- Clarithromycin
- HIV protease inhibitors (ritonavir, saquinavir and indinavir): Ritonavir has an unusually high effect on systemic exposure of vardenafil, and 50% dose reduction is warranted
- Grapefruit juice
- Cimetidine
- Antacids: tadalafil's rate of absorption decreased by 30%; no interaction with sildenafil or vardenafil

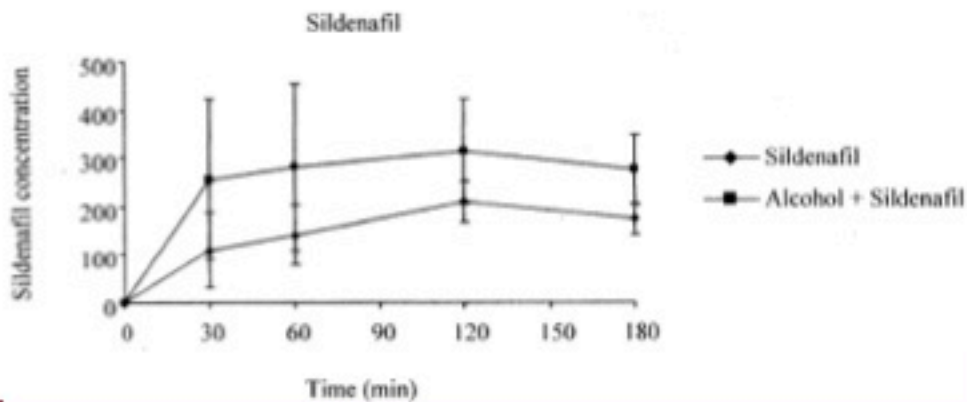
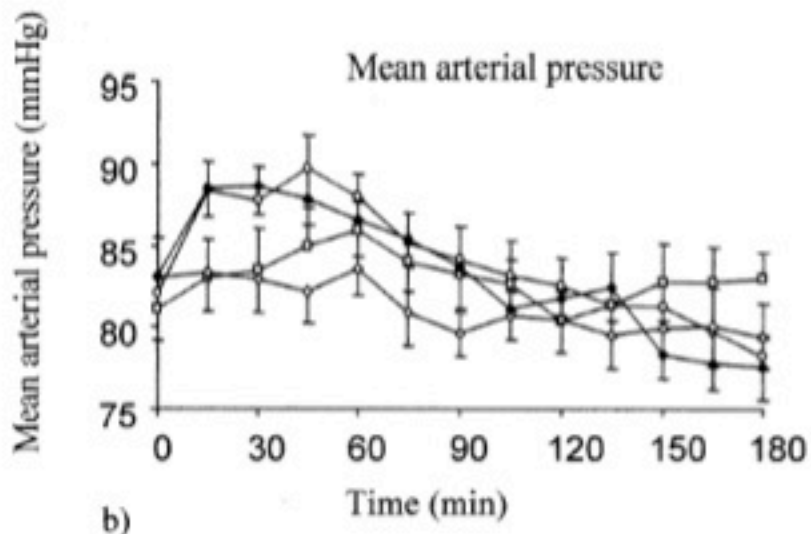
Concomitant medications potentially requiring higher doses of PDE5 inhibitors

- Rifampin
- Phenobarbital
- Phenytoin
- Carbamazepin

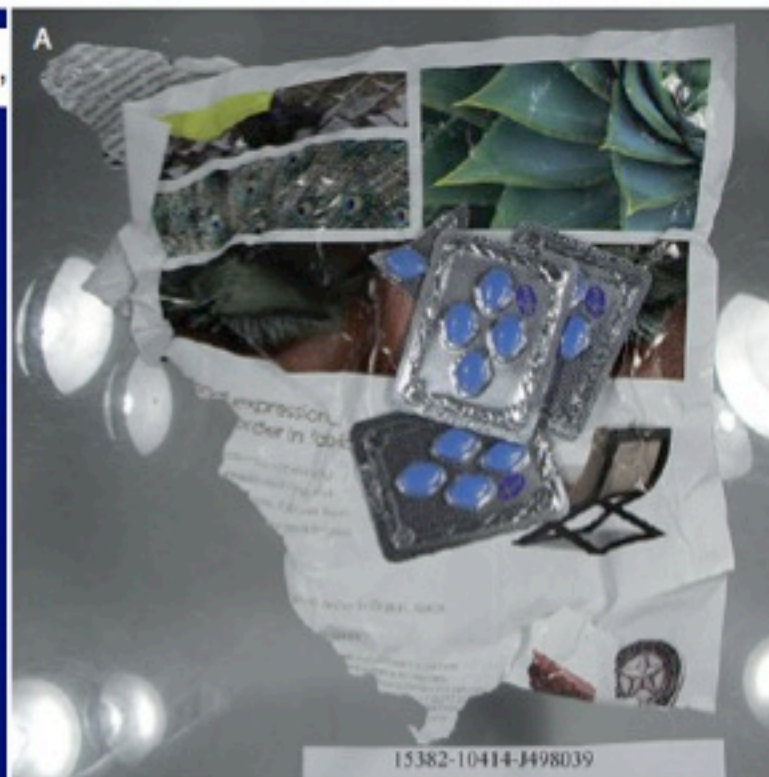


No adverse hemodynamic interaction between sildenafil and red wine

Stephen J. Leslie, MRCP, Graham Atkins, BSc, James J. Oliver, MRCP, and David J. Webb, FRCP *Edinburgh, United Kingdom*



Internet-Ordered Viagra (Sildenafil Citrate) Is Rarely Genuine



Ottimizzare la terapia

“Timing”

Interazioni

Posologia corretta

Stimolazione sessuale

Almeno 6-8 tentativi

Visite di follow-up

Partner





I PDE5i, quale scegliere?



Bari,
7-10 novembre 2013

Ricapitolando:

- **Breve emivita** (“pillola occasionale”)
 - **Sildenafil**: più studiato e conosciuto
 - **Vardenafil**: più recente, maggiori effetti sull’ eiaculazione precoce
- **Lunga emivita** (“pillola da week-end”):
 - **Tadalafil**: meno “a domanda”, possibilità di una terapia in cronico con 5mg/die

Mettersi in gioco - II



- Seconda domanda: che cosa fare?



- In presenza di una disfunzione erettile, è indispensabile la determinazione del testosterone, è anche suggerito un dosaggio della prolattina.
- In caso di sospetto ipogonadismo, per praticità sarebbe indicato includere tra gli esami anche una valutazione dell'emocromo e del PSA (pur con recenti riserve).
- In caso di sospetta componente vascolare si ipotizzi l'ecocolodoppler penieno dinamico

- La principale differenza tra i PDE5i consiste nell'emivita; da segnalare la diversa azione sull'eiaculazione.
- In terapia sostitutiva con **Testosterone** monitorare sempre **emocromo** e **PSA**.
- Proporre al paziente una terapia adatta alla sua vita di relazione ed alla sua sessualità, ascoltando i suoi bisogni ed assecondando le sue necessità; sono indispensabili counseling e follow up.

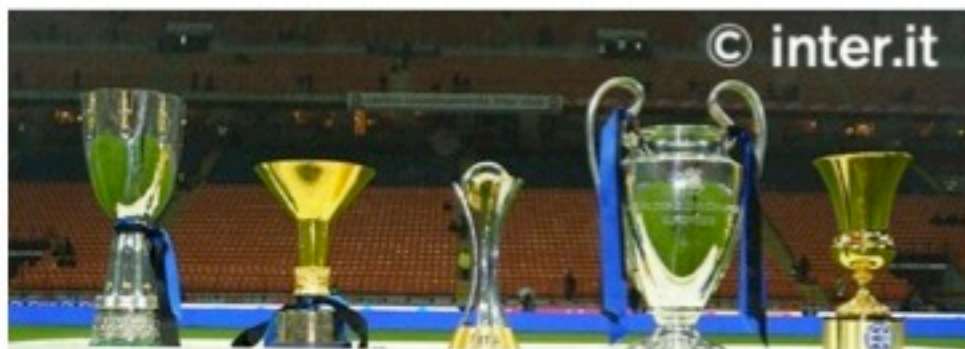
“Parlare è un po' come il sesso quando si invecchia: cominciare diventa ogni giorno un po' più difficile, ma quando hai cominciato non vorresti mai finire.”

Stephen King





Quinto titolo: campioni del mondo



Sesto titolo: tim cup...ero là...

*E ora tristemente
Inter-Roma 0-3
E DE del relatore
che vive a Roma!*

DISFUNZIONE ERETTILE

Terapia farmacologica

SISTEMICA: ENDOCRINA
NON ENDOCRINA

LOCALE: INTRACAVERNOSA
INTRAURETRALE
TRANSDERMICA

DISFUNZIONE ERETTILE

Terapia farmacologica sistemica

TERAPIA ENDOCRINA

TERAPIA NON ENDOCRINA

Testosterone

hCG

GnRH

DHT

DHEA

Naltrexone

Dopaminoagonisti

Androstenedione

Altre

Sildenafil

Vardenafil

Tadalafil

Apomorfina

Yohimbina

Trazodone

Fentolamina

Arginina

Altre

DISFUNZIONE ERETTILE

Terapia farmacologica locale

INTRACAVERNOSA

PGE-1

Papaverina

Fentolamina

Linsidomina

Moxisylyte

VIP

Altre

INTRAURETRALE

PGE-1

Papaverina

Prazosin

TRANSDERMICA

PGE-1

Papaverina

Nitroglicerina

Minoxidil

Novel therapeutic targets for erectile dysfunction

Steve K. Williams, Arnold melman*

Maturitas 71 (2012) 20–27

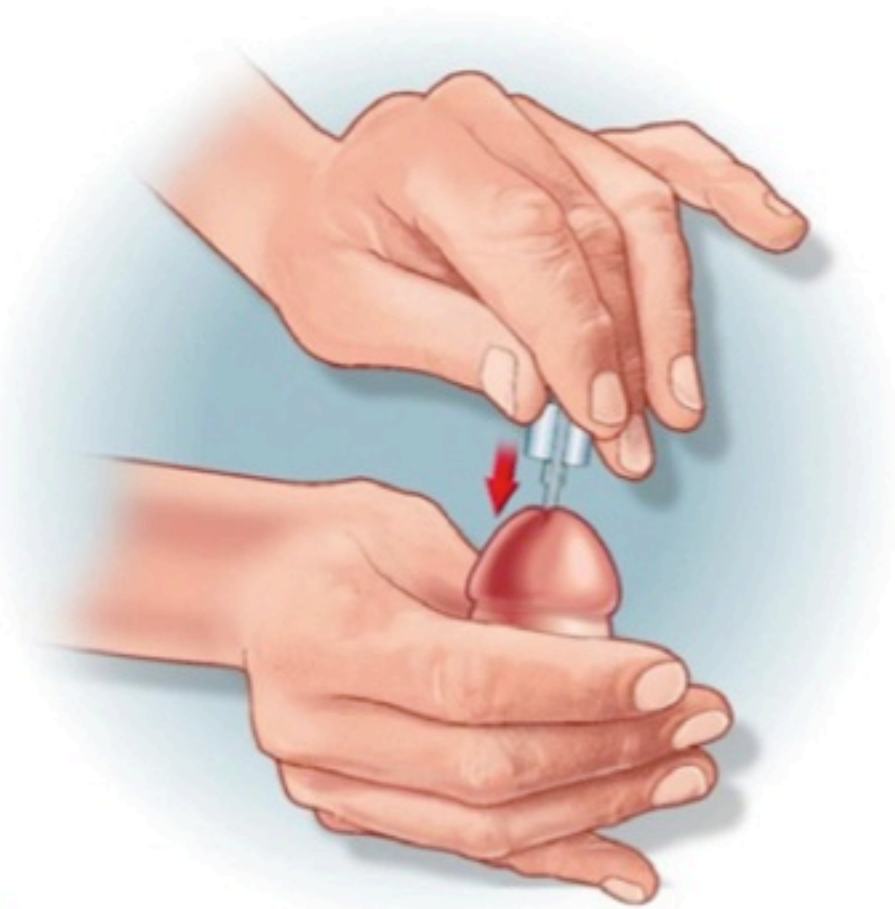
Department of Urology, Albert Einstein College of Medicine, Bronx, NY, United States

- Pharmacotherapy
- 2.1. PDE 5 inhibitors
- 2.2. Melanocortin receptors
- 2.3. Endothelins
- 2.4. Dopamine receptor agonists
- 2.5. Prostaglandin E1 (PGE1).....
- 2.6. Gene therapy
- 2.7. Potassium channels
- 2.8. Nitric oxide synthase (NOS) isoforms.....
- 2.9. Growth factor targets.....
- 2.10. Tissue engineering
- 2.11. Neural auto transplantation
- 2.12. Cavernous muscle cell auto transplantation.....
- 2.13. Penile cartilage rods.....

SOP Conservative (Medical and Mechanical) Treatment of Erectile Dysfunction

Porst ISSM Standards Committee for Sexual Medicine J Sex Med 2013;10:130

MUSE (= Medical Urethral System for Erection):
Einmalsystem zur Verabreichung von Alprostadil (PGE1) in die Harnröhre



SOP Conservative (Medical and Mechanical) Treatment of Erectile Dysfunction

Porst ISSM Standards Committee for Sexual Medicine J Sex Med 2013;10:130

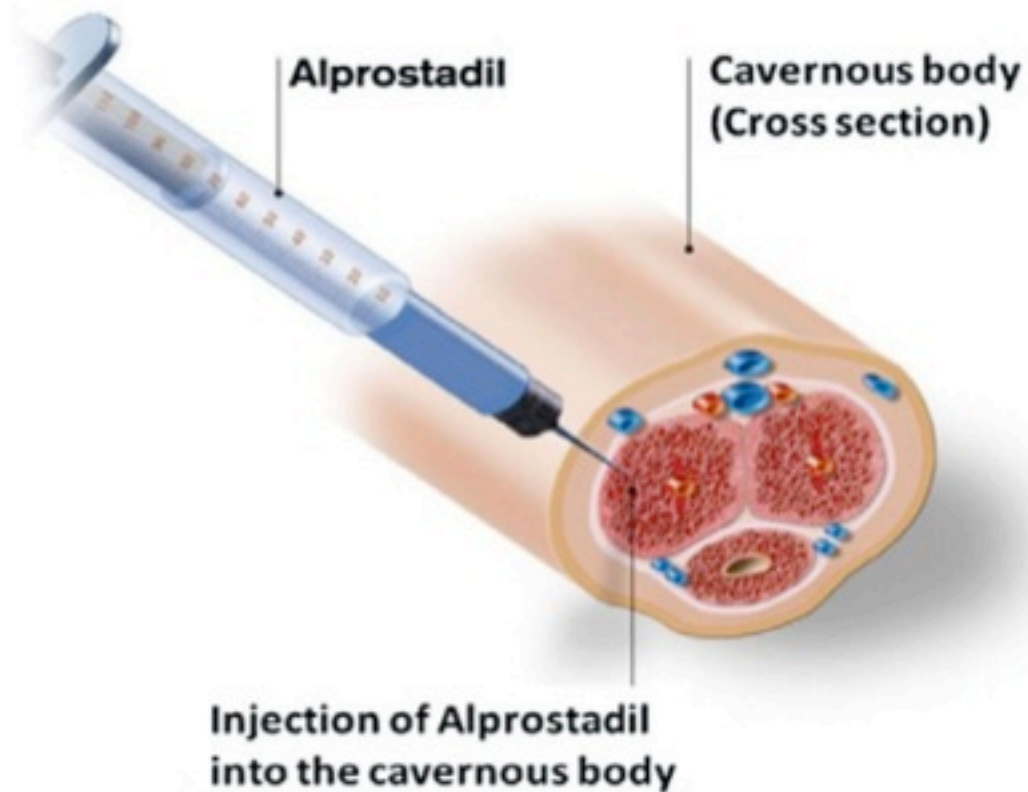
Table 23 Review of the literature: efficacy rates of transurethral alprostadil (MUSE®) vs. self-injection therapy with alprostadil (Caverject®, Viridal®, and Edex®) (from Porst and Adaikan [123])

Author	No. of patients	MUSE®	i.c. alprostadil
Ghazi, 1998 [124]	125	48% (61)	79% (98)
Werthman, 1997 [125]	100	37%	89%
Porst, 1997 [126]	103	43% (44)	70% (72)
Shabsigh, 1998 [127]	106	27%	66% (buckling test)
Shabsigh, 2000 [128]	68	53%	83% (at home use)
Flynn, 1998 [129]	Literature review	45%	>70%

MUSE = Medicated Urethral System for Erection

SOP Conservative (Medical and Mechanical) Treatment of Erectile Dysfunction

Porst ISSM Standards Committee for Sexual Medicine J Sex Med 2013;10:130



SOP Conservative (Medical and Mechanical) Treatment of Erectile Dysfunction

Porst ISSM Standards Committee for Sexual Medicine J Sex Med 2013;10:130

Table 24 Efficacy of vasoactive substances in the diagnosis of ED. Literature review of evaluable publications (from Porst [133])

Substance	Dose (min/max)	Publications	No. of patients	Responders
Papaverine	30–110 mg	19	2,161	61% (987 out of 1,616)
Papaverine/phentolamine	15 mg/1.25 mg	13	3,016	68.5% (2,065 out of 3,016)
PGE1 (alprostadil)	60 mg/2 mg			
	5 µg–40 µg	27	10,353	72.6% (7,519 out of 10,353)

Table 26 Side effects of vasoactive drugs in ED. Review of the literature (Porst [133])

Substance	N	No. of publications	Priapism > 6 hours	Fibrosis	Pain	Elevated liver enzymes
Papaverine	1,527	15	7.1% (92 out of 1,300)	5.7% (60 out of 1,056)	4% (18 out of 452)	1.6% (5 out of 314)
Papaverine/phentolamine	2,263	22	7.8% (122 out of 1,561)	12.4% (288 out of 1,843)	11.6% (141 out of 1,215)	5.4% (43 out of 799)
PGE1 (alprostadil)	2,745	10	0.36% (10 out of 2,745)	0.8% (18 out of 2,180)	7.2% (40 out of 558)	0%

Table 28 Various dose combinations with trimix combinations have been reported in the literature (from Porst and Adaikan [123])

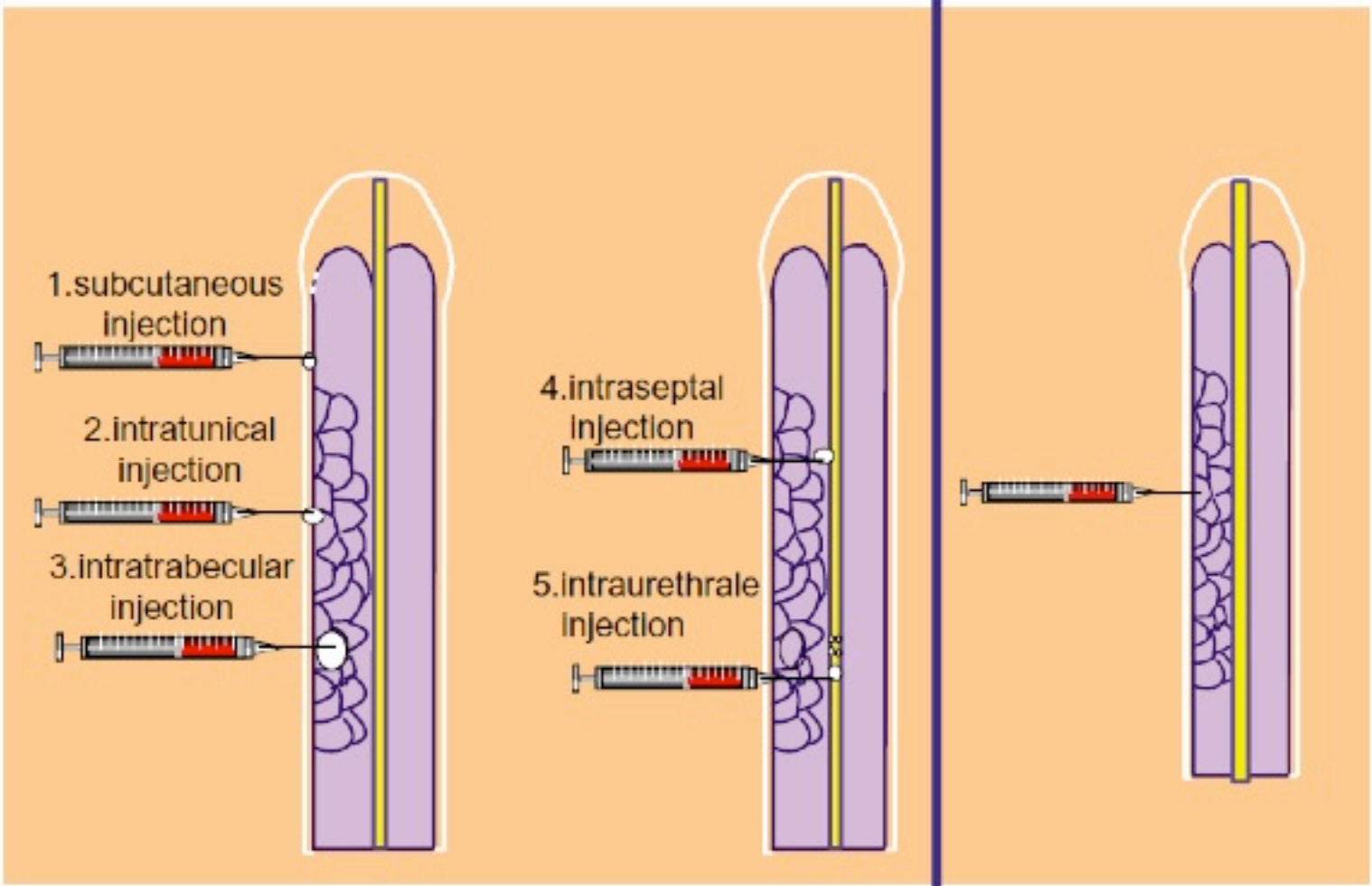
Reference	Trimix stock solution			Injection volume (mL)
	Papaverine per mL	PGE1 per mL	Phentolamine per mL	
Bennett et al., 1991 [145]	17.6 mg	5.9 µg	0.59 mg	0.25
Govier et al., 1993 [146]	22.5 mg	8.3 µg	0.83 mg	0.36
Israilov et al., 2002 [147]	19.4 mg	16.4 µg	1.6 mg	NA
Marshall et al., 1994 [148]	12 mg	9 µg	1 mg	0.1–0.8
Shenfeld et al. 1995 [149]	4.5 mg/0.5 mL	5 µg/0.5 mL	0.25 mg/0.5 mL	0.5
Mulhall et al., 1999 [150]	30 mg	10 µg	1 mg	NA
	30 mg	25 µg	2 mg	NA
	150 mg	30 µg	5 mg	0.18–0.21
Montorsi et al., 2002 [151]	300 mg	100 µg	10 mg	0.18–0.21
	300 mg	200 µg	20 mg	0.18–0.21

SOP Conservative (Medical and Mechanical) Treatment of Erectile Dysfunction

Porst ISSM Standards Committee for Sexual Medicine J Sex Med 2013;10:130

Potential of Malinjection in Self-Injection Technique

Correct Intra sinusoidal Injection



SOP Conservative (Medical and Mechanical) Treatment of Erectile Dysfunction

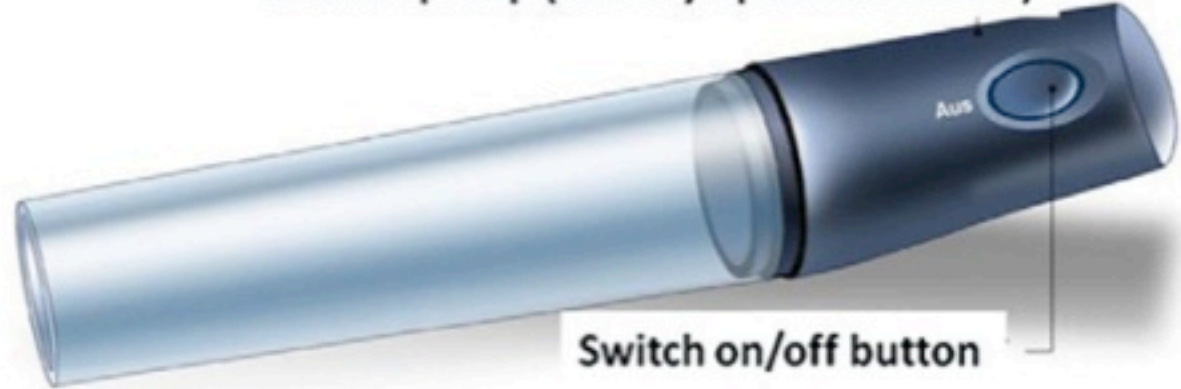
Porst ISSM Standards Committee for Sexual Medicine J Sex Med 2013;10:130



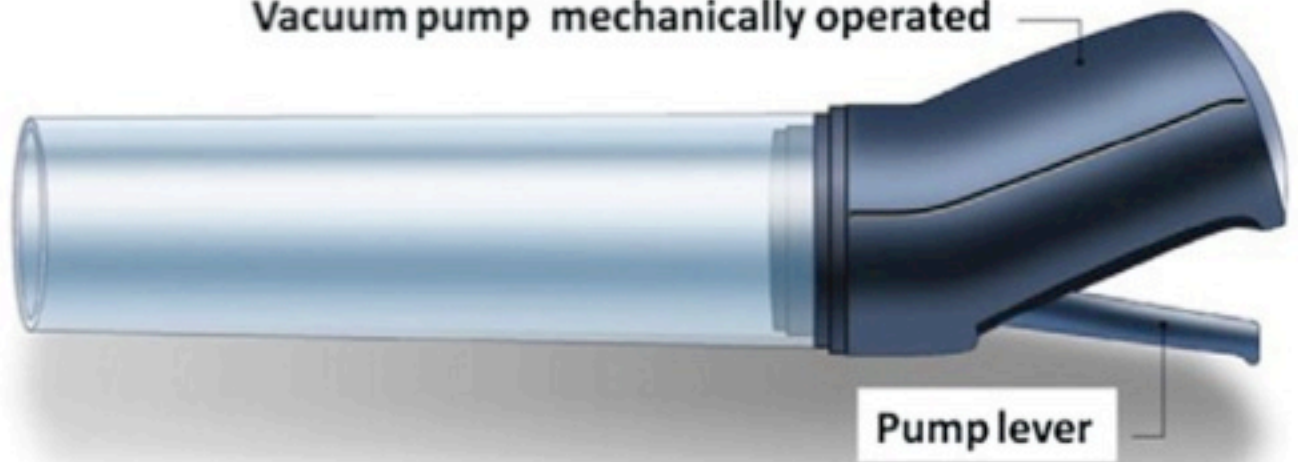
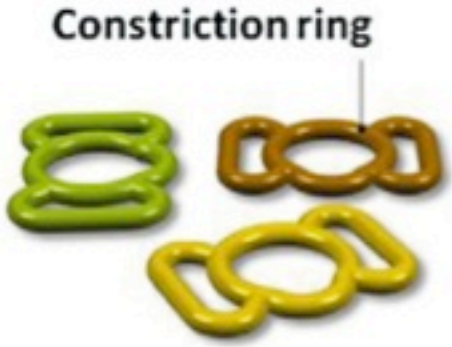
SOP Conservative (Medical and Mechanical) Treatment of Erectile Dysfunction

Porst ISSM Standards Committee for Sexual Medicine J Sex Med 2013;10:130

Vacuum pump (battery operated motor)



Vacuum pump mechanically operated



SOP Conservative (Medical and Mechanical) Treatment of Erectile Dysfunction

Porst ISSM Standards Committee for Sexual Medicine J Sex Med 2013;10:130

Table 32 Outcome of VCD therapy—overviews of the literature (source: Glina and Porst [169])

Author	Device	N	Evaluable	Mean age (years)	Follow-up (months)	Satisfaction
Nadig, 1987 [170]	Osbon Erec-Aid®	302	81% (244)	?	up to 72	83%
Witherington, 1989 [171]	Osbon Erec-Aid®	15,000	10% (1,517)	64	8.6	92% good erections
Blackard, 1993 [172]	Osbon Erec-Aid®	47	96% (45)	?	?	42%
Derouet, 1993 [173]	Osbon Erec-Aid®	90	100%	32–75	?	37%
Baltaci, 1995 [174]	Osbon Erec-Aid®	61	80% (49)	?	12.8	67%
Lewis, 1997 [175]	Osbon Erec-Aid®	34,777	17% (5,847)	?	1974–1992	65–83%
Meinhardt, 1993 [176]	Post-T VED	74	100%	55	3 weeks	30%
Fedel, 1995 [177]	Innovital	100	40%	52.4	6	90%
Cookson, 1993 [178]	?	216	53% (115)	65	29	84%
Graham, 1998 [179]	?	323	100%	61	2 weeks	23%
Droupy, 1998 [180]	?	53 (RRP)	55% (29)	66.5	27	52%
Opsomer, 1998 [181]	?	170	?	66	48	55%

Post-T VED – post-testosterone vacuum-erection device; RRP – radical retropubic prostatectomy; VCD – vacuum constriction device

Guidelines on Male Sexual Dysfunction: Erectile Dysfunction and Premature Ejaculation

Hatzimouratidis EUROPEAN UROLOGY 57 (2010) 804–814

Table 1 – Indications for specific diagnostic tests

Patients with primary erectile disorder (not caused by organic disease or psychogenic disorder)

Young patients with a history of pelvic or perineal trauma who could benefit from potentially curative vascular surgery

Patients with penile deformities (eg, Peyronie's disease, congenital curvature) that might require surgical correction

Patients with complex psychiatric or psychosexual disorders

Patients with complex endocrine disorders

Specific tests may also be indicated at the request of the patient or his partner

For medicolegal reasons (eg, penile prosthesis implant, sexual abuse)

Table 2 – Specific diagnostic tests

Nocturnal penile tumescence and rigidity using Rigiscan

Vascular studies

- Intracavernous vasoactive drug injection
- Duplex ultrasound of the cavernous arteries
- Dynamic infusion cavernosometry and cavernosography
- Internal pudendal arteriography

Neurologic studies (eg, bulbocavernosus reflex latency, nerve-conduction studies)

Endocrinologic studies

Specialised psychodiagnostic evaluation

Table 1

Ideal Candidates for Intracavernous Injection Therapy

Failure of first-line oral therapy
Patient use of nitrates or potential use of nitrates
Neural injury from pelvic surgery, trauma, or radiation
Diabetic patients or severe vasculopathies (often after failed first-line therapy)
Patient desire for rapid onset of erection
Patient desire for greater rigidity and duration of erection than achievable with oral agents

Table 2

**Absolute and Relative
Contraindications for Intracavernous Injection Therapy**

History of priapism with vasoactive drug use
Severe penile fibrosis
Use of MAOIs (monoamine oxidase inhibitors) which would limit use of phenylephrine for potential priapism
Poor visual acuity limiting needle delivery

Potential Sites of Injection

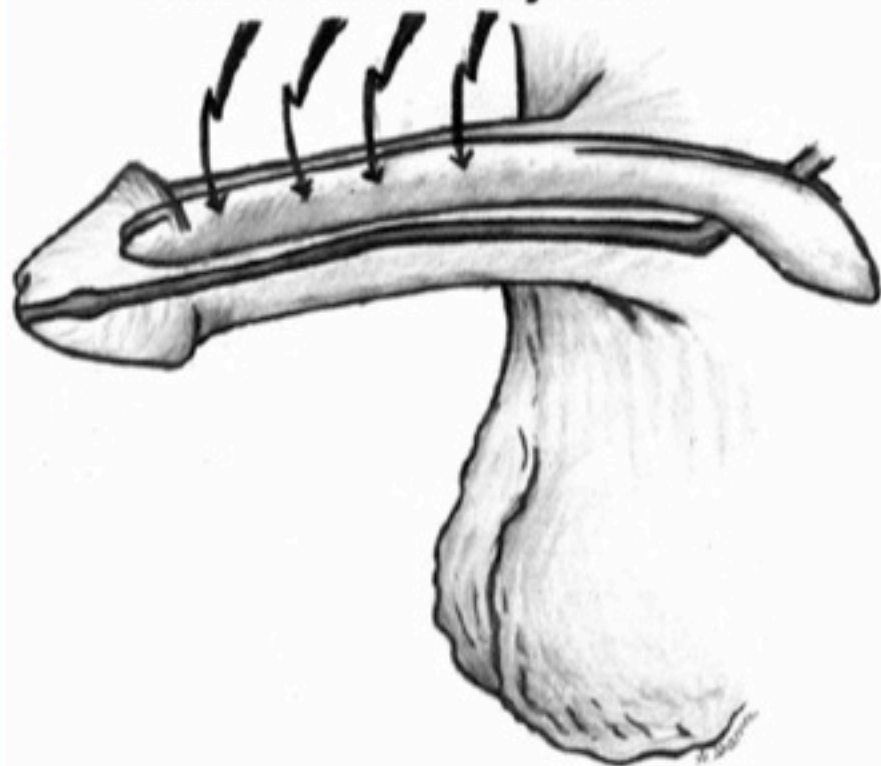


Fig. 2. Sites for intracavernous injection therapy.

Table 3

Strategies to Optimize Intracavernous Injection Therapy

Direct injection into proximal corpora
Gentle local pressure applied to injection site (2-3 min)
Comfortable, stress-free environment
Sexual stimulation following injection
Incremental dose increases if unsuccessful, until recommended dose maximum achieved (minimum 24 h between attempts)
Patient information and support

Intracavernous Pharmacotherapy for Erectile Dysfunction

Anthony J. Bella and Gerald B. Brock

Table 4
Inadequate Response
to Intracavernous Injection Therapy: Common Causes

Inadequate dose
Misdirected injection into wrong location (subcutaneous or trabecular)
Leakage of vasoactive agent prior to injection
Inadequate sexual stimulation
Premature ejaculation

Table 5
Common Steps
to Correct Inadequate Therapeutic Response

Reassess dose and increase until therapeutic response achieved
Review of injection technique
Evaluate timing with regards to injection and sexual stimulation
Change to more potent vasoactive agent or combination therapy if at maximum recommended dose
Use combination therapy if pain is limiting factor
Involve partner and reassure

Table 6
Comparison of Single Agent Vs Combination Intracavernous Injection Therapy

Drug	Dose	Efficacy (%)	Priapism > 6 hours (%)	Fibrosis (%)	Drop-out rate (%)
Prostaglandin E-1	12-15 mg (range 5-40 mg)	70-75	1	1-3	40-60
Papaverine	20-80 mg (range 5-160 mg)	55	1-6	6-12	35-50
Phentolamine/papaverine	10 mg/1.25 mg-60 mg/2 mg	70	7	6-12	30-45
Trimix (PGE-1, papaverine, phentolamine)	10 mg/8 mg/0.2 mg-20 mg/20 mg/0.5 mg	75-85	1-3	2-5	25

MUSE (= **M**edical **U**rethral **S**ystem for **E**rection):
Einmalsystem zur Verabreichung von Alprostadil (PGE1) in die Harnröhre

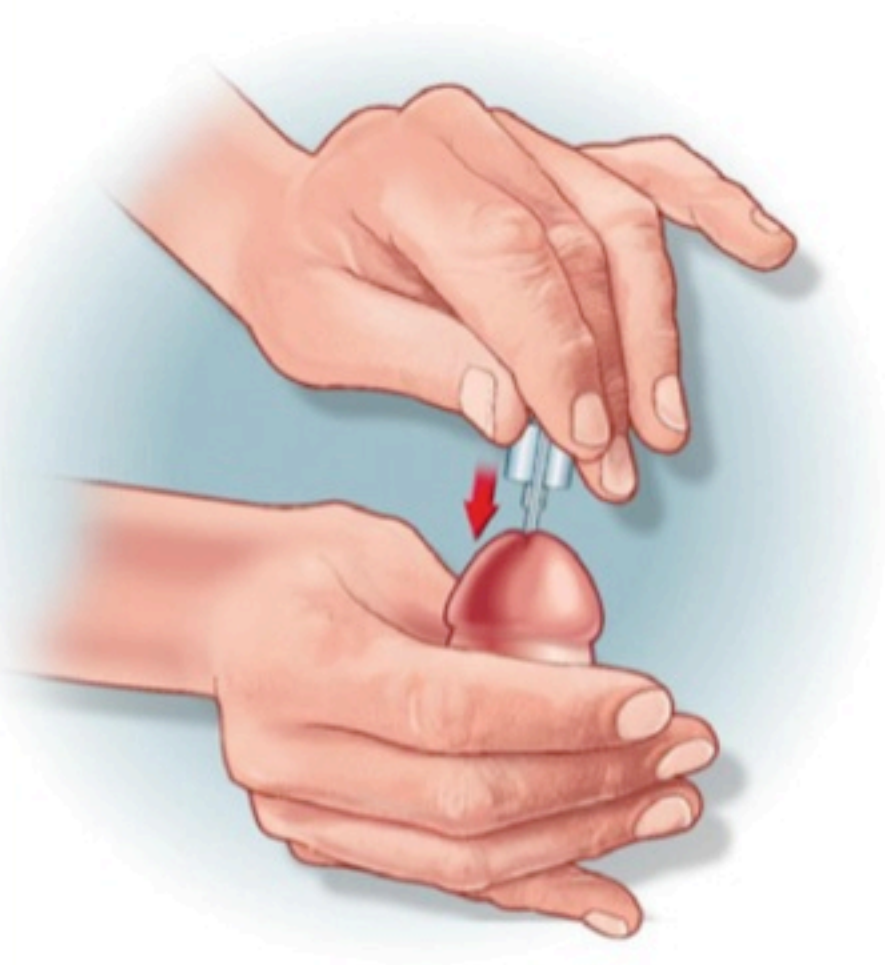




Figure 2. Erec-Tech vacuum therapy system.



Figure 3. Coloplast Alpha-1 inflatable penile prosthesis.

Regular Intercourse Protects Against Erectile Dysfunction: Tampere Aging Male Urologic Study

Juha Koskimäki,

The American Journal of Medicine (2008) 121, 592-596

Table 3 Incidence Rate Ratio of Moderate or Complete Erectile Dysfunction by Frequency of Intercourse and Morning Erections in Men Free of Moderate or Complete Erectile Dysfunction at Baseline, Adjusted for Age, Diabetes, Heart Disease, Hypertension, Cerebrovascular Disease, Depression, Body Mass Index, and Smoking

Determinant	Baseline (No. of Men)	Cases (No. of Cases)	Incidence (per 1000, 95% CI)	Incidence Rate Ratio (95% CI)
Frequency of intercourse (No. per week)				
<1	73	24	79 (53-117)	2.20 (1.27-3.79)
1	375	55	32 (24-41)	1 (reference)
2	223	21	20 (13-30)	0.61 (0.35-1.07)
≥3	129	10	16 (9-30)	0.63 (0.31-1.29)
				$P_{\text{trend}} < .001$
Frequency of morning erections (No. per week)				
<1	351	54	33 (25-43)	0.88 (0.57-1.38)
1	161	22	29 (19-45)	0.96 (0.55-1.67)
2-3	289	41	31 (22-41)	1 (reference)
Daily	84	12	31 (17-54)	1.04 (0.53-2.06)
				$P_{\text{trend}} = .52$
Overall	890	131	32 (27-38)	

Table 3 Suggested comprehensive general and specific lifestyle changes with clinical evidence to be included in sexual dysfunction guidelines and that could be utilized with or without conventional medicines by health care professionals and patients^a

<i>Lifestyle/health parameter</i>	<i>General recommendation for men</i>
Alcohol	Eliminate or reduce when dieting; otherwise, 1–2 standard drinks per day maximum
Calories (dietary)	Reduce by 100–600 calories day ⁻¹ according to weight-loss goals
Dairy	Low-fat and low-calorie dairy
Carbohydrates	Reduce simple sugars and increase consumption of complex carbohydrates including fiber (see below)
Cardiovascular risk markers	Review the overall numbers to achieve or maintain heart-healthy parameters (blood pressure, cholesterol, glucose, heart rate, C-reactive protein, etc.). Heart health = sexual health.
Exercise	Approximately 30 min minimum per day on average or at least 300–500 calories expended per daily physical activity. Resistance exercise should also occur 1–2 times a week.
Fat (dietary)	Reduce saturated fat to less than 10% calories, increase intake of monounsaturated and other healthy fat (omega-3 for example)
Fiber	20–30 g day ⁻¹ of a combination of soluble and insoluble fiber, or 15 g of fiber per 1000 kcal consumed per day
Fruits and vegetables	Several servings per day of whole fruits and vegetables (not processed)
Meat	Lean, game and grass-fed meats should be encouraged over high-saturated-fat meat, and moderate to minimal consumption should also be encouraged.
Medications (prescriptions and supplements)	Review the list on a regular basis to determine the impact on sexual health
Mental health (depression/stress/anxiety)	Awareness and discussion and evaluation on a regular basis
Nuts and seeds	Several servings a week (high in fiber, magnesium, potassium and healthy fats)
Omega-3 fatty acids	Consume healthy fatty fish at least twice a week and increase consumption of plant omega-3 (chia, flaxseed, soy, etc.)
Processed food	Choose unprocessed options when possible (whole fruit instead of juice, whole grain, etc.)
Protein consumption	0.8–1.0 g kg ⁻¹ of body weight; utilize low-calorie whey, casein, egg white or plant (soy, etc.) protein powders if needed
Sleep	A total of 6–8 h on average per night and become educated on specific sleep issues (apnea, nocturia, snoring, etc.)
Sodium (or potassium/sodium ratio)	Consume less than 2500 or 1500 mg day ⁻¹ if salt-sensitive or highly salt-sensitive; otherwise, choose foods with high potassium/sodium ratio (>2:1) (unsalted nuts, seeds, fruits, vegetables, etc.)
Tobacco (including cigars, smokeless and secondhand/passive)	Eliminate or educate on current cessation options
Weight and waist size	Maintain a healthy weight/waist, or a 5%–10% weight reduction over several years is associated with sexual and overall health improvements. Become educated on local weight-loss medical organizations and publications.

^a Discussion with a hospital, clinic or community nutritionist should also be encouraged, and a goal of reducing cardiovascular risk to as close to zero as possible with the primary care doctor or specialist should be discussed with each patient.

Sexual Activity, Erectile Dysfunction, and Incident Cardiovascular Events

Susan A. Hall

Am J Cardiol 2010;105:192–197

A low frequency of sexual activity (once a month or less vs >2 times weekly) was associated with increased risk of CVD (hazard ratio 1.45, 95% confidence interval 1.04 to 2.01).

In conclusion, our results suggest that a low frequency of sexual activity predicts CVD independently of ED and that screening for sexual activity might be

“COUNSELING”

STRATEGIE ALTERNATIVE

Modificazione fattori di rischio

Correzione ipogonadismo

Trattamento continuativo

Switch terapeutico

	Main benefits	Limitations
Questionnaires	Easy to administer, well tested, and validated. Assess presence and severity of erectile dysfunction	Do not define the cause of erectile dysfunction
Intracavernosal injection	Rapid and easy. Can assess severity of erectile dysfunction	Risk of prolonged erection, priapism, and faulty injection
Colour doppler ultrasound	Tested against a historical gold standard (pharmaco-arteriography) to diagnose arteriogenic erectile dysfunction. Might suggest other vascular disease (eg, coronary artery disease)	Less reliable in diagnosing venogenic erectile dysfunction. Incomplete smooth muscle relaxation due to anxiety or sympathetic overtone might lead to false-positive results. Redosing and retesting are frequently needed
Pharmaco-arteriography	Outlines arterial anatomy before arterial surgery in post-traumatic and congenital cases	Invasive. Affected by methodology and timing
Pharmaco-cavernosometry or cavernosography	Suggests venogenic erectile dysfunction. Delineates site of leak and cavernosal abnormalities	Moderately invasive. Incomplete smooth muscle relaxation due to anxiety or sympathetic overtone might lead to false-positive results
Neurological testing	Assess somatic pathways	Does not directly assess autonomic nerve function. No universally accepted and reproducible criteria. Complex and time consuming
Nocturnal penile tumescence testing	Closest to a gold standard in differentiating between psychogenic and organic erectile dysfunction	Nocturnal erections might be regulated by different pathways. Does not detect sensory deficit impotence. False-positive results can occur if patients do not sleep well. Physical disorders might alter nocturnal penile tumescence testing. Assesses only radial not axial rigidity. Does not correlate well with International Index of Erectile Function domain scores

Table 2: Uses and limitations of commonly used specific erectile dysfunction investigations

	Recommended treatment
Low risk (asymptomatic after moderate-intensity exercise): asymptomatic and less than three major risk factors—controlled hypertension, mild valvular disease, LVD (NYHA class I), and NYHA class II	Sexual activity can be continued and oral PDE5-Is can be given
Intermediate or indeterminate risk: asymptomatic and at least three coronary artery disease risk factors—mild stable angina pectoris, asymptomatic after MI (>6–8 weeks), moderate stable angina pectoris, MI for over 2 weeks but less than 6 weeks, LVD or CHF (NYHA class III) peripheral arterial disease, history of stroke, or transient ischaemic attack	In-depth cardiovascular assessment to re-categorise the patient is needed before treatment of erectile dysfunction
High risk: unstable or refractory angina, uncontrolled hypertension, CHF (NYHA class IV), recent MI (<2 weeks), high-risk arrhythmias, obstructive hypertrophic cardiomyopathies, or moderate-to-severe valve disease	Sexual activity stopped. Stabilise cardiovascular condition first then proceed to treatment for erectile dysfunction

MI=myocardial infarction. LVD=left ventricular disease. NYHA=New York heart classification. CHF=congestive heart failure. PDE5-Is= phosphodiesterase type 5 inhibitors. Adapted from Nehra and colleagues.⁴⁸

Table 1: Risk stratification and treatment of men with erectile dysfunction and cardiovascular disease

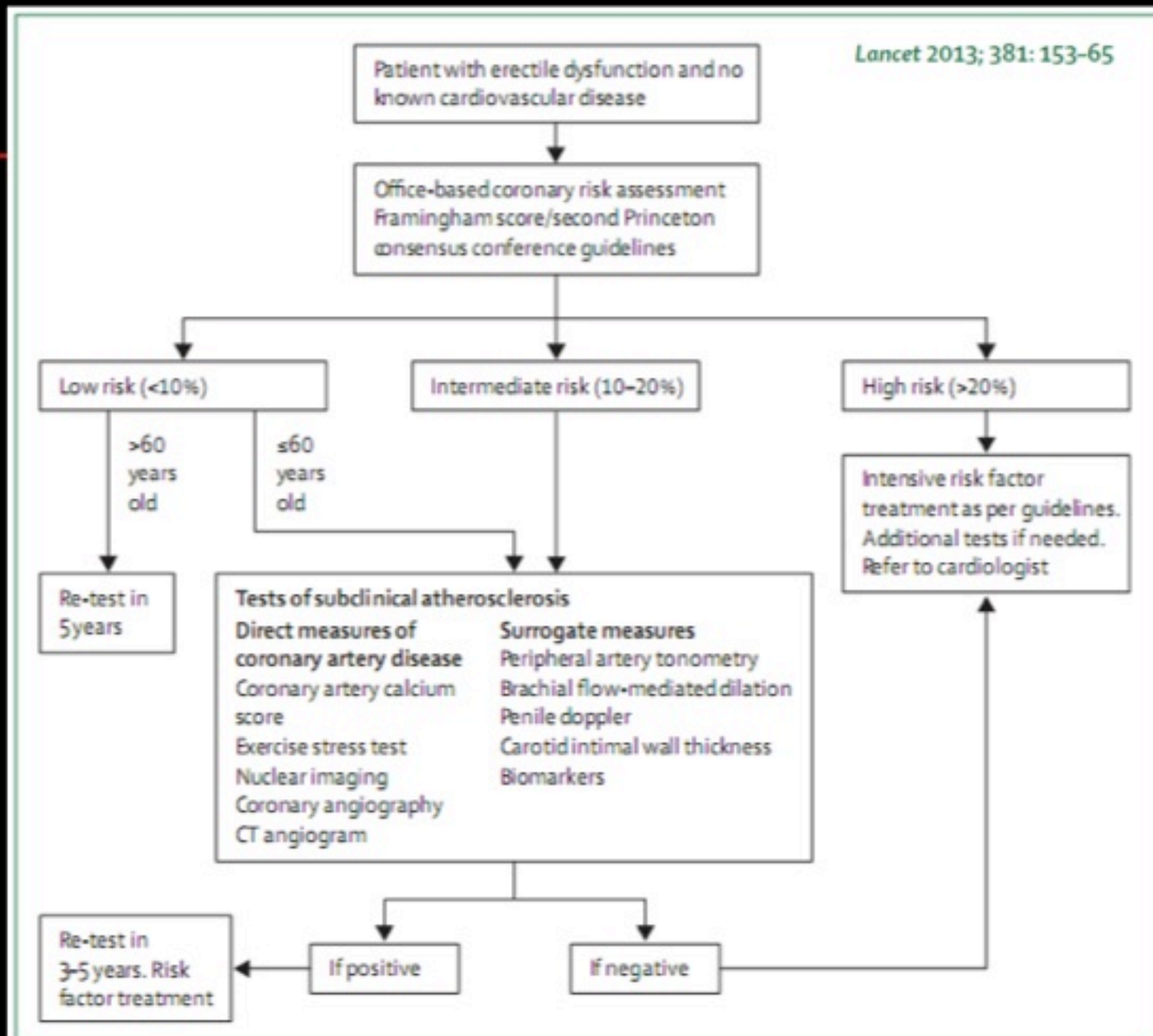


Figure 3: Algorithm for coronary risk assessment in erectile dysfunction



Lower urinary tract symptoms improve with testosterone replacement therapy in men with late-onset hypogonadism: 5-year prospective, observational and longitudinal registry study

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Mean IPSS at baseline was 10.35 ± 5.02 and decreased significantly with time after initiation of TU therapy (ANOVA $p < 0.05$). Mean IPSS between weight losers (L, $n = 186$) and non-losers (NL, $n = 68$) showed an erratic pattern with no statistical difference between the 2 groups (Fig. 1a). Furthermore, mean IPSS was not significantly altered by the use of vardenafil over the time course of the treatment (Fig. 1b).

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These results demonstrate that testosterone replacement in men with LOH alleviates symptoms of LUTS which is independent of the effects on weight or use of the PDE5i vardenafil. It remains to be seen whether preemptive



La letteratura



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The Effect of Androgen-replacement Therapy on Prostate Growth: A Systematic Review and Meta-analysis

*Yuanshan Cui, Yong Zhang**

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This meta-analysis shows that regardless of the administration method, neither short-term nor long-term ART increases the risk of prostate growth. Further high-quality, prospective studies are required to confirm this observation.

Is Testosterone Replacement Therapy in Males with Hypogonadism Cost-Effective? An Analysis in Sweden

J Sex Med **;***:**_**.

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In conclusion, the presented analyses indicate that the lifelong treatment with TU depot injection is a cost-effective treatment option for men diagnosed with hypogonadism in Sweden. The benefits of TRT outweigh the treatment costs, and long-term complications could be substantially reduced at an acceptable investment.

