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REVIEW ARTICLE

Penile rehabilitation in men after radical robotic prostatectomy: Fact or fiction?

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Abstract

Erectile dysfunction (ED) is one of the most frequent and distressing complications after radical prostatectomy (RP), significantly impairing patients' quality of life and intimate relationships. Penile rehabilitation (PR) aims to preserve erectile tissue integrity, prevent fibrosis, and facilitate early functional recovery by restoring oxygenation to the corpora cavernosa. Current PR strategies include oral phosphodiesterase type 5 inhibitors (PDE5is), intracavernosal injections, and vacuum erection devices, used alone or in combination. Adjunctive options, such as low-intensity shockwave therapy, stem cell therapy, and platelet-rich plasma, are currently under investigation. Despite widespread use, there is no standardized PR protocol, and evidence remains mixed regarding optimal timing, dosage, and duration. This review summarizes contemporary and emerging PR modalities, highlighting evidence-based principles, patient selection, and integration of preoperative counseling to set realistic expectations. Psychosocial support, partner involvement, and multidisciplinary collaboration are essential to maximize adherence and recovery. Future research should prioritize high-quality randomized controlled trials to define standardized, evidence-based PR protocols tailored to individual risk profiles and preferences, ultimately improving functional recovery and quality of life after RP.

KEYWORDS

erectile dysfunction, penile rehabilitation, radical prostatectomy, sexual function recovery

1 | INTRODUCTION

Prostate cancer (PCa) is the second most frequently diagnosed malignancy among men worldwide, affecting approximately 1.4 million new cases in 2020[1]. Its incidence is rising steadily due to widespread prostate-specific antigen (PSA) screening and an aging population[1]. Radical prostatectomy (RP) remains a cornerstone curative treatment for patients with low- to intermediate-risk, organ-confined disease, especially those with a life expectancy over 10 years[2]. Advances in surgical techniques, such as nerve-sparing approaches and robot-assisted procedures, have improved perioperative outcomes but have not eliminated the risk of treatment-related sexual dysfunction[3].

RP commonly results in long-term sexual health side effects such as erectile dysfunction (ED) and penile length loss[4]. Reported rates of ED after RP vary widely, ranging from 25% to over 90%, depending on baseline

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erectile function, patient comorbidities, surgeon experience, and definition of recovery[5–8]. The impact of post-prostatectomy ED extends beyond sexual health, affecting self-esteem, mental well-being, interpersonal relationships, work productivity, and overall quality of life[9].

The concept of penile rehabilitation (PR) emerged in the early 2000s as a proactive strategy to preserve penile tissue health, ensure proper oxygenation, speed up the return of spontaneous erectile function after RP, and prevent length loss[7]. Interventions such as phosphodiesterase type 5 inhibitors (PDE5is), intracavernosal injections (ICIs), vacuum erection devices (VEDs), and emerging modalities, including low-intensity shockwave therapy (LiSWT) and regenerative approaches, have been studied with mixed results[10–12]. Figure 1 illustrates potential treatments for PR. Despite its potential advantages and widespread use, there is currently no standardized, evidence-based PR protocol, and the optimal timing, duration, and combination of treatments are still debated.

This review summarizes the current evidence on PR strategies following RP, highlights patient-centered factors that affect adherence and outcomes and explores future directions with novel and investigational therapies.

2 | DEFINITION AND RATIONALE FOR PENILE REHABILITATION

The rationale for PR lies in the mechanism of ED after RP. The pathophysiology of ED involves injury to the cavernous nerves, neuropraxia, and vascular injury, leading to structural changes and apoptosis in the smooth muscle and endothelium[7]. Notably, the loss of EF and prolonged flaccid state after RP causes reduced oxygenation, resulting in pro-apoptotic and pro-fibrotic changes in the corpora cavernosa that further worsen ED after RP[13]. These structural changes predispose patients to venous leak, as the smooth muscle fails to expand fully. Venous leak is associated with poor EF recovery and reduced responsiveness to PDE5i, and its severity increases with the duration of post-operative ED[7]. Therefore, the goal of PR protocols is early EF recovery by enhancing cavernous oxygenation, preserving penile tissue integrity, and preventing smooth muscle atrophy[14].

A major challenge in evaluating PR efficacy is accurately measuring post-RP EF recovery. EF is affected by multiple variables, including patients' age, baseline erectile function, comorbidities, surgical technique, surgeon skill, length of follow-up, and differences in how "recovery" is defined[8]. Additionally, the lack of a validated, procedure-specific sexual health questionnaire for post-RP EF hampers efforts to standardize outcome reporting.

Given these limitations, the International Index of Erectile Function (IIEF) remains the most widely used tool to assess EF recovery after RP[9]. Efforts to identify an optimal cutoff score have yielded varying results. Terrier et al. (2017) prospectively monitored men for 24 months after RP and concluded that an erectile function domain (EFD) score of ≥24, combined with an intercourse satisfaction domain (ISD) score, is a valid threshold for defining functional erections in this population[9]. Similarly, a post-hoc analysis of the REACTT trial showed that changing the EF recovery definition from ≥22 to >26 did not significantly impact outcomes[15].

Nevertheless, the IIEF may not fully capture the complex aspects of post-RP sexual health, as it overlooks changes in penile length, orgasmic function, and psychosocial well-being[16]. The development of a standardized, RP-specific EF assessment tool would improve reporting consistency and enhance the evaluation of PR interventions.

3 | ESTABLISHED TREATMENT MODALITIES FOR PENILE REHABILITATION

3.1 | Oral phosphodiesterase type 5 inhibitors (PDE5i)

According to the American Urological Association (AUA) guideline on ED, the use of PDE5i to improve EF after RP currently has a Grade C recommendation, reflecting limited but supportive evidence[17]. Table 1 summarizes key studies evaluating PDE5i use for erectile function recovery after radical prostatectomy. The REACTT trial, which enrolled 423 men after bilateral nerve-sparing RP, showed that daily tadalafil 5 mg was more effective than on-demand tadalafil 20 mg or placebo in improving EF after surgery[15].

A 2021 meta-analysis by Sari et al. further supported these findings, showing that daily use of sildenafil 100 mg was significantly associated with EF recovery (OR: 4.00, 95% CI: 1.40–13.4)[18]. In contrast, on-demand PDE5i use did not achieve statistical significance. Notably, this analysis identified only sildenafil 100 mg and pelvic floor therapy as interventions significantly associated with EF recovery[18]. Despite these improvements, there is still no consensus or guideline-defined optimal dosing regimen for PDE5i in penile rehabilitation protocols.

The timing of PDE5i initiation is another critical factor. Evidence suggests that starting therapy immediately after surgery results in better EF recovery compared to delayed treatment[19–21]. In an RCT, Jo et al. found that initiating PDE5i right after catheter removal significantly increased EF recovery rates compared to starting at 3 months post-surgery (41% vs. 18%)[20].

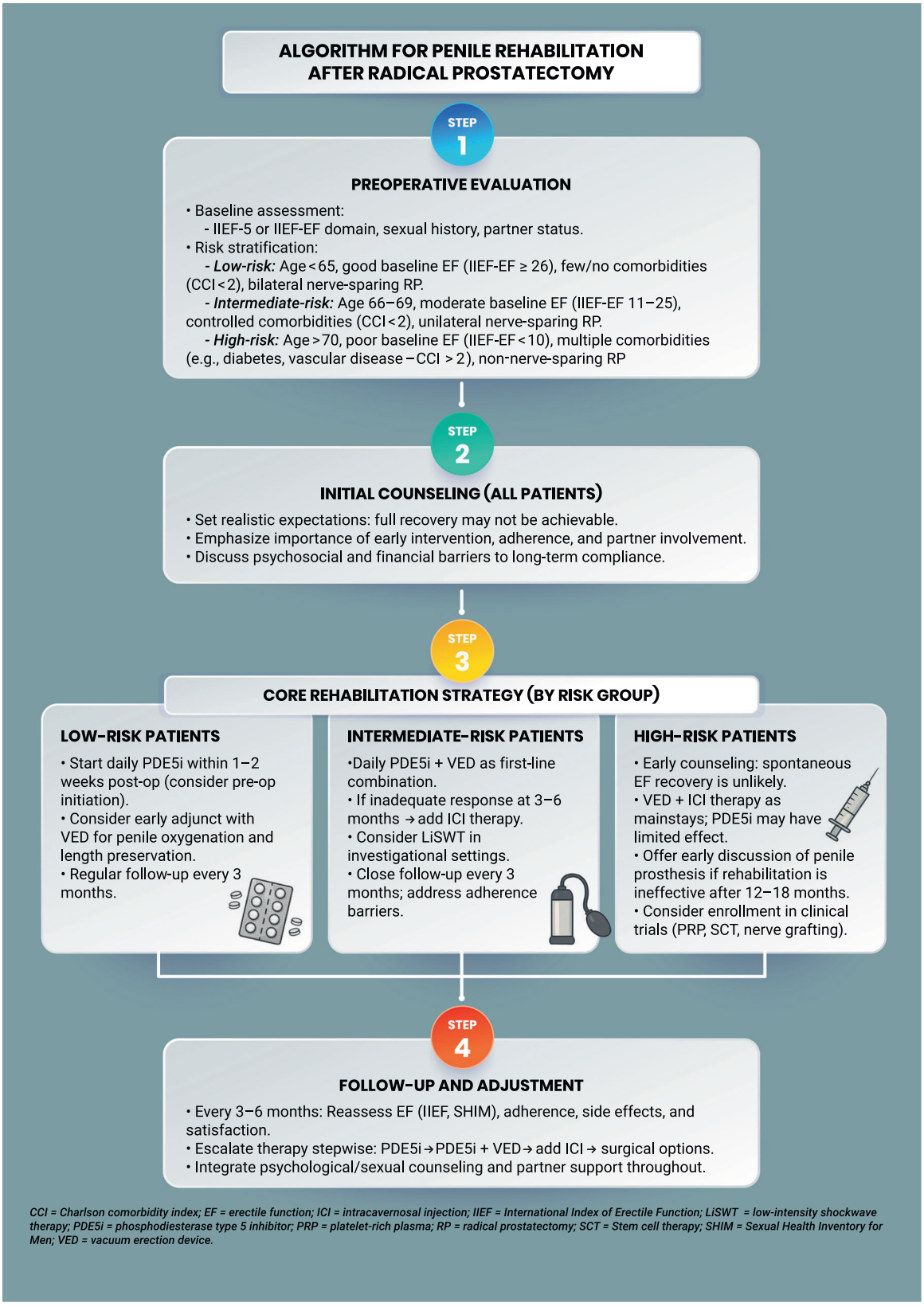

FIGURE 1 Proposed algorithm for penile rehabilitation after radical prostatectomy, stratified by patient age, baseline erectile function, comorbidities, and surgical technique. The algorithm highlights the importance of early counseling, individualized therapy selection, and regular follow-up to optimize outcomes and adherence.

TABLE 1 Major studies assessing PDE5 inhibitors for erectile function recovery following radical prostatectomy.

Author, year	Study design	Population	Intervention	Timing of initiation	Duration	Main findings
REACTT Trial, 2014[15]	Randomized controlled trial	423 men post–bilateral nerve-sparing RP	Tadalafil 5 mg daily vs. tadalafil 20 mg on-demand vs. placebo	Early postoperative	9 months	Daily tadalafil superior to on-demand and placebo for EF recovery
Sari et al., 2021[18]	Meta-analysis	Multiple RCTs	Sildenafil 100 mg daily vs. on-demand PDE5i	Variable	Variable	Daily sildenafil significantly associated with EF recovery (OR = 4.00); on-demand not significant. Sildenafil 100 mg and pelvic floor therapy were the only interventions significantly associated with EF recovery
Jo et al., 2010[20]	Randomized controlled trial	Men after RP	PDE5i daily	Immediately after catheter removal vs. 3 months post-RP	12 months	Immediate initiation improved EF recovery (41% vs. 18%)
Noh et al., 2022[22]	Double-blind, prospective pilot study	Men undergoing RP	Tadalafil 5 mg daily	2 weeks before RP vs. 4 weeks after RP	12 months	Preoperative initiation improved IIEF-5 scores (15.6 ± 2.1 vs. 12.8 ± 3.5; $p < 0.001$)
Osadchiy et al., 2020[23]	Retrospective review	Men after RP	Tadalafil-based PR protocol	Preoperative vs. postoperative initiation	Variable	Preoperative protocol associated with superior EF recovery
Tian et al., 2017[24]	Meta-analysis	Post-RP men	PDE5i therapy	Postoperative	> 6 months vs. < 6 months	Longer therapy (> 6 months) improved EF recovery (mean IIEF-EF difference: 3.9; 95% CI: 3.01–4.8; $p < 0.00001$)

Abbreviations: EF, erectile function; IIEF, International Index of Erectile Function; PDE5i, phosphodiesterase type 5 inhibitor; PR, penile rehabilitation; RP, radical prostatectomy.

Some data suggest that starting treatment before surgery may provide additional benefits[22,23]. In a 2022 double-blind, prospective pilot study, Noh et al. compared tadalafil started 2 weeks before RP versus 4 weeks after surgery, reporting significantly higher 12-month IIEF-5 scores in the postoperative group (15.6 ± 2.1 vs. 12.8 ± 3.5, $p < 0.001$)[22]. This aligns with a retrospective review by Osadchiy et al., which also found better outcomes with preoperative tadalafil[23]. Finally, Tian et al. showed that PDE5i therapy for more than 6 months after RP was associated with significantly greater EF recovery compared to shorter treatment durations (mean IIEF-EF difference: 3.9; 95% CI: 3.01–4.8; $p < 0.00001$)[24]. These findings suggest that starting daily PDE5i therapy 2 weeks before RP and continuing it long-term may yield the most favorable EF recovery, a strategy endorsed by the authors of this review.

3.2 | Intracavernosal injection (ICI) therapy

ICI therapy with vasoactive agents such as alprostadil, phentolamine, papaverine, and/or atropine has been a long-standing cornerstone of PR. Of these, only alprostadil is approved by the US Food and Drug Administration (FDA) for ICI use. However, combination formulations, often called Bimix, Trimix, and Quadmix, are widely available from compounding pharmacies.

The efficacy of ICI in PR has been demonstrated in both randomized and observational studies[10,25–27]. In one of the pioneering trials in this field, Montorsi et al. randomized 30 men with good EF prior to RP into two groups: ICI three times per week for 12 weeks versus observation. At follow-up, erectile function recovery was achieved in 67% of patients receiving ICI compared to only 20% in the control group[10].

Similarly, an observational study by Claro et al. reported a 94.6% success rate among 168 patients with ED after RP using ICI, defined as achieving sexual intercourse with a rigid erection[28]. The prescribed ICI volume ranged from 0.1 mL to 0.8 mL based on patients' in-office response to 0.2 mL of a compounded mixture containing papaverine (22.6 mg), prostaglandin E1 (13.4 mg), and phentolamine (1.34 mg). Follow-up ranged from 5 months to 72 months (median: 29 months). All patients who achieved successful intercourse received injections weekly or more frequently, with explicit instructions to avoid using injections on consecutive days. There were no significant side effects, with all patients reporting mild pain, around 15% developed ecchymosis during the first three to four home self-injections, and 19 patients (11.3%) reported prolonged erection, lasting from 3 h to 10 h, with all self-resolving at home[28]. Key studies evaluating ICI therapy for erectile function recovery after radical prostatectomy can be found in Table 2.

3.3 | Vacuum erection device (VED)

A VED is a cylindrical, closed-end plastic tube that uses negative pressure to increase blood flow into the corpus cavernosum. A battery-powered suction or a manual pump can create this vacuum. A constriction ring may be used and is placed at the base of the penis to prevent blood from leaking out of the corpus cavernosum, which can be useful during intercourse. Regarding the use of VEDs after RP, the theory is that VEDs can serve as a temporary solution during the neuropraxia period following RP[29]. This is achieved by negative pressure that dilates the cavernosal arteries. The increased arterial blood flow reduces hypoxia, fibrosis, and apoptosis, which helps preserve penile length, girth, and overall sexual function[30,31]. VEDs are a well-established and well-researched treatment for ED after RP. Both the AUA[17] and the International Society of Sexual Medicine (ISSM)[32] recommend their use, and they are considered the second-line therapy after PDE5is[33].

In the latest meta-analysis on post-RP therapy, Feng et al. identified two studies comparing VED monotherapy to no treatment and three studies comparing VED combined with phosphodiesterase type 5 inhibitor (PDE5i) therapy to PDE5i alone[34]. In the VED versus control studies, the VED group showed significantly higher IIEF-5 scores (mean difference [MD] = 6.70; 95% CI: 2.30–11.10; $p = 0.003$). The timing of initiation (1 month vs. 6 months postoperatively) yielded similar IIEF-5 outcomes at 12 months; however, late initiation was associated with a higher proportion of patients experiencing a loss of ≥2 cm in stretched penile length (SPL). The three combination-therapy studies showed significantly higher IIEF-5 scores with VED + PDE5i compared to PDE5i alone at 3 months after surgery (MD = 3.73; 95% CI: 2.85–4.61; $p < 0.00001$). Long-term benefits were supported by Engle et al., who found that the combination group maintained higher IIEF-5 scores at 6 months, 9 months, and 12 months[35].

Recently, an RCT involving 100 patients followed for 12 months after nerve-sparing RP compared four groups: (1) VED only; (2) tadalafil only; (3) a combination of tadalafil and VED; and (4) no treatment[36]. The study showed that the group receiving tadalafil plus VED not only had improved IIEF-5 scores but also achieved a higher rate of successful penetration (SEP-2) compared to the other groups. However, there were no significant differences in the recovery of target erectile function among the groups. Notably, VED alone or in combination with tadalafil helped maintain penile length compared to no treatment or tadalafil alone. Table 3 provides an overview of major studies evaluating VED in post-radical prostatectomy EF recovery.

VED-related adverse effects are generally mild and temporary in nature. They include device malfunction, penile bruising, pain, and numbness[37–39]. VED is

TABLE 2 Key studies evaluating intracavernosal injection therapy for erectile function recovery after radical prostatectomy.

Author, year	Study design	Population	Intervention	Timing and frequency	Follow-up	Main findings
Montorsi et al., 1997[10]	Randomized controlled trial	30 men with good preoperative EF undergoing RP	ICI with alprostadil/papaverine/phentolamine	3 times/week for 12 weeks	Not specified	EF recovery in 67% of ICI group vs. 20% in observation group
Claro et al., 2001[28]	Observational study	168 men with ED after RP	Papaverine (22.6 mg) + PGE1 (13.4 mg) + phentolamine (1.34 mg)	Weekly or more frequent injections; avoid consecutive days	5–72 months (median 29 months)	94.6% success rate (sexual intercourse with rigid erection). Mild pain common; around 15% ecchymosis early; 11.3% prolonged erection (3–10 h, all self-resolving)
Bock et al., 2024[88]	Review/summary of studies	Post-RP patients (multiple cohorts)	Alprostadil monotherapy or combination (Bimix/Trimix/Quadmix)	Variable	Variable	Evidence supports ICI efficacy in EF recovery; widely used in PR protocols despite limited RCTs

Abbreviations: EF, erectile function; ICI, intracavernosal injection; PGE1, prostaglandin E1; PR, penile rehabilitation; RP, radical prostatectomy.

TABLE 3 Clinical studies investigating vacuum erection device (VED) therapy in post-radical prostatectomy erectile function recovery.

Author, year	Study design	Population	Intervention	Timing and frequency	Follow-up	Main findings
Feng et al., 2022[34]	Meta-analysis	Post-RP patients	VED vs. no treatment; VED + PDE5i vs. PDE5i alone	3 months, 6 months, 9 months, and 12 months	VED vs. control: higher IIEF-5 (MD = 6.70; 95% CI: 2.30–11.10; $p = 0.003$). Combination therapy: higher IIEF-5 at 3 months (MD = 3.73; 95% CI: 2.85–4.61; $p < 0.00001$)	Early use of VED contributed to significantly higher IIEF-5 scores, and preserve penile length
Engel et al., 2011[35]	Randomized prospective study	Post-robotic RP patients	VED + PDE5i vs. PDE5i alone	3 months, 6 months, 9 months, and 12 months	Combination maintained higher IIEF-5 scores across all time points, greater penile hardness scores at 6 months and 9 months postoperatively, and significantly higher percentage of patients achieving completion of orgasm at 12 months post-RP	Combination therapy resulted in a more rapid and completed return of sexual function compared to PDE5i alone
Zhang et al., 2022[36]	Randomized controlled trial	100 patients after nerve-sparing RP	4 groups: VED only ($n = 25$); tadalafil only ($n = 25$); tadalafil + VED ($n = 25$); no treatment ($n = 25$)	Up to 12 months	Tadalafil + VED improved IIEF-5 and SEP-2 compared to others; VED preserved penile length; no significant difference in recovery of target EF	Combination therapy (PDE5i + VED) not only improved EF recovery, but also prevent penile length shrinkage post-RP

Abbreviations: CI, confidence interval; EF, erectile function; IIEF, International Index of Erectile Function; MD, mean difference; PDE5i, phosphodiesterase type 5 inhibitor; RP, radical prostatectomy; SEP, Sexual Encounter Profile; VED, vacuum erection device.

contraindicated in patients with bleeding disorders or on anticoagulant therapy.

The main challenge is long-term adherence: several retrospective reviews report significant discontinuation by 12 months post-op, citing pain, perceived lack of effectiveness, dislike of the device, cost, and inconvenience as primary reasons[40–43]. This highlights the importance of thorough pre-treatment counseling and ongoing follow-up to improve adherence.

4 | EMERGING AND INVESTIGATIONAL THERAPIES

Over the past decade, several new interventions have been explored for managing ED after RP. This section highlights LiSWT, stem cell therapy, and platelet-rich plasma (PRP) injections, as well as methods for nerve regeneration.

4.1 | Low-intensity shockwave therapy (LiSWT)

LiSWT is a non-invasive method that utilizes low-intensity acoustic shockwaves to stimulate tissue regeneration. Proposed mechanisms include stimulating angiogenesis, recruiting stem and progenitor cells, promoting nerve regeneration, and regulating smooth muscle activity within the corpora cavernosa[44].

The first report of LiSWT in the post-RP setting was a pilot study by Frey et al., which enrolled 16 men with ED persisting for at least 1 year after RP[45]. Patients underwent six weekly sessions over 6 weeks. The median baseline IIEF-5 score was 9.5 (range 5–20). At 1 month, the median change in IIEF-5 was +3.5 (IQR = 4.25; SD = 2.66; $p = 0.0049$), and at one year, the change was +1 (IQR = 3.5; SD = 2.46; $p = 0.046$). These results indicated short-term benefits, but long-term efficacy remained uncertain.

The first RCT was conducted by Baccaglini et al.[46]. Patients were randomized to receive either tadalafil alone (control) or tadalafil plus LiSWT, which was started 6 weeks after surgery. The treatment protocol involved 2400 shocks per session, given once weekly for 8 weeks, at a maximum energy of 5 Hz. At 4 months postoperatively, the treatment group had a higher median IIEF-5 score than the control group (12.0 vs. 10.0; $p = 0.006$), but the proportion achieving an IIEF-5 score of 17 or higher was not significantly different (17.1% vs. 22.2%; $p = 0.57$).

Long-term follow-up (average 45 months) of the same cohort showed no statistically significant difference in mean IIEF-5 scores between the treatment and control groups (18.85 vs. 16.63; $p = 0.42$)[12]. Importantly, since most participants had moderate-to-severe ED, the observed differences did not reach the minimal clinically significant difference (MCSD) threshold for IIEF-5, which means an improvement of at least 4 points[47]. Subsequent studies have largely confirmed these findings, indicating that LiSWT combined with PDE5i offers limited short- and long-term benefits compared to PDE5i alone[48–50]. Overall, current evidence does not support a clinically significant benefit of LiSWT over standard PDE5i therapy in post-RP ED. Furthermore, high-quality RCTs are needed to define their role in penile rehabilitation.

4.2 | Platelet-rich plasma (PRP)

PRP is an autologous, blood-derived preparation widely used for its regenerative and healing properties[51]. PRP is enriched with growth factors, including platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), and vascular endothelial growth factor (VEGF), which may promote angiogenesis and tissue repair[51]. Although its mechanism of action in EF recovery remains incompletely understood, preclinical evidence suggests that CXC ligand 5 (CXCL5) and its receptor CXC chemokine receptor 2 (CXCR2) may mediate neuroprotection of the cavernous nerves (CNs) following injury, such as that encountered in RP[52].

The therapeutic potential of PRP for ED after RP was first studied in 2009 in an animal experiment involving bilateral CN injury in rats[53]. PRP treatment increased the number of myelinated axons within the CN and improved EF compared with the control group, indicating a potential role for PRP in neuroprotection. Later animal studies have supported these results, showing enhanced neurogenesis, decreased smooth muscle apoptosis, and increased proliferation of corporal smooth muscle cells after PRP treatment[52,54,55].

To date, three RCTs have assessed intracavernosal PRP injections in humans with ED of mixed etiologies, although none have specifically targeted post-RP patients. Shaher et al. examined 100 men with mild-to-moderate ED who were randomly assigned to receive either PRP (three injections, 15 days apart) or a placebo, and they found significantly higher rates of achieving the MCSD in IIEF-EF scores at 1 month, 3 months, and 6 months in the PRP group (76% vs. 18%, 72% vs. 16%, and 70% vs. 16%, respectively; all $p < 0.001$)[56]. Poulios et al. employed a similar design with two PRP injections spaced 1 month apart and observed consistent benefits, with significantly higher MCSD achievement rates at all follow-up points (1 month = 76% vs. 25%, $p < 0.001$; 3 months = 69% vs. 39%, $p = 0.018$; 6 months = 69% vs. 27%, $p < 0.001$)[57]. However, Masterson et al. later repeated Poulios's protocol but found no significant differences between PRP and placebo at 1 month, 3 months, or 6 months (58.3% vs. 53.6%, $p = 0.730$; 41.7% vs. 52%, $p = 0.469$; 60% vs. 41.7%, $p = 0.226$)[58].

Overall, although animal models support a biological rationale for PRP in neuroprotection and EF recovery,

human clinical data remain inconsistent, and no published trials have specifically investigated PRP for post-RP ED. Future research should focus on standardized PRP preparation protocols, adequately powered RCTs, and long-term follow-up to determine its role in penile rehabilitation.

4.3 | Stem cell therapy (SCT)

SCT has been studied by a few authors as a potential method for PR after RP. The proposed mechanisms include cellular differentiation and paracrine signaling, which may promote neuronal repair, smooth muscle regeneration, and endothelial cell growth[59–61]. SCT is most commonly administered intravenously or via ICI, with cells usually sourced from bone marrow or adipose tissue[62].

Two early-phase clinical trials have assessed the effectiveness of SCT in treating ED after RP[63,64]. In 2016, a phase I trial enrolled 12 men with ED following RP who received four ICIs of bone marrow–derived mononuclear cells[63]. After 6 months, notable improvements were observed in the mean scores for intercourse satisfaction (IIEF-IS) domain (6.8 vs. baseline 3.9; $p = 0.044$) and erectile function (IIEF-EF) domain (17.4 vs. baseline 7.3; $p = 0.006$) on the IIEF-15. In 2017, the phase II findings extended the follow-up to 12 months for the original cohort and included six additional patients[64]. The new cohort demonstrated similar improvements in IIEF-5 scores (from 18.7 to 46.6), whereas the original cohort showed minor declines at 12 months, which were not statistically significant.

Another phase I trial investigated the use of autologous adipose-derived stem cells in 17 men with post-RP ED[65]. After a single ICI, 47% (8/17) regained erections sufficient for intercourse at 6 months. In 2018, Haahr et al. published results from a similar study involving 21 patients: 38% achieved intercourse-quality erections at 12 months. Median IIEF-5 scores increased modestly from 6.0 (IQR = 3) at baseline to 7 (IQR = 17) after 6 months and to 8 (IQR = 14) at 12 months[66]. However, these improvements did not exceed the MCSD, which limits their clinical significance.

These early studies show the potential of SCT for ED recovery after RP. However, the results remain inconsistent and are limited by small sample sizes, varied protocols, and a lack of controls, and therefore, SCT remains investigational. Future research should include larger, well-designed RCTs with standardized protocols and long-term follow-up to accurately assess its safety and effectiveness.

4.4 | Nerve grafting

Neuropraxia of the cavernous nerves is a common cause of ED following RP, caused by mechanical trauma, ischemia, thermal injury, and inflammation[67]. Even with nerve-sparing techniques, injury to these nerves remains relatively common[68]. Cavernous nerve damage results in structural changes within the corpora cavernosa, including fibrosis and loss of smooth muscle, ultimately impairing erectile function[67].

The rationale for nerve grafting and regeneration is to provide a scaffold that supports axonal regrowth and reinnervation of the penile tissue. Three main techniques are described: sural nerve grafting, genitofemoral nerve grafting, and end-to-side nerve grafting. Among these, sural and genitofemoral grafts have been studied more extensively. Unfortunately, clinical data have shown mixed results, with recent comparative studies reporting no significant difference in erectile function between nerve grafting and conventional nerve-sparing RP[69,70].

End-to-side grafting is a newer technique where the end of a donor nerve is attached to the side of a damaged nerve to promote regeneration[71]. So far, only two studies have been published on this technique. Reece et al. conducted a retrospective review of 17 post-RP men with ED who underwent sural nerve grafting as a bridge from the femoral nerve to the corpora cavernosa[71]. At 12 months, 71% recovered enough sexual function for intercourse, and 94% showed clinically meaningful improvements. Trindade et al. reported a case series of 10 patients, with 60% achieving intercourse-quality erections at an average of 13 months after treatment[72]. These initial results are promising but require confirmation through larger, multicenter clinical trials.

Alternative autologous scaffolds for nerve regeneration, such as peptide-impregnated nanoparticles and spider silk, have also shown promise in preclinical studies and initial human trials[73,74]. However, further research with standardized methods and larger patient groups is essential before these techniques can be adopted into routine clinical practice.

5 | MULTIMODAL THERAPY AND THE ROLE OF PREOPERATIVE COUNSELING

Preoperative counseling is essential for improving patient adherence to PR protocols. In a qualitative study, Nelson et al. examined men's experiences with PR and ED after RP[75]. A lack of clear information about post-surgical complications, especially ED, was among the most common frustrations reported by patients. Many felt that recovery of EF had been "over-promised" and expected to return to baseline function easily. Therefore, setting realistic expectations during preoperative consultations is essential for improving patient satisfaction and functional outcomes.

Albaugh et al. (2019) conducted a longitudinal, cross-sectional study of men followed for two years after RP[42]. Patients were assessed at 1 month, 3 months, 6 months,

12 months, and 24 months using the Sexual Health Inventory for Men (SHIM) within the IIEF. Although some improvements in EF and orgasmic function were observed, only 28.6% of men with normal preoperative SHIM scores returned to baseline EF after two years. Adherence to PDE5i and VEDs was poor, even with comprehensive instructions and regular follow-up. Common barriers included cost, inconvenience, and perceived ineffectiveness. Attrition rates were also high, with only 55.8% completing 12 months and 45% achieving 24 months of PR therapy. These findings highlight the importance of counseling to identify potential barriers and provide ongoing education, as well as the need for urologists to address dropout rates throughout rehabilitation proactively.

Predictive tools, like nomograms, can help make pre- and post-surgery discussions more systematic. Mulhall et al. developed nomograms for the preoperative, early postoperative, and late postoperative periods to predict EF recovery 2 years after RP[76]. Variables included age, baseline IIEF-EF scores, PDE5i use, comorbidities (e.g., cardiovascular disease, diabetes, obesity, smoking), and nerve-sparing status. All three nomograms showed good calibration and high predictive accuracy (c-index > 0.78). These tools provide a structured approach for counseling patients and help men monitor their recovery expectations over time.

Finally, multimodal approaches may improve outcomes and increase adherence. Basal et al. compared men undergoing PR with PDE5i alone, VED alone, a combination of PDE5i and VED, or no treatment. Combination therapy was associated with the shortest EF recovery time and was believed to enhance adherence by providing earlier and more noticeable improvements[77]. Similarly, a meta-analysis by Feng et al. reported significantly higher IIEF-5 scores and better penile hardness at 3 months in men treated with PDE5i plus VED compared with those treated with PDE5i alone[34]. These findings suggest that multimodal approaches not only speed up EF recovery but may also increase adherence through improved treatment effectiveness.

Although no universally accepted method exists for risk stratification, we suggest a practical classification into low-, intermediate-, and high-risk groups based on consistently reported predictors of erectile function recovery, including age, baseline IIEF score, comorbidities, and surgical nerve-sparing status[78–80]. This framework aims to improve patient counseling and support tailored rehabilitation strategies, as outlined in the algorithm.

6 | BARRIERS TO SUCCESS: COMPLIANCE AND PSYCHOSOCIAL FACTORS

Compliance remains a significant challenge with ICI therapy in PR. In a cohort of 430 men undergoing RP, Polito et al. reported that 37% refused to start a PR program, including ICI, beginning 4 weeks postoperatively, and among those who did participate, 19% stopped therapy within 6 months[81]. The main reasons for refusal were lack of sexual interest from the patient and/or partner and temporary urinary incontinence. At the same time, dropout was mostly due to poor treatment response, pain during injection, and fear or difficulty with administration. Despite these barriers, a survey of providers in the ISSM found that 75% reported using ICI as a primary rehabilitation approach[82].

Adverse events related to ICI can further reduce adherence. Patients should be informed about the risks of priapism, penile fibrosis, deformities, and the high incidence of pain, especially after RP[83–85]. West et al. evaluated 566 men after RP and observed significant differences in pain associated with ICI based on surgical technique: 10% in bilateral nerve-sparing, 32% in unilateral nerve-sparing, and 92% in non-nerve-sparing procedures ($p < 0.001$)[86]. Additionally, pain was independently associated with poorer EF recovery. In another study of 464 patients after RP, Tsikis et al. showed that moderate-to-severe ED was an independent predictor of stress urinary incontinence (OR = 1.88; 95% CI: 1.21–2.90), suggesting a potential shared underlying mechanism[87]. Overall, the combination of comorbidities, side effects from treatment, and compliance challenges emphasizes the impact of ICI on both functional recovery and overall quality of life.

Sexual response in men is a complex process involving physical, psychological, and relational factors[88,89]. A systematic review by McCabe and Althof, which included 40 studies (32 RCTs), found that ED treatment improved sexual satisfaction, confidence, self-esteem, and depressive symptoms[90]. Corona et al., in a study of 1140 men in stable relationships, showed significant associations between ED and relational issues, such as decreased desire, delayed ejaculation, and lower frequency of intercourse, using the SIEDY Scale 2[89]. These findings highlight the importance of including psychological support and partner involvement in PR programs, especially when ICI therapy is used, to improve adherence, sexual satisfaction, and quality of life.

7 | PATIENT ADHERENCE AND LONG-TERM FOLLOW-UP

Adherence to PR protocols after RP remains below optimal levels, despite evidence supporting their potential role in preserving EF[42]. Several factors contribute to this issue. Psychosocial barriers such as postoperative depression, anxiety, and altered self-image are common and can reduce patient engagement[42]. The invasiveness and discomfort of widely used treatments, including VEDs, ICIs, and penile traction therapy, often lead to early discontinuation.

Additionally, the lack of immediate or noticeable improvements in EF decreases patient motivation, given the extended time needed for neural recovery. Financial burden is another significant factor, as many PR methods are not routinely covered by insurance, resulting in significant out-of-pocket costs. Lastly, inadequate preoperative counseling and limited postoperative follow-up hinder patient understanding of the rationale, expectations, and importance of adherence, further damaging long-term outcomes.

Although patients face many barriers to maintaining rehabilitation, several strategies can boost adherence. Clear and consistent communication is essential: when patients understand the purpose and benefits of therapy, they are more likely to stay engaged and follow their regimen. Routine follow-up visits also support adherence by providing ongoing assistance, tracking progress, and addressing any challenges that may arise.

An example of a structured approach is the Indiana University protocol, which emphasizes patient education and regular follow-up to improve compliance[91]. Patients are ideally seen before surgery or within 6 weeks of RP to start rehabilitation quickly. During the initial visit, a detailed sexual, reproductive, and medical history is taken, and patients are encouraged to include their partners in treatment planning. Counseling centers on education, managing expectations, and shared decision-making to align therapy with patient goals. Patients are then followed every 3 months, with reassessment of EF and evaluation of side effects. This structured, patient-centered model demonstrates how early intervention, partner involvement, and ongoing follow-up can boost adherence and ultimately improve outcomes in penile rehabilitation.

8 | CONCLUSION

PR aims to preserve erectile function and accelerate recovery; however, established options such as PDE5i, ICI, and VEDs demonstrate variable effectiveness and lack standardized protocols. We propose an evidence-based algorithm for PR after RP, stratified by patient age, baseline erectile function, comorbidities, and surgical technique. The algorithm emphasizes early counseling, individualized therapy selection, and regular follow-up to optimize outcomes and treatment adherence.

Successful PR requires patient-centered care, including preoperative counseling, partner involvement, and structured follow-up to improve adherence and outcomes. Emerging regenerative therapies—including LiSWT, PRP, SCT, and nerve grafting—remain investigational, with limited and inconsistent evidence.

Multimodal therapies can enhance recovery, although long-term benefits require further research. High-quality, multicenter trials are essential to develop evidence-based protocols tailored to individual patients. By integrating advances in therapy with psychological and relational support, penile rehabilitation shows potential to enhance sexual health outcomes after PCa surgery.

AUTHOR CONTRIBUTIONS

Karen Zhang, Arnold P. P. Achermann, Hunter Hasley, Richard Bennett, Andrew Guo, Mohammed Mahdi, Lucas G.C.R. de Amorim, Helen L. Bernie, and Thairo A. Pereira all participated in data acquisition, data analysis, and drafting. Arnold P. P. Achermann, Helen L. Bernie, and Thairo A. Pereira participated in the study concept and design, and critical revision of the manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest. No generative AI tools were used in the writing of this manuscript.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This study did not involve human subjects, patient data, or any intervention, and therefore was exempt from institutional ethics review.

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