



## Platinum Priority – Collaborative Review – Sexual Medicine

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# Prevention and Management of Postprostatectomy Sexual Dysfunctions Part 2: Recovery and Preservation of Erectile Function, Sexual Desire, and Orgasmic Function

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Published online ahead of print on May 2, 2012**Keywords:**Radical prostatectomy  
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Climacturia[www.eu-acme.org/europeanurology](http://www.eu-acme.org/europeanurology)Please visit [www.eu-acme.org/europeanurology](http://www.eu-acme.org/europeanurology) to read and answer questions on-line. The EU-ACME credits will then be attributed automatically.**Abstract****Context:** Sexual dysfunction is common in patients who undergo radical prostatectomy (RP) for prostate cancer (PCa).**Objective:** Review the available literature concerning prevention of, and management strategies for, post-RP sexual dysfunction in terms of postoperative treatments for erectile function (EF), sexual desire (SD), and orgasmic function (OF) impairment.**Evidence acquisition:** A literature search was performed using Google and PubMed databases for English language original and review articles either published or e-published up to November 2011.**Evidence synthesis:** We propose a rational description of many of the clinically available preventive and therapeutic strategies for the preservation and recovery of post-RP EF. A huge amount of preclinical data show that tissue damage ultimately leads to structural alterations, and the literature stresses that rehabilitation and treatment are undoubtedly better than leaving the erectile tissue to its unassisted fate; likewise, the timing of any rehabilitation and treatment is of major clinical importance. However, no specific recommendation emerges regarding the structure of the optimal rehabilitation or treatment regimen. The role of postoperative erectile dysfunction (ED) treatment of those patients who received a non-nerve-sparing RP was also extensively discussed. The literature almost completely lacks a systematic and comprehensive debate about SD (ie, low libido) and OF (ie, decreased intensity of orgasm, dysorgasmia, and climacturia) in patients undergoing RP. Psychological and sexual counseling is of major importance to improve any rehabilitation and treatment of postoperative EF, SD, and OF impairment. **Conclusions:** Despite the great number of possible rehabilitation approaches proposed, these approaches should be considered only as strategies, since incontrovertible evidence of their effectiveness for improving natural EF recovery is limited. Conversely, numerous effective therapeutic options are available for treating post-RP ED. SD and OF have not yet been fully assessed in patients who underwent RP.

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## 1. Introduction

Radical prostatectomy (RP) is a recommended curative procedure for patients with low- and intermediate-risk localized prostate cancer (PCa) and a life expectancy of  $\geq 10$  yr (level of evidence [LE]: 1b) [1]. The most updated European Association of Urology (EAU) guidelines report that either bilateral nerve-sparing RP (BNSRP; LE: 3) or unilateral nerve-sparing RP (UNSRP; LE: 4) represents the recommended approach of choice for all men with both normal preoperative erectile function (EF) and organ-confined disease [1]. EAU guidelines suggest, as an option, a non-nerve-sparing (NNS) surgical approach for selected patients with low-volume, high-risk, localized PCa and highly selected patients with very high-risk, localized PCa in the context of multimodality treatment [1].

Therefore, the population of patients with PCa who may benefit from an RP is clearly quite large. More important, it is evident that many patients who undergo RP are not receiving an operation with nerve-sparing (NS) intent. Yet even these patients have had, keep having, and probably in large part would continue to have satisfactory sexual activity that included at least an adequate level of sexual desire (SD), adequate erections, and an appropriate orgasmic function (OF). Our unfortunate patients might also feel distress related to their own sexuality or might even be bothered by pain related to sexual activity [2].

It is easy to see that post-RP sexual dysfunction—mainly erectile dysfunction (ED)—remains a challenge for the urologist. Part I of this review paper [3] comprehensively addressed the point that optimal post-RP EF outcomes may be achieved by the careful choice of the correct patient (ie, patient factors and cancer selection) at the right time, for the correct type of surgery (ie, surgical techniques and surgeon factors). Part II is aimed at defining a shareable road map for preventing and managing sexual dysfunction (ie, EF, SD, and OF impairments) in those patients who wish to continue to be sexually active postoperatively.

## 2. Evidence acquisition

A literature search for English language original and review articles either published or e-published up to November 2011 was performed using Google and the National Library of Medicine's PubMed database. Keywords included *radical prostatectomy*, *erectile function*, *erectile dysfunction*, *phosphodiesterase-5 inhibitors*, *intracavernosal injection*, *penile prosthesis*, *sexual desire*, *orgasmic function*, and *climacturia*. The retrieved articles were gathered and examined. Reference lists of retrieved articles, as well as relevant review articles, were also studied. This review paper is the result of an interactive peer-reviewing process by an expert panel of coauthors.

## 3. Evidence synthesis

### 3.1. Management of postoperative erectile function impairment

Many authorities have carefully reviewed the scientific literature aimed at defining indications for, types of, and

limitations of proper management of postoperative recovery of EF and post-RP EF impairment treatments [4–7]. A detailed analysis of all these studies will not be the goal of our collaborative review; this paper aims to emphasize the importance of any type of rehabilitation and therapy after surgery, regardless of the therapeutic method used [4,8,9].

#### 3.1.1. Postoperative erectile function rehabilitation: just a never-ending story?

Regardless of the surgical technique, the removal of the prostate may result in an almost obligatory period of dormancy of the nerves that govern the functional aspects of erection. This situation may lead to a loss of daily and nocturnal erections associated with persistent failure of cavernous oxygenation and secondary erectile tissue damage resulting from the production of pro-apoptotic factors (ie, loss of smooth muscle) and pro-fibrotic factors (ie, an increase in collagen) within the corpora cavernosa [4,5,10]. These changes are coupled with postoperative ED of varying degrees and the development of venous leakage, which portends a poor prognosis for EF recovery [4,5,11]. The importance of promoting erectile tissue preservation is obvious, and the practice of suggesting and applying any form of rehabilitative strategy in post-RP patients has been widely reported in the everyday clinical setting. Using an Internet-based survey, Teloken et al. assessed whether such an approach was actually being used among members of the International Society for Sexual Medicine and/or its affiliated societies [12]. The survey showed that 87% of the 301 physicians who completed the questionnaire (82% were urologists) performed some form of rehabilitation. As part of the primary rehabilitation strategy, 95% of the physicians used phosphodiesterase type 5 inhibitors (PDE5-Is), 75% used intracavernous injections (ICIs), 30% used a vacuum device, and 9.9% used intraurethral prostaglandin. Among the primary reasons for avoiding EF rehabilitation, the authors found excessive cost (50% of the time); even more important,  $\leq 25\%$  of the physicians said that the explanation for not performing any EF rehabilitation was the fact that there were no supportive clinical evidence-based data [12].

Although this latter aspect is frustrating, it is unfortunately true that sufficient clinical evidence supporting such rehabilitation is still lacking [13]. In fact, almost all the available data refer to in vitro studies or studies in animals [4,5], and concerns exist regarding the translatability of those data to humans. An increasing amount of experimental data, for instance, support the concept of cavernosal damage and suggest a protective role for prolonged dosage with a PDE5-I [14–19]; however, similar data have not yet been clearly and uniquely replicated in humans [13,20].

Penile rehabilitation programs using PDE5-Is are common in clinical practice, but there is no definitive evidence to support their use or the best treatment strategy [5,13,20,21]. The International Consensus of Sexual Medicine (ICSM) committee recommended that clinicians instruct patients on the essential elements of the pathophysiology of postoperative ED (grade C recommendation) [4]. The ICSM committee listed very precisely five different types of rehabilitative approaches: (1) PDE5-Is, (2) ICIs,

(3) intraurethral alprostadil, (4) vacuum therapy, and (5) neuromodulatory agents. No specific recommendation can be given regarding the optimal rehabilitation regimen (grade D recommendation) [4]. Because of such a prestigious recommendation and recent literature reviews, this collaborative paper will focus on only some specific practical aspects of rehabilitation (Table 1).

First, the authors strongly believe that *rehabilitation and treatment are undoubtedly better than leaving the erectile tissue to its unassisted, unfavorable fate* [8,13,20]. In support of this resolute attitude is a plethora of preclinical data showing that structural alterations may lead to veno-occlusive dysfunction [13–19], whose incidence ultimately increases in a time-dependent fashion after surgery. These observations may provide a robust clinical rationale for early penile rehabilitation prior to penile fibrosis development [5,22–24].

The idea that treating is at least better than doing nothing certainly derives from the historical studies of Montorsi et al. [23] and, subsequently, Mulhall et al. [24] concerning the use of relatively early postoperative ICIs. As for today, the concept can be more easily applied after learning from experiences with PDE5-Is. Indeed, it has been extensively demonstrated that sildenafil [5,25], tadalafil [5,26], and vardenafil [5,27,28] taken when needed may be successfully used out of the scope of rehabilitation in men who underwent an RP with a clear bilateral nerve-sparing (BNS) intent. Likewise, a few and not widely appreciated data suggested that bedtime sildenafil (25 mg [21] or 50–100 mg [20] daily) led to a significant improvement in EF recovery. Bannowsky et al. [21] specified that sildenafil was significantly active in cases of early postoperative nocturnal erections. The findings obtained with the small patient sample of Padma-Nathan et al. [20] showed that nightly sildenafil administration for 9 consecutive months, beginning 1 mo postoperatively, resulted in a

greater return to baseline EF—arbitrarily defined as a combined score of  $\geq 8$  on questions 3 and 4 of the International Index of Erectile Function (IIEF).

More recently, a randomized, double-blind, double-dummy, multicenter, parallel group study compared 9-mo 10-mg nightly dosing of vardenafil (which could be decreased to 5 mg if required) and flexible-dose on-demand vardenafil (starting at 10 mg, with the option to titrate to 5 or 20 mg) in patients who had a BNSRP [13]. This paper has been the center of much discussion, since the results clearly but unexpectedly showed that nightly dosing with vardenafil did not have any effect beyond that of on-demand use. Even more clinically relevant is the fact that this study confirmed that vardenafil taken when needed during the double-blind treatment period was associated with significantly better results compared with placebo. The authors thus concluded that the use of on-demand vardenafil was of greater benefit than nightly treatment in men following NS surgery [13].

Those results support a concept strongly shared by the authors of this collaborative review: *Treating patients early postoperatively is of major importance and may certainly lead to better long-term results in terms of either EF recovery or ED treatment possibilities*. Translating this concept to the everyday clinical practice setting, Briganti et al. [8], in a large contemporary series of patients treated by high-volume surgeons, showed that the 3-yr EF recovery rates were significantly higher in patients who did use postoperative PDE5-Is compared with patients who did not use any postoperative PDE5-Is (73% and 37%;  $p < 0.001$ ), regardless of the class of risk to which patients belonged according to their own preoperative characteristics. Even more impressive, EF recovery rates were not significantly different according to the PDE5-I treatment schedule

**Table 1 – Practical road map for erectile function rehabilitation and erectile dysfunction treatment after nerve-sparing radical prostatectomy: a schematic reappraisal**

- Rehabilitation and treatment are undoubtedly better than leaving the erectile tissue in its unassisted, unfavorable fate.
- Penile rehabilitation (any form) should start as early as possible and certainly prior to penile fibrosis development.
- Treating patients early on postoperatively may lead to better long-term results in terms of both EF recovery and ED treatment possibilities.
- Sildenafil, tadalafil, and vardenafil taken when needed may be used successfully in patients who underwent RP with a clear bilateral NS intent. There are no definitive conclusions on the superiority of daily use of PDE5-Is with rehabilitative intent compared with as-needed use of PDE5-Is.
- Young patients with good preoperative EF who underwent RP with a clear BNS intent may experience good EF recovery rates even without any treatment; however, using PDE5-Is after a clear BNSRP may further improve postoperative EF outcomes.
- Ideally, PDE5-Is could be initiated as early as the removal of the catheter or during the very first month after surgery.
- When ICI is the treatment of choice—mainly because of the relative ineffectiveness of PDE5-Is, even in a number of post-NSRP patients—timing for starting ICI should be accurately defined because of a relatively high probability of alprostadil-associated painful erection. Penile pain may diminish with time. Despite being off-label, injectable erectogenic preparations other than alprostadil may ultimately lead to less frequent pain, both after injection and during erection.
- It is not possible to make a clear final suggestion for the best timing to begin postoperative early ICI in men who received either interfascial or intrafascial RP.
- Psychological and sexual counseling is of major importance to improve any rehabilitation and treatment of postoperative EF impairment. A combined approach of psychological and sexual counseling with “organic” therapies for patients who underwent either BNSRP or NNSRP is certainly suggested.
- *Postoperative EF rehabilitation* could mean interventions designed to achieve faster and better natural EF recovery, but the term could also mean interventions that preserve sexual continuity without necessitating natural EF.
- In eugonadal patients with PCa, serum testosterone is positively correlated with sexual activity (ie, EF). Although the role of T replacement in postoperative ED recovery could be of great significance, hypogonadal men are not usually treated with T after RP because of the fear of stimulating dormant PCa cells. Over the last decade, exploratory data from some relatively small series of patients who have been treated with T replacement after RP showed positive results in terms of EF recovery and without significant increases in PSA values.
- Patients with ED after BNSRP or NNSRP may benefit from penile prosthesis implantation after failure of less invasive treatments.

EF = erectile function; ED = erectile dysfunction; RP = radical prostatectomy; NS = nerve-sparing; PDE5-I = phosphodiesterase type 5 inhibitor; BNS = bilateral nerve-sparing; BNSRP = bilateral nerve-sparing radical prostatectomy; ICI = intracavernosal injection; NSRP = nerve-sparing radical prostatectomy; NNSRP = non-nerve-sparing radical prostatectomy; PCa = prostate cancer; T = testosterone; PSA = prostate-specific antigen.

(chronic compared with on-demand) after BNSRP [8]. More recently, Gallina et al. [29] also showed that after a mean follow-up of >2 yr, only 35.8% of patients left untreated after open BNSRP recovered EF after surgery, reaching an IIEF-EF domain score  $\geq 22$ . However, these authors also demonstrated that for patients <55 yr old with a preoperative IIEF-EF score  $\geq 22$ , the rate of EF recovery at the 1-yr assessment was  $\leq 69\%$ ; this rate increased up to 88% ( $p = 0.11$ ) for patients receiving PDE5-Is of any type and with any posology. Even though such a difference did not reach statistical significance, a higher EF also was associated with the use of PDE5-Is among patients with such excellent preoperative characteristics. Taken together, all these data could suggest that although younger patients with good preoperative EF may experience good EF recovery rates even without any treatment, using PDE5-Is after BNSRP further improves their functional outcomes [29].

The recent literature, however, showed that treating is still not the most favored approach in many cases in the real-life scenario. Giuliano et al. [30], for instance, reporting the results of a cross-sectional survey of urologic practices representative of the French Urological Association in 2005, outlined that only 38% of the responders systematically prescribed postoperative ED therapy to their patients. Sixty-two percent provided treatment either at the patients' request (49%) or at the physicians' own discretion (13%). Those data also suggested that a pharmacologic treatment with a rehabilitative intent (ie, regardless of intercourse and sexual attempts) was chosen in 54% of the prescriptions, and this rate was even higher in routine prescribers (67%) [30].

In addition, *timing of rehabilitation and treatment is of major clinical importance* [4,5,30,31]. Giuliano et al. [30,31] clearly reported that 9% of all urologists recommended that ED treatment—of any type—be initiated within the first few days after surgery, whereas 79% of all urologists (92% of routine prescribers) recommended initiation  $\leq 3$  mo after surgery. This recommendation led to having a third of the patients under treatment 1–2 mo postoperatively and half of the patients under treatment 3–4 mo after the RP. However, at  $\geq 8$  mo, 46% of patients still were not being treated at all [30]. Given what we now know from animal studies—that is, treating is of great importance for endothelial and smooth muscle protection, neuromodulation, and reduction of corporal fibrosis [4,14–19]—the literature today tries to stress that any form of rehabilitation or treatment should begin as early as possible, and certainly as close to the surgery as possible [4,5].

This recommendation is certainly easily applicable for PDE5-Is, which have a relatively low probability of side effects [4,5,13,20,21,32]; PDE5-Is could be initiated as early as the removal of the catheter or during the very first month after surgery. In a “massive attack” program for EF preservation, for instance, Moskovic et al. instructed their patients to take 25 mg of sildenafil nightly, as well as to use 250- $\mu$ g alprostadil urethral suppositories three times per week, even beginning 1 wk prior to surgery [33]. Patients also had to restart 25 mg of sildenafil nightly 3 d after BNSRP with the addition of 250- $\mu$ g alprostadil urethral suppositories three times per week once the catheter was removed.

One month after RP, the patients were even instructed to use a vacuum erection device at least 10 min/d, and they were also clearly encouraged to engage in sexual activity and to use 100 mg of sildenafil on demand prior to sexual attempts. When needed, ICIs were introduced in the EF preservation program  $\geq 3$  mo after surgery [33]. Of 29 patients originally included, 3 and 6 of the 24 patients who did not discontinue the program (10.3% and 25%, respectively) had reported a return to natural unassisted EF sufficient for penetration at 3- and 6-mo assessment, respectively. Preoperative female partner sexual function correlated with greater patient compliance with the localized component of the EF rehabilitation program [33]. In a manner substantially comparable to treatment with PDE5-Is only, McCullough reported the results of a prospective, randomized, open-label, multicenter study comparing nightly intraurethral alprostadil and oral sildenafil in men with preoperative fully normal EF (IIEF-EF  $\geq 26$ ) who underwent BNSRP (either open or robot-assisted laparoscopic prostatectomy) [34]. Both nightly treatments were started  $\leq 1$  mo after surgery, at the catheter removal visit, to be continued for 9 consecutive months. Their findings suggested that there were no statistically significant differences between the two groups in terms of IIEF-EF domain scores and intercourse success rates, both at the end of the treatment period and at the completion of the study itself. Similarly, patients began both treatments as early as 1 mo after RP without significant treatment-emergent side effects [34].

When ICI is the treatment of choice—mainly in those patients in whom PDE5-Is are relatively ineffective [4,5,24]—*timing for starting ICI should be accurately defined* [6,35,36]. Indeed, ICI often causes penile pain [6,35,37], which may ultimately lead to a high treatment discontinuation rate [35,38]. Yiou et al. recently reported the results of a prospective study aimed at assessing safety and efficacy of intracavernosal alprostadil in a cohort of men who underwent laparoscopic nerve-sparing RP (NSRP) by high-volume surgeons and started self-injection treatment 1 mo after surgery [35]. Patients were advised to start with 2.5  $\mu$ g of alprostadil twice a week, which was then uptitrated till they were able to reach an erection hard enough to allow vaginal penetration; at the same time, it was also suggested that patients attempt intercourse as often as possible. Both pain during injections and pain during erections were assessed using two different Lickert scales; 15 of the 142 originally enrolled men (11%) discontinued because of painful erection since the beginning, and they were offered different treatment modalities. Among those who continued the treatment, pain intensity during erection significantly decreased over time (ie, between 6 and 12 mo after RP). Likewise, at the 6-mo assessment, pain scores correlated negatively with the IIEF-EF, IS, OS, and erection hardness; in contrast, neither of the two pain scales correlated significantly with any of the sexual scores at 12 mo, suggesting that the adverse impact of pain diminished throughout time. Of importance, patients with greater pain scores at 12 mo also reported the lowest SD scores. The authors did not find any significant dose correlation between alprostadil and pain intensity after ICI or during erection [35].

In a prospective nonrandomized study, Mulhall et al. [24] evaluated the postoperative outcome of men with functional preoperative erections who underwent either BNSRP or UNSRP or non-nerve-sparing RP (NNSRP) and were challenged early on postoperatively with oral sildenafil. Nonresponders were switched to ICI and were instructed to either self-inject three times a week, as for rehabilitative purposes, or to use on-demand ICI. TriMix (30 mg/ml papaverine, 1 mg/ml phentolamine, 10 µg/ml prostaglandin E1) was the medication of choice as a starting agent for the penile injection program; on average, self-injection was started 4 mo postoperatively, with a range of 1–10 mo. At 18 mo after RP, all patients who had used TriMix did not report either pain or prolonged erections [24]. These results seem to support the concept that *injectable erectogenic preparations other than alprostadil may ultimately lead to less frequent pain, both after injection and during erection.*

The coauthors of this collaborative paper agree that caution should be paid in regard to this issue because (1) the pathophysiology of penile pain after ICI is still controversial; (2) alprostadil is still the only drug approved for intracavernosal treatment of ED; and (3) none of the studies dealing with ICI after NSRP comprehensively assessed the potential fluctuation of the painful penile symptomatology on a time-by-time basis, thus not allowing a clear final suggestion on the best time to begin postoperative early ICI in men who received either an interfascial or intrafascial RP.

This text has proposed a reasoned description of many of the clinically available preventive and therapeutic strategies for the preservation and recovery of post-RP EF. *Postoperative EF rehabilitation could mean interventions designed to achieve faster and better natural EF recovery, but it could also mean interventions that preserve sexual continuity without necessitating natural EF.*

It is certainly also important to specify that early postoperative treatment should not be limited to patients who have undergone surgery with neurovascular nerve bundle bilateral preservation. Indeed, the many patients who underwent RP with an extrafascial approach may also benefit from early therapy for the treatment of ED.

The literature suggests that patients undergoing NNSRP are not expected to regain any spontaneous erection; lack of natural erections produces cavernosal hypoxia, and prolonged periods of cavernosal hypoxia induce fibrosis, which later increases the incidence of venous leakage [39–44]. It is a common clinical experience that any severe impairment of the native structure of the corpora cavernosa may ultimately lead to greater difficulty even in the use of second-line treatment of ED [37,45,46]. In men who received an NNSRP, Gontero et al. showed a trend toward a progressively decreasing erectile response with time from the operation [6]. Interestingly, by using a 4-mo interval cut-off, Gontero et al. outlined that ≤70% of the patients who received ICI ≤3 mo after RP did also achieve an erection sufficient for sexual intercourse; after that period of time, the chances of an acceptable response to alprostadil decreased to 40% [6], with a sort of age-related responsiveness. The study of Gontero et al. acquires even greater importance when one considers the temporal aspect in terms of adherence to, and rate of

tolerability for, the same treatment; indeed, despite reporting the highest response rate to alprostadil, patients scheduled for an injection as early as 1 mo postoperatively also more frequently experienced complications in terms of prolonged painful erections and ICI-related discomfort [6]. The authors suggested 3 mo after surgery as a reasonable compromise in terms of effectiveness and patient compliance [6]. Particular care is also advisable before introducing ICI too early because of psychosexual concerns associated with self-administered penile injections [6,47].

*Psychological and sexual counseling is of major importance to improve any source of rehabilitation for, and treatment of, postoperative EF impairment.* An aspect that must be considered by even the most skeptical surgeon is the importance of a multimodal approach. This approach implies that several factors should certainly be taken into account, including the patient's awareness of being diagnosed with cancer [9], the patient's age and sociocultural background (among other factors, those related to the relationship and family context), clinical and sexological history before surgery, the starting time of the treatment, the patient's compliance with the therapy, any adjuvant treatment, and the follow-up terms [9,48,49]. At the same time, many studies have shown that sexual counseling would eventually contribute to better treatment efficacy and patient acceptance and compliance, which is generally quite poor [50]. Salonia et al. analyzed acceptance and discontinuation data for 100 consecutive, age-comparable, pre-open BNSRP self-reported potent patients who at discharge from the hospital received a PDE5-I prescription [51]. Thereafter, patients did not receive any further specific counseling throughout an 18-mo follow-up period, being completely free to use or not use any ED therapy. Surprisingly, the results indicated that up to 49% of the patients—preoperatively self-reporting to be fully potent and strongly motivated to maintain postoperative EF—actually decided not to even start any ED treatment after hospital discharge. In addition, an increasing number of men did not even attempt sexual intercourse over the course of the follow-up period; up to 72.5% of the patients who freely decided to begin PDE5-Is but who did not receive formal and adequate counseling over time eventually discontinued the therapy [51]. The authors thus concluded that specific counseling on ED treatment modalities, coupled with reeducation of the patients, could represent key points in promoting a higher initial acceptance rate and a reduction of the postoperative discontinuation rate for PDE5-Is [51].

These issues seem to match the recommendations of the ICSM committee, which outlined (1) that, to facilitate the discussion on EF rehabilitation, clinicians should debate the essential elements of the pathophysiology of post-RP ED and (2) that penile rehabilitation has significant potential benefits for the patient/partner and should be considered after RP [4]. This is also the case for patients who underwent an NNSRP, for whom ICI alprostadil may be of great benefit. To this aim, Titta et al. reported the results of a prospective study considering a small cohort of patients who completed the IIEF 1 mo after NNSRP and were shown how to use ICI [48]. Patients were then randomized to either a group treated with ICI only or a group who received

ICI-focused sexual counseling for 18 consecutive months. At the end of the study protocol, the analyses showed that men who received sexual counseling coupled with ICI therapy reported the best quality in all IIEF domains (namely, all  $p < 0.05$ , except for OS), the lowest discontinuation rate, and the highest degree of couple's satisfaction compared with men who did not receive any proper counseling. Sexual counseling reduced patients' feeling of lack of sexual spontaneity, dissatisfaction, and fear of needles [48].

Along with the importance of the interdigitation of psychological and biologic aspects, it is important to remember that sexual function per se is multifaceted, and the effect of RP on the specific domains of sexual function is even more varied and difficult to interpret. Le et al, for instance, showed that surgery may affect specific domains of sexual function (eg, erections, desire, and orgasm) to different degrees. However, in a cohort of 620 men treated with RP, none of the domains of sexual function were closely linked to sexual bother [49]. The authors concluded that these findings outlined even more the importance of appropriate counseling in setting patient expectations for the outcomes of sexual function, mainly in specific domains such as EF [49]. Conversely, Nelson et al. [2], using the sexual bother and the sexual function subscale from the Prostate-Health Related Quality-of-Life Questionnaire [52], showed that in patients who underwent RP (laparoscopic or open), mean IIEF-EF scores decreased from baseline to a 24-mo follow-up, while sexual bother was significantly increased over the same follow-up dates compared with the baseline value (all  $p < 0.01$ ); this finding indicated a higher degree of sexual bother. When considering the group as a whole, the authors did not find a significant difference between sexual bother scores over time, meaning that sexual bother did not significantly decrease during the follow-up time points; even more important, this finding was true for men both with and without postoperative ED. The authors concluded that those men were not psychologically "adjusting" to having ED [2]. Changes in EF scores were the only significant predictor of sexual bother scores [2].

Taking all these observations together, we would like to translate this concept even further into the need for implementing effective psychosexual counseling from the preoperative period, so that patients (1) are actually aware of the possible sequelae in terms of sexual difficulties and sexual recovery; (2) are informed about the existence of appropriate therapies; (3) may be encouraged to undergo early ED treatment after RP; and (4) may eventually understand the importance of, and need for, an objective use of compounds and suppositories.

These recommendations could certainly help overcome unwanted misconceptions regarding spontaneous recovery of sexual function, and particularly EF [53]. To this aim, *patients' education should become an essential part of the preparations before RP and continue after RP* [4,53], with information preferably delivered by a combination of meetings and written handouts [53]. Sexual counseling should also stress to both men and their partners that even if EF is not restored quickly after surgery, it may be partially or fully regained after multifaceted combined approaches [53].

### 3.1.2. *The case for testosterone replacement therapy after radical prostatectomy*

Late-onset hypogonadism in the male general population can be defined by the presence of at least three sexual symptoms—decreased frequency of morning erections, ED, and decreased frequency of sexual thoughts—associated with a total testosterone (T) level  $< 11$  nmol/l (320 ng/dl) and a free T level  $< 220$  pmol/l (64 pg/ml) [54]. The importance of an age-related reduction in the circulating T level in men remains clinically controversial [54]. Although several reports suggest that T administration may produce significant benefits for hypogonadal men, many concerns remain about the prevalence and severity of potential treatment-emergent adverse events [55,56], with much attention paid to the correlation between T administration and the eventual risk of developing PCa [56]. Androgens are vital for growth and maintenance of the prostate [57–59]. However, an association between circulating androgens and PCa has not been clearly confirmed in epidemiological studies [57,59,60]; the impact of circulating androgens after RP has been even more neglected [61].

Gacci et al. [62] recently considered 257 patients who consecutively underwent RP and both fulfilled a number of psychometric instruments addressing health-related quality-of-life (HRQoL) and sexual functioning issues and measured preoperative circulating T. Hypogonadism was found in 61 patients (23.7%); those men showed a slightly significant correlation between preoperative sexual functioning and T values ( $p = 0.05$ ), while preoperative sexual functioning parameters were significantly higher in patients with normal T compared with patients with low T levels. This finding led the researchers to conclude that in eugonadal patients with PCa, T was positively correlated with sexual activity (ie, EF) [62]. Likewise, Gacci et al. agreed with the conclusions of Khera [61], suggesting that although the relationship between T and improvement in EF should be well established, the role of T in postoperative ED recovery could be of even greater significance [62]. It has been suggested that T replacement may have a major role in regulating nitric oxide formation [61], regulating phosphodiesterase type 5 expression at the cavernosal levels [61,63,64], maintaining innervation of penile tissue [61], and protecting the corpora cavernosa from veno-occlusive disease and increased collagen deposition [61].

Hypogonadal men are not usually treated with T after RP because of the fear of stimulating dormant PCa cells. Over the last decade, however, the scientific literature has reported data from some relatively small series of patients who have been treated with T replacement after RP with positive results regarding at least EF recovery, but without significant increases in prostate-specific antigen values [65–68].

### 3.1.3. *Penile prosthesis implantation for end-stage erectile dysfunction after radical prostatectomy*

Patients with ED after NSRP may benefit from penile prosthesis implantation after failure of less invasive treatments [7,37,69–71]. Likewise, as previously outlined, many patients received an operation with NNS intent and continue

to desire satisfactory sexual activity, which includes adequate erections. Penile implant surgery is a well-recognized ED treatment even for cancer survivors who wish to remain sexually active and for whom nonsurgical treatments are ineffective, unpalatable, or even unacceptable [7,69,70,72]. As summarized by the experts of the ICSM committee on implants, mechanical devices, and vascular surgery for ED [7], penile prostheses are indicated as a third-line treatment (LE: 3).

Tal et al. recently published the results of a crucial analysis aimed at describing the utilization of penile implants after RP or radiation therapy (RT) for PCa, using Surveillance Epidemiology and End Results cancer registry data linked with Medicare claims (SEER-Medicare database) [70]. The analysis considered 68 558 men aged  $\geq 66$  yr, of whom 52 747 (77%) had RT and 15 811 (23%) had RP as their initial PCa treatment between 1998 and 2005. The study cohort also included 2722 patients (17%) who had RP and subsequently received adjuvant RT and men who were treated with androgen deprivation therapies for metastatic diseases. A total of 533 men had a claim for penile implant surgery, yielding a penile implant utilization rate of 0.78% (95% confidence interval [CI], 0.71–0.85). Patients who underwent RP also received penile implants earlier after the PCa initial treatment compared with patients who underwent RT (median interval: 18.3 vs 24.3 mo;  $p < 0.0001$ ). At multivariate analysis, predictors of penile implant surgery were younger age ( $p < 0.0001$ ), being unmarried ( $p < 0.05$ ), and having a greater number of comorbidities ( $p < 0.05$ ) [70]. Men who had undergone RP were more likely than men who had RT to receive a penile implant, after adjusting for other variables (2.3% compared with 0.3%; odds ratio [OR]: 5.4;  $p < 0.0001$ ), and the same was found for men who received adjuvant RT compared with patients who had RT as primary treatment (2.4% and 0.3%; OR: 5.5;  $p < 0.0001$ ). More important, the penile implant utilization rate was dramatically low, being 0.31% (95% CI, 0.26–0.36) in the RT group and 2.3% (95% CI, 2.1–2.6) in the RP group. Patient's age, being unmarried, and RT emerged as independent predictors of a reduced utilization rate among patients (all  $p < 0.001$ ) [70].

The results of these analyses clearly highlight that penile prostheses are scarcely requested after PCa treatment. Although the analyses could be limited by the entry criteria (ie, age  $\geq 66$  yr, potential use of androgen deprivation therapy with its consequent reduction of SD, and so on), the paper clearly raises the question of whether prostheses are uncommonly implanted after both RP and RT because of a poor outcome. This is not the case, according to most of the published literature that demonstrates the technical feasibility of placing a penile implant in men who have had RP [7,71,73], safety with a low morbidity rate [71], highly effective ED treatment with higher treatment satisfaction compared with PDE5-Is or ICI in both patients [7,70,71,74] and partners [7,75] (although data in post-RP women populations are almost absent), and excellent long-term mechanical reliability of contemporary penile implant models [76]. Akin-Olugbade et al. [76] reported that having a history of RP was predictive of lower patient satisfaction with penile implant surgery compared with non-RP patients.

This finding outlines the importance of giving the RP candidates and, subsequently, patients who have undergone surgery for PCa multimodal support both in terms of “organic treatment” and psychological and sexual counseling that includes the patient's expectations and his actual needs and desires.

Looking at the problem from the other side, it has also been demonstrated that in patients who have already received a three-piece inflatable penile prosthesis, performing either an open RP [77] or an RARP [78,79] is safe and does not represent a technical contraindication when nontraumatic handling of the pelvic reservoir was ascertained to preserve the integrity of the prosthesis. Even more important, postoperative implant use was not affected by RP [77]. Similarly, for those men who are ab initio candidates for an NNSRP, simultaneous placement of a penile prosthesis and RP has been rarely, but satisfactorily, reported [80]. There are no sufficient published data that rigorously consider this approach, especially in the new era of strict intrafascial RP and RARP.

### 3.2. Prevention and management of postprostatectomy sexual desire impairment

The historical data of Laumann et al. [81] showed that the prevalence of low SD ranged from 14% (for men 18–29 yr old) to 17% (for men 50–59 yr old). Men in the oldest cohort (50–59 yr) were three times more likely than men in the younger cohorts to experience low desire. In terms of health-related indicators, men who were in poorer health and experienced emotional problems or stress were two to three times more likely to experience low desire [81]. Even the analysis of the findings of the nationally representative Swedish survey of 1475 men (aged 18–74 yr) showed that the frequency of decreased “interest in sex” emerged as the most frequent sexual complaint (16% of men) [82]. The prevalence of low sexual interest was confirmed as being significantly higher in the oldest age group (ie, 41% of men aged 66–74 yr), and 45% of men with low sexual interest also had erectile difficulties [82]. Although once again the data are indirect, it is certainly evident that all the features previously mentioned are also features of men diagnosed with PCa and subject to RP; the probability of having this latter combination reported in the clinical setting by men who had undergone RP is even higher. However, the scientific literature almost completely lacks a systematic and comprehensive evaluation of issues relating to SD in patients undergoing RP [83,84]; similarly, to the best of our current knowledge, the prevalence and predictors of hypoactive SD disorder in this category of patients have been never evaluated [85]. Loss of SD has been reported to occur in 60–80% of patients after RP [9,86,87].

The psychological impact of PCa per se and its uncertain outcome may diminish male SD and subjective arousability. Dahn et al. [84] evaluated the relationship between SD and quality of life (QoL) in patients who had undergone either RT ( $n = 29$ ) or RP ( $n = 62$ ) during the previous 18 mo for localized PCa, using items from a number of different tools, including the Functional Assessment of Cancer Therapy-General

Module [88], to assess QoL. The mean score for SD was 2.0, corresponding to a rating of “fair”; the SD response range included “very poor” in 24%, “poor” in 15%, “fair” in 15%, “good” in 23%, and “very good” in 22 of the patients. SD per se was not independently related to QoL, whereas whole sexual functioning items demonstrated a significant relationship with QoL ( $\beta = 0.25$ ;  $p = 0.01$ ). Even more interesting, post hoc regression analyses revealed that for men with lower sexual functioning ratings, more SD was significantly associated with lower levels of QoL, whereas less SD was related with higher QoL. An opposite trend was found for men with higher sexual functioning scores. Translating these findings into the clinical setting, this means that for those PCa survivors who were not adequately sexually functioning (ie, did not have adequate EF), having high SD levels would mean being more distressed.

Patients undergoing curative surgery for PCa are distressed not only about loss of EF but also about decreased SD [83,86,88,89]. In 2636 men initially treated with definitive therapy for localized PCa from the Prostate Cancer Registry of the Cleveland Clinic Foundation, including 1207 post-RP men, Schover et al. [86] reported low SD in 45% of the sample throughout the last 6 mo since therapy. SD impairment emerged as distressful in 60% of those patients [86]. More specifically, Messaoudi et al. segregated their cohort of 63 patients who consecutively underwent RP according to the level of sexual motivation, using a self-administered questionnaire [90]; after RP, patients reported lower SD (52.4%), reduced intercourse frequency (79%), anorgasmia (40%), less satisfying orgasm (38%), climacturia (25%), greater distress (68%), and/or lower partner satisfaction (57%). In addition, among the most sexually motivated patients, 76% reported loss of masculine identity, 52% reported loss of self-esteem, and 36% reported anxiety about performance. These rates were lower among less motivated patients (53%, 29%, and 18%, respectively) [90]. The authors thus concluded that the more motivated patients experienced greater distress and were less satisfied.

To translate current considerations into clinical practice, we consider that an adequate surrogate for the intensity of post-RP SD can be indirectly derived and be correlated with the positive attitudes of men toward seeking help for sexual problems. Jenkins et al. [83] reported the results of a mailed questionnaire that detailed data from the Prostate Cancer Registry of the Cleveland Clinic Foundation; according to the specific purpose of the study, data were segregated according to patient ethnicity and included only African American and white men. A greater number of African American than white men (41% compared with 22%;  $\chi^2 = 23.69$ ;  $p < 0.0001$ ) indicated that a wish to preserve erections had a major influence on their choice of treatment of PCa. African American men also were significantly more likely than white men to report current problems with loss of SD after PCa (61% compared with 43%;  $\chi^2 = 12.91$ ;  $p = 0.0003$ ). The authors did not find a significant ethnic difference in level of distress over lack of SD among those men who reported SD impairment or in the relationship between SD and current rates of hormonal therapy [83]. According to the Help-Seeking scale [91] African American men had attitudes

significantly more indicative of a willingness to seek help for a sexual problem ( $p = 0.0002$ ) than white patients [83].

Schover et al. reported that men who had been more recently diagnosed with PCa were also more likely to intend to seek help in the near future (ie, over the next year) [91]; the same cohort of patients were more dissatisfied with their sexual function and had higher levels of distress about subsequent ED and loss of SD, thus leading to a greater probability of seeking help for sexual disorders [90]. Similarly, Miller et al. [92] evaluated the potential association between sexual motivation and patterns of ED therapy among a large cohort of PCa treatment survivors. Data collection considered 896 consecutive patients treated with RP ( $n = 665$ ), external RT ( $n = 147$ ), or brachytherapy ( $n = 84$ ). For analytic purposes, men who reported the concurrent outcomes of unassisted erections insufficient for intercourse and moderate to big problems with current sexual function were classified as “sexually motivated”; men who reported unassisted erections insufficient for intercourse and no or small problems with current sexual function were classified as “sexually indifferent.” Patients who had undergone RP and were classified as “sexually motivated” clearly reported the highest rates of previous use of PDE5-Is, ICI, intraurethral alprostadil, and vacuum therapy (all  $p < 0.01$ ). The same study also outlined that current therapy use for ED recovery achieved independent predictor status for better sexual HRQoL [92].

Although we have taken the license to attempt to translate the results of these two studies into the clinical setting, one major aspect that could be derived from previous observations is the fact that the level of sexual motivation—arbitrarily translated into SD—is closely related to the request for help and the use of specific therapies for post-RP ED. Therefore, the prevention and management of a poor functional outcome in terms of loss of SD would necessarily pass through a comprehensive prevention and management of postoperative EF recovery and satisfactory ED treatment (see previous comments throughout this paper). This idea emerges as even more true when considering the findings of Dahn et al. [84], already mentioned. Although data from the Cancer of the Prostate Strategic Urologic Research Endeavor registry showed that SD was relatively preserved in men undergoing RP and that sexual function was only weakly correlated with SD [49], once again, psychological and sexual counseling are of major importance to improve postoperative EF and, consequently, the level of SD [9,48,50,51,53]. These authors found the conclusive sentences of a review paper from McCabe et al. [93] to be of major importance; there is need for collaboration between health care practitioners from different disciplines in the evaluation, treatment, and education issues surrounding sexual dysfunction, particularly for SD disorders in men who have been diagnosed with, and treated for, PCa.

Special mention must be made of the correlation between hypoactive SD and hypogonadism and T deficiency; reduced sexual interest is a well-documented symptom of low androgen levels, and T supplementation among hypogonadal men with low desire may be an effective treatment [54,94]. As we have outlined, the scientific

literature has reported very limited data from some small series of patients who have been treated with T replacement after RP, with positive results regarding at least EF recovery [61,65–68]. The impact of T replacement therapy in terms of SD recovery has been even more scarcely investigated.

### 3.3. Postprostatectomy orgasmic function impairment

While substantial attention has been given to postoperative EF, OF has not yet been fully assessed in patients who underwent RP [95–98], and almost all the available data concern only open surgery. One possible explanation has been furnished by Koeman et al. [96], who said that it is difficult to define *orgasm* objectively because it is a subjective experience, usually occurring when the power of observation is limited, if not even suspended. It is of major importance to combine the latter observation with the sort of definition recently reported by the ICSM committee on male orgasmic disorders, which described the experience of orgasm as a distinct cortical event, experienced phenomenologically both cognitively and emotionally, associated with the perception of striated muscle contractions and resulting in semen expelled during ejaculation, mediated through sensory neurons in the pelvic region [99]. Orgasm remains the least understood phase of the sexual response cycle, although from a certain point of view, the fact that the ejaculatory apparatus (prostate, seminal vesicles, and ejaculatory ducts) is removed with RP may certainly partly explain any eventual postoperative orgasm impairment [97,99]. Orgasmic modifications, including complete absence of orgasm, alterations in orgasm intensity, and orgasmic pain, are not uncommon in men after RP [95–97,100]. Patients also may report postoperative orgasm-associated urinary incontinence (UI) (ie, climacturia) [17,101–104].

The data available in the literature on post-RP OF are objectively few and fragmented, so tackling a project of prevention or even only management of postoperative OF impairment is extremely difficult. There is no orgasm-specific questionnaire able to standardize the results, making them a matter of common discussion among researchers. This situation eventually makes it necessary to use non-validated interviews, thus making it impossible to obtain clear prevalence figures for the different orgasm disorders. In their historical retrospective small cohort of patients who underwent open RP, Koeman et al. [96] reported that 14 of 17 men (82%) experienced orgasm, which was normal (ie, comparable to the preoperative figure) in 4 men (29%), whereas 7 men (50%) reported a weakened orgasmic sensation. Also, 8 men (57%) explained that the absence of ejaculation had decreased their pleasure at orgasm. Pain at orgasm (dysorgasmia) was reported by only 2 men (14%) [96]. More recently, Barnas et al. [97] analyzed the results of a retrospective survey of 239 patients who underwent open RP at a single center. A total of 37% reported a complete absence of orgasm, 22% had no change in orgasm intensity, orgasm intensity was decreased in 37%, and orgasm intensity even increased in 4%. Dysorgasmia occurred in 14% of the patients; pain was reported in the penis (63%), abdomen (9%), rectum (24%), and other areas (4%). In those men who reported

having dysorgasmia, pain occurred with every orgasm in 33%, frequently in 13%, occasionally in 35%, and rarely in 19% [97]. Schover et al. [86] reported that of their whole cohort of patients (ie, patients treated with RT and RP),  $\leq 65\%$  reported a problem with their orgasms (including 31% who no longer tried to reach orgasm and 28% with orgasms that were disappointingly weak). Of these men, 64% rated themselves distressed about orgasm problems [86]. Of the 458 men who have been investigated concerning preoperative and postoperative OF by Dubbelman et al. [100], 306 men (67%) confirmed that orgasm was present after surgery.

Decreased intensity of orgasm or even anorgasmia has been considered most probably a psychological event after RP [97]. Therefore, optimally any therapy should be accompanied by sexual counseling that addresses the ability to reach an orgasm and the quality of orgasm without emission and ejaculation. We would like to emphasize some prerequisites in the management of postoperative OF recovery.

Even relating to OF, patient selection is critical, and even better is adequate preoperative counseling that makes the patient aware that some factors may be crucial for the recovery of his postoperative orgasm sensation. Dubbelman et al. [100], for instance, reported that postoperative OF showed an age-related decline; indeed, in their cohort, OF was preserved in 77% of the men  $< 60$  yr old but in only 61% of men  $> 60$  yr old ( $p < 0.0001$ ). Likewise, men who received an NNSRP were more likely to have orgasmic dysfunction compared with men who had an NS surgery ( $p = 0.001$ ), with both variables emerging as independent predictors at multivariate analysis (ie, age OR: 2.003,  $p = 0.002$ ; and NNSRP vs BNSRP OR: 0.454,  $p = 0.001$ ). Severe UI after RP showed a negative effect on OF ( $p = 0.021$ ) [100]. In addition, assessing data from 334 consecutive preoperatively sexually active patients who underwent open BNSRP and using question 10 of the IIEF (“When you had sexual stimulation or intercourse, how often did you have the feeling of orgasm or climax?”), Salonia et al. [98] showed that OF progressively ameliorates over a 48-mo postoperative follow-up ( $F = 4.02$ ;  $p = 0.007$ ). While considering the full IIEF-OF domain score within the whole cohort of patients, OF linearly decreased with patient’s age, thus confirming the findings of Dubbelman et al. [100]. After adjusting for patient’s age, EF, rate of UI, and use of any PDE5-I, OF linearly increased with the postoperative improvement of the EF at any single follow-up assessment (ie, hazard ratio [HR]: 0.425,  $p = 0.015$ ; HR: 0.454,  $p < 0.001$ ; and HR: 0.454,  $p < 0.001$  at 12, 24, and 36 mo, respectively). Younger age, NS surgery, and time since RP also emerged as independent predictors of better sexual health in the prospective study of Hollenbeck et al, who considered the ability to achieve an orgasm as an item of their postoperative assessment [104]. Starting from the idea that the higher the postoperative EF score, the higher the OF throughout the follow-up time frame, some parceled and sporadic reports seemed to suggest that PDE5-Is may improve OF after NSRP [28,105,106]. However, it is also important to counsel patients that despite the absence of erections, OF can still be normal after RP, and orgasm with a flaccid penis is a possibility [100].

The few available data seem to suggest that dysorgasmia occurred in 14% of the patients [96,97]. The cause of dysorgasmia is not yet well understood; Barnas et al. [97] postulated that the physiologic bladder-neck closure that occurs during orgasm in these men may translate into postoperative spasm of the vesicourethral anastomosis, or pelvic floor musculature dystonia. This hypothesis led them to experimentally use the  $\alpha$ -blocker tamsulosin in a relatively small cohort of 98 men; of those men, 77% reported an improvement in pain, and 8% reported complete resolution of pain at the posology of 0.4 mg tamsulosin daily [97,105]. This pattern of results could be partially explained by the possibility of dealing with benefit patients with chronic prostatitis/chronic pelvic pain syndrome using  $\alpha$ -blockers [107]. However, the scientific literature completely lacks rigorous trials aimed at assessing potential treatments for orgasm-associated pain after RP.

As previously mentioned, climacturia, or orgasm-associated UI, is a known complication of open RP [96,101–104]. In light of the complete absence of standardized objective assessment tools, the exact rate is unknown, varying from 20–93% according to different cohorts [96,101–103]. Koeman et al. reported a prevalence of 64% [96], and the prevalence even reached 93% in the cohort of men analyzed by Barnas et al.; orgasm-associated UI occurred with every orgasm in 16%, occurred occasionally in 44%, and occurred rarely in 33% of the men [97]. Data addressing potential differences among types of surgery are virtually absent; solely, Choi et al. [103] showed a 20% rate of climacturia in patients who underwent open RP, which was 24% in men submitted to laparoscopic RP. In their small cohort of 42 post-RP men, Lee et al. [101] stated that 21% of the patients did experience climacturia only rarely after RP, 47% experienced it occasionally, 11% often, 16% most of the time, and 5% all the time. In terms of volume of urine leakage, 58% reported only a few drops. Interestingly, climacturia rates were higher in patients presenting within the first 12 mo postoperatively compared with rates in those presenting after year 1 (relative risk [RR]: 1.82;  $\chi^2 = 8.38$ ;  $p < 0.01$ ). The development of climacturia based on time since surgery was 22% at 0–6 mo, 27% at 6–12 mo, 17% at 12–24 mo, and 9% at >24 mo [103]. These latter findings seem comparable to those even more optimistic findings from Blaivas [108], who previously reported that orgasmic-associated UI usually disappears within the first 5 mo postoperatively, although in 5–10% of patients this leakage may persist. Lee et al. [101] found that men with climacturia were comparable to those without climacturia in time since surgery.

In terms of management of this orgasmic dysfunction, it is important to know that no differences in terms of rate of climacturia have been found based on patient age, preoperative EF, last reported postoperative erection grade, NS status, presence or strength of nocturnal erections, libido level, or—surprisingly—daytime UI. Conversely, Lee et al. found a higher—although not significant—number of patients with climacturia who also experienced UI (11% and 4%). Climacturia rates were higher in men who also reported dysorgasmia (RR: 1.09;  $\chi^2 = 10.24$ ;  $p < 0.01$ ) [103].

Various coping strategies and therapies have been suggested and applied with anecdotal success in men with climacturia. Usually, men who report urine leakage are advised to empty the bladder before sexual relations; this means even before foreplay, since UI has also been described as loss of several drops to a teaspoon of urine during kissing, hugging, and genital foreplay up to 38% of times after RP [109]. The use of condoms has also been suggested to address patient concerns that climacturia would negatively affect sexual relationships. Anecdotally, daily use of the tricyclic antidepressant imipramine or antimuscarinic compounds has also been suggested, but to our knowledge no formal outcome analyses have been done. Similarly, Abouassaly et al. reported that three of their patients (11.5%) described an improvement in the amount of orgasm-associated UI after the application of a constricting band at the base of the penis [102]. Similarly, one patient opted for placement of a bulbourethral sling, subsequently reporting a complete resolution of the leakage [102]. Sighinolfi et al. [110] reported the use of a pelvic floor rehabilitation program consisting of active pelvic floor muscle exercises, electromyography biofeedback for strength and endurance, and electrical stimulation in three patients who had undergone open BNSRP and presented with UI, climacturia, and ED. After a 4-mo program with weekly sessions, climacturia episodes seemed to be significantly decreased after the rehabilitation in all the subjects, with urine leakage very rare or absent [110].

Absence of orgasm, decreased orgasm intensity, dysorgasmia, and climacturia may make a man feel uncomfortable or ashamed and cause psychological distress potentially resulting in a loss of self-confidence and self-esteem, avoidance of sexual contact with discord in relationships, and a reduction of HRQoL [81,97,101,102]. This underlines the importance of counseling patients both preoperatively and postoperatively to reduce the risk of complete sexual avoidance, which—as we extensively discussed—may result in serious damage to the structure of the penis and negatively affect a patient's psychological and emotional state.

#### 4. Conclusions

Several preventive and therapeutic strategies for the preservation and recovery of post-RP EF are available in the everyday clinical setting. However, no specific recommendation emerges regarding the optimal rehabilitation or treatment regimen. It is of major importance to stress that *postoperative EF rehabilitation* could mean interventions designed to achieve faster and better natural EF recovery, but the term could also mean interventions that preserve sexual continuity without necessitating natural EF. Rehabilitation and treatment, as early as possible, are undoubtedly better than leaving the erectile tissue to its unassisted, unfavorable fate. Likewise, the role of postoperative ED treatment (ie, ICI and penile prosthesis implantation) for those patients who received an NNS surgical approach also deserves the highest attention of clinicians. The literature almost completely lacks a systematic and comprehensive debate about SD and OF in patients undergoing RP.

Psychological and sexual counseling emerges as a cornerstone of any rehabilitation and treatment of postoperative EF, SD, and OF impairment.

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