Γνωρίζετε καλά τα φάρμακα της στύσης;

Ενα τεστ 12 ερωτήσεων για ειδικούς

Δημήτρης Χατζηχρήστου

Δ. Χατζηχρήστου

Δήλωση συμφερόντων

Ερευνητής / μέλος advisory board:

- GSK
- Lilly
- Medispec
- Menarini
- Donier

The Journal of Urology

Volume 168, Issue 2, August 2002, Pages 615–620

OLOGY: Original Articles

tic Steps In The Evaluation Of Patients With Erectile tion

ichristou, Konstantinos Hatzimouratidis, Michael Bekas, Apostolos Apostolidis, Vasilios tantinos Yannakoyorgos

Table 3.
Evaluation of diagnostic potential of basic evaluation tests

	% Diagnostic Potential	
Tests	Stepwise	Total
Medical, sexual history	57	57
Laboratory evaluation	6.2	63.2
Physical examination	13.9	77.1
Intracavernous injection	2.6	79.7

Table op

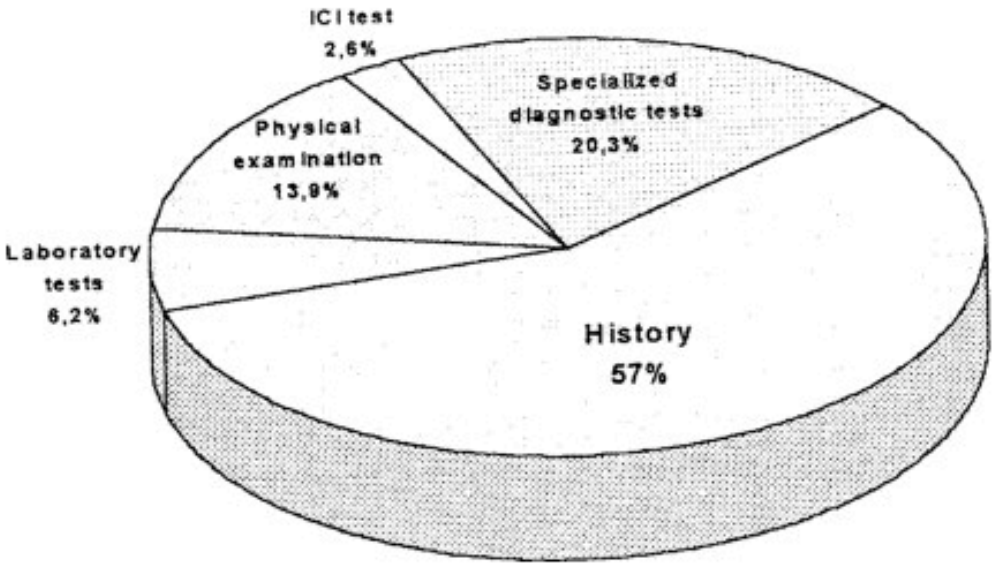


Fig. 4.
Diagnostic potential of each diagnostic step. *ICI*, intracavernous injection

Figure op

ΘΕΡΑΠΕΙΕΣ
ΣΤΥΤΙΚΗΣ ΔΥΣΛΕΙΤΟΥΡΓΙΑΣ

Τα κάτω...**πάνω!**

ΙΝΣΤΙΤΟΥΤΟ ΜΕΛΕΤΗΣ ΟΥΡΟΛΟΓΙΚΩΝ ΠΑΘΗΣΕΩΝ

ΚΕΝΤΡΟ ΣΕΞΟΥΑΛΙΚΗΣ ΚΑΙ ΑΝΑΠΑΡΑΓΩΓΙΚΗΣ ΥΓΕΙΑΣ

ΤΑ ΦΑΡΜΑΚΑ ΤΗΣ ΣΤΥΣΗΣ

Κανένα φυτικό σκεύασμα ή συμπλήρωμα διατροφής δεν έχει αποδείξει ότι βοηθά τη στύση!

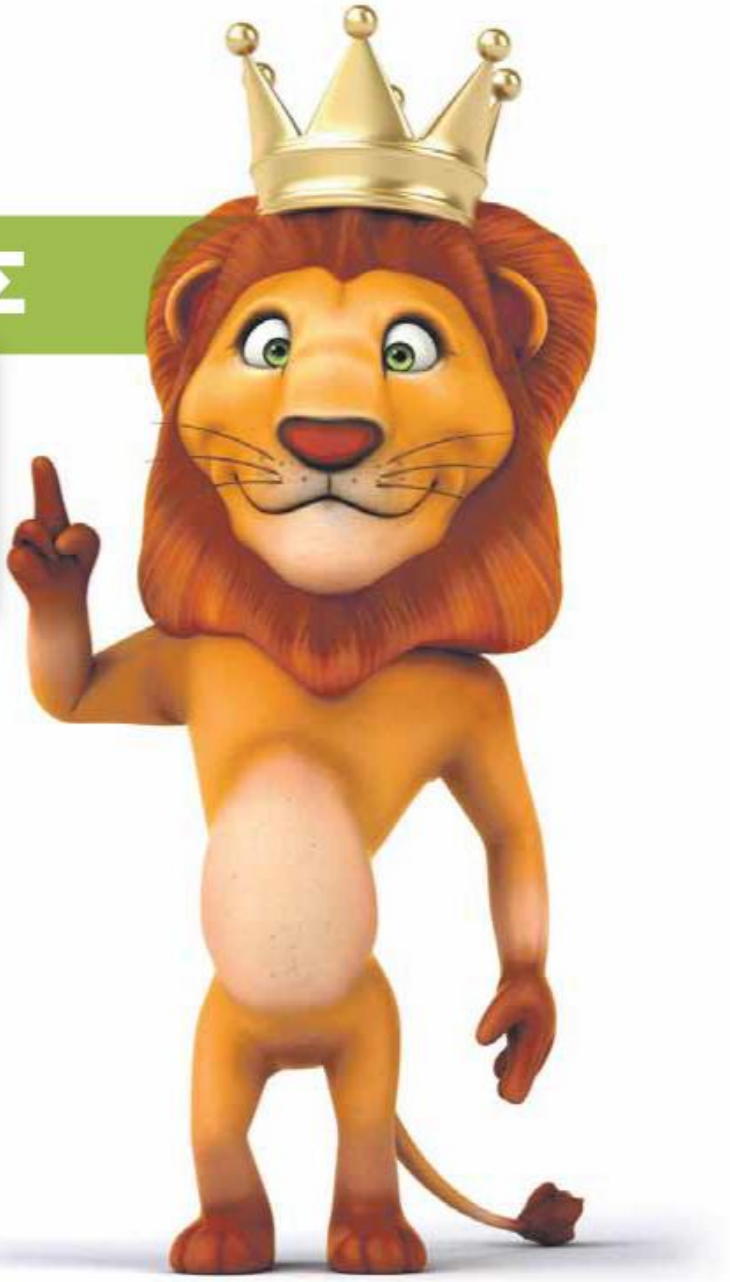
Όλα τα αποτελεσματικά φάρμακα χορηγούνται με ιατρική συνταγή.

Η μόνη ένδειξη είναι στυτική δυσλειτουργία οργανικής και ψυχογενούς αιτιολογίας. Στη 2η περίπτωση συνδυάζεται με θεραπεία από σεξολόγο

Κανένα από αυτά δεν είναι αφροδισιακό, δηλαδή δεν επηρεάζει την ερωτική διάθεση/ επιθυμία

Όλα τα φάρμακα προκαλούν αγγειοδιαστολή και αύξηση της αιμάτωσης του πέους

Χωρίζονται σε 2 κατηγορίες: σε χάπια και ενέσεις



ΤΑ ΦΑΡΜΑΚΑ ΑΠΟ ΤΟ ΣΤΟΜΑ

ΔΙΑΤΙΘΕΝΤΑΙ ΣΤΗΝ ΕΛΛΑΔΑ

(όλα είναι σε μορφή δισκίου για λήψη από το στόμα)

- **ΑΒΑΝΑΦΙΛΗ**
- **ΒΑΡΔΕΝΑΦΙΛΗ**
- **ΣΙΛΔΕΝΑΦΙΛΗ** → κυκλοφορεί και σε μορφή διαλυόμενου, στο στόμα, δισκίου 10mg
- **ΤΑΔΑΛΑΦΙΛΗ** → κυκλοφορεί και σε 5mg δόση για καθημερινή λήψη ανεξάρτητα από την επαφή

Η ΜΟΡΦΗ ΑΥΤΗ ΕΧΕΙ **2 ΕΝΔΕΙΞΕΙΣ**

άντρες με συχνές ερωτικές επαφές

μεγαλύτεροι άντρες που πάσχουν και από καλοήθη υπερπλασία προστάτη (η συχνότερη αιτία για προβλήματα ούρησης μετά τα 50 έτη).

! Είναι απαραίτητη η **ΕΡΩΤΙΚΗ ΕΠΙΘΥΜΙΑ** για να προκληθεί στύση

ΑΠΟΤΕΛΕΣΜΑΤΙΚΟΤΗΤΑ

70% ενώ **ΜΕΙΩΝΕΤΑΙ** σε 50%

σε άντρες με σοβαρό οργανικό πρόβλημα

(σακχαρώδης διαβήτης, νευρολογικές παθήσεις, μετά ριζική προστατεκτομή)

ΑΠΟΛΥΤΗ ΑΝΤΕΝΔΕΙΞΗ

Η ΛΗΨΗ ΝΙΤΡΩΔΩΝ ΦΑΡΜΑΚΩΝ

ΣΥΝΗΘΕΙΣ ΠΑΡΕΝΕΡΓΕΙΕΣ

ΠΟΝΟΚΕΦΑΛΟΣ
ΔΥΣΠΕΨΙΑ
ΜΥΑΛΓΙΑ

ΠΩΣ ΕΠΗΡΕΑΖΕΙ Η ΤΡΟΦΗ...

Η τροφή καθυστερεί την απορρόφηση, άρα και την δράση στα δισκία για λήψη από το στόμα, εκτός της ταδαλαφίλης.

Τα δισκία που διαλύονται στο στόμα δεν επηρεάζονται

Η κοινωνική χρήση **αλκοόλ ΔΕΝ ΕΠΗΡΕΑΖΕΙ** τη δράση τους

ΧΑΡΑΚΤΗΡΙΣΤΙΚΑ ΤΩΝ ΦΑΡΜΑΚΩΝ ΤΗΣ ΣΤΥΣΗΣ

	ΑΒΑΝΑΦΙΛΗ	ΒΑΡΔΕΝΑΦΙΛΗ	ΣΙΛΔΕΝΑΦΙΛΗ	ΤΑΔΑΛΑΦΙΛΗ	ΑΛΠΡΟΣΤΑΔΙΛΗ
ΤΡΟΠΟΣ ΛΗΨΗΣ	Από το στόμα	Από το στόμα ή διαλυόμενα δίσκια στο στόμα	Από το στόμα	Από το στόμα	Ενεση στο πέος
ΟΣΟΛΟΓΙΑ	mg 100 & 200	mg 10 & 20	mg 25 50 & 100	mg 5 10 & 20	μg 20
ΙΣΤΗ συνήθης **ηγούμενη δόση ρησίως** (σε mg)	mg 200	mg 20	mg 100	mg 20	μg 40
ήθης χρόνος λήψη **μέχρι ράσει** (σε ώρες)	ώρες περίπου 0,5	ώρες περίπου 1	ώρες περίπου 1	ώρες 1-2	ώρες 0,2
ήθης **διάρκεια σης** από λήψη ώρες)	>6	6 έως 12	6 έως 12	έως 36	1 έως 2
άζεται **σεξου-ός ερεθισμός;**	ΝΑΙ	ΝΑΙ	ΝΑΙ	ΝΑΙ	**ΟΧΙ**

Η: Hatzichristou D. Erectile Dysfunction. In V. Mirone: Uroandrology, Springer, 2014

6+8
ερωτήσεις

ΕΡΩΤΗΣΕΙΣ

Ερώτηση 1

Γιατί μόνο 1 στους 10 ασθενείς με πρόβλημα στύσης μιλάνε σε γιατρό για το πρόβλημα;

Το πρόβλημα της περιορισμένης αναζήτησης θεραπείας για ΣΔ

- Πολλοί ασθενείς δεν αισθάνονται άνετα να αναζητήσουν θεραπεία
- Η ΣΔ δεν σχετίζεται πάντα με αυξημένη δυσαρέσκεια του ασθενή*
- **Μήνυμα προς το ασθενή (TALK)**

Talk	**Εμπιστευθείτε το γιατρό σας**
Ask	**Ρωτήστε για το σεξουαλικό σας πρόβλημα**
Learn	**Μάθετε για τις θεραπευτικές επιλογές**
Keep	**Κρατήστε στην σύντροφο σας σύμμαχο**

*Evangelia N, Kirana PS, Chiu G et al. (2010) Level of bother and treatment---seeking predictors amor
male and female in---patients with sexual problems: a hospital--- based study. J Sex Med 7:700---711.

l. 2006 Jan;3(1):47-55.

ting physicians to treat erectile dysfunction patients: development and evaluation of a course on unication and management strategies.

adis L[1], Papaharitou S, Salpiggidis G, Tsimtsiou Z, Nakopoulou E, Kirana PS, Moisidis K, Hatzichristou D.

or information

ct

SE: To describe the development and assess the outcome of a workshop on erectile dysfunction (ED) management based on particip ns evaluations.

D: The study involved physicians who attended a workshop offered throughout the country, during a 3-year period. The workshop incl video-based dramatizations, and role-play sessions. A pilot study investigated the workshop's impact on physicians' attitudes toward ness and sexual behavior issues; Patient-Practitioner Orientation Scale (PPOS) and Cross Cultural Attitude Scale (CCAS) were adm nd after the course. New knowledge acquisition, quality of presentation, and workshop's usefulness in their clinical practice were the ns used for workshop's evaluation. Analysis used quantitative and qualitative methods.

S: A total of 194 questionnaires were administered during the pilot study and the response rate was 53.6%. A shift in attitudes toward ness and less judgmental attitude toward patients' sexual attitudes were revealed (total PPOS score and Sharing subscale: $P < 0.05$ 1). Six hundred physicians were asked to evaluate the workshops and the response rate was 62.3%. The tutorial session for "medica t of ED" ($P < 0.001$) and the role-play on sexual history taking ($P < 0.05$) received higher evaluation scores. Qualitative analysis show frequently reported category referred to the appropriateness of role-play as a teaching and awareness-raising technique (31.25%); a ges in clinical practice and communication patterns was identified by 20% of the participants who stressed the necessity for multidisci n, as well as the adoption of a nonjudgmental attitude toward patients.

USION: Training courses on ED management, using a combination of tutorial and interactive sessions, constitute an effective way of ge, enhancing physicians' communication skills with ED patients, and influencing attitudes toward patient-centeredness in sexual issu sults strongly support the establishment of sexual medicine courses at continuing medical education curricula.

Συζητώντας στο ιατρείο για την Στυτική Δυσλειτουργία

- Τα σεξουαλικά προβλήματα υγείας συχνά παραμελούνται στην κλινική πράξη
- Οι ασθενείς αισθάνονται αμηχανία και ότι οι γιατροί δεν έχουν την ειδίκευση για να διαχειριστούν το πρόβλημα τους
- Οι γιατροί διστάζουν να ρωτήσουν, έχουν περιορισμένο χρόνο και έτσι αυξάνεται το χάσμα μεταξύ σεξουαλικής ιατρικής και κλινικών δεξιοτήτων.

Προϋποθέσεις που πρέπει να δημιουργήσει ο γιατρός:

- Δημιουργείστε μια ατμόσφαιρα ασφάλειας και σεβασμού
- Η συζήτηση να είναι πολιτισμένη
- Σεβαστείτε τις σεξουαλικές προτιμήσεις του κάθε ατόμου
- Παρουσιάστε τεκμηριωμένα τις θεραπευτικές επιλογές
- Οργανώστε μια στενή παρακολούθηση

Athanasiadis L, Papaharitou S, Salpiggidis G et al. (2006) Educating physicians to treat erectile dysfunction patients: development and evaluation of a course on communication and management strategies. J Sex Med
Hatzichristou D, Rosen RC, Derogatis LR et al. (2010) Recommendations for the clinical evaluation of men and women with sexual dysfunction. J Sex

ΕΡΩΤΗΣΕΙΣ

Ερώτηση 2

Τι πρέπει να καθορίσουμε μετά τη διάγνωση της στυτικής δυσλειτουργίας;

Καθορισμός σοβαρότητας της Στυτικής Δυσλειτουργίας

Δύο βασικές ερωτήσεις:

- Είστε σε θέση να επιτύχετε μια στύση σκληρή ώστε να επιτευχθεί η διείσδυση;
- Είστε σε θέση να διατηρήσετε την στύση αυτή μέχρι της εκσπερμάτιση;

Βαρύτητα

- **Ήπια:** Υπάρχουν σεξουαλικές επαφές πάνω από τις μισές φορές, αδυναμία επίτευξης πολύ σκληρής στύσης
- **Μέτρια:** Ανεπαρκή σκληρότητα και/ή διατήρηση, διείσδυση με βοήθεια κάποιες φορές.
- **Σοβαρή:** Δεν είναι δυνατή η σεξουαλική επαφή λόγω της ποιότητας των στύσεων

Hatzimouratidis K, Amar E, Eardley I et al. (2010) Guidelines on male sexual dysfunction: erectile dysfunction and premature ejaculation. Eur Urol

Οργανικά αίτια στυτικής δυσλειτουργίας
Ανατομικά/Τραύμα • Μέγεθος (μικροφαλία /πεεκτομή) • Φίμωση • Συγγενής κάμψη του πέους • Νόσος Peyronie
Αγγειακά • Αρτηριακά • Μηχανισμού φλεβικής σύγκλεισης • Μικτά
Ορμονικά
Νευρογενή • Κεντρικά • Περιφερικά
Από φάρμακα
Άλλα (π.χ. αιματολογικά νοσήματα / πριαπισμός)

Η δύσκολη πρώτη επίσκεψη

1. Προσδιορίστε το σεξουαλικό πρόβλημα
2. Διάρκεια και σοβαρότητα της ΣΔ
3. Συνύπαρξη άλλων σεξουαλικών προβλημάτων
4. Καθορισμός της ποιότητας της στύσης
5. Κλινική εξέταση
6. Εργαστηριακός έλεγχος
7. Αξιολόγηση αποτελεσμάτων / Εκπαίδευση

ΕΡΩΤΗΣΕΙΣ

Ερώτηση 3

Γνωρίζετε την

φαρμακολογία των PDE5i;

ΦΑΡΜΑΚΟΛΟΓΙΚΑ ΧΑΡΑΚΤΗΡΙΣΤΙΚΑ ΑΝΑΣΤΟΛΕΩΝ PDE5

ΠΑΡΑΜΕΤΡΟΙ	ΣΙΛΔΕΝΑΦΙΛΗ 100 mg	ΤΑΔΑΛΑΦΙΛΗ 200 mg	ΒΑΡΔΕΝΑΦΙΛΗ 20 mg	ΑΦΑΝΑΦΙΛΗ 200 mg	ΟΥΝΤΕΝΑΦΙΛΗ 200 mg
Cmax	560 μg/L	378 μg/L	18.7 μg/L	2920 μg/L	1139 μg/L
Tmax	0.8-1 h	2 h	0.9 h	45 min	1 h
T1/2	2.6-3.7 h	17.5 h	3.9 h	5.1 h	11 – 13 h
AUC	1685 μg.h/L	8066 μg.h/L	56.8 μg.h/L	8490 μg.h/L	7898 μg.h/L
Πρωτεϊνική δέσμευση	96%	94%	94%	99%	94%
Βιοδια-θεσιμότητα	41%	NA	15%	NA	NA

Έναρξη της δράσης

Παρόλο που κάποιοι ασθενείς θα ανταποκριθούν σε 15’, χρειάζονται 30’ για να ανταποκριθεί το 50% των ασθενών.

Διάρκεια της δράσης

- Σιλδεναφίλη και βαρδεναφίλη: 6-12 h
- Αβαναφίλη: >6 h
- Ταδαναφίλη: έως 36 h

Τρόφιμα και αλκοόλ: αλληλεπιδράσεις

Σιλδεναφίλη και βαρδεναφίλη: Καθυστέρηση της Τ και μείωση Cmax
Ταδαλαφίλη,αβαναφίλη, βαρδεναφίλη/σιλδεναφιλη ODT: Δεν επηρεάζεται

Αποτελεσματικότητα των PDE5i

- Είναι ιδιαίτερα αποτελεσματικά φάρμακα (περίπου 75% των χρηστών απαντούν **ναι στο SEP3**)
- Η αποτελεσματικότητα είναι δοσοεξαρτώμενη
- Οι ασθενείς με μακροχρόνιο σακχαρώδη διαβήτη, μετά από ριζική και με νευρολογικές νόσου αποτελούν ειδικές κατηγορίες με ανταπόκριση μέχρι 50%

Κατ' επίκληση ή καθημερινή λήψη;

- Η καθημερινή λήψη φαίνεται να έχει καλύτερα αποτελέσματα για επιτυχή συνουσία σε σύγκριση με την κατ' επίκληση λήψη ταδαναφίλης
- Η ημερήσια δοσολογία είναι καλά ανεκτή
- Σε ζευγάρια με συχνές σεξουαλικές επαφές που επιθυμούν αυθορμητισμό

- McMahon C (2005) Comparison of efficacy, safety and tolerability of on---demand tadalafilb and daily dosed tadalafil for the treatment of erectile dysfunction. J Sex Med
- Rajfer J, Aliotta PJ, Steidle CP et al. (2007) Tadalafil dosed once a day in men with erectile dysfunction: a randomized, double---blind, placebo---controlled study in the US. Int J Impot Res

Ασθενείς με Σακχαρώδη Διαβήτη

- Η παθοφυσιολογία είναι πολυπαραγοντική
- Η αποτελεσματικότητα είναι μέτρια, δεν επηρεάζονται τα επίπεδα σακχάρου
- Βελτίωση αποτελεσματικότητας: Ρύθμιση επιπέδων γλυκόζης αίματος και συνοδών νοσημάτων

Ασθενείς με ριζική προστατεκτομή

- Η παθοφυσιολογία είναι πολυπαραγοντική
- Αξιολόγηση της στυτικής ικανότητας πριν το χειρουργείο
- PDE5i μετεγχειρητικά (Tadanafil 5mg καλύτερα αποτελέσματα) Ενημέρωση για τις δυσκολίες αποκατάστασης

Ασθενείς με νευρολογικά νοσήματα

- Περιορισμένα στοιχεία για αποτελεσματικότητα & ασφάλεια
- Sildenafil: Αποτελεσματική σε ασθενείς με Parkinson και MS
- Sildenafil: Σε ασθενείς με πολλαπλή συστηματική ατροφία παρατηρείται σοβαρή υπόταση

ΕΡΩΤΗΣΕΙΣ

Ερώτηση 4

Ποιον PDE5i προτιμούν οι ασθενείς;

Προτίμηση PDE5i

- Διακοπή περίπου στο 50%
- Οι μεγαλύτεροι σε ηλικία άνδρες με λίγες επαφές τείνουν να προτιμούν σιλδεναφίλη και βαρδεναφίλη ενώ οι νεότεροι ταδαλαφίλη καθημερινής λήψης
- Η επιλογή PDE5i θα πρέπει να είναι συνάρτηση της συχνότητας επαφών και της ανάγκης για αυθορμητισμό
- Δυνατότητα στον ασθενή να δοκιμάσει όλους τους PDE5 ώστε να επιλέξει ποιος ανταποκρίνεται στις ανάγκες του
- Ασθενείς που δοκίμασαν όλους του PDE5i: συνέχιση χρήσης στα 3 χρόνια σε ποσοστό 86%.

- Hatzimouratidis K, Hatzichristou DG (2009) Phosphodiesterase type 5 inhibitors: unmet needs. Curr Pharm Des
- Ljunggren C, Hedelin H, Salomonsson K et al. (2008) Giving patients with erectile dysfunction the opportunity to try all three available phosphodiesterase type 5 inhibitors contributes to better long---term treatment compliance. J Sex Med

ract. 2014 Sep;68(9):1087-99. doi: 10.1111/ijcp.12449. Epub 2014 Aug 14.

uation and effectiveness of tadalafil once daily during a 6-month observational study in erectile ction: the EDATE study.

Hatzichristou D, Boess FG, Büttner H, Gehchan N, Henneges C, Porst H.

Table 4 Reasons for discontinuation of tadalafil OaD treatment

	Number (%) of patients		
	PDE5-I naïve *N* = 510	PDE5-I pretreated *N* = 267	Overall *N* = 778*
Discontinued TAD-OaD†	71 (100.0)	36 (100.0)	107 (100.0
Reasons			
Lack of efficacy (hardness of erection)	18 (25.4)	15 (41.7)	33 (30.8)
Adverse event	16 (22.5)	6 (16.7)	22 (20.6)
Cost of medication	12 (16.9)	4 (11.1)	16 (15.0)
Did not want to take a pill every day	7 (9.9)	5 (13.9)	12 (11.2)
Patient discontinued study	8 (11.3)	1 (2.8)	9 (8.4)
Partner's request	3 (4.2)	2 (5.6)	5 (4.7)
Felt that medication controlled his sexual life	3 (4.2)	0	3 (2.8)
Slow onset of action	3 (4.2)	0	3 (2.8)
Lack of efficacy (duration of erection)	0	2 (5.6)	2 (1.9)
Lack of confidence in medication	0	1 (2.8)	1 (0.9)
Non-desired spontaneous erections	1 (1.4)	0	1 (0.9)

*For one patient, previous PDE5-I treatment status was unknown. †Includes all patients with documented end date of tadalafil OaD treatment, irrespective if the patient completed or discontinued the study. *N*, number of patients; OaD, once a day; PDE5-I, phosphodiesterase type 5 inhibitor; TAD, tadalafil.

ract. 2014 Sep;68(9):1087-99. doi: 10.1111/ijcp.12449. Epub 2014 Aug 14.

uation and effectiveness of tadalafil once daily during a 6-month observational study in erectile ction: the EDATE study.

Hatzichristou D, Boess FG, Büttner H, Gehchan N, Henneges C, Porst H.

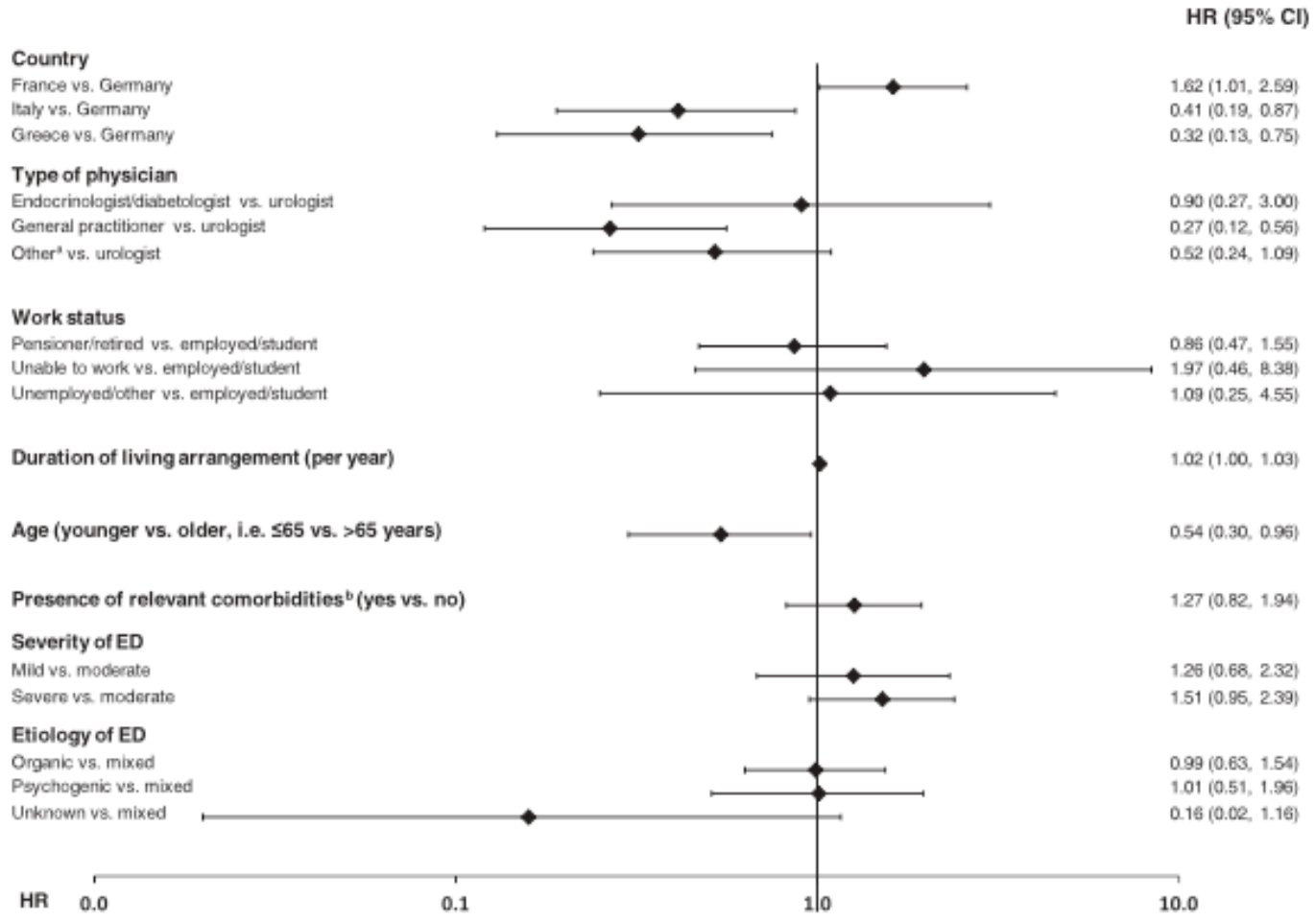


Figure 3 Factors associated with time to discontinuation of tadalafil OaD treatment (Cox proportional hazards mod patients included in model). Model goodness of fit (AIC): 1267.347. AIC, akaike information criterion; CI, confiden interval; ED, erectile dysfunction; HR, hazard ratio; OaD, once a day. [a]'other' includes: sexual medicine specialist, cardiologist, psychiatrist or other specialty. [b]Based on presence or absence of ≥ 1 of the following pre-existing condi hypertension, dyslipidaemia, diabetes, benign prostate hyperplasia, cardiovascular disease.

ract. 2014 Sep;68(9):1087-99. doi: 10.1111/ijcp.12449. Epub 2014 Aug 14.

uation and effectiveness of tadalafil once daily during a 6-month observational study in erectile ction: the EDATE study.

Hatzichristou D, Boess FG, Büttner H, Gehchan N, Henneges C, Porst H.

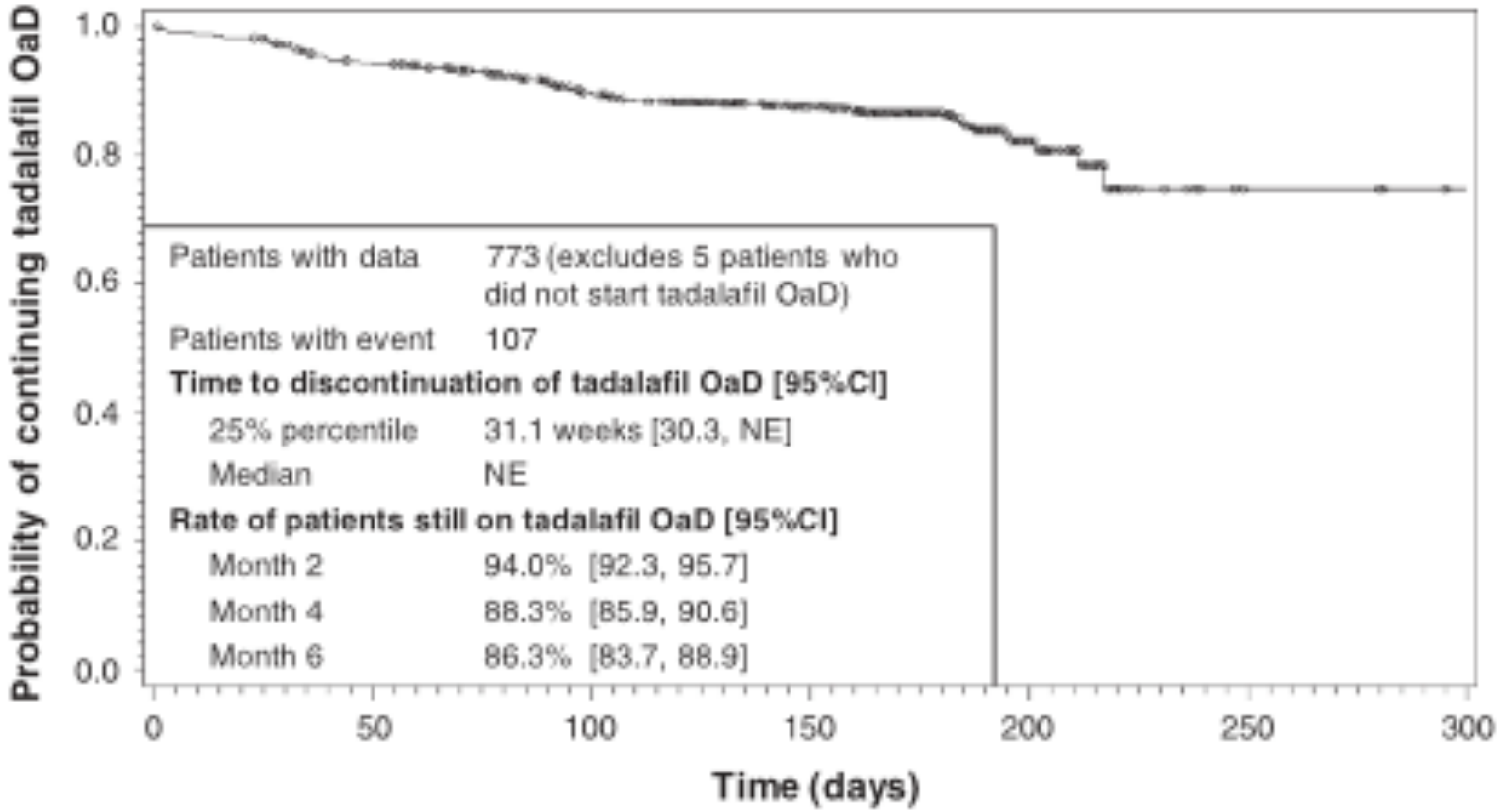


Figure 2 Kaplan–Meier estimation for time to discontinuation of tadalafil OaD treatment. CI, confidence interval; NE, estimable; OaD, once a day.

ΕΡΩΤΗΣΕΙΣ

Ερώτηση 5

Πως χειρίζεστε ασθενείς που δεν απαντούν στους PDE5i;

International Journal of Impotence Research (2004) 16, 207–213

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ffectiveness' scale—therapeutic outcome of pharmacologic ies for ED: an international consensus panel report

, F Giuliano[2], I Goldstein[3], D Hatzichristou[4], W Hellstrom[5], T Lue[6], F Montorsi[7], R Munarriz[3]*, H Porst[9] and R Rosen[10]

Clinical trials in ED are generally characterized by:

- Motivated patients, with a high degree of compliance in treatment administration and reporting of results.
- Rigorous criteria for inclusion/exclusion, administration and evaluation.
- Narrow emphasis on measurable results from the specific treatment under study.

In contrast, clinical practice of ED is characterized by:

- Differing expectations and motivation for treatment.
- Variability among patients in medical and psychological comorbidities, degree of compliance and consistency of reported results.
- A broad range of possible approaches for managing ED (including counseling and other first- or second-line therapies).

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omplete response This term describes consistent achievement and maintenance f full erection with the ability to engage and complete sexual intercourse. Such rectile response for ED patients is synonymous with 'complete or nearly complete emission of all symptoms'.

he panel agreed that complete response should include the patient's ability to lerate side effects, without necessarily including the use of concomitant edication for side-effect relief, if any, at the clinically effective dose. Side-effect rofiles in this category would not be expected to interfere significantly with the atient's functioning.

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Partial response This category is regarded as the most difficult to define, and also likely to include a large proportion of patients. As with the discussion of complete response, the possibility of basing the definition of partial response o specific scale scores was considered, although a broader definition was selecte There was general agreement that *partial response* refers to a degree of sympt improvement and/or partial remission of symptoms, as described below

1. Achievement of a degree of erection that is clearly discernible, but not adequate for intercourse or complete, or
2. Ability to achieve full erection, but not on a consistent basis over time.
3. Ability to achieve full erection, which is not maintained until completion o intercourse on a consistent basis.

The role of side effects in defining partial response was considered. The panel included in the definition of a partial responder any patient for whom treatment efficacy was adequate, but who was bothered by the side effects of treatment. effects were deemed in this case to be, significantly interfering with patient's u the treatment.

Patients who had adequate efficacy with a given agent or dose, but were reluct to use the drug due to bothersome side effects of treatment (eg, headache, dyspepsia) were defined as having a partial response to treatment.

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NONRESPONDERS: definitio

ny patient who, after four successive or closely timed trials of the maximu
erated dose of the medication, in accordance with the regulatory agency's
idelines with respect to timing relative to meals, alcohol ingestion, use of
ncomitant medications and adequate sexual stimulation, is unable to achie
sustain adequate penile rigidity until completion of sexual performance".

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Nonresponse This category is relatively straightforward in cases in which treatment fails to produce an ability to achieve and maintain adequate erection for sexual activity, including either slight improvement that makes no clinical difference or results in the patient's status as unchanged/worse.

The panel proposed adding to the nonresponder category patients whose burden of side effects outweighes their therapeutic gain.

Nonresponders, in general:

- Fail to respond in a clinically significant manner to the treatment,
- Experience intolerable side effects at any dosage or
- Cannot be titrated to a dose that would produce a response, due to intolerable side effects associated with treatment.

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Treatment response: this dimension refers to pharmacologically based (ie, *response-based*) aspects, including both treatment efficacy and tolerability (side effects). These effects are typically self-reported by the patient and serve as surrogate end points for objective, physiological changes in penile firmness or rigidity. The 'therapeutic index' has previously been reported as a summary measure of this variable.

Treatment satisfaction: this includes both patient and partner subjective responses and overall satisfaction with treatment. Treatment satisfaction may be assessed by means of interview or self-report questionnaires.

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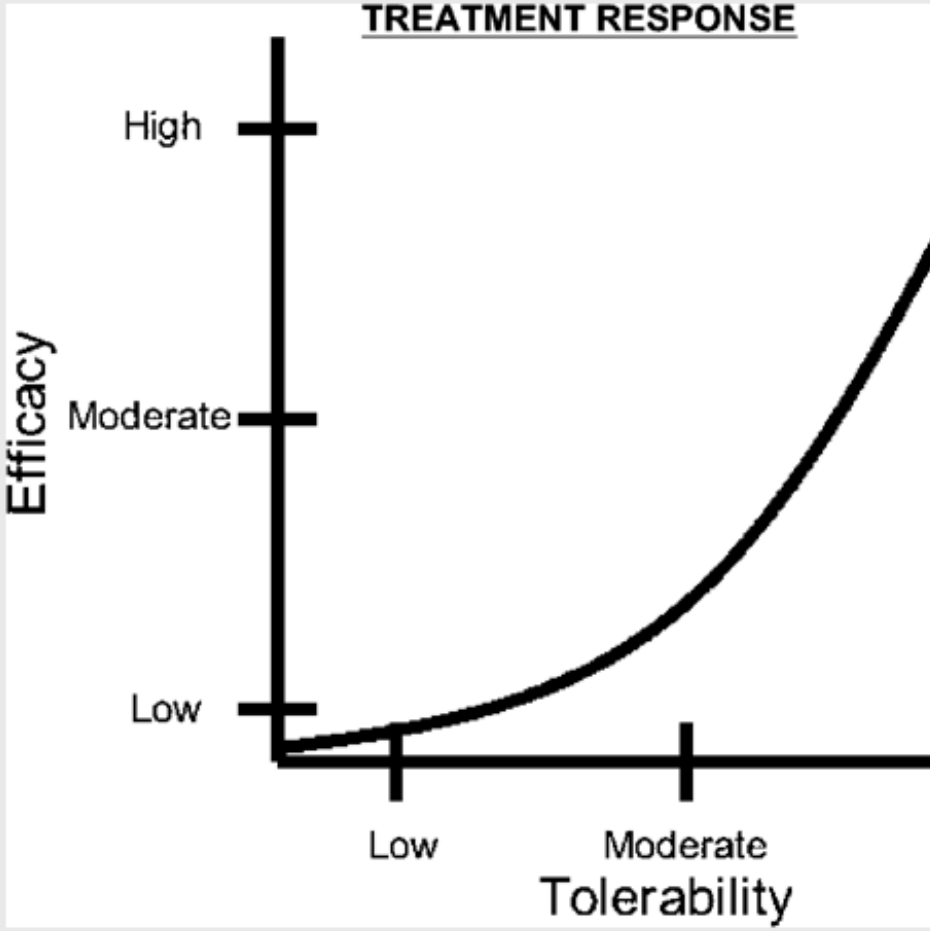

Ασθενείς που δεν ανταποκρίνονται στους PDE5i

Αίτια μη ανταπόκρισης

- Μη σωστή λήψη του φαρμάκου
- Προβλήματα ψυχολογικά και σχέσης
- Σεξουαλική δυσλειτουργία της συντρόφου
- Σοβαρή οργανική στυτική δυσλειτουργία

Urology

Volume 60, Issue 2, Supplement 2, August 2002, Pages 28–38

ving treatment optimization with sildenafil citrate a®) in patients with erectile dysfunction[1]

McCullough · [a], James H Barada[b], Ahmed Fawzy[c], Andre T Guay[d], Dimitrios Hatzichristou[e]

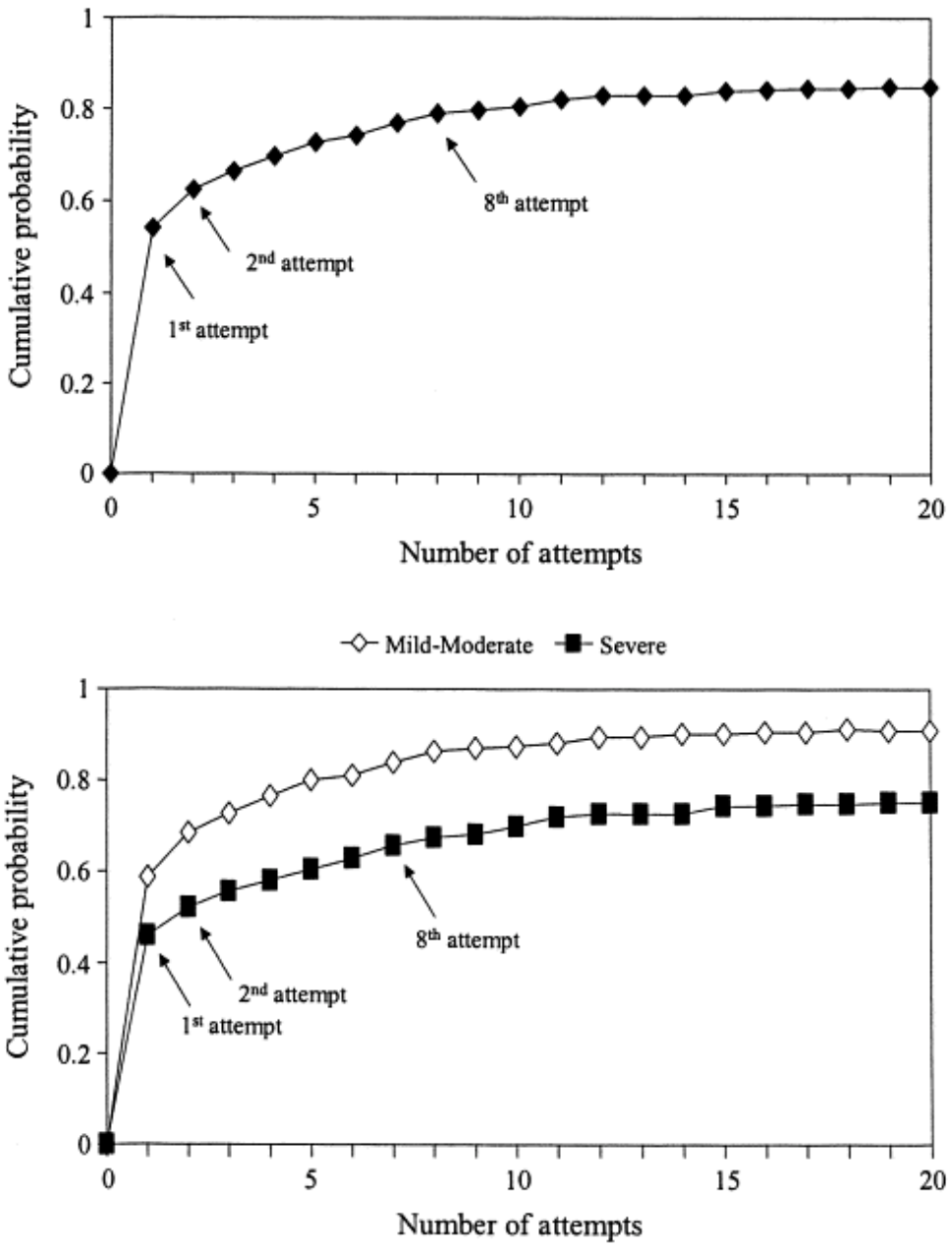

FIGURE 2.
Intercourse success rates, as determined from event log data, in men with erectile dysfunction sildenafil (*top*). Intercourse success rates in men stratified by erectile dysfunction severity (*bot*

Urology

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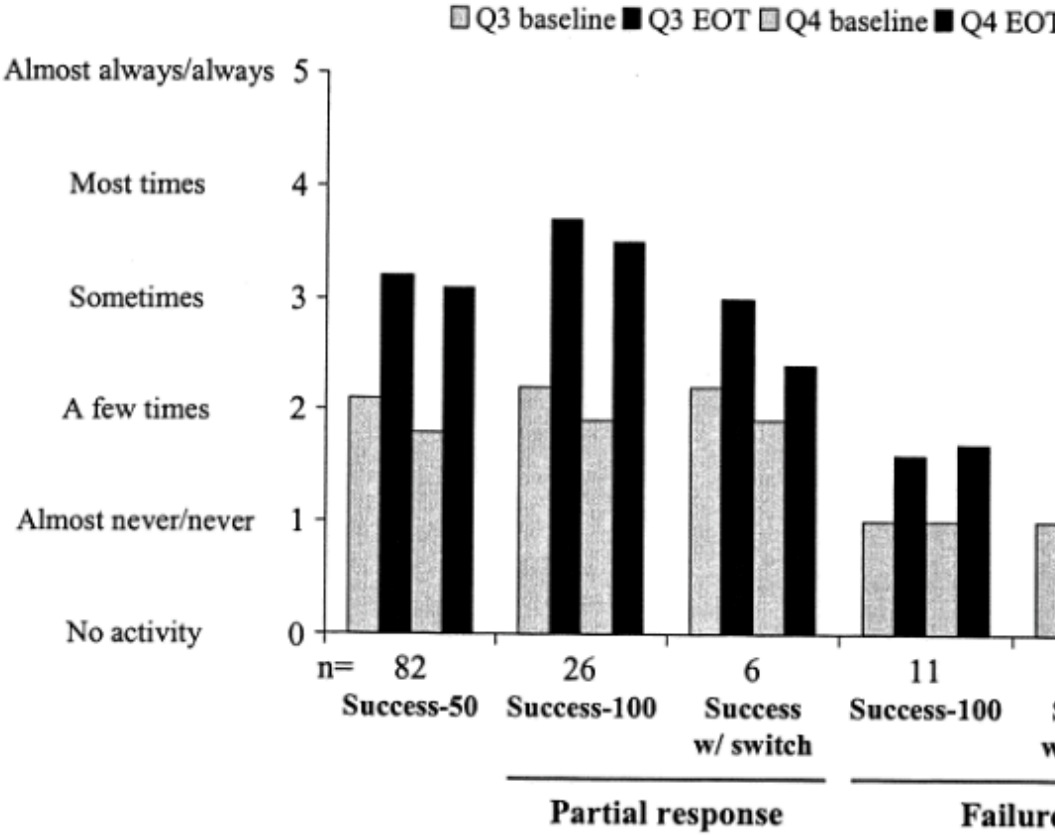

FIGURE 4.

Efficacy results in a disease management program. Baseline and end-of-treatment (EOT) score International Index of Erectile Function question (Q)3 and Q4. EOT scores are patient response Q4 at the stage they reached "success" (ie, 50 mg sildenafil, 100 mg sildenafil, switch to another modality).

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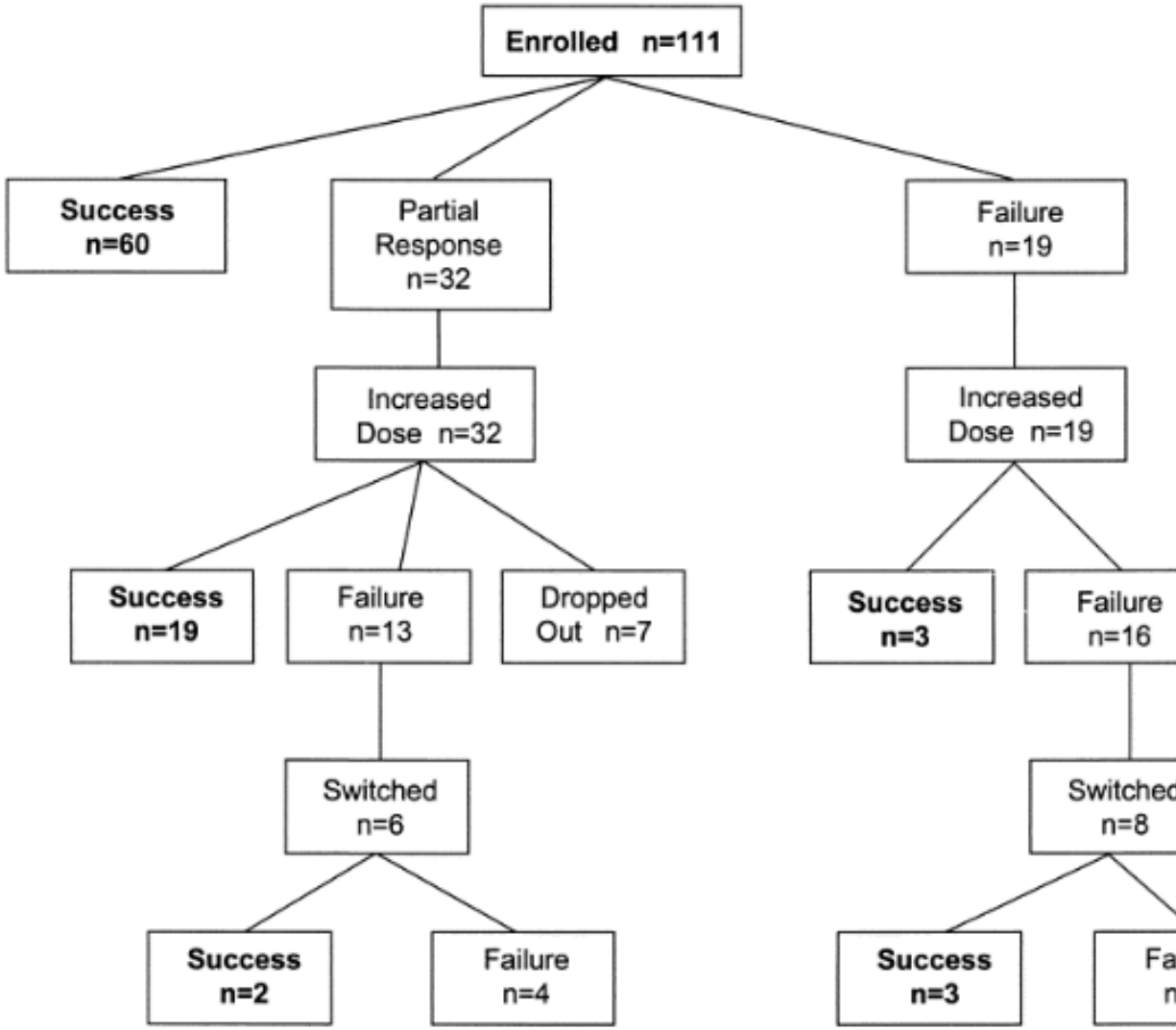

FIGURE 3.
Patient disposition in a disease management program.

International Journal of Impotence Research (2002) 14, Suppl 1, S43–S52
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denafil citrate: lessons learned from 3 years of clinical experie

Hatzichristou[1]*

ble 2 Essential aspects in managing patients with erect
sfunction: the 'FAST' acronym

low-up of patients
justment of dosing
xual stimulation
ration to the maximum tolerated dose

European Urology

Volume 47, Issue 4, April 2005, Pages 518–523

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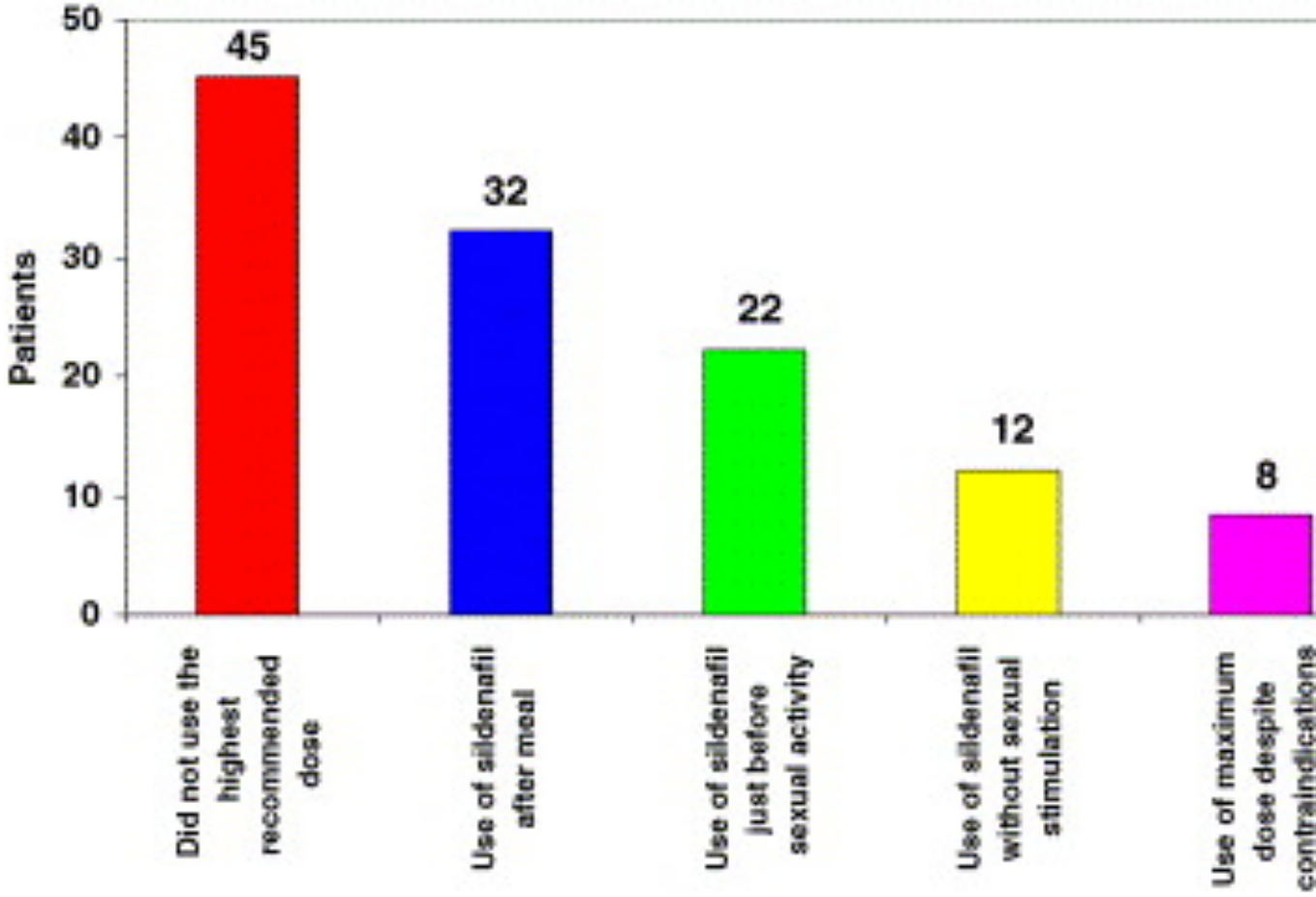
tzichristou · , Kyriakos Moysidis, Apostolos Apostolidis, Athanasios Bekos, Vasilios



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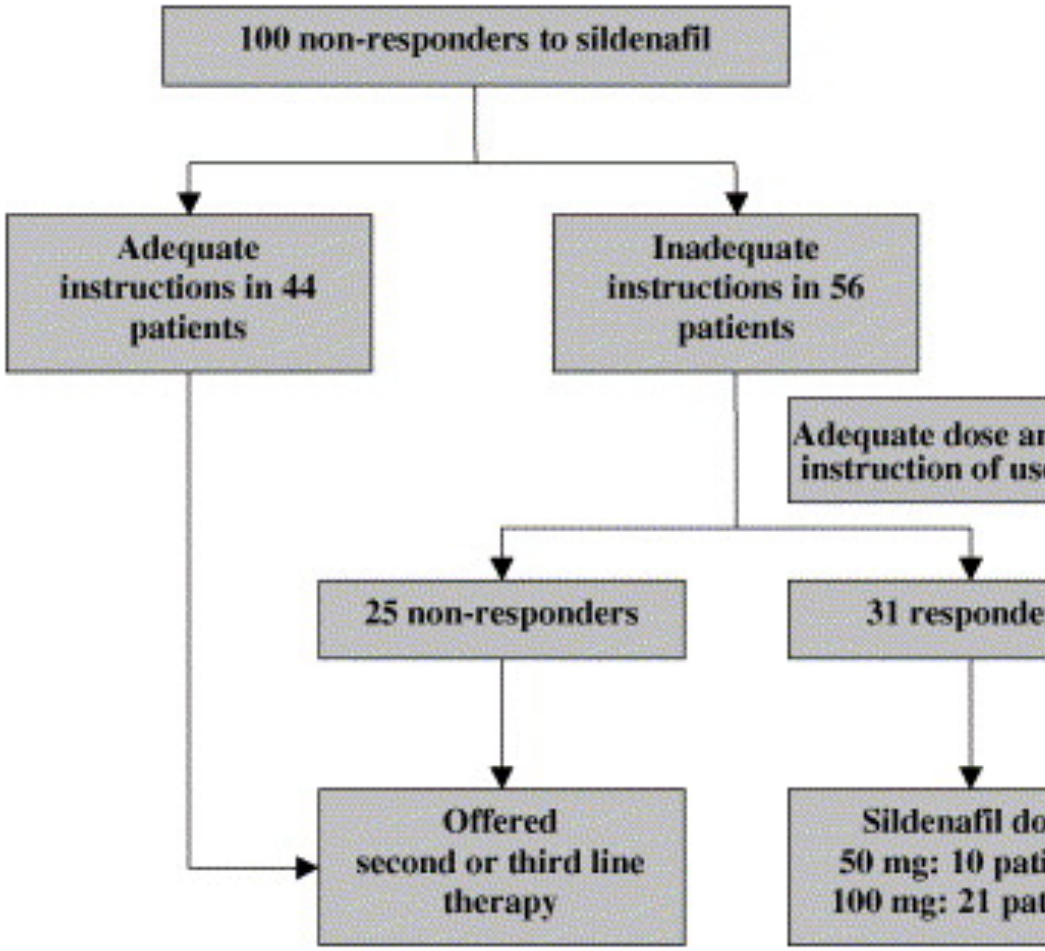

European Urology

Volume 51, Issue 1, January 2007, Pages 75–89

al Medicine

diesterase Type 5 Inhibitors: The Day After

latzimouratidis, Dimitrios Hatzichristou

Table 1 – Reasons for inadequate use of PDE5-Is and treatment strategy

Study	PDE5-I used	Reasons for inadequate use	Treatment strategy	Resu trea
McCullough [97]	Sildenafil	• Only 50 mg used and <5 attempts (55%)	• Re-education (proper administration and expectations) • Retrial with at least 8 attempts (100 mg if needed)	54% cor respond
Atiemo [40]	Sildenafil	• Use after meal (13.3%) • No sexual stimulation (33.7%) • Timing of sex (14.3%) • Too few attempts (20.4%)	• Re-education (videotape, personal instructions, instruction sheets for patient and partner) • Retrial (100 mg if 50 mg after one attempt was inadequate)	41.5% c to respo
Jiann [41]	Sildenafil	• No sexual stimulation (30%) • <4 attempts (60%) • Maximum dose <100 mg (45%)	• Adequate instructions • Retrial with 4 doses (100 mg)	58.5% c to respo
Hatzichristou [39]	Sildenafil	• Maximum dose <100 mg (44%) • Use after meal (32%) • Use just before sex (22%) • No sexual stimulation (12%)	• Adequate instructions • Retrial with 4 doses (100 mg if needed)	55.4% c to respo
Gruenwald [43]	Sildenafil	• Maximum dose <100 mg (76%) • 2.5 attempts (average)	• Adequate instructions (oral and written, videotape in some cases) • Retrial with 8 doses (100 mg)	23.6% a normal functio
Hatzimouratidis [35]	Tadalafil	• Maximum dose <20 mg (10%) • <4 attempts (29%)	• Adequate instructions • Retrial with 4 doses (100 mg if needed)	43.75% to respo
Hatzimouratidis [35]	Vardenafil	• Maximum dose <20 mg (3%) • <4 attempts (38%)	• Adequate instructions • Retrial with 4 doses (100 mg if needed)	31.6% c to respo

PDE5-I = phosphodiesterase type 5 inhibitor.

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e 3 – What can we expect in the future for PDE5-Is?

ntial indication	Rationale
nic administration PDE5-Is (everyday, low-dose use)	Chronic dosing may safely maximise efficacy improving endothelial dysfunction, although there are limited data on the systemic effects of the continuous inhibition of PDE5
evention/cure	Current evidence supports the potential of prevention/cure mainly through improving endothelial dysfunction
ment of LUTS due to BPH	PDE5-Is may relieve obstruction, improve LUTS, potentiate NO-mediated relaxation in prostate
-risk factor treatment	Beneficial effects of PDE5-Is in treating patients with cardiovascular risk factors or disease have been shown.
bination multimodal pills	A single compound can target a number of risk factors to improve patient compliance.

-I = phosphodiesterase type 5 inhibitor; ED = erectile dysfunction; LUTS = lower urinary tract symptoms; BPH = benign pr
rplasia; NO = nitric oxide.

European Urology

Volume 50, Issue 1, July 2006, Pages 126–133

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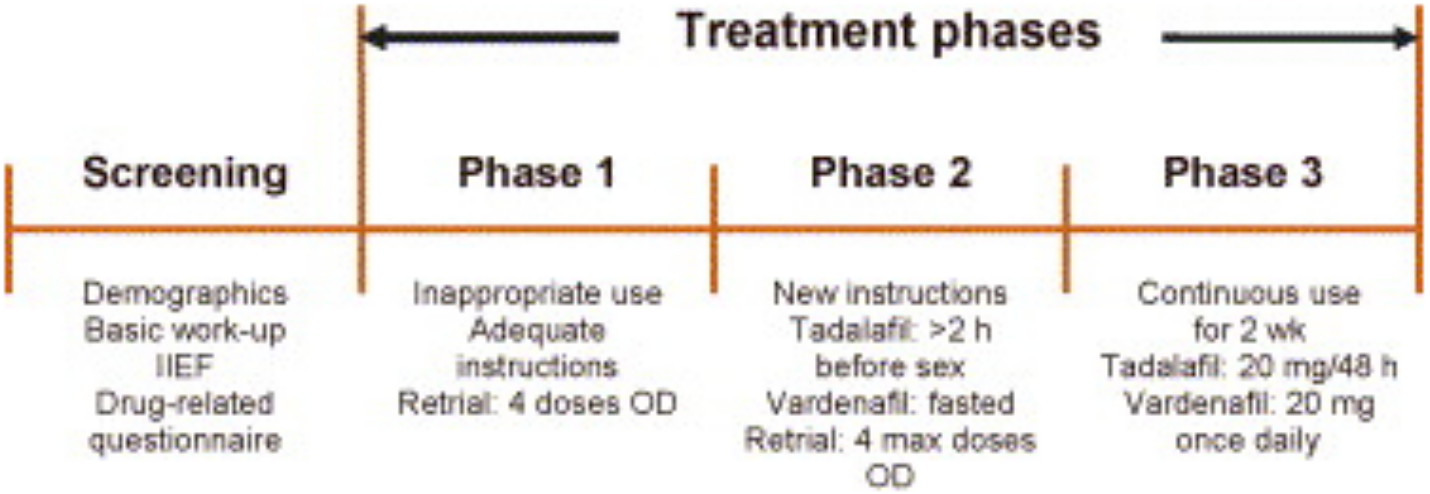
ent Strategy for “Non-Responders” to Tadalafil and afil: A Real-Life Study ☆

os Hatzimouratidis, Kyriakos Moysidis, Athanasios Bekos, Zoi Tsimtsiou, Evangelos Ioannidis, atzichristou ·

epartment of Urology, Papageorgiou General Hospital, and the Center for Sexual and ve Health, Aristotle University of Thessaloniki, Greece



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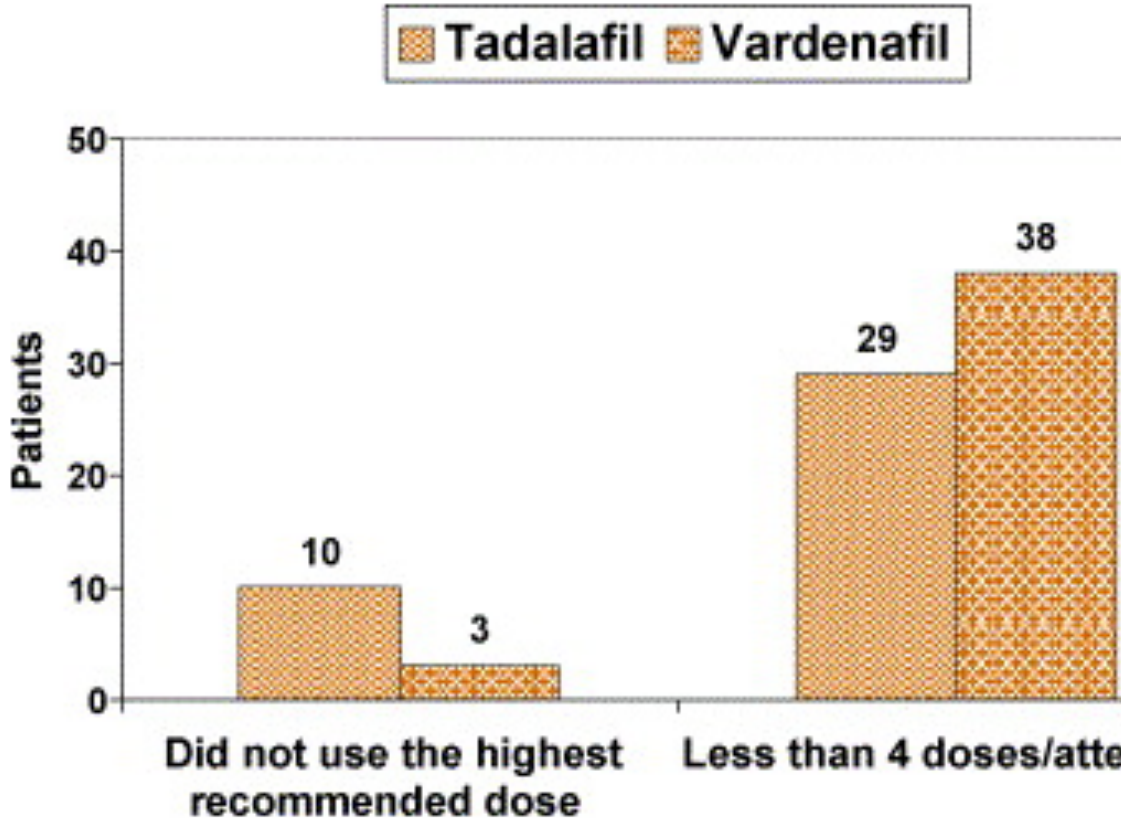

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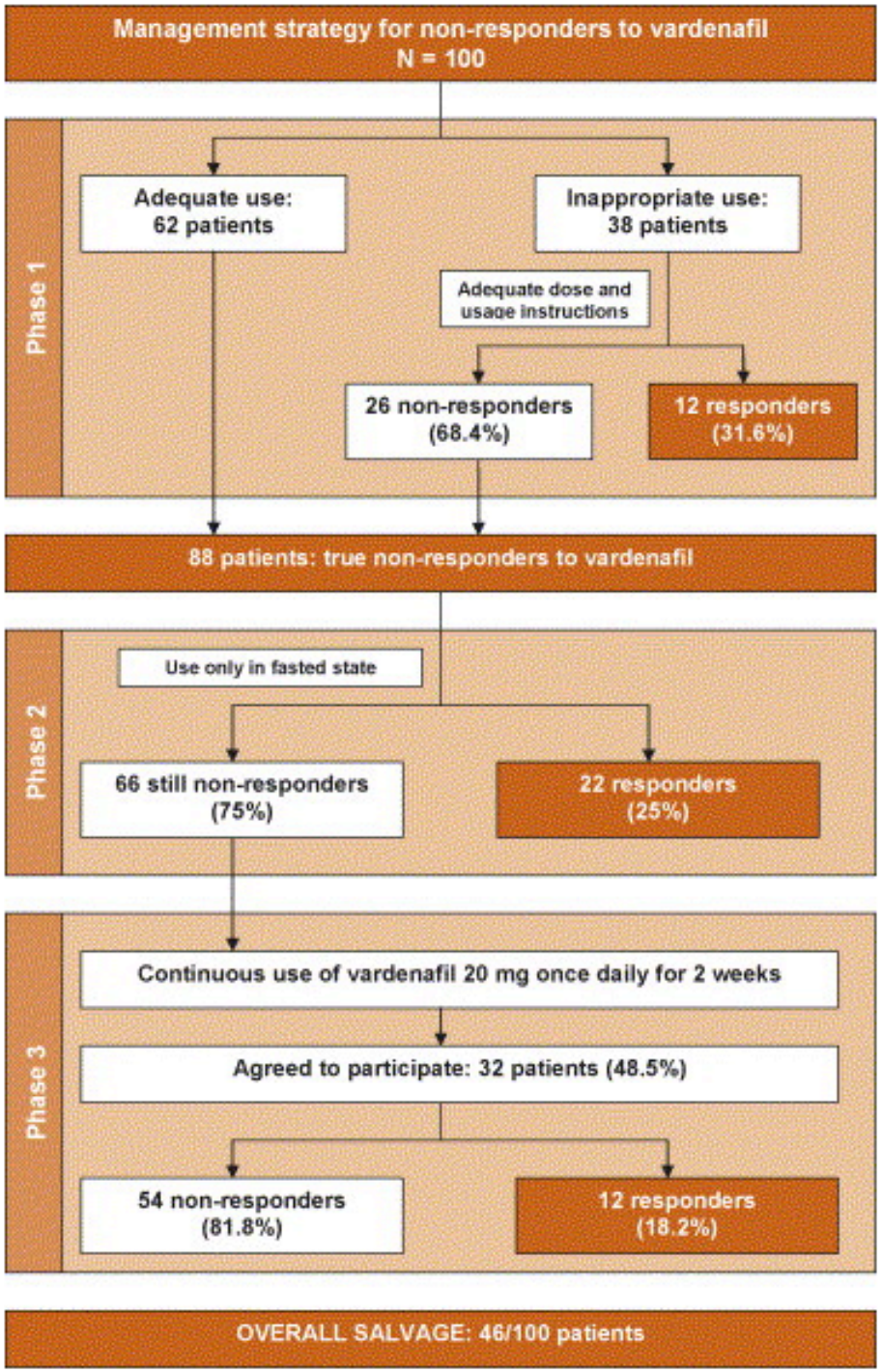

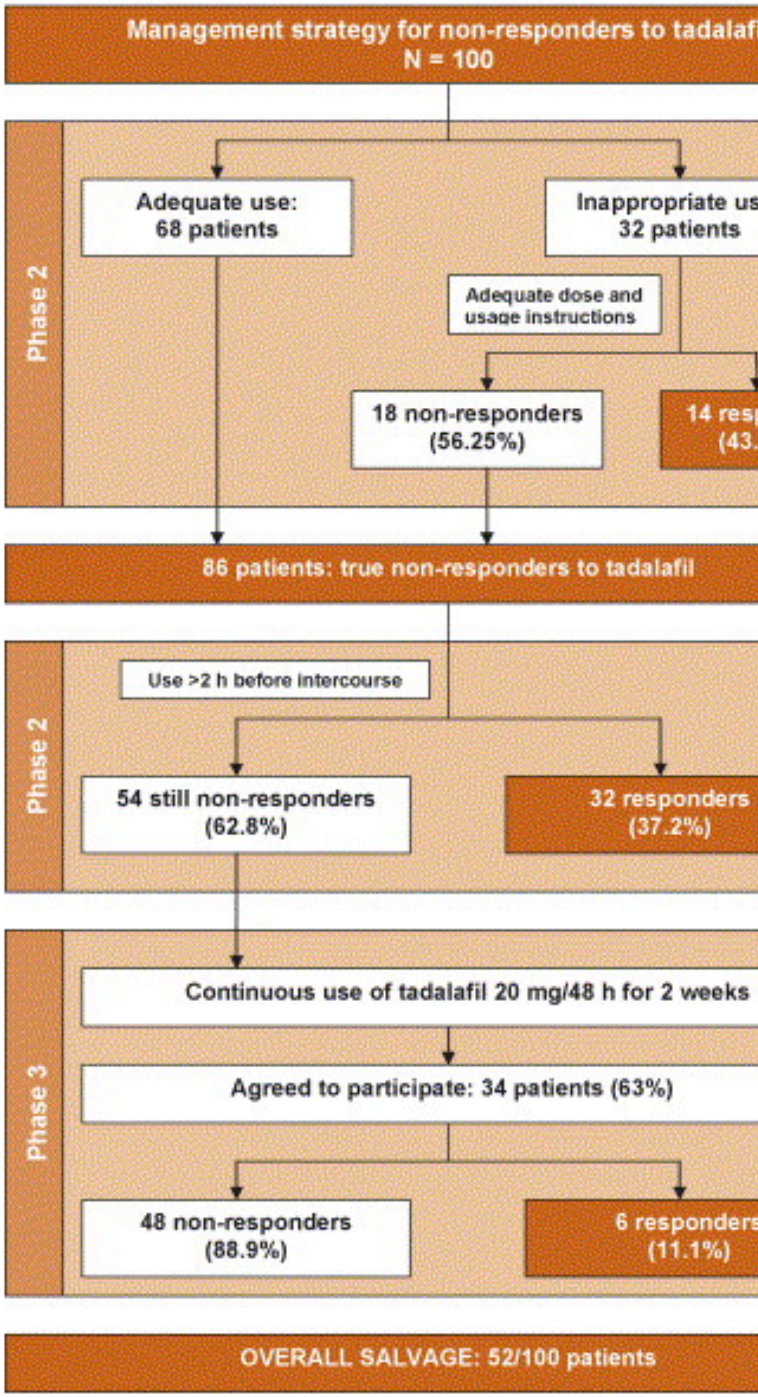

94 May;151(5):1209-16.

tive intracavernous injection test implies normal veno-occlusive but not necessarily normal arterial on: a hemodynamic study.

i ES[1], Hatzichristou DG, Namburi S, Goldstein I.

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mpotence evaluations a positive intracavernous injection test has been presumed to signify normal erectile hemodynamics. This premis y obtaining hemodynamic data in 80 patients 17 to 65 years old with positive injection tests: patients achieved maximal circumference es and equilibrium intracavernous pressures of 80 mmHg or more (range 80 to 136) sustained for 30 minutes or longer. Corporeal veno e testing revealed that flow-to-maintain (0.5 to 3 ml. per minute) and pressure decay (0 to 47 mmHg) values as well as pharmaco- sography findings (absent or minimal contrast medium in venous structures in 92% of the cases) were all consistent with low outflow er Arterial testing revealed right and/or left cavernous systolic arterial blood pressures always at 80 mmHg or more, consistent with a prere us artery pressure value for a positive injection test. Systemic-cavernous systolic arterial blood pressure gradients were 0 to 24 mmHg, lg and 35 mmHg or more in 47 (59%), 18 (22%) and 15 (19%) patients, respectively. Large systemic-cavernous pressure gradients sug ence of arterial occlusive disease. In 8 patients with positive injection tests and gradients of 35 mmHg or more pharmaco-arteriography d hemodynamically significant arterial occlusions. In conclusion, hemodynamic data in selected patients with positive injection tests reve ow erection states, threshold cavernous artery pressures and disparities in systemic-cavernous systolic pressure gradients that sugges disease in 19% of the cases. The erectile response in a positive test is equal to or greater than a threshold response, not always the ma e as determined by the systemic blood pressure. A positive intracavernous injection test did not necessarily signify normal erectile namics.

1999;36(1):60-7.

dynamic characterization of a functional erection. Arterial and corporeal veno-occlusive function in ts with a positive intracavernosal injection test.

stou DG[1], Hatzimouratidis K, Apostolidis A, Ioannidis E, Yannakoyorgos K, Kalinderis A.

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TIVES: To characterize hemodynamically a functional/rigid erection and study the hypothesis that a positive intracavernosal injection t s normal arterial and corporeal veno-occlusive function.

DS: 33 patients (mean age 39.5 +/- 9 years), who developed rigid erection during pharmacocavernosometry, included in the present s sence of axial rigidity was determined at steady state equilibrium intracavernosal pressure, by absence of buckling to axial force of 1 k o the erect penis and sustained for >/=15 min. Arterial and veno-occlusive hemodynamic parameters were analyzed.

TS: Flow-to-maintain at intracavernosal pressure 150 mm Hg and mean pressure decay values ranged between 0.5-13 ml/min and 5-8 ectively. Flow-to-maintain values >5 ml/min were noticed in 8 patients (24. 24%), while pressure decay values >45 mm Hg in 13 patie). Pharmacocavernosography revealed moderate opacification of venous structures in 7 cases (21.21%). Abnormal systemic-caverno arterial pressure gradients in both cavernosal arteries were noticed in 9 patients (27.27%). All patients with flow-to-maintain values >5 mal arterial function.

USIONS: A functional/rigid erectile response may coexist with arterial insufficiency or corporeal veno-occlusive dysfunction. Presence r borderline arterial inflow may compensate minimal or moderate veno-occlusive dysfunction, resulting in a functional - but not norma . Such information is critical when the intracavernosal injection test is used for diagnostic purposes.

International Journal of Impotence Research (2003) 15, 99–104
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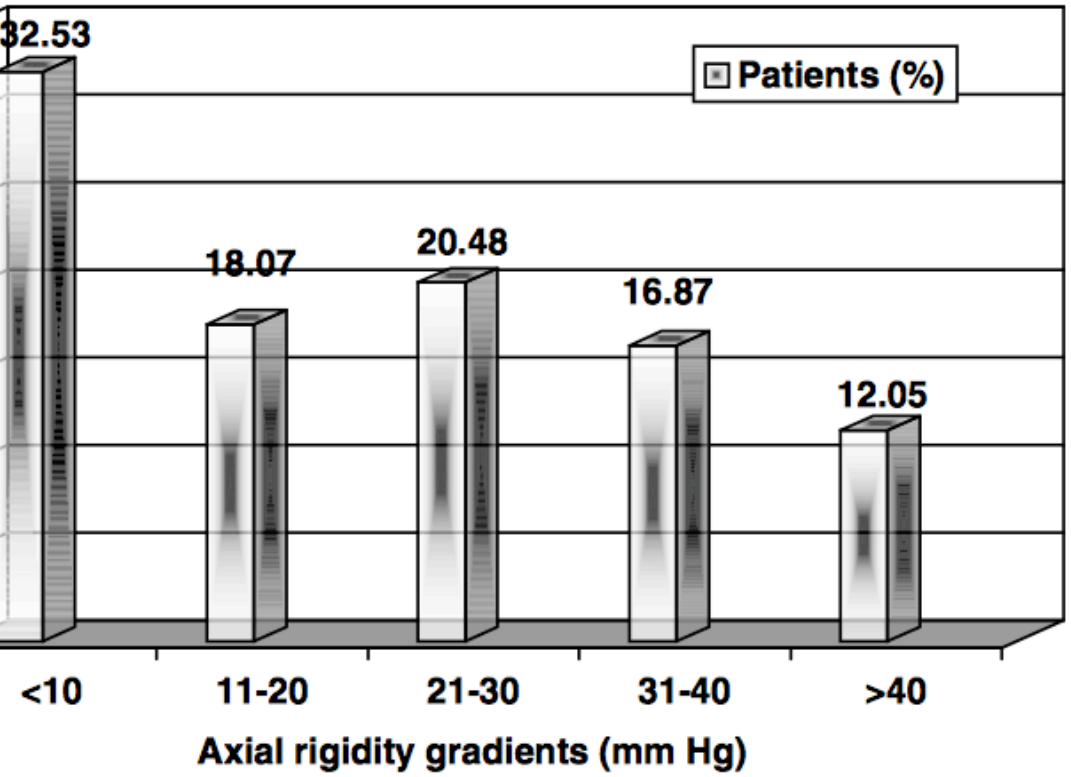
nal hemodynamic parameters do not always predict the ence of a rigid erection: a quantitative assessment of tional erectile impairment

zichristou[1]*, K Hatzimouratidis[1], V Tzortzis[1], A Apostolidis[1], A Bekos and E Ioannidis[1]



3 ARGs in the study sample.

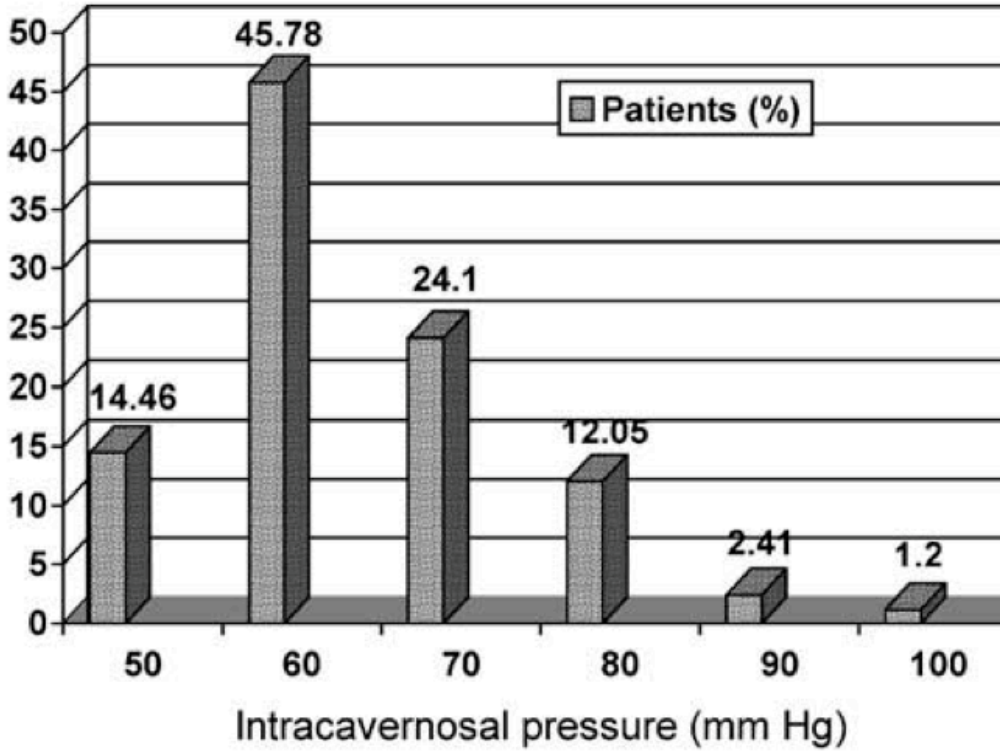


Figure 2 Intracavernosal pressure associated with presence penile rigidity in the study sample.

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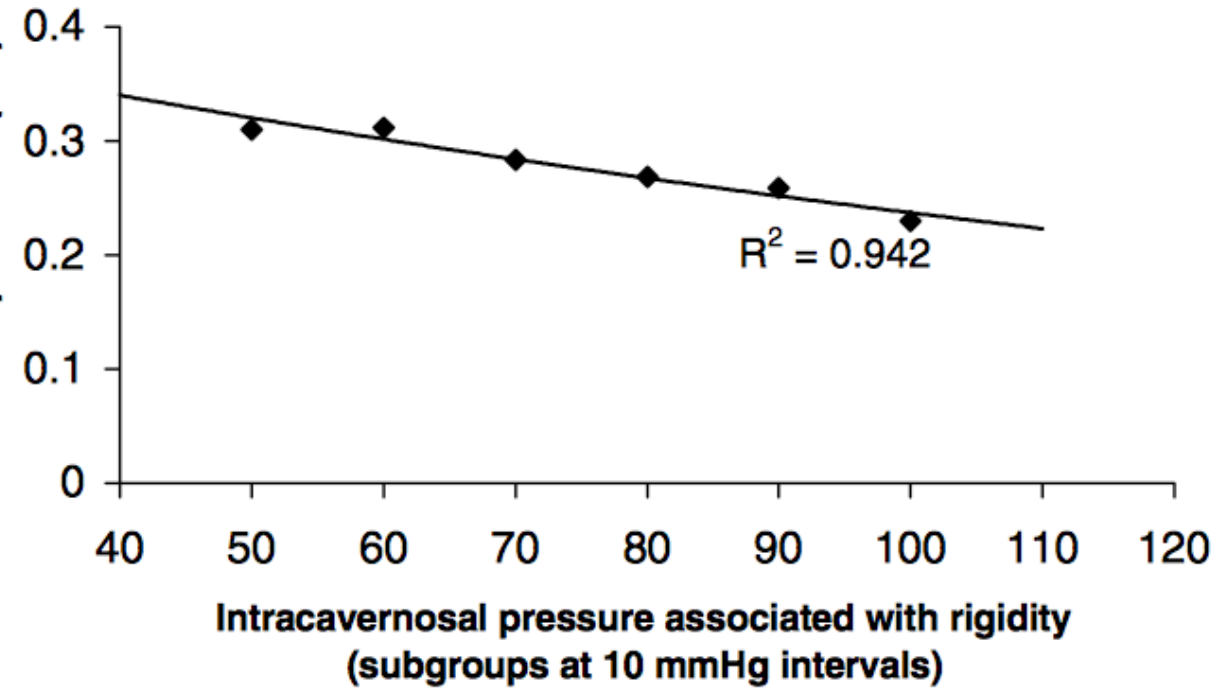


ure 1 Relation between intracavernosal pressure associated th rigidity values and mean penile aspect ratio values rrelation coefficient 0.942).

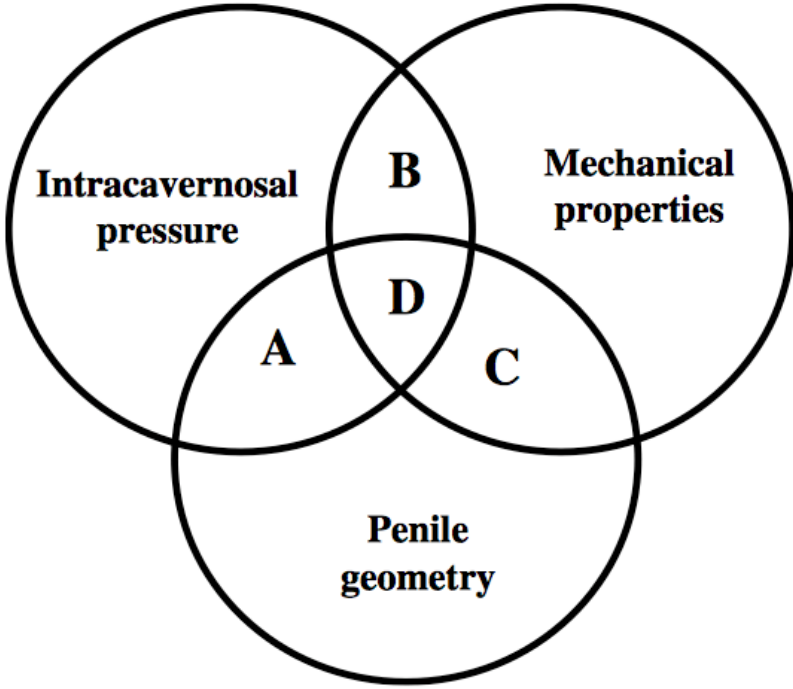


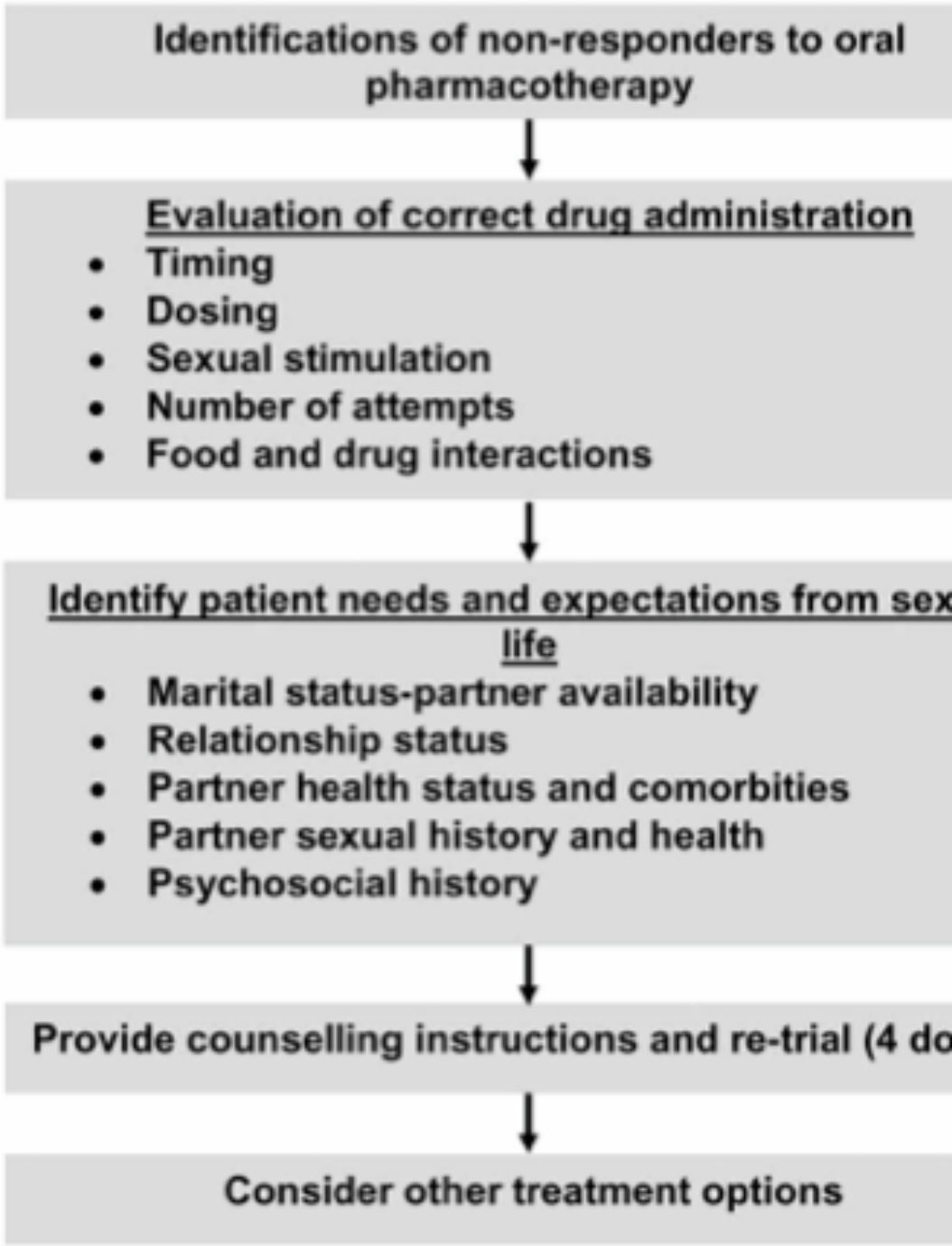
Figure 4 A conceptual model on the pathophysiol impotence, in which impotence may be because of r intracavernosal pressure, altered tissue mechanical pro unfavorable penile geometry (*D*/*L*) ratio or any combina these: (a) normal tissue expandability, low intracav pressure and low *D*/*L* ratio, (b) normal penile geomet intracavernosal pressure and altered tissue expandability ties, (c) normal intracavernosal pressure altered tissue e ability and low *D*/*L* ratio. (d) low intracavernosal pressur altered tissue expandability and low *D*/*L* ratio.

Current Pharmaceutical Design, 2009, *15*, 3476-3485

hodiesterase Type 5 Inhibitors: Unmet Needs

nouratidis and D. G. Hatzichristou*

ment of Urology, Center for Sexual and Reproductive Health, 'Papageorgiou' General Hospital, Aristotle of Thessaloniki, Thessaloniki, Greece



European Urology

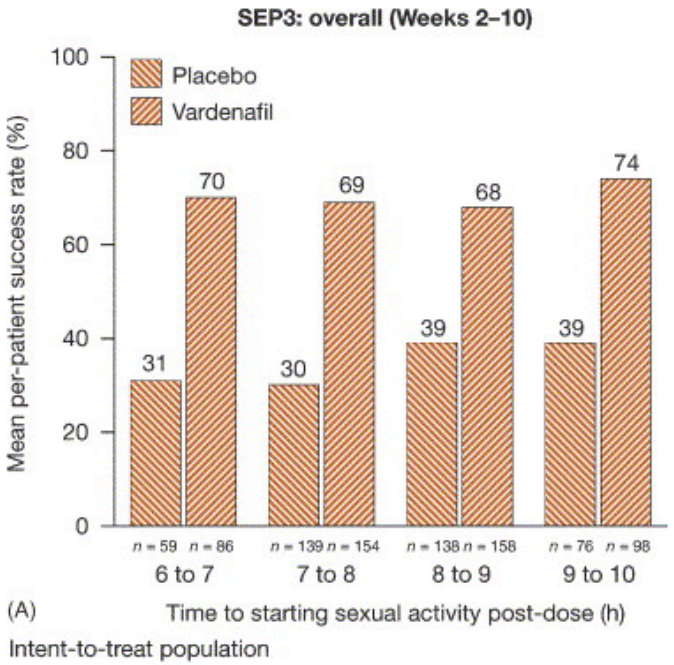
Volume 50, Issue 5, November 2006, Pages 1086–1095

European Urology goes Platinum

cine

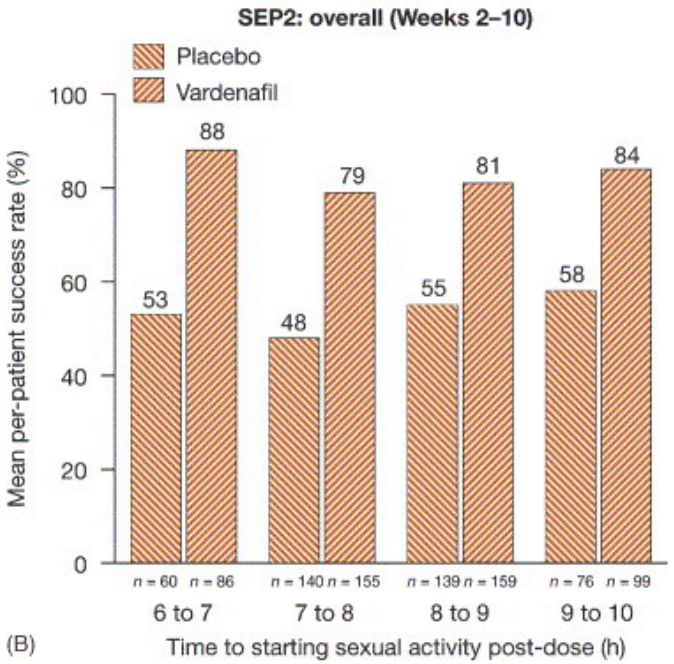
ed Duration of Efficacy of Vardenafil When Taken 8 Before Intercourse: A Randomized, Double-Blind, o-Controlled Study

t[a], Ira D. Sharlip[b], Dimitris Hatzichristou[c], Eusebio Rubio-Aurioles[d], Marc Gittelman[e], tancil[f], Peter M. Smith[f], H. Jeffrey Wilkins[g], Peter Pommerville[h], for the Vardenafil Study



(A)

Intent-to-treat population



(B)

, tolerability and satisfaction with sildenafil citrate 100-mg titration ed with continued 50-mg dose treatment in men with erectile tion

Buvat, Dimitrios Hatzichristou, ggi, Ian Farmer, Jose M. Jabaloyas, Paul J. Miller iel Schnetzler

Issue

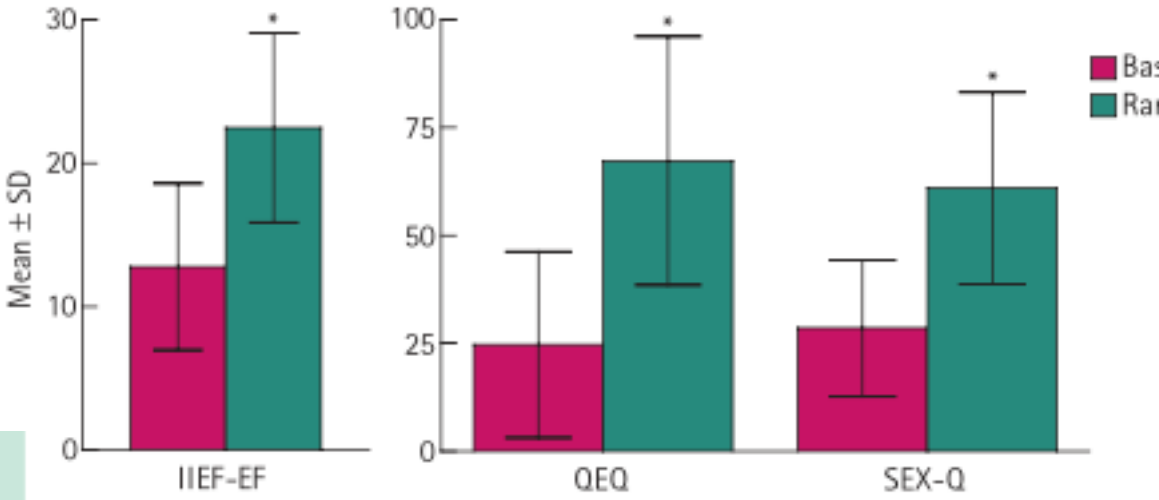
BJU International
Volume 102, Issue 11, pages 1645–1650, December 2008

FREE

	Single-blind	Double-blind	
	50 mg	50 mg	100 mg
	492	239	236
	6.5	7.1	3.0
	3.5	4.6	3.8
	1.6	1.3	2.1
	1.2	2.1	0.8
	0.2	0	1.3
estion	1.2	1.7	0.4
ngitis	0	1.7	0

TABLE 2
The most frequently reported AEs (≥1% of participants; expressed as % of patients)

*FIG. 1. Mean change from baseline to randomization in the IIEF-EF domain, QEQ and SEX-Q; *P*



Urology

Volume 68, Issue 3, Supplement, September 2006, Pages 38–46

Sildenafil Citrate (Viagra): Redefining Efficacy in the Treatment of Erectile Dysfunction

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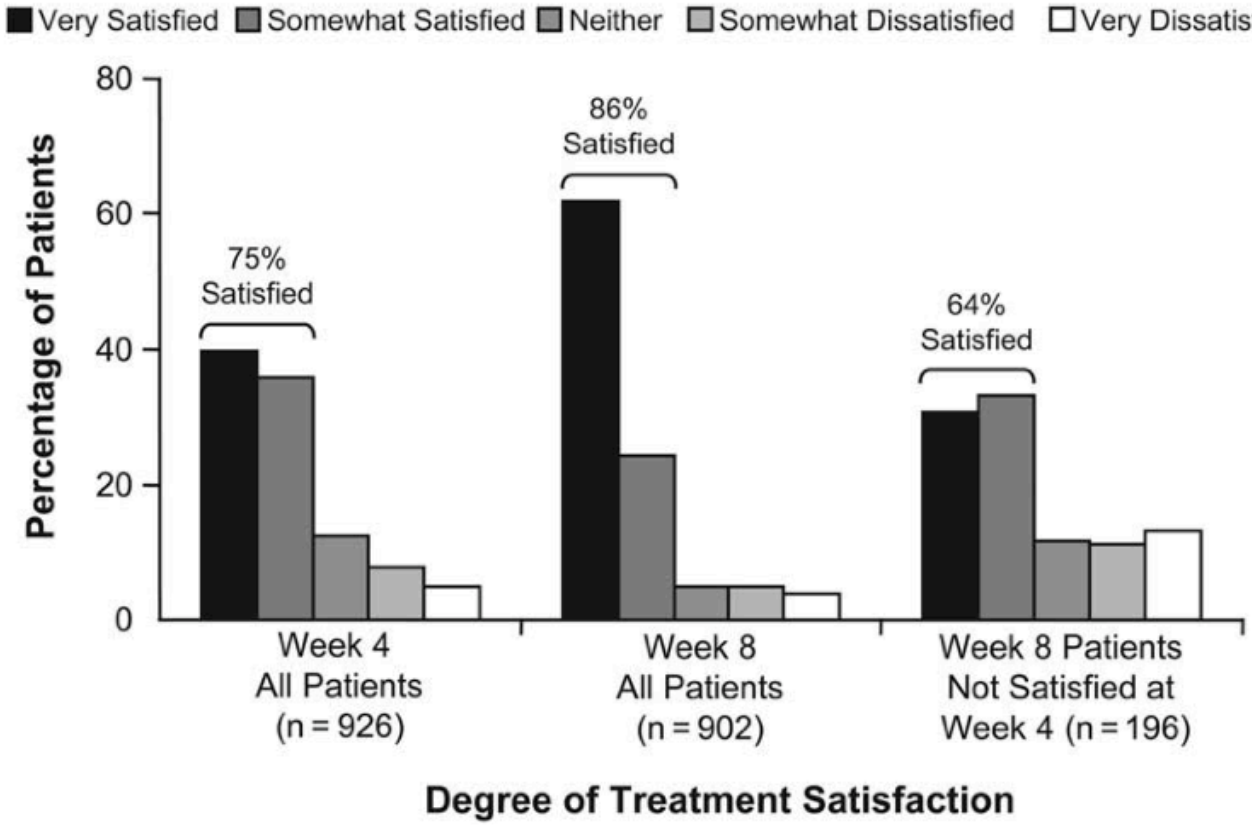
R. Mccullough[a, 1], Culley C. Carson[b, 2], Dimitrios Hatzichristou[c, 3]



Urology

Volume 68, Issue 3, Supplement, September 2006, Pages 38–46

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Mccullough[a, 1], Culley C. Carson[b, 2], Dimitrios Hatzichristou[c, 3]

TABLE I.

Information provided to patients in the Viagra® sample package

Viagra works only when you are sexually stimulated (such as kissing or touching)
For most men, Viagra works the first or second time they try it. Some men may need more attem So keep trying. Viagra can be taken as often as once a day
If you take any medicines that have nitrates in them (such as nitroglycerin for chest pains)—eve or even once in a while—you should not take Viagra
Viagra works in as quickly as 30 minutes. And it stays ready to work for at least 4 hours
If you are not pleased with your results, talk to your doctor. Your doctor can increase your dose t mg or decrease your dose to 25 mg

Στρατηγικές διάσωσης για ασθενείς που **ΔΕΝ ΑΠΑΝΤΟΥΝ** στη θεραπεία με αναστολείς φωσφωροδιεστεράσης τύπου-5 (PDE-5)

ΨΕΥΔΟΑΠΑΝΤΗΤΕΣ

Ακολουθούν τις οδηγίες σωστά;

>4 λήψεις φαρμάκου με μικρή χρονικά απόσταση μεταξύ τους

Μέγιστη ανεκτή δόση

Λήψη δισκίου>1 ώρα πριν τη σεξουαλική δραστηριότητα

4 ώρες πριν από λιπαρό γεύμα, εφ' όσον το απαιτεί το φάρμακο που χορηγήθηκε

Χρήση συνοδών φαρμάκων, σύμφωνα με οδηγίες γιατρού

Επαρκής σεξουαλική διέγερση!

Είναι το ζευγάρι έτοιμο να επανέλθει στη σεξουαλική δραστηριότητα;

Αντιμετώπιση σεξουαλικής δυσλειτουργίας συντρόφου, εφόσον υπάρχει

Εντοπισμός/ Επίλυση προβλημάτων στη σχέση του ζευγαριού

Συνδυασμός με ψυχοσεξουαλική θεραπεία

Αποδοχή θεραπείας από σύντροφο

ΜΗ ΑΠΑΝΤΗΤΕΣ

Επόμενα βήματα...

Συνταγογράφηση άλλου αναστολέα PDE-5

Λήψη ημερήσιας δόσης

ΛΗΨΗ ΣΥΝΔΥΑΣΤΙΚΗΣ ΘΕΡΑΠΕΙΑΣ:

1. Συμπληρωματική τεστοστερόνη, εφόσον ενδείκνυται
2. Στυτική συσκευή κενού
3. a-blockers, στατίνες ή συνεχής πίεση αεραγωγών, όταν υπάρχουν συννοσηρότητες

Ενδοσπραγγώδεις ενέσεις συν/πλην αναστολείς PDE5

Πεϊκή πρόθεση

The Journal of Urology

Volume 164, Issue 4, October 2000, Pages 1197–1200

FIL VERSUS INTRACAVERNOUS INJECTION
Y: EFFICACY AND PREFERENCE IN PATIENTS ON
VERNOUS INJECTION FOR MORE THAN 1 YEAR

ATZICHRISTOU, APOSTOLOS APOSTOLIDIS, VASILIOS TZORTZIS, EVANGELOS
NSTANTINOS YANNAKOYORGOS, ATHANASIOS KALINDERIS

Table 3.

Sildenafil responder preferences at 1 month and at study end

	No. Pts.	No. Injection (%)	No. Sildenafil (%)	No. Injection + Silden
		After 1 mo.		
Alprostadil (μg.):				
10 or Less	54	13 (24.1)	35 (64.8)	6 (11.1)
Greater than 10–20	28	7 (25)	17 (60.7)	4 (14.3)
Combined papaverine, phentolamine + prostaglandin E1 (ml.):				
0.05–0.3	19	5 (26.3)	12 (63.2)	2 (10.5)
0.35–0.6	12	5 (41.7)	5 (41.7)	2 (16.6)
0.7–1	3	1 (33.3)	2 (66.7)	0
		After 3 mos.		
Alprostadil (μg.):				
10 or Less	54	13 (24.1)	39 (72.2)	2 (3.7)
Greater than 10–20	28	8 (28.6)	19 (67.8)	1 (3.6)
Combined papaverine, phentolamine + prostaglandin E1 (ml.):				
0.05–0.3	19	6 (31.6)	12 (63.1)	1 (5.3)
0.35–0.6	12	8 (66.7)	4 (33.3)	0
0.7–1	3	3 (100)	0	0

The Journal of Urology

Volume 164, Issue 4, October 2000, Pages 1197–1200

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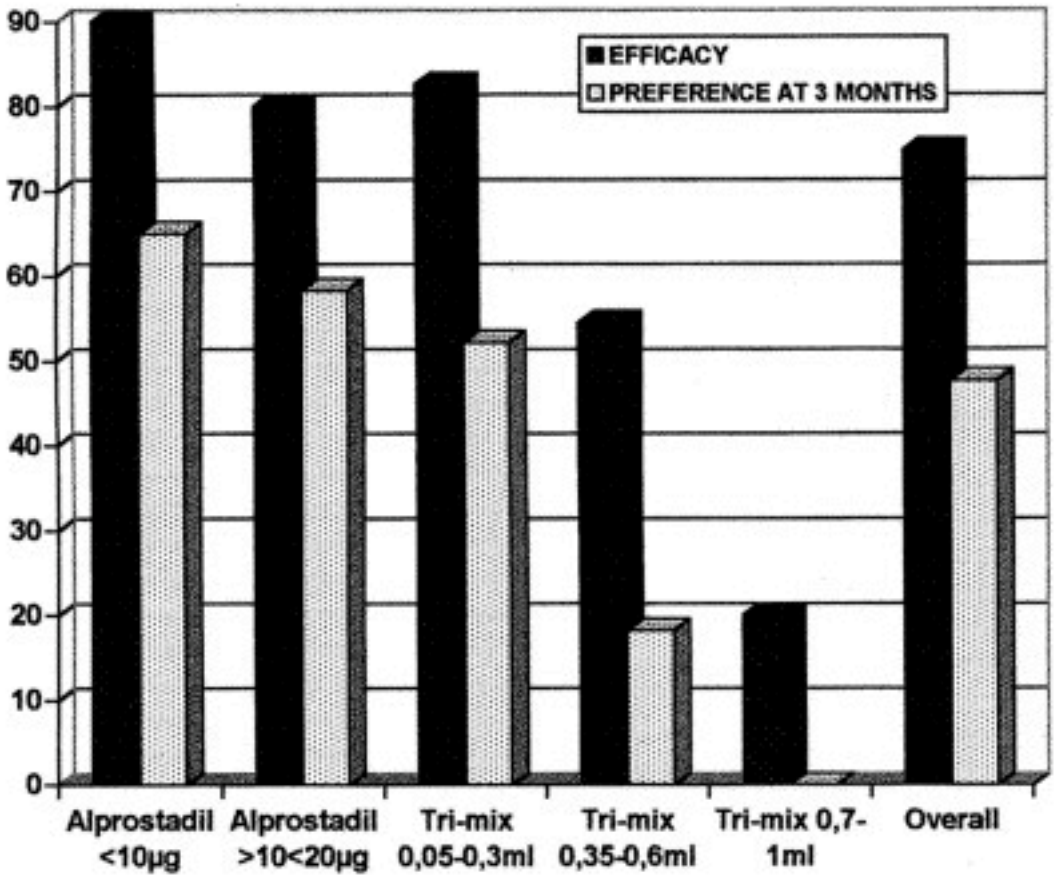


Fig. 2.

Differences in efficacy of sildenafil and preference by group in overall study sample of 155 patients combined papaverine, phentolamine and prostaglandin E1.

Συνδυασμοί με PDE5i

PDE5i και PDE5i

- Ταδαλαφιλη 5 + 5
- Ταδαλαφιλη 5 + άλλος **PDE5i** .

PDE5i και VED

- Βελτίωση του IIEF-EF.
- Νέοι ασθενείς, μετά από ριζική.

PDE5i και ενδοπεϊκές ενέσεις

- Ανταπόκριση έως 31%
- Παρενέργειες σε ποσοστό 33%
- 20% ζάλη

PDE5i και Τεστοστερόνη

- Βελτίωση σε ασθενείς με επίπεδα T <300ng/dl

ΕΡΩΤΗΣΕΙΣ

Ερώτηση 6

Ποιος PDE5i έχει το καλύτερο προφίλ ασφάλειας;

ΑΝΕΠΙΘΥΜΗΤΕΣ ΕΝΕΡΓΕΙΕΣ ΤΩΝ ΑΝΑΣΤΟΛΕΩΝ ΤΗΣ PDE5

Ανεπιθύμητη ενέργεια	ΣΙΛΔΕΝΑΦΙΛΗ	ΤΑΔΑΛΑΦΙΛΗ	ΒΑΡΔΕΝΑΦΙΛΗ	ΑΦΑΝΑΦΙΛΗ	ΟΥΝΤΕΝΑΦΙΛΗ
Κεφαλαλγία	12.8%	14.5%	16%	9.3%	8.9%
Ερύθημα πρόσωπου	10.4%	4.1%	12%	3.7%	23.2%
Δυσπεψία	4.6%	12.3%	4%	1%	2.1%
Ρινική συμφόρηση	1.1%	4.3%	10%	1.9%	7.1%
Ζάλη	1.2%	2.3%	2%	<1%	< 1%
Διαταραχές όρασης	1.9%		< 2%	1.9%	
Οσφυαλγία		6.5%			
Μυαλγία		5.7%			

ΚΕΝΤΡΟ ΣΕΞΟΥΑΛΙΚΗΣ ΚΑΙ ΑΝΑΠΑΡΑΓΩΓΙΚΗΣ ΥΓΕΙΑΣ

ΙΝΣΤΙΤΟΥΤΟ ΜΕΛΕΤΗΣ ΟΥΡΟΛΟΓΙΚΩΝ ΠΑΘΗΣΕΩΝ

Ασφάλεια των PDE5i

Καμιά διαφορά

- Εμφάγματα μυοκαρδίου
- Τέστ κόπωσης: στον συνολικό χρόνο και τον χρόνο μέχρι τη ισχαιμία σε ασθενείς με σταθερή στηθάγχη

Συνχορήγηση

Νιτρώδη

- Αντένδειξη: σοβαρή αγγειοδιαστολή και πτώση ΑΠ

Αντιυπερτασικά - ablocker

- Κίνδυνος υπότασης – παράθυρο 4 ωρών
- Αντικατάσταση τεραζοσίνης, δοξαζοσίνης με αλφουζοσίνη ή ταμσουολσίνη
- Έναρξη με χαμηλότερη δόση PDE5i

CYP34A

- Μείωση δόσης

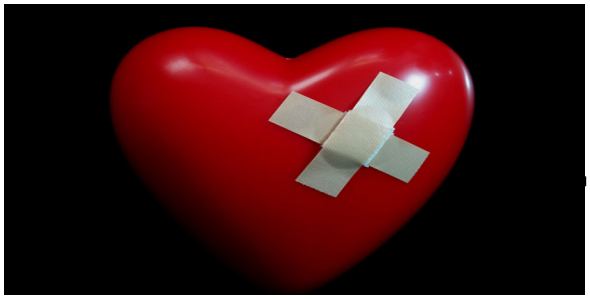
Kloner RA (2004) Novel phosphodiesterase type 5 inhibitors: assessing hemodynamic effects parameters. Clin Cardiol

ΣΑΣ ΕΥΧΑΡΙΣΤΩ

ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

Ερώτηση 1

Τι να δίνω στους καρδιολογικούς ασθενείς;



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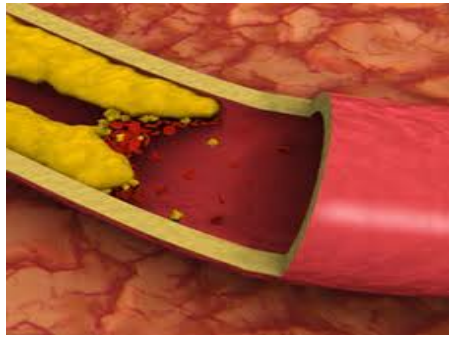


- ED not only shares risk factors with CVD but also constitutes itself an independent marker of increased risk for CVD.

- The relevant CV risk is higher in men **40-49 years** with ED (Vlachopoulos et al. 2013) and those with **diabetes** (Miner et al. 2012)

The American Journal of Cardiology

Volume 96, Issue 12, Supplement 2, 26 December 2005, Pages 80–84

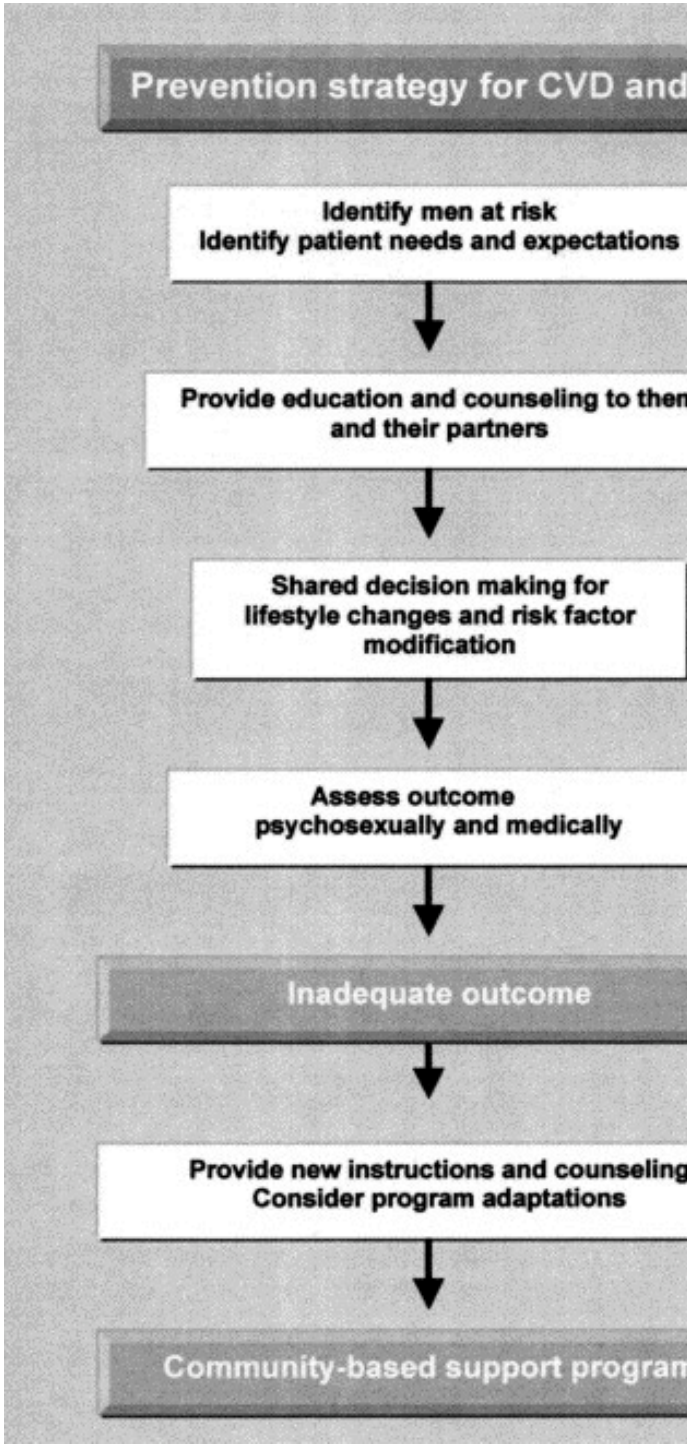
A Symposium: Sexual Dysfunction and Cardiac Risk — The Second Princeton Consensus Conference

A Symposium: Sexual Dysfunction and Cardiac Risk

ntion and Management of Cardiovascular Disease and le Dysfunction: Toward A Common Patient-Centered, Model

Hatzichristou, MD · , Zoi Tsimtsiou, MD

online 6 December 2005



PRINCETON
sensus
ommendations
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ease

e: www.imop.gr

Sexual inquiry of all men

ED CONFIRMED

Exercise ability (1)

(1)
Sexual activity is equivalent to walking 1 mile on the flat in 20 minutes or briskly climbing 2 flights of stairs in 10 seconds.

(2)
Sexual activity is equivalent to 4 minutes of the Bruce treadmill protocol

Low risk

Indeterminate risk

High risk

stress test (2)

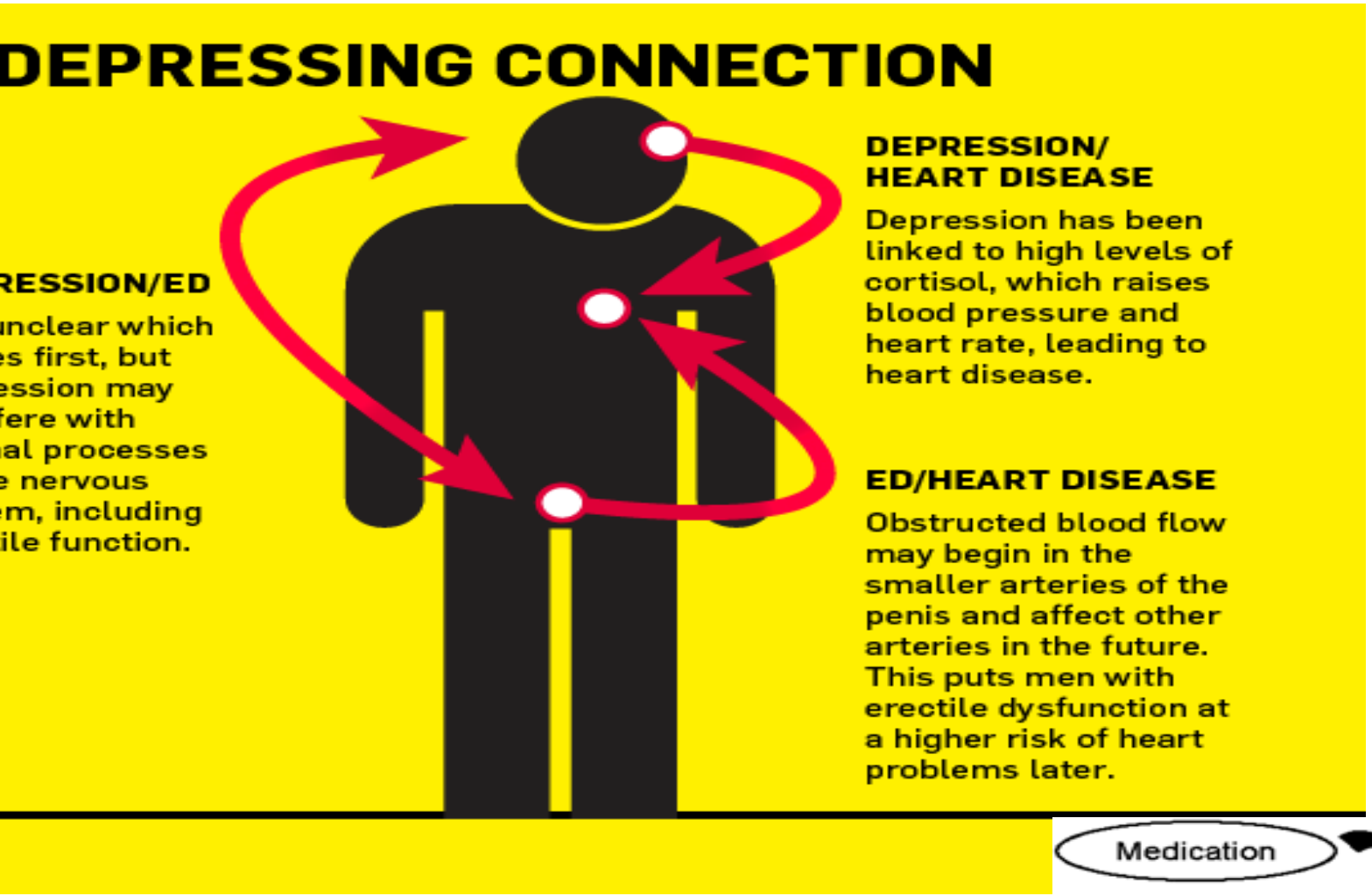
Low risk

High risk

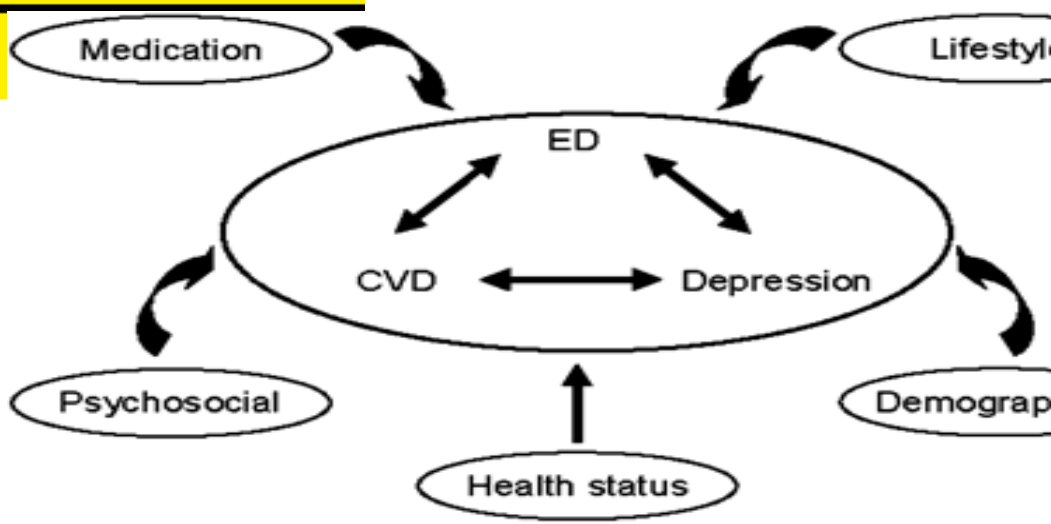
Advice, Treat ED

Cardiologist

R, et al: Am J Cardiol. 2000; 86(2):175-81 * Kostis JB et al: Am J Cardiol. 2005; 26:96(12B):85M-93M * Nehra A, et al:Mayo Clin Proc. 2012;87(8):766



CVD, ED Depression: the fatal triad

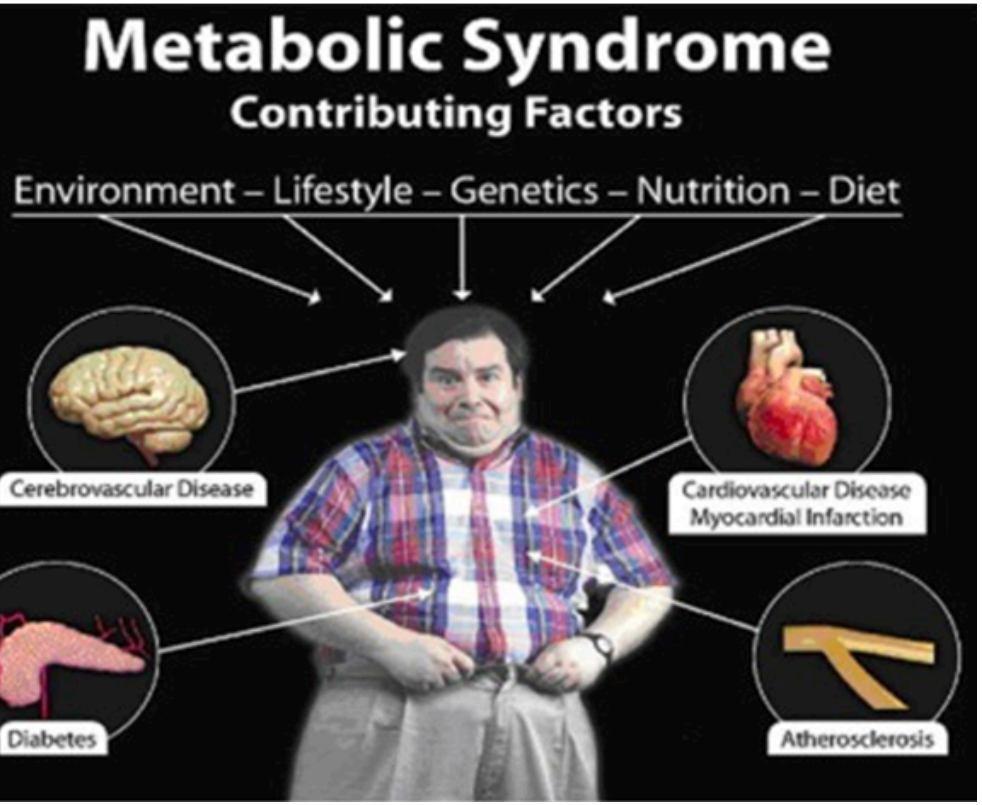


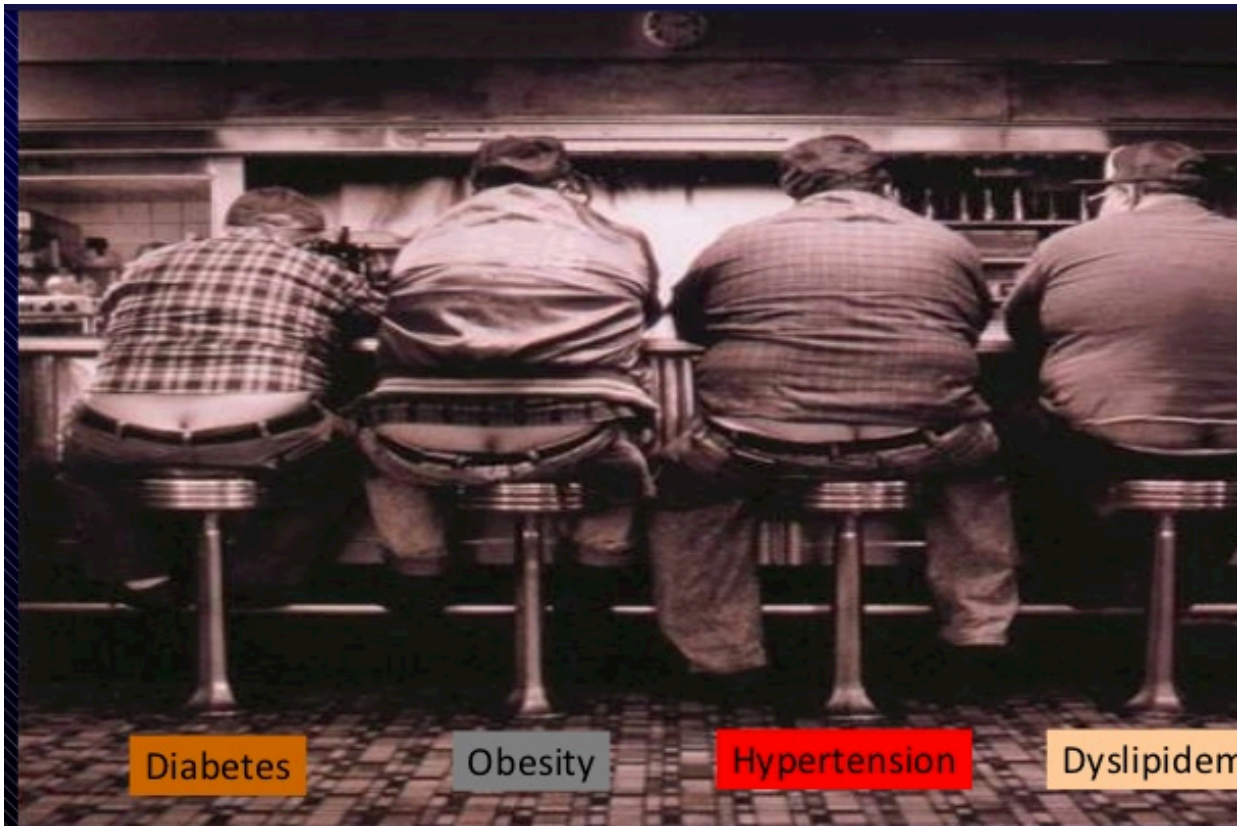
Goldstein I: Am J Cardiol 2000; 86(S1):41-5

ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

Ερώτηση 2

Πως να χειρίζομαι τους διαβητικούς;

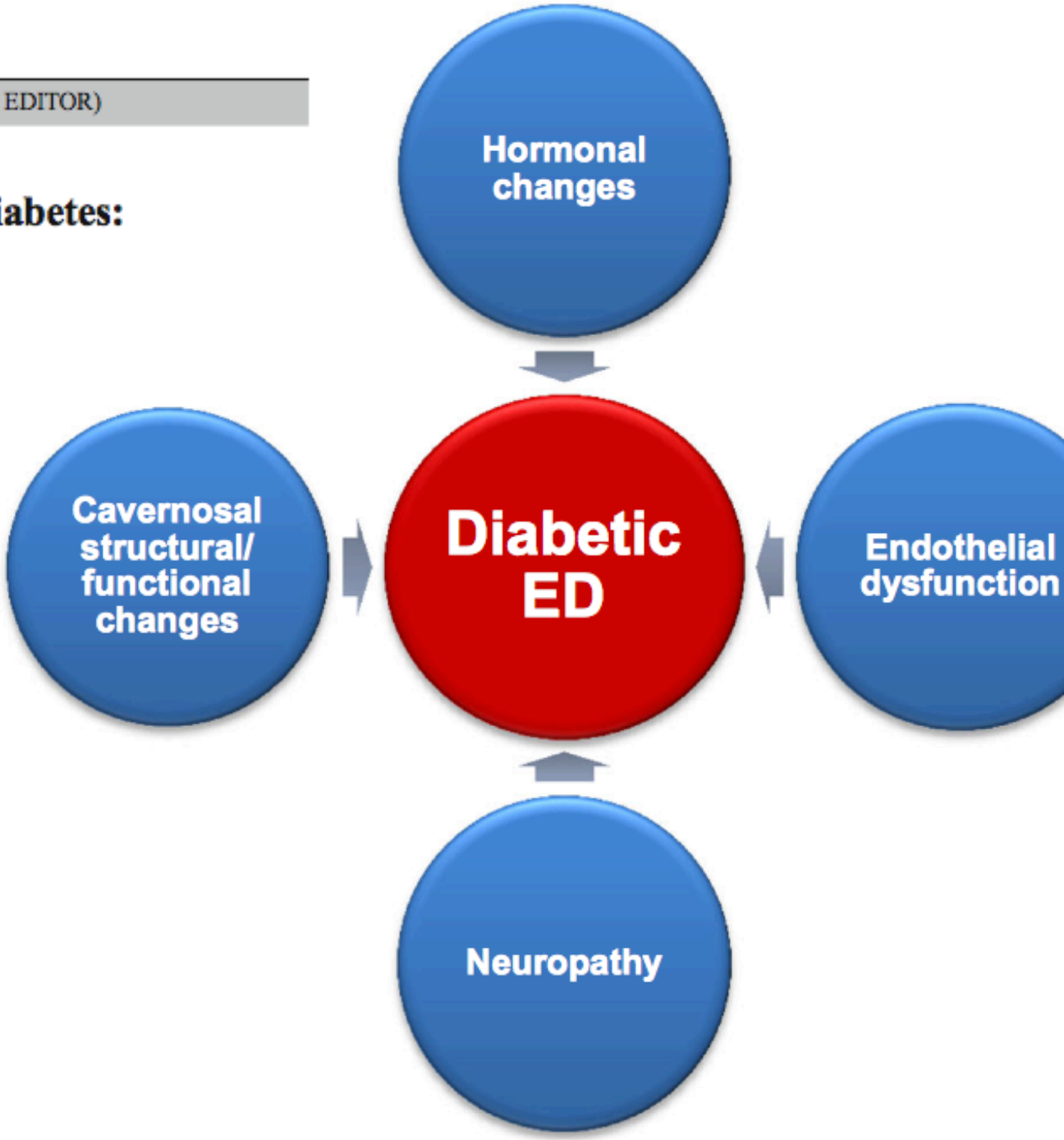

Metabolic Syndrome
Contributing Factors
Environment – Lifestyle – Genetics – Nutrition – Diet
Cerebrovascular Disease
Cardiovascular Disease
Myocardial Infarction
Diabetes
Atherosclerosis


Diabetes
Obesity
Hypertension
Dyslipidem

Rep (2014) 14:545
07/s11892-014-0545-6

to Treat Erectile Dysfunction in Men with Diabetes: Pathophysiology to Treatment

tinos Hatzimouratidis · Dimitrios Hatzichristou



p (2014) 14:545
s11892-014-0545-6

ASCULAR COMPLICATIONS—NEUROPATHY (D ZIEGLER, SECTION EDITOR)

o Treat Erectile Dysfunction in Men with Diabetes: Pathophysiology to Treatment

os Hatzimouratidis · Dimitrios Hatzichristou

Table 1 Efficacy of PDE5i in diabetic men (updated from [9])

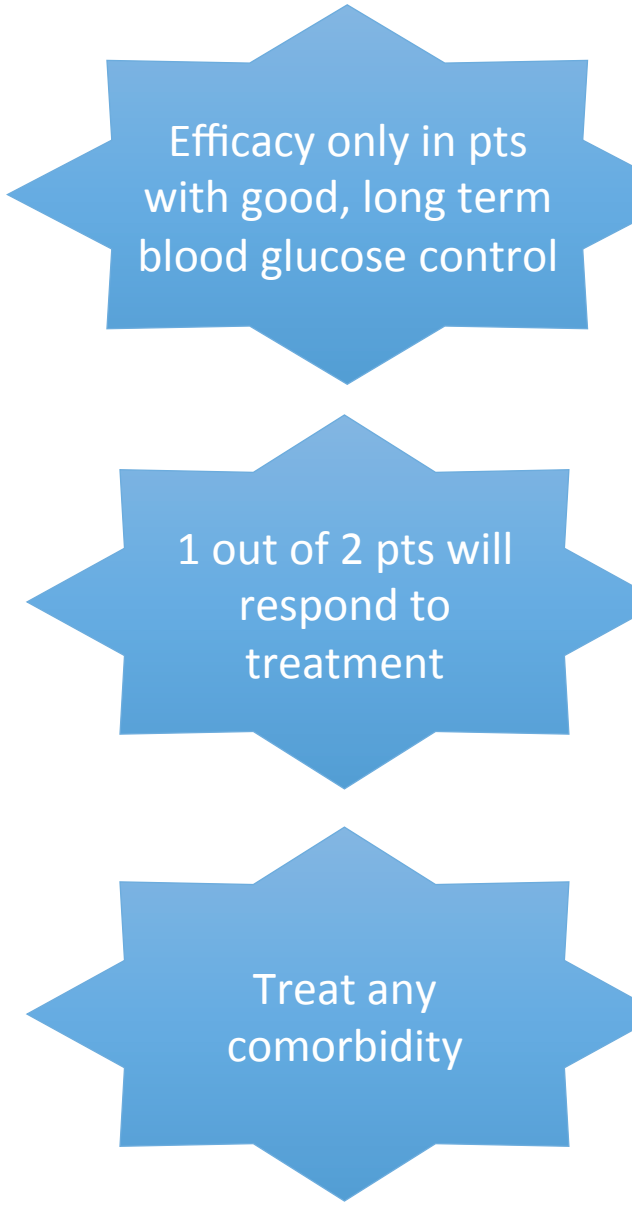
Study	Drug	Diabetes type	Outcome measure	Efficacy (%)
Rendell et al., 1999 [58]	Sildenafil (25–100 mg)	Type 1 (n=50) and type 2 (n=136)	IIEF Q4	Placebo 1.6 Sildenafil 2.7 (mean scores, p
Boulton et al., 2001 [59]	Sildenafil (25–100 mg)	Type 2 (n=110)	IIEF Q4	Placebo 1.84 Sildenafil 3.35 (mean scores, p
Stuckey et al., 2003 [60]	Sildenafil (25–100 mg)	Type 1 (n=188)	IIEF Q4	Placebo 2.19 Sildenafil 3.25 (mean scores, p
Goldstein et al., 2003 [61]	Vardenafil (10 and 20 mg)	Type 1 (n=51) and type 2 (n=387)	SEP3	Placebo 23 % Vardenafil 10 mg 49 % Vardenafil 20 mg 54 % (p<0.0001 for both 10 and 20
Safarinejad, 2004 [62]	Sildenafil (100 mg)	Type 1 (n=48) and type 2 (n=234)	IIEF Q4	Placebo 2.9 Sildenafil 2 (mean scores, p<0
Fonseca et al., 2004 [63]	Tadalafil (10 and 20 mg)	Type 1 (n=210) and type 2 (n=427)	SEP3	Placebo 21.5 % Tadalafil 10 mg 48.6 % Tadalafil 20 mg 52.8 % (p<0.001 for both 10 and 20
Ziegler et al., 2006 [64]	Vardenafil (5–20 mg)	Type 1 (n=154)	SEP3	Placebo 28 % Vardenafil 50 % (p<0.0001)
Hatzichristou et al., 2008 [65]	Tadalafil (2.5 and 5 mg)	Type 1 (n=33) and type 2 (n=265)	SEP3	Placebo 28.2 % Tadalafil 2.5 mg 46 % Tadalafil 5 mg 41.1 % (p≤0.005 for both 2.5 and 5
Park et al., 2010 [66]	Mirodenafil 100 mg	Type 1 and type 2 (n=55 for both types, stratification not reported)	SEP3	Placebo 22.3 % Mirodenafil 69 % (p<0.0001)
Moon du et al., 2011 [67]	Udenafil (100 and 200 mg)	Type 1 and type 2 (n=174 for both types, stratification not reported)	SEP3	Placebo 22.6 % Udenafil 100 mg 53.13 % Udenafil 200 mg 63 % (p<0.0001 for both 100 and 2
Goldstein et al., 2012 [68]	Avanafil (100 and 200 mg)	Type 1 (n=11) and type 2 (n=349)	SEP3	Placebo 20 % Avanafil 100 mg 34 % Avanafil 200 mg 40 % (p<0.002 for 100 mg and p<0

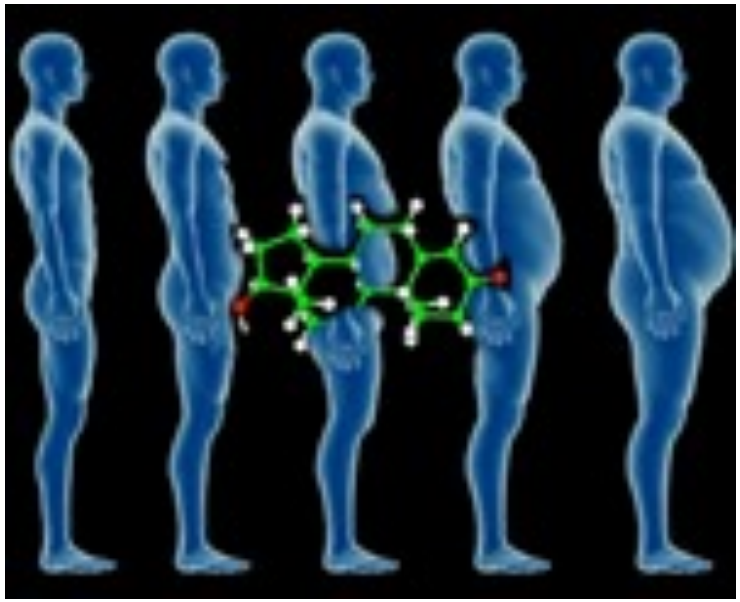
IIEF Q4 International Index for Erectile Function Question 4 (During sexual intercourse, how often were you able to maintain completion of intercourse? Scale 0–5), *SEP3* Sexual Encounter Profile question 3 (Did your erection last long enough for you t intercourse?)

PDE5i in patients with diabetes mellitus

In a review of randomized clinical trials of PDE5i in diabetic patients, the weighted mean difference for the IIEF-EF and the percentage of successful attempts in the PDE-5 inhibitors and in the control arm was 26.7 (95% CI 23.1 to 30.3) and 6.6 (95% CI 5.2 to 7.9) respectively (Vardi and Nini 2007). This is mainly because the pathophysiology of diabetes-induced ED is multifactorial, including elevated advanced glycation endproducts, high levels of oxygen free radicals, impaired nitric oxide synthesis, increased endothelin B receptor binding sites and up-regulated RhoA/Rho-kinase pathway, neuropathic damage and impaired cyclic guanosine monophosphate (cGMP)-dependent protein kinase-1 (Thorve, Kshirsagar et al. 2011).

The only existing strategy to improve response rates include initially **management of the underlying hyperglycemia and comorbidities, as well as to start early treatment with PDE5i** (also to prevent or halt the progression of disease).





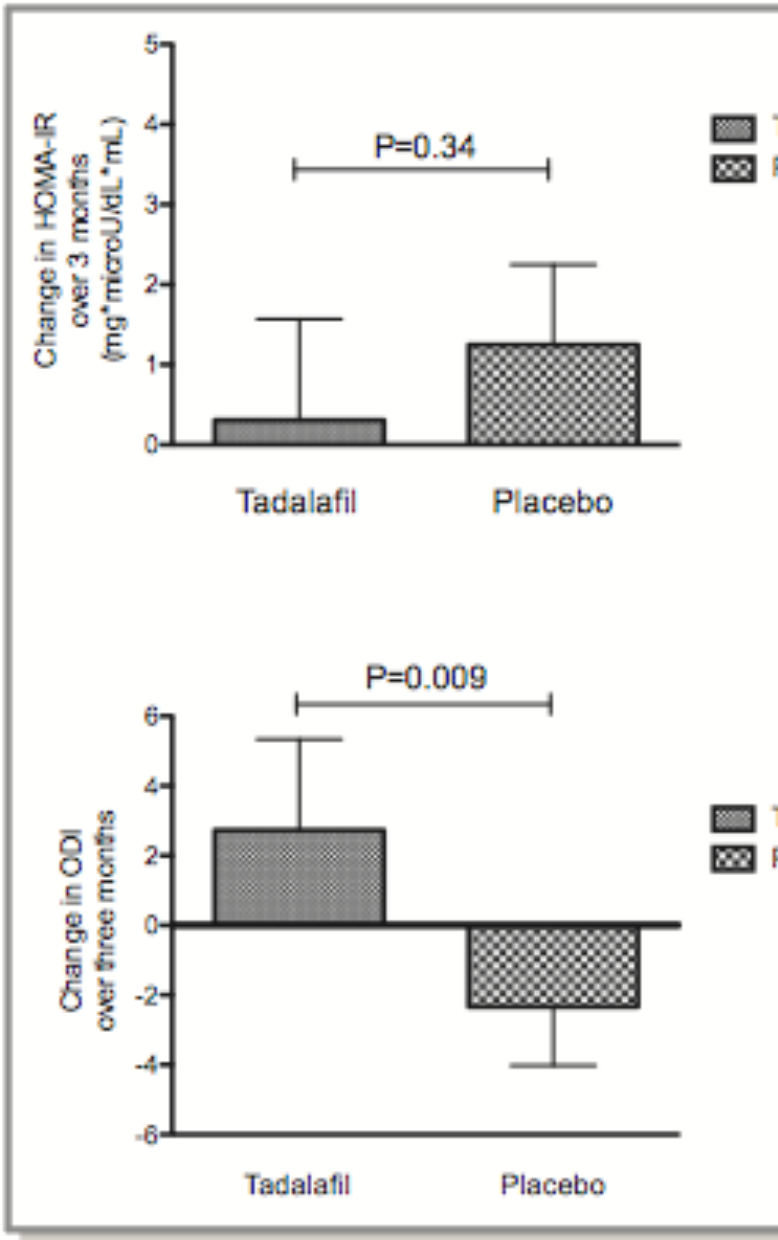
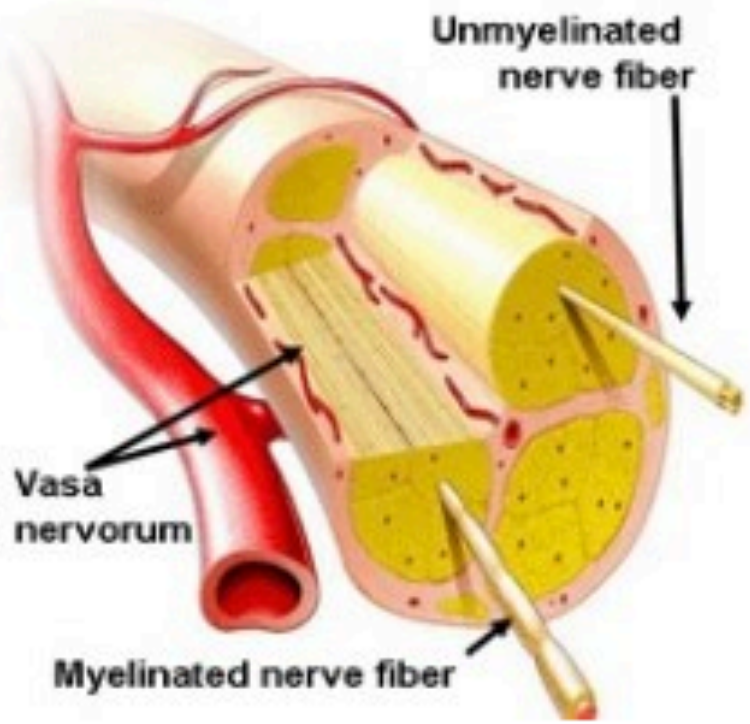


Figure 2. Change in HOMA-IR and oral disposition i
3 months of treatment with tadalafil vs placebo gro
represent means±standard deviations. HOMA-IR indicate
static model of insulin resistance, ODI indicates oral disposit

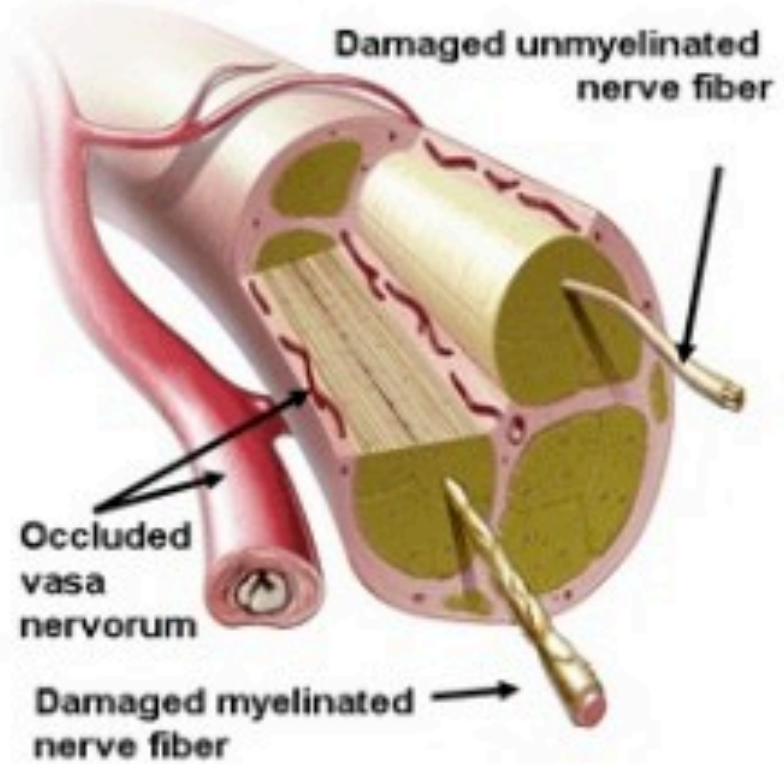
Ho JE, Arora P, Walford GA, Ghorbani A, Guanaga DP, Dhakal BP et al. Effect of phosphodiesterase inhibition on insulin resistance in obese individuals. J Am Heart Assoc 2014; 3

Diabetic Peripheral Neuropathy

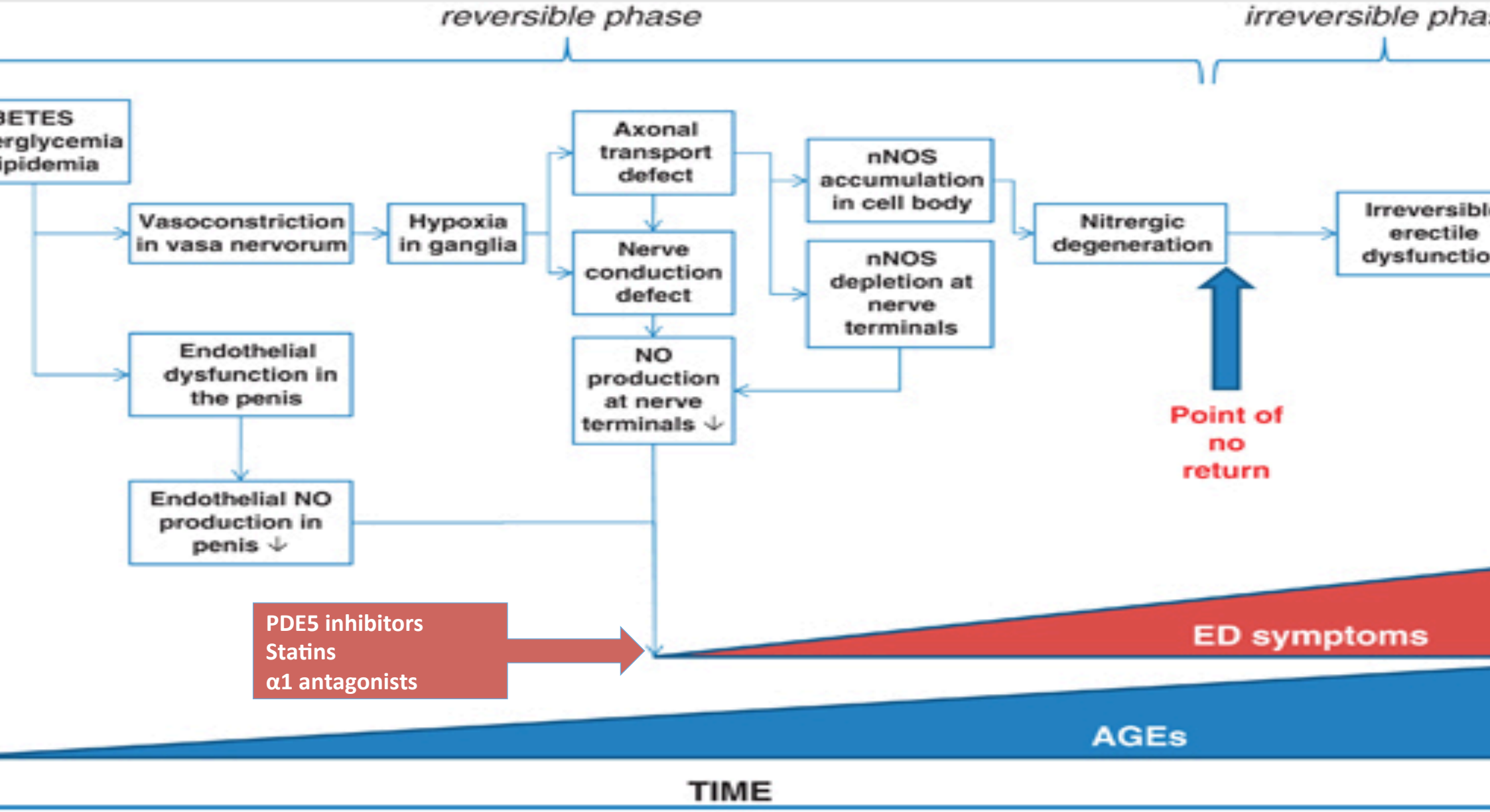
Healthy Nerves and Blood Vessels



Nerves and Blood Vessels Damaged by DPN



Diabetes mellitus and ED



, et al. Int J Impotence Res (2013) 25, 1–6.

ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

Ερώτηση 3

Πως να χειρίζομαι τους ασθενείς με ΚΥΠ;

Common pathophysiologic mechanisms of **Erectile dysfunction** and **Benign Prostatic Hyperplasia**

LIFESTYLE
Vascular risk factors

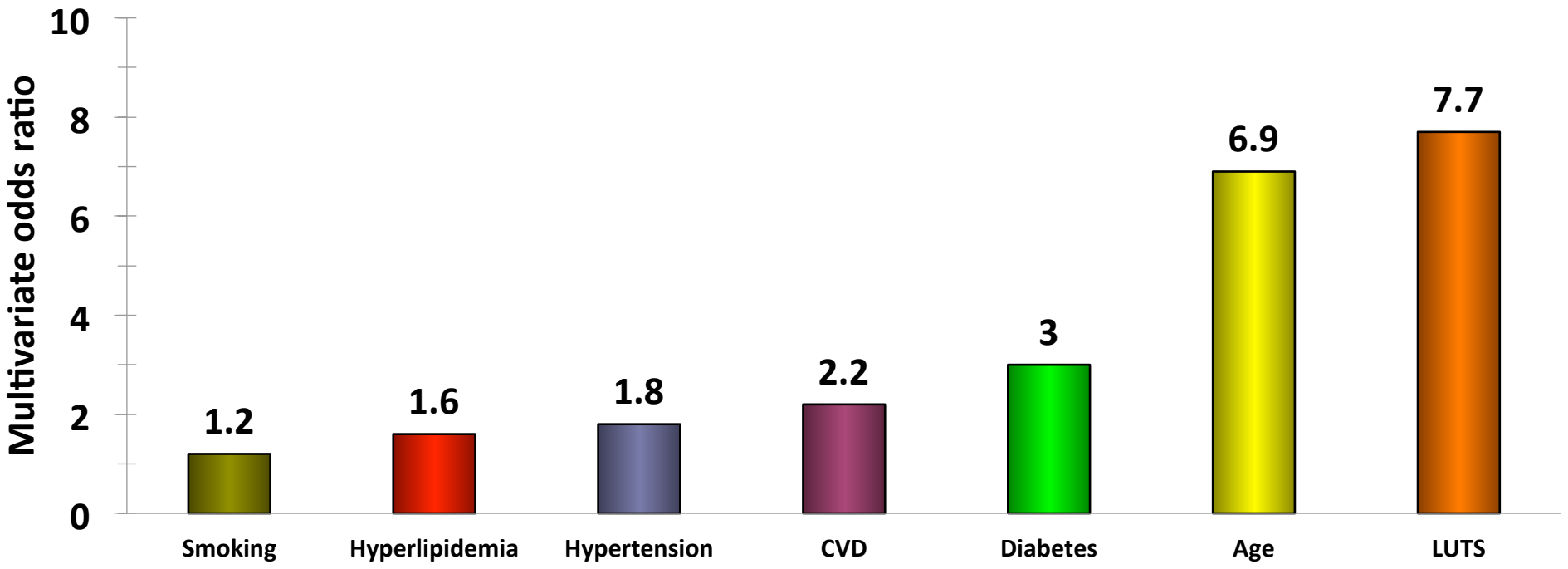
1.	2.	3.	4.
lteration of the tric oxide (NO)- yclic guanosine onophosphate GMP) pathway	Increased Rho-kinase (ROCK) contractile signalling	Autonomic adrenergic hyperactivity	Pelvic atherosclerosi
Decreased mooth muscle relaxation	Increased smooth muscle tone	Adrenergic receptor imbalance /dysregulation	Structural and function impairment

rectile dysfunction + Lower urinary tract symptoms (BPH-associated

M, et al: Eur Urol. 2011; 60: 809-25

source: www.ir

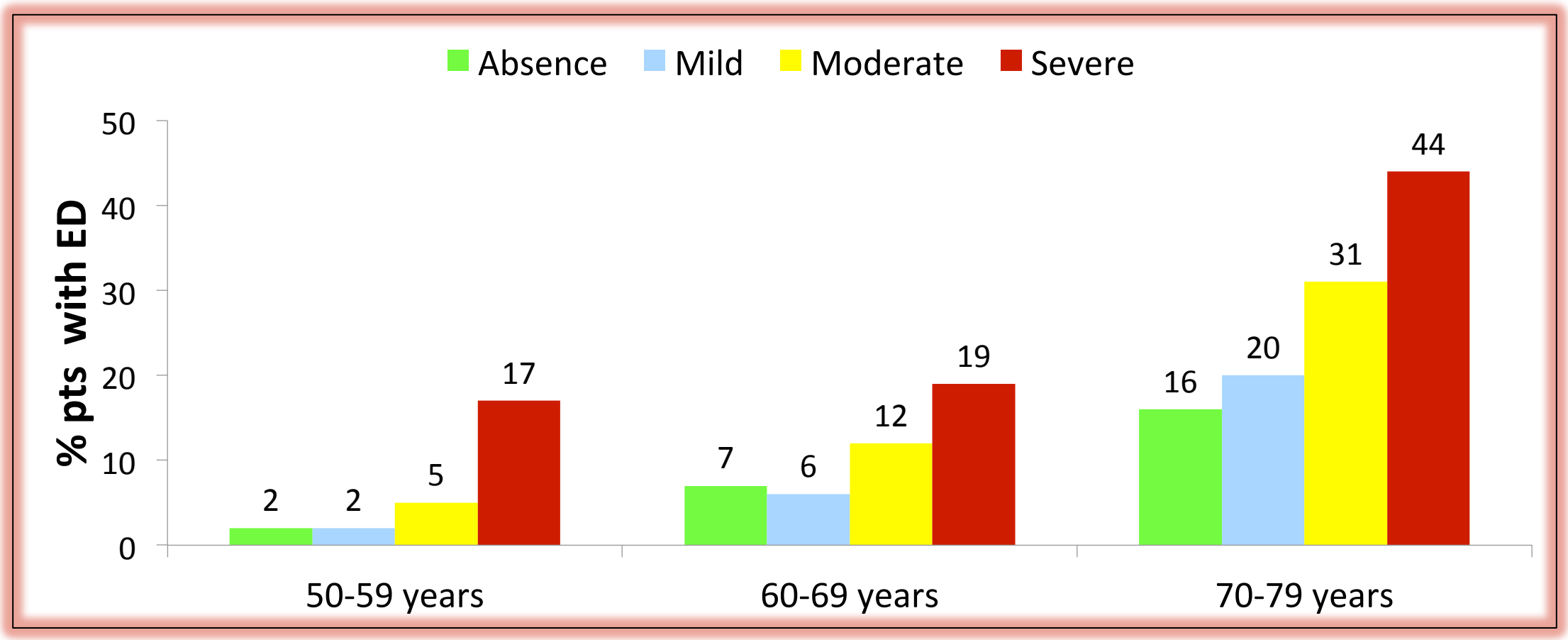
BPH-associated LUTS is strong predictor of ED



Rosen R et al. Eur Urol 2003, 44:637-649

- 24.8% had reduced or no sexual activity because of LUTS (Wein, Coyne et al. 2009)
- 31.1% of those with ED+BPH are treated for ED; 51.7% of men with BPH were under treatment (Foster, Annunziata et al. 2013).

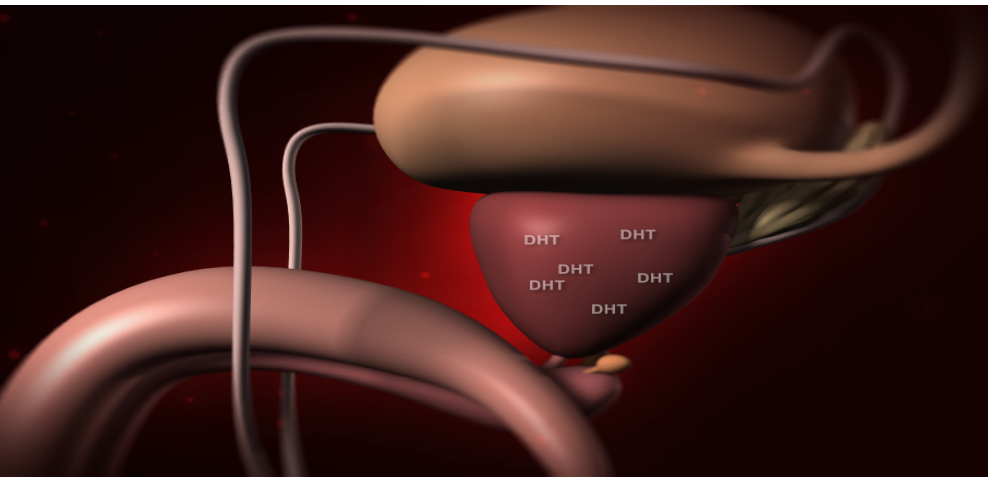
Severity of LUTS predicts severity of ED

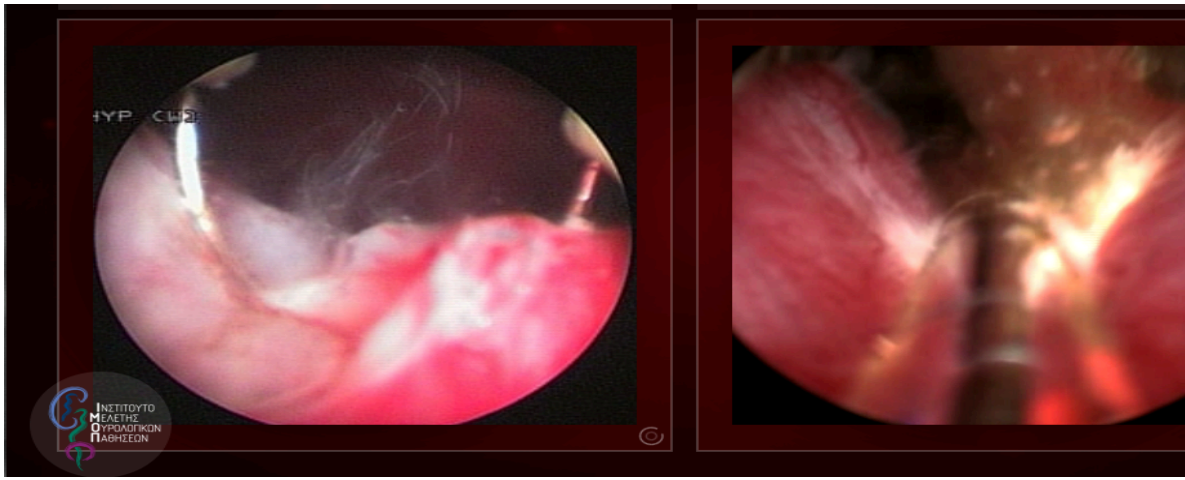


Rosen et al. Eur Urol 2003, 44:637-649

BPH-therapies and ED

- Clinical trials with 5ARI report prevalence rates of de novo erectile dysfunction of 5 - 9%, while decreased circulating dihydrotestosterone (DHT) in diminished sexual desire and/or orgasm (Gur et al. 2013).
- Prolonged adverse effects on sexual function are reported by a subset of men, raising the possibility of a causal relationship(Traish et al. 2011)
- A systematic review of 33 randomized controlled trials and cohort studies showed that minimally invasive surgeries for BPH have comparable effects to those of TURP on erectile function (Frieben, Lin et al. 2010).
- Bipolar and monopolar TURP have no difference on overall sexual function (Mamoulakis et al. 2013).





ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

Ερώτηση 4

Πως να χειρίζομαι ασθενείς
που λαμβάνουν φάρμακα
που βλάπτουν την στύση;

Drug-induced ED

- Antihypertensives, antidepressants and antiandrogens are the 3 most harmful drug categories for EF (Simonsen 2010)
- From a clinical practice point of view, the only way to identify the effect of a drug is to order a drug holiday, if indicated (Taylor et al. 2013).

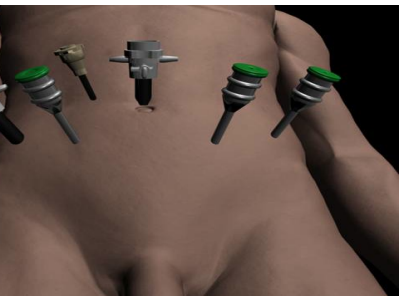
Clinical strategies to restore drug-induced ED:

- Dose reduction, if indicated;
- Dose schedule after sexual activity;
- Scheduling a drug holiday periodically, e.g. a two-day drug holiday (weekends) of an antidepressant may restore sexual function without the drug losing its efficacy.

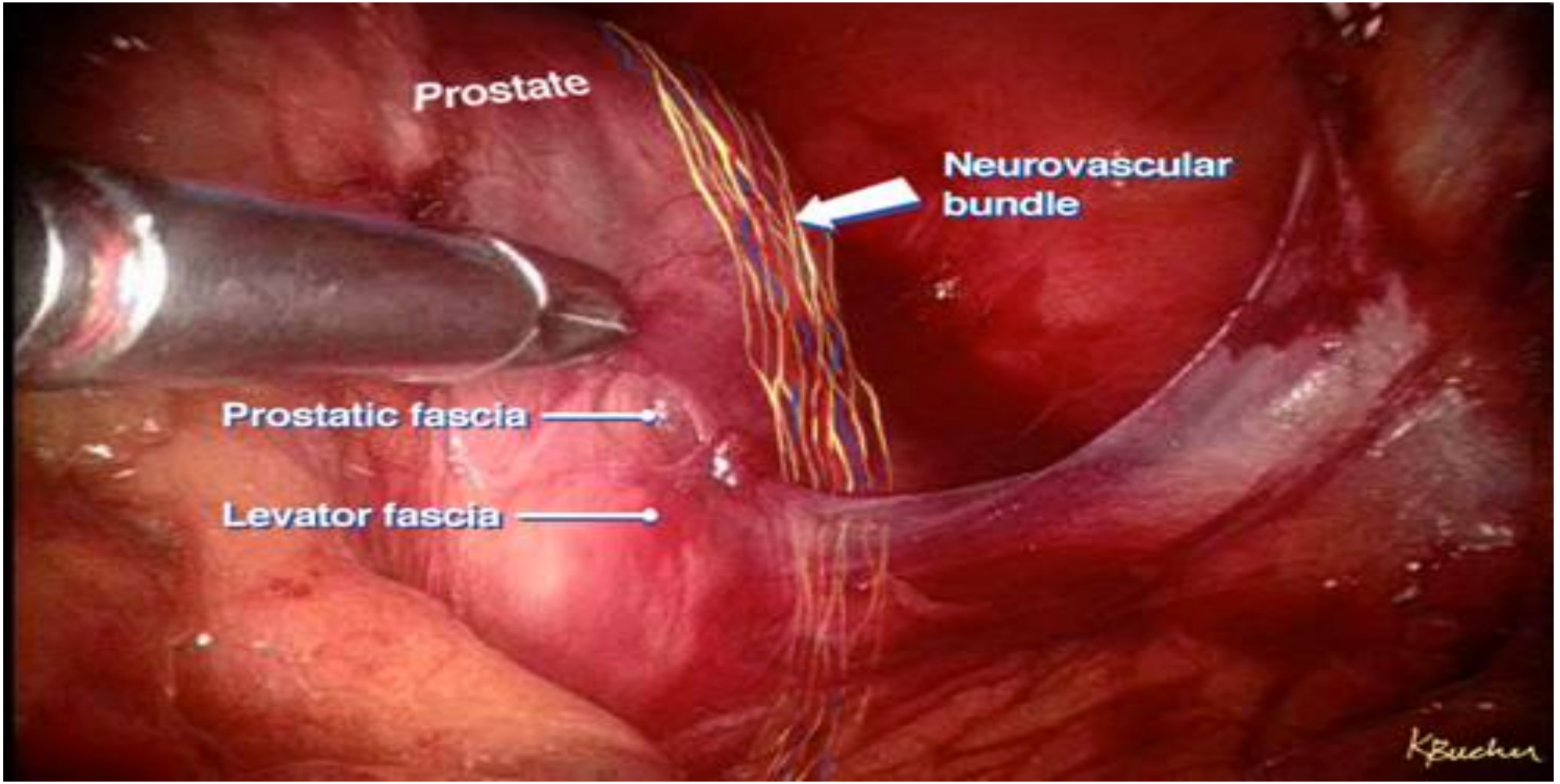
ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

Ερώτηση 5

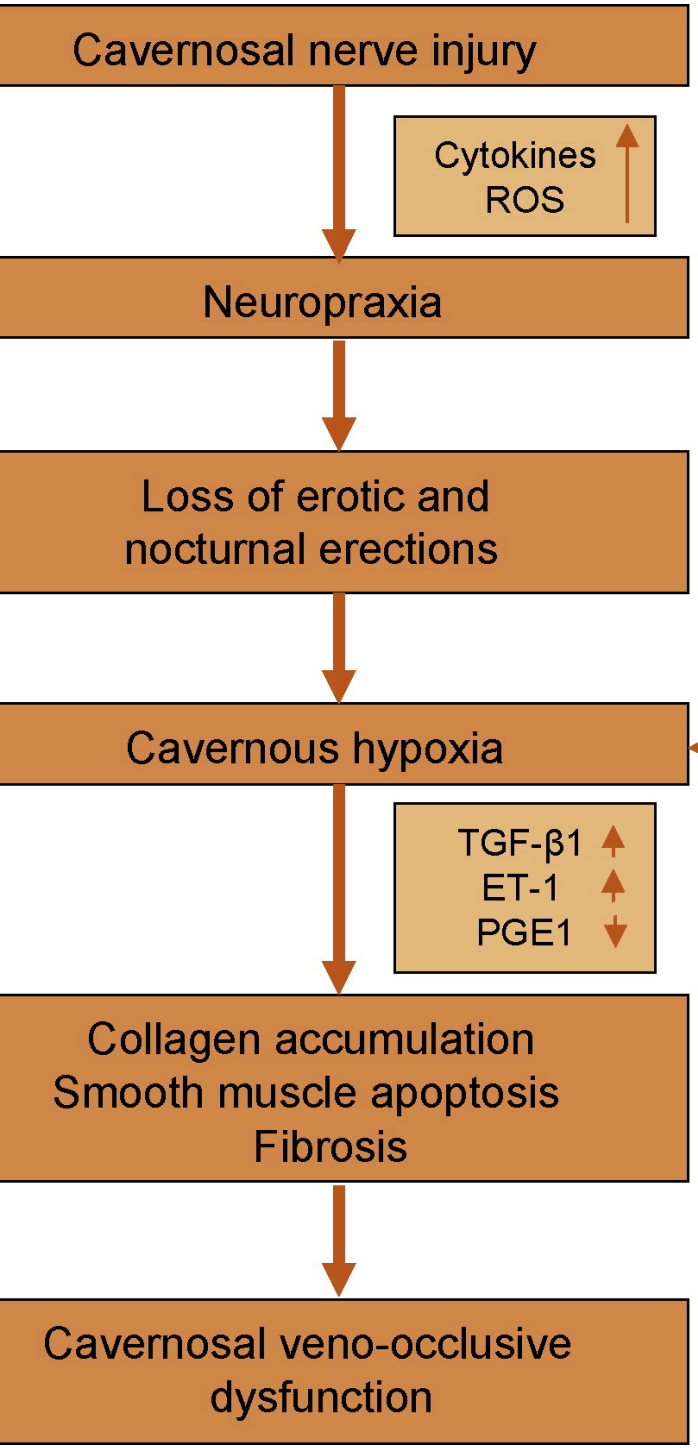
Τελικά η προστασία των νεύρων στη ριζική προστατεκτομή σώζει τη στύση;



The incredible nerve-sparing surgery



//urology.ufl.edu/patient-care/robotic-laparoscopic-urologic-surgery/procedures/robotic-nerve-sparing-radical-prostatectomy/



ELSEVIER

European Urology

Volume 55, Issue 2, February 2009, Pages 334–347

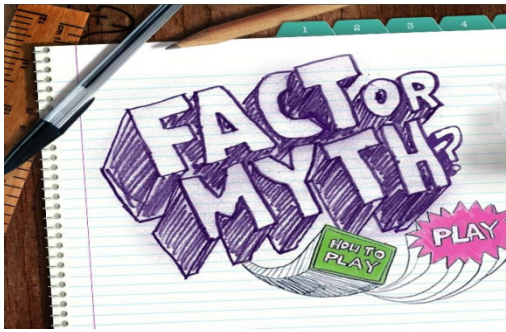
Collaborative Review – Prostate Cancer

Phosphodiesterase Type 5 Inhibitors in Postprostatectom Erectile Dysfunction: A Critical Analysis of the Basic Scie Rationale and Clinical Application

Konstantinos Hatzimouratidis[a], Arthur L. Burnett[b], Dimitrios Hatzichristou[a], Andrew R. Mc Francesco Montorsi[d], John P. Mulhall[e]

Nerve-sparing Radical Prostatectomy: myth or fact?

- Post-radical prostatectomy ED prevalence varies in different studies between 25-75% (Sanda et al. 2008)
- Such discrepancy in success rates allows clinicians to bypass the lack of well-designed head-to-head, comparative studies on different surgical techniques and eventually provide patients with unrealistic expectations (Hatzichristou 2012).
- The primary parameters contributing to EF recovery (Salonia, Burnett et al. 2012):
- ✓ Patient factors, including age, baseline EF and comorbid conditions),
- ✓ Cancer location (unilateral vs bilateral nerve-sparing),
- ✓ Technical aspects (i.e. intra- vs inter- vs extrafascial technique), surgical approach (i.e. open, laparoscopic and robot-assisted RP), as well as
- ✓ Surgeon factors (i.e. surgical volume and surgical skill)



Radical prostatectomy and erectile function: the end of the miracle

A randomized, double-blind, double- dummy, multicentre, parallel group study conducted at 87 centres worldwide, included 628 patients scheduled to undergo bilateral NSRP within 1 month of screening and having a normal IIEF-EF score of >26 at screening.

Three significant observations are of particular interest:

In 87 centers of excellence worldwide, 9 months postoperatively, only **16.8% of the patients in the placebo group had normal erectile function**, as they had preoperatively;

ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

Ερώτηση 6

Να χορηγώ PDE5i μετά τη ριζική προστατεκτομή;

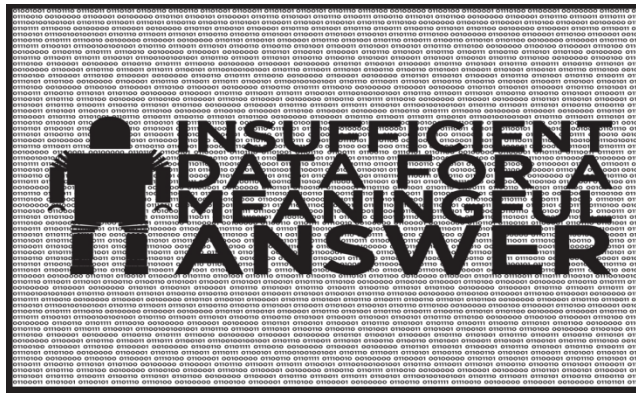
Rehabilitation Program: is it time to forget about it?

- Two double-blind studies have found no difference between nightly vs on-demand use of vardenafil or sildenafil after nerve-sparing radical prostatectomy (Montorsi et al. 2008; Pavlovich et al. 2013)
- A goal-oriented treatment paradigm has been recently proposed, where any chosen treatment may actually induce erections that allow sexual intercourse (Fode, Ohl et al. 2013)

ne must be very careful not to repeat the statement that penile
nabilitation regimens improve erectile function after radical prostatectomy
many times that it becomes a truth, even without the proper scientific
cking"

Fode, Ohl et al. 2013

Radical prostatectomy and erectile function: the end of the miracle



A randomized, double-blind, double- dummy, multicentre, parallel group study conducted at 87 centres worldwide, included 628 patients scheduled to undergo bilateral NSRP within 1 month of screening and having a normal IIEF-EF score of >26 at screening.

Statistically significant difference compared to placebo was noticed only at the vardenafil on-demand group (p = 0.0003);

On-demand administration of PDE5i **one year postoperatively reached mean IIEF3 success rates of approximately 60%**

1 out of 5 will be responder to PDE5i

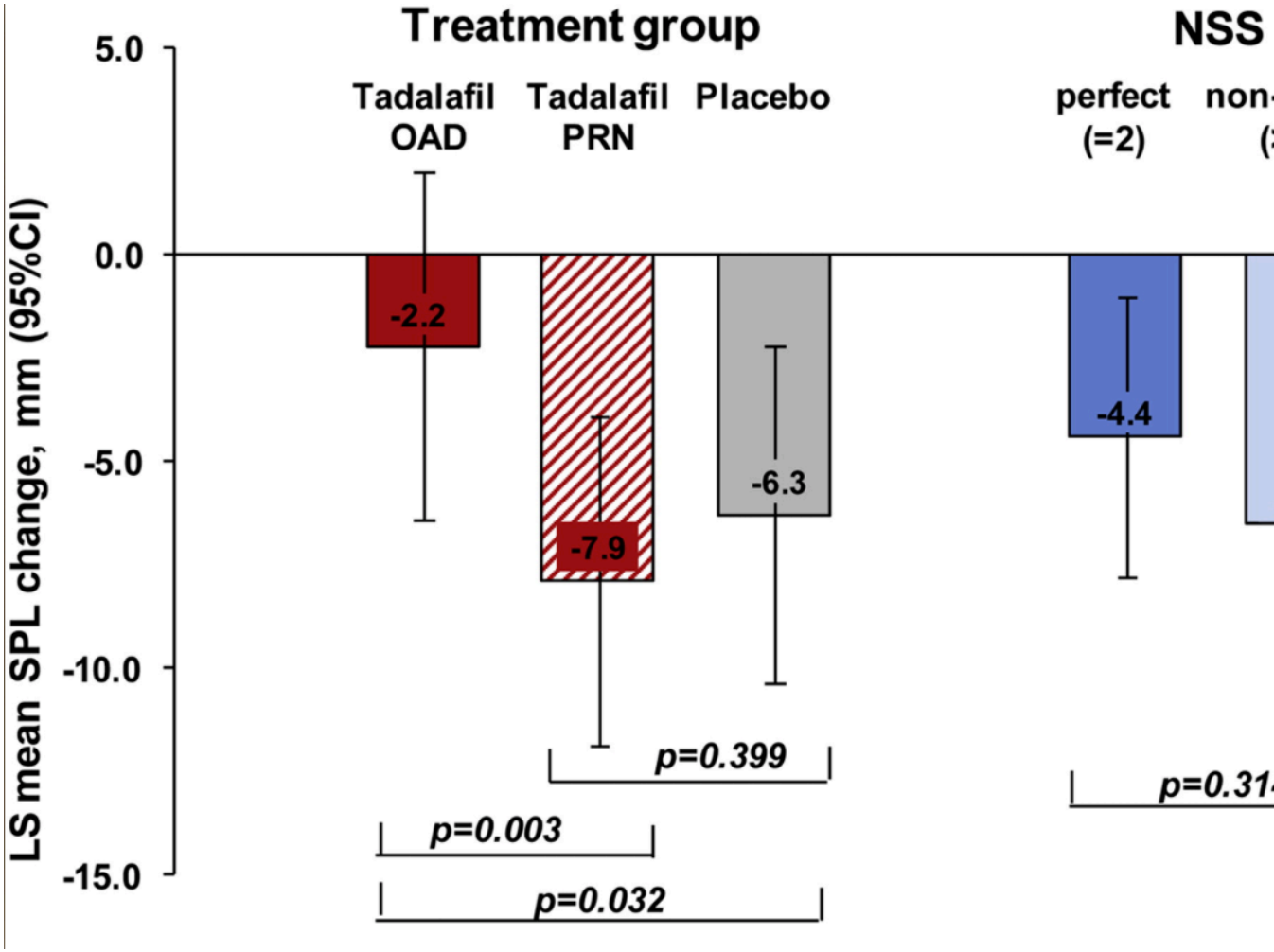
Urology

Volume 85, Issue 5, May 2015, Pages 1090–1096

Dysfunction

# of Tadalafil Once Daily on Penile Length Loss and g Erections in Patients After Bilateral Nerve-sparing l Prostatectomy: Results From a Randomized led Trial

k[a], Francesco Montorsi[b], Pierre Costa[c], Nimish Shah[d], Jose Maria Martinez-Jabaloyas[e], erer[f], Giuseppe M. Ludovico[g], Jay C. Lee[h], Carsten Henneges[i], Karim Hamid[j], Andrea Rossi[k], [l], Hartwig Büttner[i]



Urology

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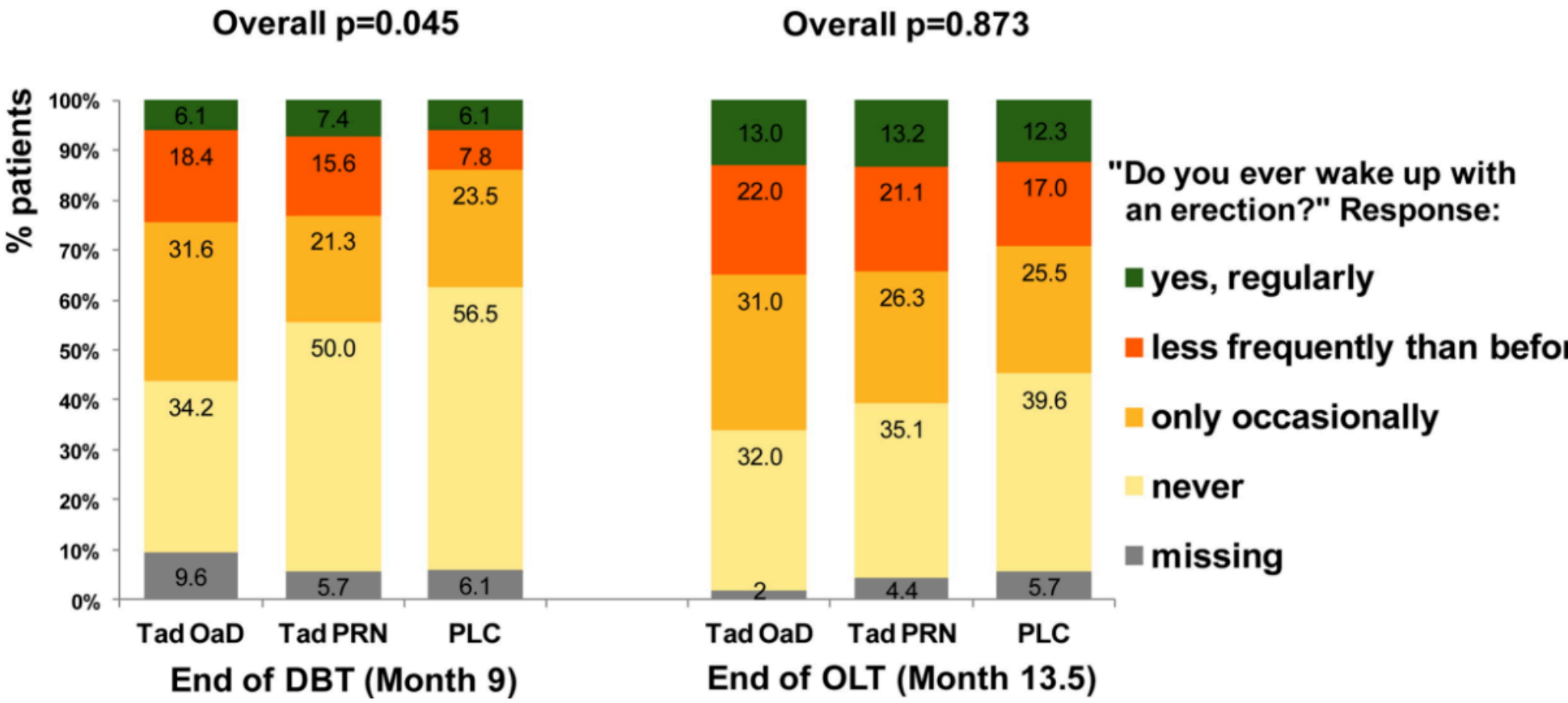


ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

Ερώτηση 7

Να χορηγώ PDE5i στην Peyronie;

Peyronie's disease: grafting procedures are not friendly to erectile function

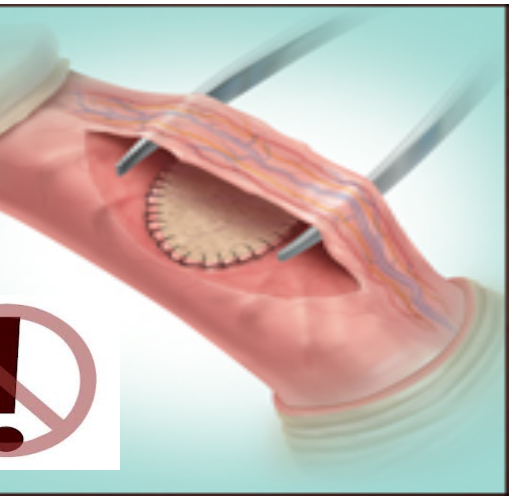
3.1% reported preoperative ED (vascular disease in 76.8%) (Kadioglu et al. 2011).

he risk of new ED with plication/tunica excision techniques is 0–13%, compared to 5–53% for grafting techniques (Hatzimouratidis et al. 2012)

5% of patients were dissatisfied with the outcome of graft surgery at 5-years (Chung et al. 2011)

minished sensation is reported in 4–21% for plication / tunica excision, with limited data for grafting procedures evine 2013).

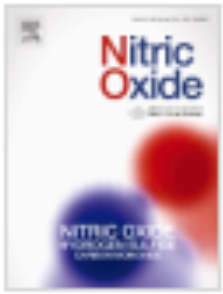
atients should be aware of grafting major drawbacks before surgery.



Based on the above, all proposed guidelines recommend tunica plication procedures curvature <60° and absence of extreme deformities (hourglass, hingle). (Hatzimouratidis, Eardley et al. 2012;Levine and Burnett 2013).

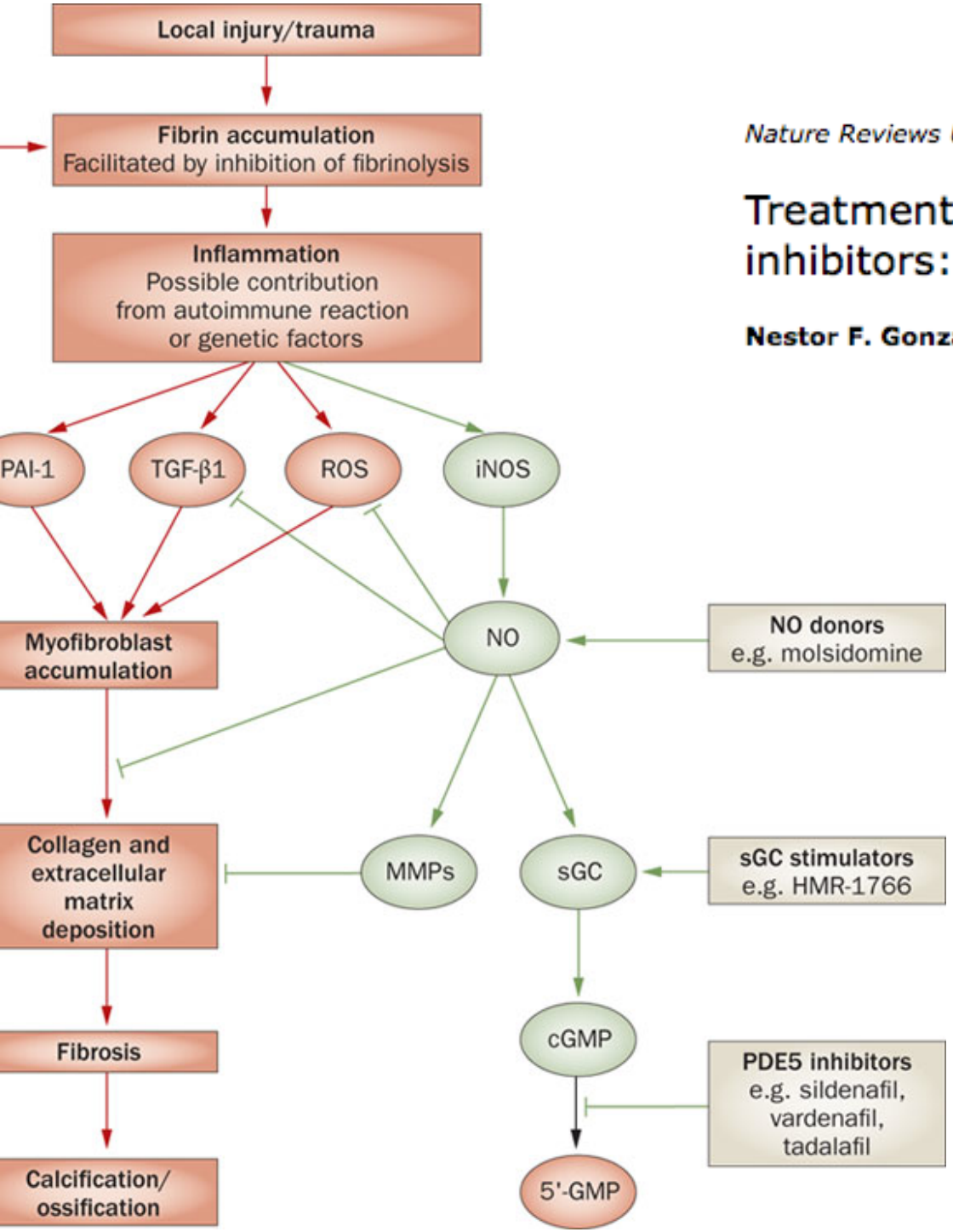
Nitric Oxide

Volume 9, Issue 4, December 2003, Pages 229–244



L-Arginine and phosphodiesterase (PDE) inhibitors counteract fibrosis in the Peyronie's fibrotic plaque and related fibroblast cultures

Eliane G.A Valente[a, 1], Dolores Vernet[a, 1], Monica G Ferrini[a, 1], Ansha Qian[a], Jacob Rajfer[a, b], Nestor F Gonzalez-Cadavid[a, b,]



Nature Reviews Urology **7**, 215-221 (April 2010) | doi:10.1038/nrurol.2010.24

Treatment of Peyronie's disease with PDE5 inhibitors: an antifibrotic strategy

Nestor F. Gonzalez-Cadavid & Jacob Rajfer

eviews Urology 7, 215-221 (April 2010) | doi:10.1038/nrurol.2010.24

ment of Peyronie's disease with PDE5 tors: an antifibrotic strategy

. Gonzalez-Cadavid & Jacob Rajfer

eyronie's disease (PD) is a localized fibrotic condition of the tunica albuginea that is associated with risk factors fo rpora cavernosa fibrosis (such as advanced age and diabetes) and Dupuytren contracture, another localized brotic process.

ost of the current pharmacological treatments for PD are not based on antifibrotic approaches that have shown romising results in animal models and clinical efficacy in other fibrotic conditions, which may explain why they are enerally unsuccessful.

idence gathered in human specimens and animal models of PD have elucidated aspects of its etiology and stopathology, showing that overexpression of transforming growth factor β1, plasminogen activator inhibitor 1, eactive oxygen species and other profibrotic factors, which are, in most cases, assumed to be induced by trauma t e tunica albuginea, leads to myofibroblast accumulation and excessive deposition of collagen.

the same time, a steady overexpression of inducible nitric oxide synthase, leading to increased nitric oxide and GMP levels, seems to act as an endogenous antifibrotic mechanism.

is process has also been reported in corporal and cardiovascular fibrosis, and has led to the demonstration that ng-term continuous administration of phosphodiesterase type 5 inhibitors counteracts the development of a PD- e fibrotic plaque in a rat model, and later extended to the prevention of corporal fibrosis in animal models of ectile dysfunction.

ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

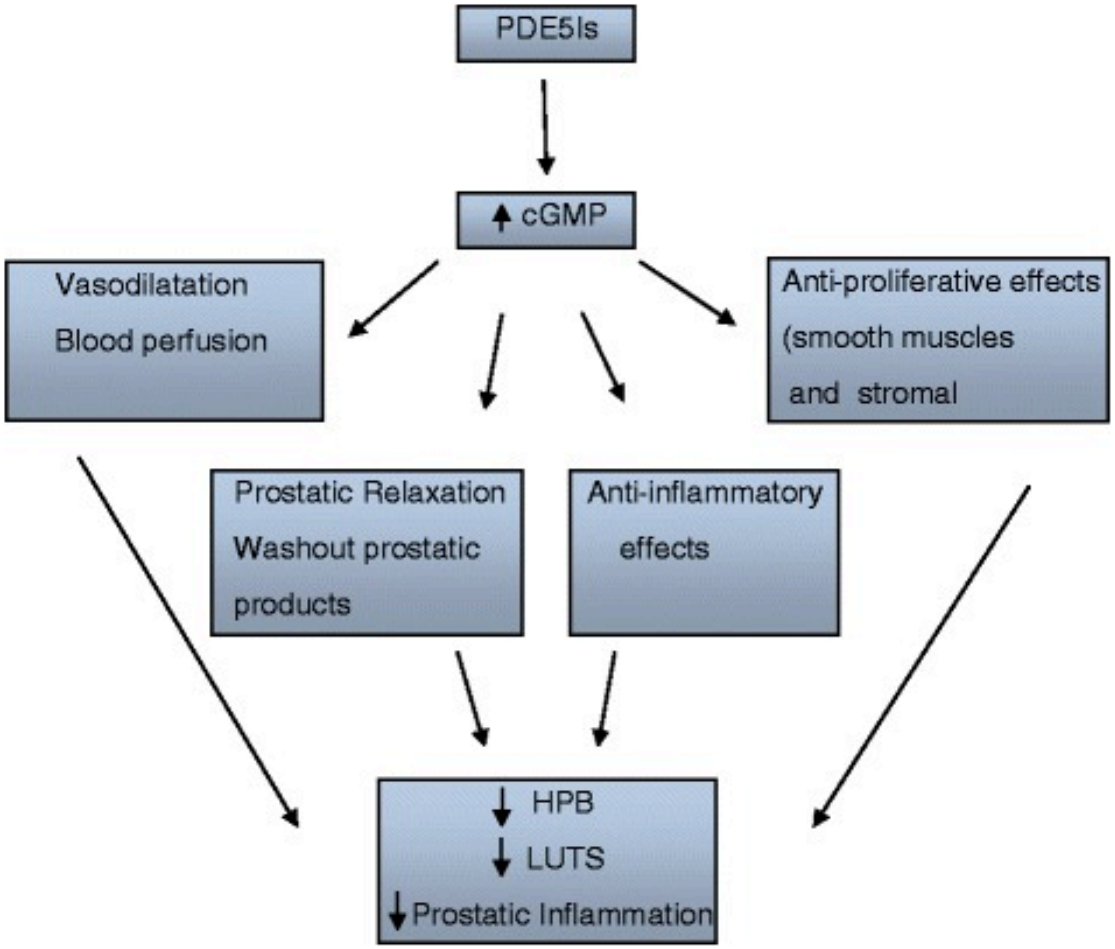
Ερώτηση 8

Να χορηγώ PDE5i στην χρόνια προστατίτιδα;

xoto CA, Gomes FO dos S. The role of phosphodiesterase-5 inhibitors in prostatic inflammation: a review. *Journal of ammation (London, England)*. 2015;12:54.

1. PDE5Is are therapeutical tools used for several urological and non-urological disorders, and experimental evidence suggest that their chronic use does not induce cellular and molecular prostatic alterations.
2. The mechanisms involved in improvements observed in BPH/LUTS possibly include relaxation of the smooth muscles of the bladder and prostate by NO/cGMPc signaling or via improving RhoA/Rho-kinase (ROCK), and by reduction of the hyperactivity of the autonomic nervous system.
3. PDE5Is can also direct and indirectly down-regulate prostatic inflammation/BPH/LUTS by inducing high levels of cGMP.
4. In conclusion, since inflammation is a major factor in benign prostatic hyperplasia (BPH) progression, PDE5Is could also restore prostatic function, as they act as potent anti-inflammatory drugs.

Fig. 1



Schematic diagram showing the hypothetical mechanism of Phosphodiesterase 5 Inhibitors (PDE5Is) on prostatic inflammmation. PD
direct and indirectly down-regulate prostatic inflammation/BPH/LUTS by inducing high levels of cGMP

o CA, Gomes FO dos S. The role of phosphodiesterase-5 inhibitors in prostatic inflammation: a review. *Journal of mation (London, England)*. 2015;12:54.

y phosphodiesterase type 5 inhibitor apy: a new treatment option for statitis/prostatodynia?

S. Kirby,* Culley Carson III† and Prokar Dasgupta*‡

*state Centre and ‡Department of Urology, Guy's Hospital, King's College, London, UK; and †Department of The University of North Carolina, Chapel Hill, NC, USA

In addition to the symptom of pelvic pain, men with chronic abacterial prostatitis/prostatodynia also frequently complain associated LUTS and ejaculatory discomfort. Consequently treatment with tadalafil at a dose of 5 mg/day for a period of time would seem logical. It could be surmised that many of its beneficial effects might stem from an improvement of blood flow to pelvic organs as a consequence of its anti-inflammatory and vasodilatory activity, as well as a relaxant effect on smooth muscle, as has been previously suggested in the case of LUTS by Andersson and others [6–8]

ly phosphodiesterase type 5 inhibitor rapy: a new treatment option for statitis/prostatodynia?

S. Kirby,* Culley Carson III† and Prokar Dasgupta*‡

*state Centre and ‡Department of Urology, Guy's Hospital, King's College, London, UK; and †Department of The University of North Carolina, Chapel Hill, NC, USA

Clearly the hypothesis that daily treatment with a PDE5 inhibitor might be beneficial in men with the prevalent condition of chronic abacterial prostatitis/prostatodynia will need to be formally tested in the context of a randomised controlled trial. If the results of such a study were to prove positive, the quality of life of very many sufferers of this disorder might be significantly improved. One might also speculate that it could provide a concomitant benefit to the partners of these often very unhappy men.

ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

Τελευταια ερωτηση

Να χορηγώ PDE5i στην νοσο Peyronie;

Μη χειρουργική αντιμετώπιση νόσου Peyronie

Oral therapies for PD.

ment (dose)	Mechanism of action	Efficacy	ICSM guidelin
0 IU daily to twice	Antioxidant reduces oxidative stress of reactive oxygen species shown to be increased in PD	NB for pain, curvature, or plaque size	NB for deformity
5 mg daily)	Inhibits fibrosis and collagen deposition by inhibiting neutrophil microtubules	NB for pain, curvature, or plaque size	NB for deformity
inobenzoate (3 g	Stabilises tissue serotonin monoamine oxidase activity; antifibrotic effect due to a direct inhibitory effect on fibroblast glycosaminoglycan secretion	Mean decrease in plaque size in 74.3%, no improvement in curvature	NB for deformity
0 mg daily)	Affects the release of TGF from fibroblasts and blocks TGF receptors	No demonstrable improvement in pain, curvature, or plaque size	NB for deformity
twice daily)	Reduces both collagen fibre deposition and elastogenesis	No significant improvement in pain, curvature or plaque size	NB for deformity
(400 mg twice	Nonspecific phosphodiesterase inhibitor, antifibrotic presumably	36.9% with mean decrease in curvature of 23°	Further studies required findings

NB, no benefit; TGF, transforming growth factor.

Levine LA. Peyronie's disease: A contemporary review of non-surgical treatment. *Arab Journal of Urology*. 2013;11(3):278-283.

J Androl. 2011 Aug;29(2):156-160. English.
ed online Aug 31, 2011. http://dx.doi.org/10.5534/kja.2011.29.2.156

ct of PDE5 Inhibitor in Nonsurgical Management of onie's Disease: Preliminary Study

Kuk Ham, Mi Mi Oh, Su Hwan Shin, Tae Yong Park, Sang Woo Kim, Jong Jin Park, Seung Min Jeong
Geon Moon

ment of Urology, Korea University College of Medicine, Korea University Institute for Regenerative e, Seoul, Korea.

Conclusions

Although the effect of PDE5 inhibitor for pain relief, successful intercourse and resolution of plaque size was not significant, patients who received PDE5 inhibitors had a more satisfaction of treatment of PD. Further prospective studies on the effect of PDE5 inhibitor in PD will be needed.

Η ΣΥΝΔΥΑΣΤΙΚΗ ΘΕΡΑΠΕΙΑ

(ΨΥΧΟΣΕΞΟΥΑΛΙΚΗ
+ ΦΑΡΜΑΚΕΥΤΙΚΗ)
ΠΡΟΣΦΕΡΕΙ:

ΠΗΓΗ: Melnik T: J. Sex. Medicine; 5(11), (2008)

ΠΕΪΚΕΣ ΠΡΟΘΕΣΕΙΣ

Αποτελούν την πιο παλιά μέθοδο αντιμετώπισης

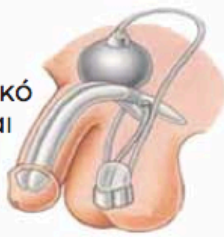
Έχει ένδειξη σε κάθε άντρα που έχει δοκιμάσει **ΑΝΕΠΙΤΥΧΩΣ** τις άλλες θεραπείες.

Υπάρχουν 2 τύποι προθέσεων:

οι **ΣΤΑΘΕΡΕΣ**

και οι **ΔΙΟΓΚΟΥΜΕΝΕΣ**

Οι σταθερές αποτελούνται από 2 κυλίνδρους από ειδικό βιο-υλικό που τοποθετούνται μέσα στα 2 σηραγγώδη σώματα.



Στις διογκούμενες, οι κύλινδροι είναι συνδεδεμένοι με σύστημα αντλίας που δίνει τη δυνατότητα πλήρωσης των κυλίνδρων με φυσιολογικό ορό. Δίνουν άριστο αισθητικό αποτέλεσμα, αλλά έχουν υψηλό κόστος.

Πιθανότητα μηχανικής βλάβης

Η τοποθέτηση της πρόθεσης γίνεται με χειρουργική επέμβαση διάρκειας 1 ώρας

ΙΚΑΝΟΠΟΙΗΣΗ:

Η ικανοποίηση των αντρών και των συντρόφων ξεπερνά το 90%

ΕΠΙΠΛΟΚΕΣ:

Σπάνιες, με πιο σημαντική την μόλυνση της πρόθεσης (χρήζει άμεσης χειρουργικής αφαίρεσης και τοποθέτηση νέας)