Review Article

The controversy surrounding penile rehabilitation after radical prostatectomy

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Abstract: Radical prostatectomy (RP) techniques have been refined in the last few decades. Despite nerve-sparing surgery, erectile dysfunction (ED) still seems to be affecting more than half of patients undergoing RP. Penile rehabilitation consists of understanding the mechanisms that affect erectile function (EF) and utilizing pharmacologic agents, devices or interventions to promote male sexual function before and after any insult to the penile erectile physiologic axis. There currently is a limited amount of clinical trials that assess treatments with the goal of recovering post-prostatectomy EF. The goal of this article is to assess a contemporary series of trials that study penile rehabilitation. Although the current evidence lacks to prove its irrefutable effectiveness, advancements in research and technology forecast a promising future in penile rehabilitation management.

Keywords: Erectile function (EF); penile rehabilitation; radical prostatectomy (RP)

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Introduction

The American Cancer Society estimated that about 1 out of 7 men will be diagnosed with prostate cancer during his lifetime (1). However, 5-year survival rates after treatment of localized prostate cancer approximates 100%. The improvement and refinement in prostate cancer detection and treatment modalities have contributed to a younger patient population undergoing radical prostatectomy (RP) (2,3). Despite its efficacy in treating prostate cancer, RP has been shown to compromise erectile function (EF) and hence, the patient's quality of life and general well-being (4).

Since the introduction of nerve-sparing techniques by Dr. Patrick Walsh in 1982, urologists can provide hope of regaining EF after RP. We currently have a better understanding of the distribution of the neurovascular bundles (NVBs) and cavernous nerves. Walsh initially stated that the NVBs had a symmetrical course through the posterolateral surface of the prostate (5). Later on, others discovered that NVBs may have either an anterolateral distribution or, occasionally, a posterolateral and lateral distribution on each side, respectively. These new concepts led to the technique of incision of the periprostatic fascia anteriorly and parallel to the NVBs to preserve both the posterolateral and anterolateral cavernous nerves covering the prostate (6-8).

Despite meticulous dissection in attempt to preserve the NVB during prostatectomy, there is evidence that neuropraxia, ischemic and hypoxic nerve insults, fibrotic remodeling, and apoptosis of cavernous smooth muscle contribute to ED (9,10). Neuropraxia is thought to arise from mechanical stretching of cavernous nerves, electrocautery-induced thermal injury and inflammation from surgical trauma. Chronic impotence reduces blood

flow to the corporeal bodies, which leads to fibrosis and transformation of trabecular smooth muscle through collagen, which itself leads to the loss of the veno-occlusive mechanism required to maintain erections (10). Furthermore, ligation of accessory internal pudendal arteries during prostatectomy decreases arterial inflow which intensifies hypoxia and ultimately leads to apoptosis (10,11).

The introduction of the robot-assisted technology was considered to refine nerve-sparing procedures through three-dimensional magnification and movement calibration and many believed it would improve post-prostatectomy erectile dysfunction (ED) rates (12). Ficarra *et al.* (13) evaluated the prevalence and the potential risk factors of ED after robotic-assisted radical prostatectomy (RARP). The systematic review analyzed comparative studies which reported EF recovery outcomes on patients undergoing prostatectomy. For patients undergoing RARP, studies showed EF rates ranging from 54% to 90% and from 63% to 94% at 12- and 24-month, respectively. They performed a cumulative analysis of the studies evaluating the EF recovery 12 months after RARP or radical retropubic prostatectomy (RRP). This showed that when compared with RRP, RARP has a statistically significant advantage over RRP with an ED prevalence of 24.2% versus 47.8% in patients undergoing RRP at 12-month. They also suggested that age, baseline EF status, comorbidities, the use of athermal dissection and extension of the nerve-sparing procedure represent the most relevant or favorable preoperative and intraoperative predictors of EF recovery after RARP. However, Woo *et al.* (14) suggest that the current high rates of EF following RP are because of the introduction of phosphodiesterase type 5 inhibitors (PDE5Is) and not surgical technique.

Rehabilitation is one of the foundations in medicine today for the successful recovery in multiple diseases. Therefore, we believe penile rehabilitation should play a role in the postoperative management of patients who undergo RP. Penile rehabilitation consists of understanding the mechanisms that affect EF and utilizing pharmacologic agents, devices or interventions to promote male sexual function before and after any insult to the penile erectile physiologic axis (15,16). Despite the understanding of the mechanisms and well-established rationale for post-RP penile rehabilitation, there is still a big controversy regarding the effectiveness of rehabilitation programs. Our goal is to provide an update of the tools clinicians have available for penile rehabilitation after RP.

PDE5Is

PDE5Is entered the market in 1998 and revolutionized the treatment of ED. PDE5Is have been shown to decrease the breakdown of cyclic guanosine monophosphate (cGMP) which then increases the efflux of intracellular calcium ions and result in smooth muscle relaxation and erection. This mechanism is potentiated by nitric oxide production stimulated by cavernous nerves (17,18). Clinical trials studying the use of PDE5Is after RP presented in this review are summarized in *Table 1*.

A number of studies have investigated the role of different PDE5Is in patients undergoing RP and many of these reported higher international index of erectile function (IIEF) scores and spontaneous erection rates (19,24-26). Padma-Nathan *et al.* (19) performed the first multicenter, double-blind, randomized, placebo-controlled trial to our knowledge investigating the effects of PDE5Is on EF after RP. They randomized 125 patients into three treatment groups: (I) placebo; (II) sildenafil citrate 50 mg; and (III) sildenafil citrate 100 mg. Out of the 125 patients, only 76 completed the post-8-week washout evaluation period. After the post-washout period, only one of 25 patients (4%) in the placebo arm had adequate EF, versus 14 of 51 patients (27%) in the sildenafil 50 and 100 mg groups combined (P=0.016). Although there was a significant dropout rate calling into question the statistical power of the study, they suggested that nightly sildenafil has a benefit for patients with post-prostatectomy ED.

Montorsi *et al.* (20) published the REINVENT trial in 2008. This multicenter, double-blind placebo-controlled trial randomized 628 patients with a baseline IIEF score of >26 into taking nightly vardenafil, on-demand vardenafil, or placebo for 9 months. After 9-month treatment period, on-demand vardenafil was associated with more patients obtaining ≥22 on the EF domain of the IIEF (IIEF-EF) score. Similarly, dropout rates were substantial, ranging between 31–35% in the study arms and there was no defined limit in the drug usage in the on-demand arm. Moreover, the data argued against the use of nightly PDE5I in the treatment of ED after RP.

Pavlovich *et al.* (21) pursued to investigate whether nightly sildenafil had an advantage over on-demand sildenafil. They randomized 100 men with good EF who had undergone nerve-sparing RP into two groups. The nightly sildenafil group consisted of patients taking nightly sildenafil and on-demand placebo; and the on-demand

Table 1 Penile rehabilitation after radical prostatectomy: summary of clinical trials using oral PDE5Is

Author	Year	N	Follow-up	Study design	ED treatment (treatment period)	Level of evidence	Significant findings
Padma-Nathan *et al.* (19)	2008	125	44 weeks	MC prospective, double blind, randomized, placebo-controlled	Nightly sildenafil *vs.* placebo (36 weeks)	1a	Sildenafil had higher IIEF score and increased nocturnal rigidity
Montorsi *et al.* (20)	2008	628	13.5 months	MC prospective, double-blind, randomized, placebo-controlled	Nightly vardenafil *vs.* on-demand *vs.* placebo (9 months)	1a	On-demand group had significantly more patients with IIEF >22. After a washout period, there was no difference in EF between groups
Pavlovich *et al.* (21)	2013	100	13 months	Prospective, double-blind, randomized	Daily sildenafil with on-demand placebo *vs.* daily placebo with on demand sildenafil (12 months)	1b	No difference in IIEF scores between treatments
Montorsi *et al.* (22)	2013	423	13.5 months	MC prospective double-blind, randomized, placebo-controlled	Tadalafil nightly *vs.* on-demand *vs.* placebo (9 months)	1a	Daily tadalafil had significantly higher IIEF at 9 months treatment period; after washout, no difference in EF between groups; tadalafil daily: protection from penile length loss
Kim *et al.* (23)	2016	74	13 months	Prospective, randomized, placebo-controlled	Daily sildenafil with on-demand sildenafil *vs.* daily placebo with on-demand sildenafil	2	No difference in IIEF-EF score or Rigiscan parameters between treatment groups

MC, multi-center; PDE5I, phosphodiesterase-5 inhibitor; IIEF, international index of erectile function; EF, erectile function.

group consisted of on-demand sildenafil (with a maximum on-demand dose of 6 tablets per month) and nightly placebo starting the day after surgery for 12 months. All men had previously completed an IIEF-EF survey before surgery and had a score of ≥26 before undergoing nerve-sparing RP. Surgeons prospectively recorded the quality of NVB preservation, and this was quantified using a nerve sparing score (NSS) of one to four, with higher scores representing better preservation. The double-blind study period included quality of life assessments every 3 for 12 months after RP, and a final assessment at 13 months after a washout period of 1 month. Compliance in returning questionnaires ranged from 60–96% per time-point but was balanced between groups. After adjusting for potential confounding factors, no significant differences were found in EF between treatments at any single time-point after RP. NSS was the only factor that was consistently found to have a significant association with EF outcomes in all longitudinal multivariable models. This study did show some limitations. First, fearing that patients would not want to be randomized to a placebo-only group, a pure placebo arm was not part of the trial. Moreover, 90% of subjects were Caucasian which is not generalizable to all populations.

Unlike the previous trials, Mulhall *et al.* (27) found that 3 months of treatment with avanafil taken on-demand significantly improved drug-assisted EF after prostatectomy. They randomized 298 patients with post-prostatectomy ED of 6 months or more to on-demand 100 or 200 mg avanafil or placebo for 12 weeks. At the end of the treatment period, 31% of the 100 mg group and 41% of the 200 mg group responded that the treatment improved their erections when compared to placebo (10.7%). Dropout rates ranged from 8% to 24% between groups, with the largest amount in the placebo group in which 14 of 24 patients withdrew their consent. This fact raises the possibility that these patients perceived lack of treatment efficacy. However, follow-up was only for 3 months and long-term response to treatment or its effect on unassisted EF were not assessed in this trial.

A recent study by Montorsi *et al.* (22) aimed to compare the efficacy of tadalafil daily and on demand versus placebo in improving unassisted EF and reducing loss of penile length following nerve-sparing RP. Four hundred twenty-three were randomized into 9 months of treatment with tadalafil 5 mg once daily, tadalafil 20 mg on demand, or placebo followed by a 6-week washout period and 3 months open-label tadalafil once daily (to all patients). At 9 months, they found a significant difference in reaching target IIEF-EF ≥22 in the tadalafil once daily group compared to placebo. However, after the drug free washout period, there was no significant difference in EF between groups. After the open-label tadalafil once daily period, IIEF-EF scores increased in all treatment groups. Regarding penile length, there was significant protection from penile length loss in the daily tadalafil group (2.2 mm) compared to other groups (7.9 mm on demand, 6.3 mm placebo) at 9 months of treatment. These data suggest that PDE5Is may play a role in the preservation of cavernosal integrity by protecting against structural changes after nerve-sparing RP (22,28-31).

All these studies evaluated the use of PDE5Is by relying on self-reported outcomes to determine efficacy of therapy which could lead to response bias. Kim *et al.* (23) conducted a study to evaluate the effects of nightly sildenafil therapy using a more objective approach with nocturnal penile rigidity (RigiScan TM, Gotop Medical, Inc., St Paul, MN, USA) in addition to the IIEF-EF score. They randomized 97 patients of which 74 completed the study into taking daily sildenafil with on-demand sildenafil or daily placebo with on-demand sildenafil. Outcomes were evaluated every 3 for 12 months and at 13 months after 1 month wash-out period. They noted no significant difference in EF between treatment groups based on IIEF-EF domain or RigiScan, suggesting that nightly sildenafil has no benefit over on-demand sildenafil.

These trials open the debate on whether the use of PDE5Is makes a significant contribution to penile rehabilitation programs. All trials had a study period of 13 months or less, which is short of the 18–24 months duration recommended by some authors. Moreover, pharmacokinetics of each of the different PDE5Is has to be taken into consideration. Tadalafil has a longer half-life than other FDA approved PDE5Is used in these trials which could suggest a higher efficacy. In most of these studies, patients were operated either by open, laparoscopic or robot-assisted approach and results were given without separate statement of the outcomes for each technique (32). There still remains an opportunity for the development of larger trials with sufficiently long-term follow-up to convince the scientific community that PDE5Is play a role in penile rehabilitation.

Intracavernosal injection (ICI) and intraurethral therapy

ICI and intraurethral therapy use alprostadil's vasodilation effects to improve EF. Alprostadil delivers prostaglandin E1 (PGE1) which increases the levels of 3',5'-cyclic adenosine monophosphate (cAMP) within the erectile tissue and result in the efflux of intracellular calcium ions and cavernosal smooth muscle relaxation. Its intraurethral form generally does not cause systemic side-effects, but locally it can elicit urethral burning and penile pain (16,18,33). Trials investigating non-oral and non-pharmacological therapies are summarized in *Table 2*.

McCullough *et al.* (33) presented the first randomized, prospective trial to study the effect of intraurethral alprostadil (IUA) with Medicated Urethral System for Erection (MUSE, Vivus Inc., Mountain View, CA, USA). Two hundred and twelve men were randomized into taking nightly IUA or nightly sildenafil for 9 months. IUA was titrated from 125 to 250 μg after 1 month of treatment for better toleration of side effects. At study end, there was no statistically significant difference in the IIEF-EF score or successful intercourse rates. They did note a significant difference between groups in erections, assessed by the global assessment question, at 6 months in favor of IUA (76% *vs.* 60%). Although compliance rates were 98% and 79% for sildenafil and IUA, respectively, dropout rates approximated 30% for the IUA group secondary to pain experienced after the increase in IUA dosage.

The pioneers in penile rehabilitation strategies were Montorsi *et al.* (34) when they published the first clinical trial to evaluate ICI in 1997. They randomized 33 patients who underwent bilateral nerve-sparing RP to receive alprostadil injections 3 times per week for 12 weeks versus no treatment. After 6 months, 67% of men in the treatment group achieved spontaneous erections sufficient for penetration when compared to 20% in the control group.

Long-term trials evaluating ICI in penile rehabilitation are limited. Mulhall *et al.* (35) published a prospective non-randomized study on 58 men with good preoperative EF that were treated with early sildenafil, and if no EF response was noted, were transitioned to ICI 3 times per week. A control group consisting of 74 patients was allowed to have treatment on-demand but off-protocol. At 18 months after prostatectomy, 52% *vs.* 19% in the rehabilitation group and

Table 2 Penile rehabilitation after radical prostatectomy: summary of clinical trials using non-oral modalities

Author	Year	N	Follow-up	Study design	ED treatment (treatment period)	Level of evidence	Significant findings
McCullough *et al.* (33)	2010	212	9 months	Prospective, randomized	IUA *vs.* sildenafil (9 months)	2	No difference in IIEF and intercourse success between treatments
Montorsi *et al.* (34)	1997	30	12 weeks	Prospective randomized	ICI *vs.* no treatment (12 weeks)	2	ICI has higher rate of spontaneous erections compared with controls
Mulhall *et al.* (35)	2005	132	18 months	Prospective, non-randomized	Sildenafil +/– ICI (12 months)	3	Treatment group had more spontaneous erections and higher IIEF compared with controls. Men on rehabilitation are more likely to respond to treatment
Mulhall *et al.* (36)	2009	84	2 years	Retrospective, no control	Sildenafil +/– ICI: early (2 months) *vs.* delayed (7 months)	4	Early better than delayed group in unassisted erections
Raina *et al.* (37)	2006	109	9 months	Prospective, randomized	Daily VED *vs.* no treatment	2	VED improved rate of spontaneous erections and decreased penile shrinkage
Raina *et al.* (38)	2010	141	5 years	Prospective, non-randomized	VED and other non-oral therapies (9 months)	3	Most men who tried non-oral agents, with or without VED, remained sexually active after 5 years
Engel *et al.* (39)	2011	23	12 months	Prospective, randomized	VED and tadalafil *vs.* tadalafil	2	Combination therapy had higher IIEF scores
Fode *et al.* (40)	2014	68	18 months	Retrospective	PVS with PDE5I *vs.* no PVS with PDE5I (6 weeks)	3	No significant difference, though trend of better IIEF score in patients using PVS
Yiou *et al.* (41)	2015	12	1 year	Phase I–II, no-control	ICSCT	4	Significant improvement in IIEF scores compared to baseline. Well tolerated

VED, vacuum erection devices; IUA, intraurethral alprostadil; ICI, intracavernosal injection therapy; PVS, penile vibratory stimulation; IIEF, international index of erectile function score; ICSCT, intracavernosal stem cell therapy.

control group, respectively, reported unassisted spontaneous erections. In a similar study in 2009, Mulhall *et al.* (36) attempted to define if EF outcomes were better with early institution of therapy. They retrospectively evaluated 48 patients in the early group and 36 patients in the delayed group who were all instructed to obtain three erections per week using sildenafil initially, and if unsuccessful, use ICI. Penile rehabilitation started at mean time of 2 months in the early group and 7 months after RP in the delayed group. After 2 years, the group of patients who started rehabilitation earlier had a significant higher percentage of unassisted erections and IIEF-EF score >25. These studies unveil evidence that not only which therapy is offered, but the timing of penile rehabilitation is of paramount importance (16,36).

ICI and IUA have been found to contribute to EF recovery after RP. However, the literature still lacks well-designed randomized prospective trials with long-term follow-up to assess its overall effectiveness in penile rehabilitation.

Non-pharmacological therapies

The corpus cavernosum usually has low oxygen tension (PO2 =25–40 mmHg) during its flaccid state. When having an erection, the tension increases up to 90–100 mmHg which enables the release of NO and PGE1. These substances prevent collagen synthesis and fibrosis by suppressing transforming growth factor-beta 1 (TGF-β1) (42). The vacuum erection device (VED) causes an erection by creating negative pressure around the penis and drawing

both venous and arterial blood into the corpus cavernosum. This increases both glanular and corporal oximetry, alleviates tissue hypoxia and prevents tissue fibrosis (43,44).

Raina *et al.* (37) were among the first to report VED use in patients undergoing RP. In their prospective clinical trial, they randomized 109 patients into using daily VED versus observation. In the VED group, 80% had erections sufficient for intercourse at 9 months and only 23% of those patients were less likely to report penile shrinkage.

Another prospective study by Raina and colleagues evaluated the effect of early use of VED in combination with sildenafil 100mg on-demand of 141 men after RP at 5 years. At 1- and 5-year follow-up, 80% and 62% of men were sexually active, respectively. After 5 years 71% of patients reported natural erections sufficient for intercourse, 8.5% were still using sildenafil, and 10% were using combination therapy of sildenafil plus VED (38). Unfortunately, this study had major limitations, as there was no control group and protocol details or nerve-sparing status were not revealed. Engel (39) did a similar study in which they randomized 23 patients undergoing bilateral nerve-sparing RARP into receiving tadalafil or tadalafil plus VED. Patients who had tadalafil plus VED had significantly higher IIEF-5 scores and greater penile hardness than the patients with PDE5I alone. After 1-year follow-up, 92% of the combination group reported engaging in vaginal intercourse versus 57% in the monotherapy group.

Penile vibratory stimulation is mostly used to stimulate an erection in men with ED and ejaculation in men with spinal cord injury. It works through the stimulation of branches of the pudendal nerves that lie along the penile shaft. The stimulation causes a reflex parasympathetic erection through the activation of nerve terminal endings that release nitric oxide and hence cGMP and cAMP that cause cavernosal smooth muscle dilation (45).

Fode *et al.* (40) reported the first human trial to investigate if PVS helps to recover EF in patients undergoing nerve-sparing RP. In their study, they randomized 68 patients into using PVS with oral PDE5Is versus oral PDE5Is alone. PVS consisted of stimulating the frenulum once daily for at least 1 week before surgery and for 6 weeks after catheter was removed. After 12 months, results showed that IIEF scores were higher in patients using the combination of PVS with oral PDE5Is, although no statistical difference was appreciated. Although they did not specify which type, frequency or dosage of the PDE5Is was used, this trial suggests that PVS may play a future role in penile rehabilitation.

Unlike PDE5Is, VED does not require intact corporal nerves and nitric oxide pathways for proper function. VED can warrant multiple erections on a daily basis early in the post-prostatectomy period, overcome RP-induced hypoxia, and prevent fibrosis that can lead to decrease in penile length and ED (16,46). The VED device contains a constriction ring used at the base of the penis that aids in maintaining erections for intercourse. However, blood gas analyses have shown hypoxia of penile blood after 30 minutes (47). Therefore, to prevent ischemic injury to the penis, a constriction ring should be avoided in penile rehabilitation unless the patient is planning vaginal intercourse. We believe that its low complication rates, lack of side effects and cost-effectiveness make VED a good addition to be taken into consideration while counseling patients for penile rehabilitation. The clinical trials investigating the use of VED and PVS showed that these non-invasive modalities are both acceptable and tolerable for patients.

Immunotherapy and stem cell therapy

Although the peripheral nervous system has the ability to regenerate after injury, this is usually limited and is not enough to prevent the pernicious effect on its end-organ function (48). Some researchers have analyzed strategies to improve regeneration and protection of cavernous nerves in order to reduce the time of denervation of the corpora cavernosa after injuries such as RP. These strategies have shown favorable results in animal models but have yet found their way into clinical practice (48,49).

In the early 2000s, several groups (50,51) discovered that immunomodulatory drugs can alleviate the inflammatory reaction that leads to cavernous nerve apoptosis and degeneration. These studies showed that immunophilin ligands can exert a neuroprotective effect on rats after cavernous nerve injury and maintain EF (52,53). However, the promising effects were not appreciated when these drugs were translated to clinical trials (54,55).

Bochinski *et al.* (56) was the first to report that neural embryonic stem cells preserved EF in rats that underwent cavernous nerve injury. Stem cells can undergo self-regeneration, differentiate into various phenotypes, and functionally and structurally regenerate injured or damaged tissues (57,58). Other researchers later validated these findings and after noticing that only a few labelled stem cells were found 4 weeks after injection, they concluded that adipose tissue-derived stem cells might exert their beneficial effects via a paracrine mechanism (59). Lin and colleagues recently attempted to counteract this 'wash-out' effect and found a

way to keep injected stem cells in the corpus cavernosum by magnetizing these with NanoShuttle magnetic nanoparticles, hence improving EF even more after stem cell therapy (60).

Evidence from animal results suggests intracavernous injection of stem cells as a promising treatment approach for ED after RP. This has motivated researchers to initiate phase I and II clinical trials in humans. Yiou *et al.* (41) recently presented their phase 1–2 pilot clinical trial of intracavernous autologous bone marrow-mononuclear cell injection in patients undergoing RP. A total of 12 patients with localized prostate cancer and vasculogenic post-prostatectomy ED refractory to medical treatment were treated with escalating doses of stem cell therapy. As any phase I study, the primary endpoint was tolerance and secondary endpoints were the effects on EF assessed with IIEF scores and penile vascularization determined by Doppler ultrasound. After 6 months of the treatment, no adverse effects occurred. When compared to baseline, there was a significant improvement in IIEF scores. They also noted an increase in Doppler peak systolic velocity which was sustained after 1 year. Although no major beneficial conclusions could be drawn due to the lack of a control group, these studies suggest that stem cell therapy could play a role in penile rehabilitation in the future.

Conclusions

Several factors contribute to post-prostatectomy EF including age, pre-existing ED, medical comorbidities, surgeon techniques, equipment and experience. The purpose of penile rehabilitation is to preserve health and minimize damage to erectile tissue during the period of neural recovery by providing adequate oxygenation to the cavernous tissues (61). Ferrini *et al.* showed that PDE5I rehabilitation has a beneficial effect on penile tissue by preventing veno-occlusive dysfunction and on the major pelvic ganglia where the medication can ameliorate the production of damaging factors and increase the expression of favorable factors after cavernous nerve injury. These results proposed for the first time that PDE5Is may be used as a neuroprotective agent to alleviate neuropathic pain and favor neuroregeneration after RP (62,63).

Although there is not enough evidence to create an algorithm for penile rehabilitation, the use of most of the therapies and modalities reviewed in this article have been well-tolerated and no significant harm of rehabilitation has been demonstrated provided the patients understand the side-effects and costs of each modality. This has driven urologists in the United States to include penile rehabilitation programs in their practices (64). Most have adopted the therapies provided in our review, either monotherapy or a combination of different modalities. We noted that research in penile rehabilitation is leading towards the use of combination therapies. Some have started to evaluate the benefits of long-term PDE5Is in combination with stem cell therapy in rats undergoing cavernous nerve injury and found that there was complete recovery of EF in rats receiving dual therapy. When given PDE5Is or stem cell therapy alone, they observed only a partial erectile response (65). Others are even combining intracavernosal stem cell injections with newer modalities such as low-energy shockwave therapy to not only improve injured cavernous nerves, but also promote angiogenesis in the corpus cavernosum (66).

We believe penile rehabilitation should be a key component in the postoperative care of patients undergoing RP. Erectile recovery should not only be focused on penile function, but also aimed to establish a satisfactory and healthy sexual life for both the patient and their partners, regardless of whether there is complete restoration of spontaneous EF. Some researchers have suggested that the application of behavioral science methods and tools by a clinical sexologist, in addition to the standard medical/surgical EF care, can improve the ability to have regular sexual activity with penetrating sex in patients undergoing robotic RP (67,68). Although there is a controversy in the effectiveness of penile rehabilitation modalities, any rehabilitation is undeniably better than no action at all. By combining excellence in the technique of robotic-assisted RP with penile rehabilitation modalities, urologists can not only improve their patients' chance of survival, but also their quality of life after surgery.

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Footnote

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