

ORIGINAL RESEARCH—ERECTILE DYSFUNCTION

Is It Worth Continuing Sexual Rehabilitation after Radical Prostatectomy with Intracavernous Injection of Alprostadil for More than 1 Year?

René Yiou, MD, PhD, PUPH,* Zentia Bütow, MD,* Juliette Parisot, MD,[†] Michele Binhas, MD,[‡] Odile Lingombet, RN,* Deborah Augustin, RN,* Alexandre de la Taille, MD, PhD,* and Etienne Audureau, MD, PhD[†]

*Department of Urology, Henri Mondor Teaching Hospital, Créteil, France; [†]Department of Public Health, LIC EA4393, Université Paris Est (UPEC), Henri Mondor Teaching Hospital, Créteil, France; [‡]Department of Anesthesiology, Henri Mondor Teaching Hospital, Créteil, France

DOI: 10.1002/sm2.51

ABSTRACT

Introduction. Intracavernous alprostadil injection (IAI) is a widely used treatment for sexual rehabilitation (SR) after radical prostatectomy (RP). It is unknown whether the continuation of IAI beyond 1 year continues to improve erectile function.

Aims. To assess evolution of sexual function in patients using IAI who are nonresponsive to phosphodiesterase type 5 inhibitors (PDE5i) between 12 (M12) and 24 (M24) months after RP.

Methods. We retrospectively studied 75 men with a nerve-sparing laparoscopic RP, who had normal preoperative erectile function, and who regularly used IAI for SR for at least 24 months. At M12, no patients had responded to PDE5i.

Main Outcome Measures. At 12 and 24 months, sexual function was assessed with the UCLA Prostate Cancer Index (UCLA-PCI), International Index of Erectile Function (IIEF)-15, and erection hardness score (EHS) with and without IAI. We also assessed the satisfaction rate with IAI, injection-related penile pain, and satisfaction of treatment. Statistical analysis was performed by using *t*-tests for paired data and Spearman's rho correlation coefficients to assess the relationships between scores at M12 and M24.

Results. Improvement of nocturnal erection was noted (UCLA-PCI, question 25); however, no significant difference was found for IIEF-erectile function with (19.60 ± 9.80 vs. 18.07 ± 10.44) and without IAI (4.63 ± 2.93 vs. 4.92 ± 4.15), UCLA-PCI-sexual bother (37.14 ± 21.45 vs. 37.54 ± 19.67), nor the EHS score with (2.97 ± 1.30 vs. 2.57 ± 1.30) and without IAI (0.67 ± 1.11 vs. 0.76 ± 0.10). The rate of satisfaction with treatment decreased over time (66.6% vs. 46.7%, *P* = 0.013). Improved response to IAI at M12 was not correlated to improvement in spontaneous erections at M24.

Conclusion. The response to IAI remained stable after 2 years of treatment, and no significant improvement of spontaneous erections during intercourse attempts was found between M12 and M24. Patients should be informed of the limited effect of IAI on natural erections after 1 year. **Yiou R, Bütow Z, Parisot J, Binhas M, Lingombet O, Augustin D, de la Taille A, and Audureau E. Is it worth continuing sexual rehabilitation after radical prostatectomy with intracavernous injection of alprostadil for more than 1 year? *Sex Med* 2015;3:42–48.**

Key Words. Erectile Dysfunction; Sexual Rehabilitation; Radical Prostatectomy; Alprostadil; Sexual Pain

Introduction

Radical prostatectomy (RP) remains the standard treatment for organ-confined prostate cancer but continues to cause erectile dysfunction related primarily to cavernous nerve injury [1]. Despite the use of nerve-sparing techniques, cavernous nerve dissection induces neuropraxia with a decrease in nitric oxide production. The resulting absence of erections during the postoperative period may cause cavernous tissue fibrosis and veno-occlusive dysfunction, ultimately leading to permanent erectile dysfunction [2]. To prevent this sequence of events, early treatment with either oral erectogenic drugs such as phosphodiesterase 5 inhibitors (PDE5i) [3–5] or intracavernous injection of vasoactive substances [6–8] is now considered in patients who wish to recover sexual activity after RP. The objective of this treatment is to resume satisfactory intercourse and prevent cavernous tissue damage by improvement in local oxygen supply [9]. The regular use of erectogenic drugs is believed to improve spontaneous erections and is therefore widely advocated for sexual rehabilitation (SR) after RP [2,9–12].

In our department, SR after RP relies chiefly on the use of intracavernous alprostadil injections (IAIs). IAI remains one of the most widely prescribed treatments for post-RP erectile dysfunction (pRPED) in France [13], predominately because the costs of this treatment following RP surgery are reimbursed by public health insurance. Several studies have demonstrated that erectile function improves with the early and regular use of IAI alone [6,14–16] or combined with other vasoactive substances [3–17]. However, it is not known how long this treatment should be continued before the maximal effect is reached. Moreover, IAI often causes penile pain [18], which leads to a high treatment discontinuation rate (35% in our experience at 1 year) and hinders the SR process [16–19]. We have previously shown in a population of patients with pRPED, and treatment with or without IAI, that erectile function improves between the 6th and 12th month after starting IAI. However, the overall erectile function remained low after 1 year, and significant pain on erection (>4/10) was still reported by some patients. Consequently, after 1 year of treatment with IAI, some patients still have insufficient erections even when using PDE5i and may express lassitude toward IAI and/or subsequently report impaired quality of life due to the constraints of the treatment. In such situations, it is unknown

whether the SR process should be continued with further IAI treatment in order to increase the chances of developing a natural erectile function or if another therapeutic strategy should be considered. Other injectable erectogenic preparations such as Tri-Mix [7] and alprostadil combined with lidocaine [20] may cause less pain than alprostadil alone and therefore may be more efficient. However, in France, one of the Tri-Mix components, phentolamine, is not available, and another, papaverine, is not licensed for intracavernous use. At present, Tri-Mix is not among the treatments recommended by the French Urological Association (AFU) for erectile dysfunction after RP [21]. As a consequence, IAI and PDE5i represent the main therapeutic options for SR in France.

Aims

In this study, we investigated whether patients using IAI for pRPED, who were unresponsive to PDE5i at 1 year following RP, would continue to improve their sexual function, whether IAI-induced or spontaneous erections, when the IAI treatment was continued for a further year.

Methods

Charts of patients undergoing bilateral nerve-sparing laparoscopic RP between July 2007 and July 2010 for localized prostate cancer and who were enrolled in a SR program consisting of IAI for at least 2 years were reviewed retrospectively. All RP procedures were performed by one of three experienced surgeons in our department.

The SR program consisted of alprostadil injections (Edex[®], Schwarz Pharma, Boulogne Billancourt, France) self-administered intracavernously commencing 1 month after RP surgery under the supervision of a physician and a nurse. An information letter explaining the concept of SR was given to all patients. Patients were advised to perform the injection at home twice a week. They received follow-up at the uro-oncology department once a week until the injections could be performed competently. Patients were then reviewed every 6 months. We advised patients to attempt intercourse as often as possible as part of the SR process. PDE5i (Viagra[®] 100 mg, Pfizer, New York, NY, USA) treatment was systematically offered after 1 year of IAI use or before if spontaneous erections were reported. PDE5i was considered a failure when patients achieved an erection hardness score (EHS) of less than two, and therefore were unable to

achieve penetration, for a minimum of eight trials with PDE5i. Patients who failed to respond to PDE5i treatment were encouraged to continue the SR process with IAI.

Included in this study were patients with an International Index of Erectile Function (IIEF)-erectile function (EF) score of over 24 preoperatively, patients without presurgery treatment of erectile dysfunction, patients reporting an EHS of ≤ 2 when using PDE5i (Viagra® 100) at the 1 year follow-up, and patients continuing the use of IAI for a minimum of 24 months following RP. Patients excluded were those who received adjuvant cancer treatment following RP.

Main Outcome Measures

Patients were invited to complete the IIEF-15 questionnaire that included scores for EF, orgasmic function, sexual drive (SD), intercourse satisfaction (IS), overall satisfaction, the EHS, and the Global Assessment Questionnaire (GAQ). The GAQ included the following questions: Q1: "Has the treatment you have been taking improved your erectile function?" and Q2: "If yes, has the treatment improved your ability to engage in sexual activity?" These were completed at 12 and 24 months after RP with reference to experiences of intercourse when using IAI or any other treatment. The patients were also invited to complete the EHS and to answer questions 1–5, and 15 on the EF domain of the IIEF, when not using any treatment. The satisfaction rate when using IAI was also identified by using the following question [22]: "On the whole, are you satisfied with IAI? 1) Very satisfied, 2) Moderately satisfied, 3) Neither satisfied nor dissatisfied, 4) Moderately dissatisfied, 4) Very dissatisfied."

The UCLA Prostate Cancer Index (UCLA-PCI) questionnaire [23] was used to measure sexual bother (score min–max: 0–100, the value of 100 corresponding to the poorest value) and the return of nocturnal erection (question 25): "How often have you awakened in the morning or night with an erection?: 1) never, 2) seldom, 3) not often (less than half the time), 4) often (more than half the time), 5) very often (more than 75% of the time)."

Pain experienced by patients during erections was assessed separately using a numeric rating scale ranging from 0 (no pain) to 10 (worst pain imaginable). We also recorded the number of injections administered per week, the dose injected and any other erectogenic treatments used at the M24 review, as well as any complications associ-

ated with the use of IAI. Finally, the patients were asked at M24 if they considered that they had recovered their preoperative erectile function. All questionnaires were handed to the patients and once completed were reviewed by the authors with each patient.

The main comorbidities at the time of RP and tumor status were also recorded.

This study formed part of a larger program based at the department of Urology to evaluate functional urological disorders occurring after RP. This program was approved by the institutional review board of the Henri Mondor Hospital.

Statistical Analysis

Descriptive results are presented as the mean (\pm standard deviation). The paired *t*-test was used for the comparison of continuous variables between paired groups (changes in scores between 12 and 24 months post-RP). A χ^2 test was used to compare the rates of nocturnal erection (UCLA-PCI) and satisfaction with treatment by IAI at M12 and M24. Spearman's rho correlation coefficients were calculated to identify the potential factors measured at M12 that may predict erectile function scores at M24 and their changes between M12 and M24. A two-tailed *P* value <0.05 was considered significant. All statistical analyses were performed by using STATA v12.1 (StataCorp. 2011, Stata Statistical Software: Release 12, StataCorp LP, College Station, TX, USA).

Results

Seventy-five patients met the inclusion criteria. Mean age \pm SD was 59.4 ± 8.2 . Characteristics of the population are presented in Table 1. Table 2 lists the mean scores at M12 and M24. No signifi-

Table 1 Comorbidities of the population at the time of radical prostatectomy and tumor status

	N (%)
Comorbidities	
Diabetes (type 2)	6 (8)
Dyslipidemia	16 (21.3)
BMI, mean \pm SD (kg/m ²)	25.6 \pm 2.6
Tobacco smoking	4 (5.3)
Hypertension	25 (33.3)
Coronary artery disease	5 (6.6)
Tumor status	
pT2	70 (93.3)
pT3a	5 (6.7)
Gleason VI	16 (21.3)
Gleason VII	51 (68)
Gleason VIII	8 (10.7)

Table 2 Mean erectile function, satisfaction, and penile pain scores at 12 (M12) and 24 months (M24) after bilateral nerve-sparing radical prostatectomy

N = 75	M12	M24	P value
Number of IAI/week	1.88 ± 0.86	1.61 ± 0.69	0.15
Dose injected (µg)	8.97 ± 5.20	10.18 ± 6.13	0.072
Pain at erection (0–10)	2.92 ± 2.70	2.52 ± 2.35	0.66
IIEF-EF with treatment	19.60 ± 9.80	18.07 ± 10.44	0.92
IIEF-EF without treatment	4.63 ± 2.93	4.92 ± 4.15	0.28
IIEF-OF with treatment by IAI	5.18 ± 3.42	5.58 ± 3.42	0.27
IIEF-SD	6.05 ± 2.32	5.93 ± 2.06	0.74
IIEF-IS	7.18 ± 4.11	6.51 ± 4.23	0.69
IIEF-OS	5.48 ± 2.70	5.62 ± 2.56	0.34
EHS with treatment by IAI	2.97 ± 1.30	2.57 ± 1.30	0.47
EHS without treatment by IAI	0.67 ± 1.11	0.76 ± 0.10	0.14
Satisfaction with treatment by IAI, n (%)			0.013
Satisfied			
Very satisfied	16 (21.3%)	9 (12%)	
Moderately satisfied	34 (45.3%)	26 (34.7%)	
Not satisfied			
Neither satisfied nor dissatisfied	9 (12%)	13 (17.3%)	
Moderately dissatisfied	8 (10.7%)	14 (18.6%)	
Very dissatisfied	8 (10.7%)	13 (17.3%)	
GAQ			
GAQ1, Yes, n (%)	65 (86.7%)	57 (76%)	0.093
GAQ2, Yes, n (%)	53 (70.7%)	46 (61.3%)	0.22
Sexual bother (UCLA-PCI)	37.14 ± 21.45	37.54 ± 19.67	0.759
Report of nocturnal erection (UCLA-PCI)			0.002
Never	60 (80.5%)	49 (64.9%)	
Less than 25%	7 (9.8%)	24 (31.6%)	
Less than 50%	4 (4.9%)	0 (0%)	
More than 50%	4 (4.9%)	1 (1.8%)	
More than 75%	0 (0%)	1 (1.8%)	

Results are means (±standard deviation). Significant values are in bold

IIEF = International Index of Erectile Function; IIEF domains: EF = erectile function; OF = orgasmic function; SD = sexual drive; IS = intercourse satisfaction; OS = overall satisfaction; EHS = erection hardness score; IAI = intracavernous alprostadil injection

cant difference was found between the 12 and 24 months scores with the exception that the satisfaction rate of treatment was lower and reports of nocturnal erection increased at 24 months postsurgery. The variation of the mean IIEF-EF scores was $+0.15 \pm 7.62$ with treatment and $+0.59 \pm 3.36$ without treatment and showed that the overall the response to IAI and achievement of spontaneous erections remained stable. The IIEF-EF score when no treatment was taken decreased in 23 patients (30.6%) remained unchanged in 19 patients (25.3%) and improved in 33 patients (44%) (min +1, max +10) at M24 in comparison to M12. No case of normalization of IIEF-EF scores without treatment (>24) was noted, and no patient considered that they had recovered their preoperative function.

Overall, 65 patients (86.8%) at M12 and 57 (76%) patients at M24 considered that the treatment improved their erection (GAQ-Q1), and 53 patients (70.7%) at M12 and 46 patients (61.3%) at M24 considered that IAI improved their ability to engage in sexual activity (GAQ-Q2).

At M24, 28 patients (37.3%) were using PDE5i (sildenafil, tadalafil or vardenafil), and two patients were using a vacuum in association with IAI.

Table 3 shows the most relevant correlation coefficients between the sexual scores of patients at M12 and M24. Significant correlations were found between the response to treatment at M12 (IIEF-EF and EHS with treatment and IIEF-IS) and in the response to treatment at M24. However, none of the sexual scores with IAI users at M12 correlated with IIEF-EF or EHS scores when not using treatment at M24, suggesting that there was no association between the response to IAI treatment at M12 and the recovery of spontaneous erections at M24. At M12, only a high sexual drive score was significantly associated with the recovery of spontaneous erection and improvement in IIEF-EF scores at M24 when the patient was not taking any treatment, indicating that patients with a higher libido achieved a better recovery of spontaneous erectile function at M24.

Table 3 Correlations between IIEF scores and satisfaction with IAI use reported at M12; IIEF and EHS scores at M24; and improvement of spontaneous erections between M12 and M24 (Δ IIEF-EF without IAI)

	M12 IIEF-SD		M12 IIEF-IS		M12 IIEF-EF (IAI)		M12 IIEF-EHS (IAI)		M12 SATISF IAI	
	Rho	P value	Rho	P value	Rho	P value	Rho	P value	Rho	P value
M24 EHS without IAI	-0.008	0.945	0.045	0.708	0.074	0.533	0.146	0.228	0.032	0.789
M24 EHS with IAI	0.267	0.025	0.273	0.021	0.368	0.002	0.294	0.015	0.235	0.052
M24 IIEF-EF without IAI	0.227	0.050	0.161	0.167	0.159	0.173	0.160	0.179	-0.069	0.566
M24 IIEF-EF with IAI	0.287	0.012	0.427	0.000	0.438	<0.0001	0.184	0.122	0.278	0.018
Δ IIEF-EF without IAI	0.277	0.016	0.204	0.080	0.073	0.533	0.061	0.614	-0.195	0.101
M24 IIEF-OF	0.332	0.004	0.422	0.000	0.485	<0.0001	0.274	0.021	0.307	0.009
M24 IIEF-IS	0.328	0.004	0.510	<0.0001	0.461	<0.0001	0.224	0.058	0.313	0.007
M24 IIEF-SD	0.418	0.000	0.299	0.009	0.249	0.031	0.134	0.263	0.167	0.161

Significant values are in bold

IIEF = International Index of Erectile Function; IIEF domains: EF = erectile function; OF = orgasmic function; SD = sexual drive; IS = intercourse satisfaction; EHS = erection hardness score; IAI = intracavernous alprostadil injection

No case of priapism or penile curvature was noted in the population studied.

Discussion

SR following RP consists of the use of a drug or device to maximize recovery of functional erections. Although specific SR programs for postprostatectomy erectile dysfunction have been developed, the best therapeutic regime remains undetermined, and the effectiveness in restoring the preoperative level of erectile function is difficult to judge [9]. The concept of early postoperative vasoactive therapy with IAI was first introduced in 1997 [6]. As IAI treatment may be painful and troublesome, concern is often expressed by patients as to how long this treatment should be continued before reaching the maximal effect concerning erectile function. Unfortunately, the rate of recovery of erectile function in patients that have already used IAI for 1 year is poorly documented [24,25].

In the present study, we found that the response to IAI treatment and the number of injection performed per week by the patient remained stable between 1 and 2 years following RP. The overall rate of nocturnal erections improved and the majority of patients responded affirmatively to GAQ 1 ("Has the treatment you have been taking improved your erectile function?") and GAC Q2 ("If yes, has the treatment improved your ability to engage in sexual activity?") at M12 and M24 demonstrating a subjective beneficial effect of IAI. However, the return of spontaneous erectile function during intercourse attempts was not significant for most patients, and the treatment satisfaction was significantly lower at M24 suggesting some lassitude toward continuing injections. Importantly, spontaneous erectile function decreased in 30.6% of patients at M24 in comparison to M12, a

fact that has never been reported in patients using IAI. Only 33 patients (44%) reported improved EF scores, but no cases of normalization of erectile function (IIEF-EF without treatment >24) were reported, and no patient considered that they had recovered their preoperative level. Only four patients had an EHS score >2 without treatment at M24, indicating that spontaneous erection after 2 years of IAI use, if present, was not rigid enough to achieve sexual penetration. Interestingly, at the M24 follow-up, 28 patients (37.3%) patients were using PDE5i or a vacuum in association with IAI. This suggests that patients had sought additional therapy to IAI in order to further improve their sexual function, even though PDE5i had previously been ineffective at 1 year.

Significant correlations were found between IIEF scores of patients receiving treatment at M12 and at M24. However, better responses to IAI at M12, as identified by using the IIEF-EF and EHS scores, were not associated with greater recovery of natural erectile function at M24. Higher SD present at M12 was the only factor associated with an improved IIEF-EF score without treatment at M24. This raises important questions concerning the concept of penile rehabilitation, since intuitively, one could have assumed that the higher the erectile function and penile rigidity obtained with IAI, the better the chances of recovering natural erection functions.

A possible explanation for the lack of erectile function recovery could be the low mean IIEF subscores with IAI. These were inferior to those reported in other settings [24–26]. In a study of patients treated with IAI after non-nerve-sparing RP, Titta et al. [24] reported an IIEF-EF subscore of 26.5 after 18 months postsurgery, compared with a score of 18.07 after 24 months in our study. All patients included in their study were alprostadil

responsive at the beginning of the study, whereas in our study, this was not an inclusion criterion. Some of our patients were poor responders to IAI but agreed to continue with the treatment with the purpose of SR. This could explain why the IIEF-EF subscores were different at a longer follow-up period. Further studies with a greater number of patients are required to confirm this hypothesis and to investigate the role of other factors that may influence the recovery of spontaneous erection in IAI users.

One of the chief questions investigated in our study was to determine how long the SR process should be prolonged in order to reach the maximal effect. Recovery of normal erection function has previously been reported up to 4 years following RP [27], with 19.8% of patients experiencing marked or moderate improvement in erectile function between 24 and 48 months after surgery. In the study, patients using IAI were excluded from analysis, and potency was defined as the ability to engage in sexual intercourse at least once per month with or without the use of PDE5i. Our study design differs radically as we included patients who did not respond to PDE5i at M12 and for whom IAI was considered the main therapeutic option to achieve sexual intercourse. Our results indicate that in such patients, the rate of recovery of erectile function may be much lower than other populations studied. The fact that 30.6% of patients in our study reported a worsened erection after 2 years of IAI use should be taken into consideration during patient counseling, particularly if use of IAIs is perceived as troublesome and can cause pain. It is unlikely that patients with an impairment of their natural erectile function after 2 years of IAI use would subsequently benefit from the same treatment regime. Due to the overall low rate of recovery of spontaneous erection at M24, it is suggested that patients who are dissatisfied with IAI after 1 year of use should be offered another therapeutic option, such as a penile implant or combination of other erectogenic drugs or devices.

Finally, the beneficial effects of IAI should be compared with those of other therapies, in particular the use of PDE5i. At present, there are no comparative studies to demonstrate a better outcome with any of the available pharmacological treatments. As a consequence, there is a lack of recommendations concerning the best regimen to use for SR [9]. Recently Mulhall et al. [9] concluded that they were unable to determine the optimal approach to SR and to define “what rep-

resents the optimal rehabilitation program in regard to strategies utilized, timing of intervention, or duration of treatment” [28].

During the time period of the study, we did not offer PDE5i treatment to patients during the first year following RP—except if the patient reported spontaneous erections—as our experience and others suggest that PDE5i is not efficient before the ninth month following surgery [5]. Since numerous studies have demonstrated that early PDE5i therapy is beneficial for SR and penile oxygenation following RP [2,9,10], we now propose that PDE5i is offered systematically 1 month after RP in combination with IAI or a vacuum and that patients may choose the best regime according to their preference and suitability, with the aim of achieving satisfactory intercourse and SR. However, in our population of patients, a significant number of patients discontinued use of PDE5i due to the costs involved and the lack of efficacy which has also been mirrored in other studies [28,29].

Consequently, IAI still represents one of the main therapeutic options for SR following RP, and we consider that the long-term outcomes of this treatment deserve particular attention. Overall, our study emphasizes that longer follow-up of patients with specific evaluation tools should be proposed in all IAI users in order to adapt the treatment and counsel patients as to other therapeutic options when results are unsatisfactory.

Conclusion

The improvement of natural erectile function after the first year of using IAI is limited, and impairment of natural erectile function may occur in some patients with pRPED. This suggests that patients using IAI who do not respond well to PDE5i within 1 year following surgery should be encouraged to continue with IAI only if it enables the patient to engage in satisfying intercourses. Patients should be informed of the limitations of using IAI and the limited effect on natural erections. Patients dissatisfied with IAI after 1 year should be offered another therapeutic option.

Corresponding Author: René Yiu, MD, PhD, PUPH, Service d'Urologie, CHU Henri Mondor, 51 av du Maréchal de Lattre de Tassigny, 94010 Créteil, France. Tel: +33-149-812-553; Fax: +33-149-812-552; E-mail: rene.yiu@hmn.aphp.fr

Conflict of Interest: The author(s) report no conflicts of interest.

References

- 1 Shikanov SA, Zorn KC, Zagaja GP, Shalhav AL. Trifecta outcomes after robotic-assisted laparoscopic prostatectomy. *Urology* 2009;74:619–23.
- 2 Montorsi F, Briganti A, Salonia A, Rigatti P, Burnett AL. Current and future strategies for preventing and managing erectile dysfunction following radical prostatectomy. *Eur Urol* 2004;45:123–33.
- 3 Mulhall JP, Parker M, Waters BW, Flanigan R. The timing of penile rehabilitation after bilateral nerve-sparing radical prostatectomy affects the recovery of erectile function. *BJU Int* 2010;105:37–41.
- 4 Montorsi F, Brock G, Lee J, Shapiro J, Van Poppel H, Graefen M, Stief C. Effect of nightly versus on-demand vardenafil on recovery of erectile function in men following bilateral nerve-sparing radical prostatectomy. *Eur Urol* 2008;54:924–31.
- 5 Zagaja GP, Mhoon DA, Aikens JE, Brendler CB. Sildenafil in the treatment of erectile dysfunction after radical prostatectomy. *Urology* 2000;56:631–4.
- 6 Montorsi F, Guazzoni G, Strambi LF, Da Pozzo LF, Nava L, Barbieri L, Rigatti P, Pizzini G, Miani A. Recovery of spontaneous erectile function after nerve-sparing radical retropubic prostatectomy with and without early intracavernous injections of alprostadil: Results of a prospective, randomized trial. *J Urol* 1997;158:1408–10.
- 7 Mulhall J, Land S, Parker M, Waters WB, Flanigan RC. The use of an erectogenic pharmacotherapy regimen following radical prostatectomy improves recovery of spontaneous erectile function. *J Sex Med* 2005;2:532–40; discussion 40–2.
- 8 Domes T, Chung E, DeYoung L, MacLean N, Al-Shaiji T, Brock G. Clinical outcomes of intracavernosal injection in postprostatectomy patients: A single-center experience. *Urology* 2012;79:150–5.
- 9 Mulhall JP, Bella AJ, Briganti A, McCullough A, Brock G. Erectile function rehabilitation in the radical prostatectomy patient. *J Sex Med* 2010;7:1687–98.
- 10 Hatzimouratidis K, Burnett AL, Hatzichristou D, McCullough AR, Montorsi F, Mulhall JP. Phosphodiesterase type 5 inhibitors in postprostatectomy erectile dysfunction: A critical analysis of the basic science rationale and clinical application. *Eur Urol* 2009;55:334–47.
- 11 Lee CH, Kim HS, Goo MJ, Kang KK, Ahn BO, Kim SH, Yang DY. Chronic administration of udenafil, a selective phosphodiesterase type 5 inhibitor, promotes erectile function recovery in an animal model of bilateral cavernous nerve crush injury. *J Sex Med* 2011;8:1330–40.
- 12 Teloken P, Mesquita G, Montorsi F, Mulhall J. Post-radical prostatectomy pharmacological penile rehabilitation: Practice patterns among the international society for sexual medicine practitioners. *J Sex Med* 2009;6:2032–8.
- 13 Giuliano F, Amar E, Chevallier D, Montaigne O, Joubert JM, Chartier-Kastler E. How urologists manage erectile dysfunction after radical prostatectomy: A national survey (REPAIR) by the French urological association. *J Sex Med* 2008;5:448–57.
- 14 Linet OI, Ogrinc FG. Efficacy and safety of intracavernosal alprostadil in men with erectile dysfunction. The Alprostadil Study Group. *N Engl J Med* 1996;334:873–7.
- 15 Porst H. The rationale for prostaglandin E1 in erectile failure: A survey of worldwide experience. *J Urol* 1996;155:802–15.
- 16 Yiou R, Cunin P, de la Taille A, Salomon L, Binhas M, Lingombet O, Paul M, Abbou C. Sexual rehabilitation and penile pain associated with intracavernous alprostadil after radical prostatectomy. *J Sex Med* 2011;8:575–82.
- 17 Porst H, Buvat J, Meuleman E, Michal V, Wagner G. Intracavernous Alprostadil Alfadex—an effective and well tolerated treatment for erectile dysfunction. Results of a long-term European study. *Int J Impot Res* 1998;10:225–31.
- 18 Kim SC, Lee SW, Seo KK. Characteristics of pain following intracavernous injection of prostaglandin E1. *J Korean Med Sci* 1997;12:327–31.
- 19 Weiss JN, Badlani GH, Ravalli R, Brettschneider N. Reasons for high drop-out rate with self-injection therapy for impotence. *Int J Impot Res* 1994;6:171–4.
- 20 Schramek P, Plas EG, Hubner WA, Pfluger H. Intracavernous injection of prostaglandin E1 plus procaine in the treatment of erectile dysfunction. *J Urol* 1994;152:1108–10.
- 21 Droupy S, Giuliano F, Costa P. [Erectile rehabilitation after radical prostatectomy]. *Prog Urol* 2009;19(suppl 4):S193–7.
- 22 Alexandre B, Lemaire A, Desvaux P, Amar E. Intracavernous injections of prostaglandin E1 for erectile dysfunction: Patient satisfaction and quality of sex life on long-term treatment. *J Sex Med* 2007;4:426–31.
- 23 Litwin MS, Hays RD, Fink A, Ganz PA, Leake B, Brook RH. The UCLA Prostate Cancer Index: Development, reliability, and validity of a health-related quality of life measure. *Med Care* 1998;36:1002–12.
- 24 Titta M, Tavolini IM, Moro FD, Cisternino A, Bassi P. Sexual counseling improved erectile rehabilitation after non-nerve-sparing radical retropubic prostatectomy or cystectomy—Results of a randomized prospective study. *J Sex Med* 2006;3:267–73.
- 25 Mulhall JP. The role and structure of a post-radical prostatectomy penile rehabilitation program. *Curr Urol Rep* 2009;10:219–25.
- 26 Brock G, Tu LM, Linet OI. Return of spontaneous erection during long-term intracavernosal alprostadil (Caverject) treatment. *Urology* 2001;57:536–41.
- 27 Glickman L, Godoy G, Lepor H. Changes in continence and erectile function between 2 and 4 years after radical prostatectomy. *J Urol* 2009;181:731–5.
- 28 Mulhall JP, Bivalacqua TJ, Becher EF. Standard operating procedure for the preservation of erectile function outcomes after radical prostatectomy. *J Sex Med* 2013;10:195–203.
- 29 Salonia A, Gallina A, Zanni G, Briganti A, Dehò F, Saccà A, Suardi N, Barbieri L, Guazzoni G, Rigatti P, Montorsi F. Acceptance of and discontinuation rate from erectile dysfunction oral treatment in patients following bilateral nerve-sparing radical prostatectomy. *Eur Urol* 2008;53:564–70.