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Original Article

Penile rehabilitation effectiveness after prostate cancer treatment: A systematic review of randomized controlled trials

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Abstract

Prostate cancer treatment can significantly impact erectile function, and penile rehabilitation has been proposed to improve the impacts. However, the effectiveness of penile rehabilitations after treatment of prostate cancer is scarce. The aim of this systematic review was to evaluate the effectiveness of different interventions of penile rehabilitation program after prostate cancer treatment. We conducted a comprehensive search of electronic databases, PubMed and Google Scholar, to identify randomized controlled trials that evaluated interventions for penile rehabilitation after prostate cancer treatment. Studies that met our inclusion criteria were systematically reviewed, and data were synthesized and analyzed. We identified 11 randomized controlled trials that evaluated different interventions for penile rehabilitation after prostate cancer treatment. The interventions included the use of phosphodiesterase type 5 inhibitors, intracavernous injections, vacuum erection devices, and penile rehabilitation programs. The data suggest that these phosphodiesterase inhibitors, intracavernous injections, vacuum erection devices, and penile rehabilitation programs are promising in improving erectile function after prostate cancer treatment. However, the optimal timing and duration of these interventions remain unclear, and there is a need for further research to determine their long-term effectiveness and safety. Healthcare providers should consider individualized approaches to penile rehabilitation, taking into account patient characteristics and preferences.

Keywords: Prostate cancer, penile rehabilitation, erectile dysfunction, randomized controlled trial, PDE5 inhibitor

Introduction

Prostatic carcinoma is a prevalent neoplastic condition primarily affecting the male population. In 2021, there were approximately 248,530 number of cases documented in the United States [1]. The therapeutic alternatives for prostatic carcinoma are contingent upon the stage and severity of the malignancy, encompassing surgical intervention, radiotherapy, hormonal manipulation, and cytotoxic chemotherapy [2]. However, these treatment modalities can engender deleterious consequences on the sexual function, particularly pertaining to erectile function, owing to the potential impairment of neural and vascular pathways governing

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the innervation and perfusion of the phallus [3,4]. Erectile dysfunction (ED) represents a prevalent and distressing sequela stemming from the management of prostatic carcinoma, significantly compromising the quality of life (QoL) experienced by the affected males and their intimate partners [5,6].

Penile rehabilitation (PR) pertains to diverse interventions targeting the reinstatement of penile functionality subsequent to prostate cancer treatment. The fundamental objective of PR is to expedite the revival of innate erectile function (EF), diminish the likelihood of ED, and heighten sexual function and gratification [7]. The interventions employed in PR encompass pharmacotherapy, vacuum erection devices (VEDs), phallic injections, intraurethral suppositories, and additional non-pharmacological strategies [8]. Nevertheless, the existing empirical support for the efficacy of these interventions is presently constrained, necessitating further investigation in this domain.

In order to evaluate the efficacy and safety of penile rehabilitation interventions post prostate cancer treatment, a systematic review of randomized controlled trials (RCTs) is considered a reliable approach to provide the trusted evidence. RCTs are widely recognized as the benchmark for assessing the effectiveness of interventions due to their ability to minimize biases and confounding factors while facilitating comparisons between different treatments [9]. Therefore, the primary objective of this systematic review was to gather evidence from RCTs regarding the effectiveness of penile rehabilitation interventions subsequent to prostate cancer treatment in order to provide a comprehensive overview of the existing knowledge on PR post prostate cancer treatment, identify gaps in the literature, and offer valuable insights for clinical practice and future research in this field. By synthesizing the findings of multiple RCTs, the systematic review will enhance our understanding of the effectiveness of diverse PR interventions and enable healthcare providers and patients to make informed decisions regarding the optimal available treatment options for restoring EF after prostate cancer treatment.

Methods

Study design and eligibility criteria

The systematic review was conducted following the updated guidelines of the preferred reporting items for systematic review and meta-analyses (PRISMA) [10] as used in the previous study [11]. The search approach encompassed RCTs that underwent a comprehensive assessment to identify penile rehabilitation after prostate cancer treatment. Online searches were conducted using Google Scholar and PubMed to locate articles published from 2000 to 2022.

The inclusion criteria were RCTs reporting PR techniques after a prostatectomy (radical or nerve-sparing) with symptoms of ED and decreased QoL. The exclusion criteria included literature reviews, editorials, commentaries, case reports, and case series. Only articles written in English included in this study. Only RCTs were included in this review.

Information source and search strategy

A comprehensive assessment to identify PR after prostate cancer treatment. The searches were conducted into two databases (Google Scholar and PubMed) to identify the articles The searches were carried out by utilizing combination keywords “penile rehabilitation”, “erectile dysfunction”, “impotence”, “prostate cancer”, “prostatectomy”, “radiation therapy”, “brachytherapy”, “randomized controlled trial” and “RCT”. Only RCTs were included in this systematic review.

Selection process and data collection process

A reference manager, Zotero (Zotero Corporation, Virginia, US), was used where all studies were imported, and duplicates were removed. The first screening was conducted on titles and abstracts of all references to identify eligible articles. The second screening was conducted on the full texts of potentially eligible studies and decided the eligibility of each study based on the inclusion criteria and the availability of the data. Data extraction included data from main

articles and supplementary materials whenever required. In addition, a list of references was also retrieved to explore additional studies. The extracted data included study characteristics of eligible studies (authors, publication year, location of the study, and study design). The information of the inclusion, purpose of the study, study groups, study outcomes of each study were also collected.

Risk of bias assessment

The assessment of risk of bias for each study was conducted using the Cochrane risk-of-bias (ROB) 2 tool [12], a revised Cochrane risk-of-bias tool for randomized trials. This tool evaluates various aspects of study design and conduct to determine the risk of bias in RCTs including random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, handling of incomplete outcome data, selective reporting, and other potential biases. The assessment was based on the information available in each study.

Results

Study selection results

The comprehensive searches yielded 479 published papers (**Figure 1**). Additional 38 were identified from the references of the papers. After thoroughly examining the titles and abstracts, 126 papers were excluded leaving 186 papers for examining the full-texts. After examining the full-texts, additional studies were excluded for some reasons and 15 RCTs were chosen for a further detailed review of the full texts (**Figure 1**). Additional four studies were excluded and 11 RCTs (7 from PubMed and 4 from Google Scholar) were included in this systematic review (**Figure 1**).

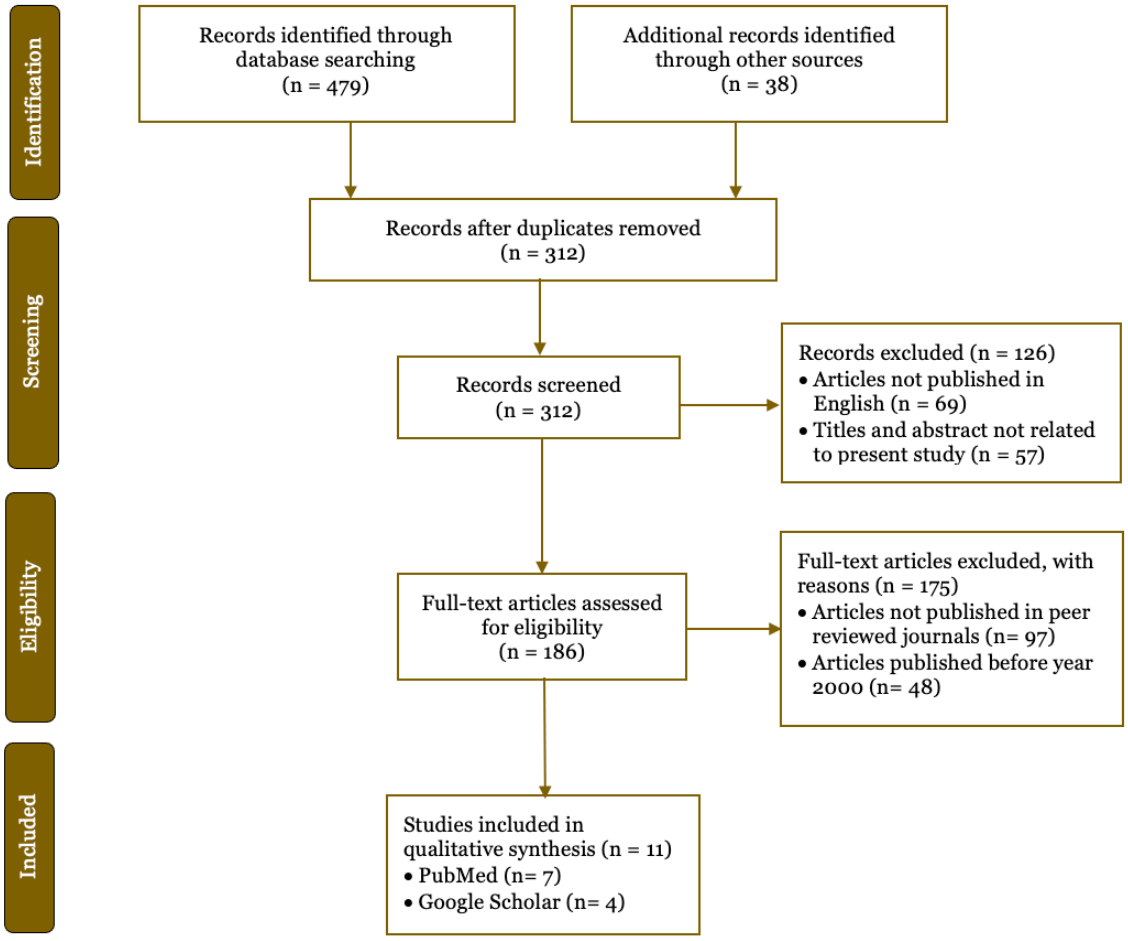

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram of the literature searches.

Effectiveness of different interventions of penile rehabilitation after prostate cancer treatment

The present study focused on comparing different interventions for prostate cancer patients and PR following radical prostatectomy (RP). Characteristics of the included studies and are presented in **Table 1.** Among the included studies, one of each study was published in 2008 [13], 2014 [14] and 2016 [15]; five studies in 2019 [16-20 and one [21] and two studies [22, 23] published in 2021 and 2022, respectively. The detailed interventions and the outcomes of the included studies are presented in **Table 1.**

Risk of bias assessment

The risk of bias assessment helps evaluate the included studies' overall quality and reliability when interpreting their findings. It provides a concise overview of multiple studies and their assessment regarding biases in research methodology. The evaluated biases include random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases.

The summary of the risk of bias assessment for each study using the ROB 2 tool are presented in **Figure 2**. Among the studies examined, Montorsi *et al.* [13], Kim *et al.* [15] and Milios e*t al.* [16] present a low risk of biases in random sequence generation and blinding of participants and personnel. However, it shows a high risk in allocation concealment. The study is considered low risk for blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases.

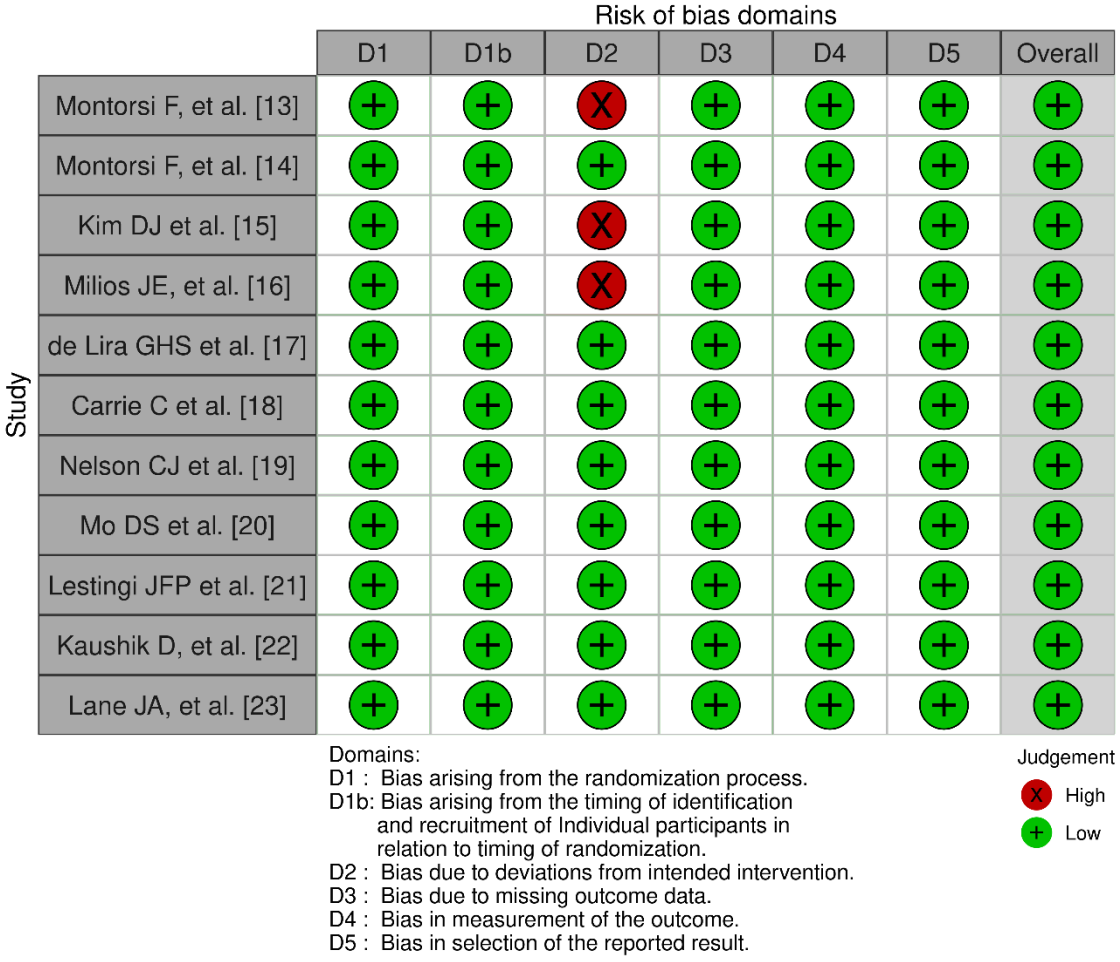

Figure 2. Assessemnt of risk of bias of included study using Cochrane risk-of-bias (ROB) 2 tool.

Table 1. Summary of the effectiveness of different interventions of penile rehabilitation after prostate cancer treatment

First author and year	Inclusion	Purpose of the study	Study groups	Study outcome
Montorsi, *et al.* 2008 [13]	Patients needed to be scheduled for bilateral nerve-sparing radical prostatectomy (NSRP) within a month of the initial assessment and possess a normal erectile function domain score of 26 or greater on the International Index of Erectile Function survey.	Investigate the influence of vardenafil, administered either nightly or upon request following bilateral NSRP surgery, on the restoration of EF in males suffering from ED. The research will assess the outcomes of vardenafil in comparison to a placebo.	A total of 628 males ranging from 18 to 64 years in age were assigned in a randomized manner to undergo the prescribed intervention. The research was carried out over a span of nine months, encompassing a double-blind phase for treatment, followed by a single-blind purging period of two months, and an additional two-month phase with the option for open-label access.	The utilization of vardenafil treatment upon request demonstrated superior enhancements in scores of an International Index of Erectile Function-Erectile Function domain (IIEF-EF) and Sexual Encounter Profile question 3 (SEP3) esponse rates compared to the utilization of a placebo over the entire treatment duration. Vardenafil showcased its efficacy when administered as needed, thus endorsing a change in treatment strategy towards on-demand dosage of Phosphodiesterase 5 inhibitors (PDE5-I) for this specific patient cohort.
Montorsi, *et al.* 2014 [14]	This research comprised male individuals aged 68 or below who were diagnosed with prostate adenocarcinoma presenting a Gleason score of 7 or less. These individuals exhibited regular erectile functionality prior to undergoing NSRP.	The objective of this study is to evaluate the efficacy of tadalafil 5 mg administered once daily and tadalafil 20 mg taken as needed in enhancing spontaneous EF following NSRP, in comparison to a placebo, over a period of nine months. The assessment of improved EF will be determined by analyzing the percentage of patients who attain an IIEF-EF score equal to or greater than 22 following a six-week period without drug usage, known as drug-free washout (DFW).	A RCT encompassing 423 participants was undertaken to investigate the effects of different treatment regimens. The participants were assigned randomly to one of three intervention groups. The initial group received a daily dose of tadalafil at 5mg (n=139), the second group received tadalafil on an as-needed basis at a dosage of 20mg (n=143), while the third group received a placebo (n=141) over a duration of nine months. Subsequently, a DFW of six weeks followed, and all participants then underwent a three-month open-label treatment phase with daily tadalafil.	The research revealed that tadalafil administered on a daily basis demonstrated the highest efficacy in treating ED among men who underwent non-nerve-sparing radical prostatectomy (non-NSRP). The average score for the IIEF-EF improved significantly and surpassed the minimum clinically significant improvement (MCID) of a 4-point increase in both groups receiving tadalafil. Only the group receiving tadalafil once daily exhibited notable enhancement in SEP3, surpassing the MCID of a 23% improvement. The therapeutic effects of tadalafil once daily were significantly superior to the placebo ($p = 0.016$ for IIEF-EF and $p = 0.019$ for SEP3). These findings imply that tadalafil once daily could serve as a valuable treatment option for restoring EF after prostatectomy and potentially preventing structural changes in the penis when administered promptly following surgery.
Kim, *et al.* 2016 [15]	The research enrolled patient diagnosed with localized prostate carcinoma who opted for surgical intervention at the WRNMM Center. Participants with	In spite of previous investigations elucidating the significance of PDE5-I in reinstating EF subsequent to Non-NSRP, a consensus has yet to be	94 individuals who satisfied the screening criteria and granted consent were recruited and subjected to randomization. Amongst them, 47	This prospective, randomized, placebo-controlled clinical trial failed to discover any indication supporting the therapeutic advantage of consuming 50 mg sildenafil

First author and year	Inclusion	Purpose of the study	Study groups	Study outcome
	documented predisposing factors for ED or medical ailments that could potentially invalidate the use of PDE5-I therapy were not considered eligible for inclusion in the study. Additionally, individuals who had previously undergone treatment with PDE5-I medications, potent cytochrome P450 inhibitors, alpha-adrenergic blocking agents (which may interact with sildenafil), or those with a confirmed hypersensitivity to sildenafil or other constituents present in Viagra were also excluded from participation.	reached regarding the optimal pharmaceutical agent, strategy (on-demand versus rehabilitative), or timing of intervention. The primary objective of this study was to assess the impact of nightly administration of sildenafil on the patterns of EF restoration following NSRP, employing both subjective and objective assessments.	individuals were randomly assigned to receive a nightly dosage of 50 mg of sildenafil, whereas the remaining 47 were randomly assigned to receive a placebo. All participants were authorized to utilize 100 mg of sildenafil as needed.	every night and 100 mg sildenafil on-demand, in comparison to solely on-demand dosage. The investigation employed two validated criteria to evaluate EF: objective assessments utilizing Nocturnal Penile Rigidity (RigiScan™) and self-reported assessments employing IIEF-EF. No noteworthy disparities were detected in the restoration of EF between the two sets of treatment.
Milios *et al.* 2019 [16]	All male individuals aged 18 years and older, who received a diagnosis of prostate carcinoma, were recommended for pelvic floor muscule (PFM) exercises and granted consent for either conventional or robotically-assisted interventions, were deemed eligible for enrolment in the research investigation. Participants with pre-existing urinary incontinence, previous prostate surgical interventions, or a medical background of undergoing radiation therapy or androgen deprivation therapy were excluded from the study.	The utilization of PFM training as a rehabilitative modality for post-prostatectomy incontinence (PPI) represents a significant field of investigation, albeit the corpus of evidence is currently in the developmental stage. We have devised an innovative PFM training regimen centered on the stimulation of rapid and slow-twitch muscle fibers to tackle this issue. Our hypothesis posits that commencing this training prior to the surgical procedure would result in enhanced PFM functionality and diminished occurrences of PPI in contrast to the control group.	In this clinical trial, a cohort of 97 patients diagnosed with Gleason 7 prostate cancer, who were scheduled for RP, were randomly allocated to either a control group (n = 47) subjected to a low-volume rehabilitation program or an intervention group (n = 50) that underwent a novel PFM training protocol specifically targeting the activation of both fast and slow twitch muscle fibers. Both groups initiated their respective interventions five weeks prior to the surgical procedure and continued for a duration of 12 weeks post-surgery. The participants' postoperative recovery was evaluated using various metrics, including 24-hour pad weights, the International Prostate Symptom Score (IPSS), the Expanded Prostate Cancer Index Composite for Clinical Practice (EPIC-CP), and Real-time ultrasound (RTUS) measurements of PFM functionality at 2, 6, and 12 weeks following the surgical intervention.	The utilization of a pre-operative regimen for PFM exercises has demonstrated positive effects on the post-operative functionality of the PFMs, reduction in the occurrence of incontinence following prostatectomy, and improvement in QoL outcomes associated with incontinence.
de Lira *et al.* 2019	All individuals within the age range of 45 to 75 years, who have been diagnosed	The primary objective of this investigation was to assess the	Among the pool of 59 eligible males, a random allocation process assigned 31	The preRP procedure, which consisted of two rounds of PFM training aided by a

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[17]	with prostate adenocarcinoma and have a scheduled RP procedure during the designated research period, were considered eligible for participation. However, patients with a prior medical record of pelvic radiotherapy, neurological ailments, laparoscopic RP, transurethral resection of the prostate, urinary incontinence, or inability to execute PFM exercises were excluded from the study.	potential benefits of a PFM training regimen administered during the perioperative period of RP in enhancing the restoration of urinary continence (UC) and EF, in comparison to conventional care. RP has been associated with the adverse effects of urinary incontinence (UI) and ED, thereby compromising the overall QoL .	individuals to two distinct cohorts. The first cohort, labelled group 1 and designated as the control group, consisted of 15 participants who underwent the customary care regimen following RP. The second cohort, referred to as group 2 and identified as the physical therapy group, comprised 16 participants who underwent two pre-RP sessions of PFM training under the guidance of a physical therapist. These sessions encompassed a series of exercises, electromyographic biofeedback, as well as oral and written instructions to continue PFM training until RP. Upon the removal of the urethral catheter, PFM training was reinstated. The assessment of UI and ED was conducted employing the International Consultation on Incontinence Questionnaire - Short Form (ICIQ-SF) and the IIEF-EF questionnaire, respectively.	physical therapist and accompanied by guidelines, did not result in a noteworthy enhancement in UC or EF at the three-month point after the surgery.
Carrie *et al.* 2019 [18]	The GETUG-AFU 16 trial was a phase 3 multicenter clinical study employing randomization and control measures. It enrolled adult males aged 18 years or older, who presented with a performance status of 0 or 1 according to the Eastern Cooperative Oncology Group criteria and were diagnosed with prostate adenocarcinoma through histological examination. Individuals who had undergone prior androgen suppression therapy or pelvic radiotherapy were excluded from participation. The trial encompassed patients with prostate cancer classified as stage pT2, T3, or T4a (limited to involvement of the bladder neck only), and their nodal status was categorized	In the realm of medical science, radiotherapy stands as the prevailing modality employed subsequent to RP. Nevertheless, the formal establishment of the efficacy pertaining to androgen deprivation therapy for this particular ailment remains wanting. Thus, our objective in this subsequent investigation was to present the latest outcomes derived from the GETUG-AFU 16 trial, wherein we assessed the effectiveness of radiotherapy in conjunction with androgen suppression versus radiotherapy in isolation.	In a RCT, a total of 743 subjects were randomly allocated to two treatment arms: radiotherapy monotherapy (n=374) or a combination regimen of radiotherapy and goserelin (n=369).	The 10-year data on progression-free survival from the study corroborated the main findings. Incorporating temporary androgen suppression alongside salvage radiotherapy notably diminished the likelihood of clinical or biochemical progression and mortality in comparison to radiotherapy as a standalone treatment. The outcomes of the GETUG-AFU 16 trial offer additional substantiation that the combination of androgen suppression and radiotherapy serves as an efficacious salvage treatment alternative for individuals experiencing escalating prostate specific antigen (PSA) levels subsequent to undergoing RP for prostate cancer.

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	as pN0 or pNx based on the TNM staging system.			
Nelson *et al.* 2019 [19]	This preliminary investigation constituted a RCT in which individuals were selected for participation by proficient research personnel associated with the Sexual Medicine Program. The primary objective of this study was to enlist a total of 60 subjects during the pilot phase.	This study aims to evaluate the effectiveness of a new psychological treatment approach based on Acceptance and Commitment Therapy-Erectile Dysfunction (ACT-ED) in assisting men with penile injections.	In this RCT, men who had undergone RP and started a structured PR program (Standard Care (SC) were recruited. SC involved penile injections 2-3 times a week. Participants were randomly assigned to either SC+ACT-ED or SC+Enhanced Monitoring (EM). SC+ACT-ED received SC along with four in-person Acceptance and Commitment Therapy (ACT) sessions and three phone calls, while SC+EM received SC and seven phone calls from an experienced sexual medicine nurse practitioner. Assessments were conducted at study entry, four months, and eight months.	In a RCT 53 participants, of whom 61% successfully completed the study, the ACT-ED group demonstrated a higher frequency of penile injections per week (1.7) and displayed superior adherence to PR (44%) in comparison to the EM group, which reported 0.9 injections per week and 10% adherence, respectively, at the four-month mark. These disparities were sustained at the eight-month milestone in terms of weekly injections (ACT=1.2; EM=0.7) and exhibited a slight enhancement in compliance (18% for ACT; 0% for EM). After four months, the ACT-ED group reported moderate effects, including heightened satisfaction with ED treatment, increased sexual self-esteem and confidence, reduced sexual distress, and diminished regret regarding prostate cancer treatment, when compared to the EM group. At the eight-month mark, the ACT-ED group still displayed greater sexual self-esteem and reduced treatment regret compared to the EM group.
Mo *et al.* 2019 [20]	The researcher conducted a comprehensive exploration across multiple databases, such as PubMed, MEDLINE, EMBASE, Cochrane Library, CNKI, VIP, CBM, and Wan fang Database, until June 2018 to identify RCTs pertaining to the treatment of ED using low-intensity extracorporeal shockwave therapy (LI-ESWT). Specific criteria were adhered to in order to screen and assess the literature, followed by the utilization of RevMan 5.3 software to conduct a meta-analysis of the acquired data.	The objective of this study is to evaluate the clinical efficacy and safety of LI-ESWT in the management of ED, utilizing the presently accessible clinical data.	This research encompassed 595 instances of ED derived from 8 double-blind, RCTs, wherein the LI-ESWT group consisted of 362 individuals and the control group comprised 233 cases.	LI-ESWT offers a safe and effective non-invasive treatment option for individuals suffering from ED. This therapeutic modality possesses the ability to significantly improve the IIEF-EF and Erection Hardness Score (EHS) in patients diagnosed with ED.
Lestingi *et al.* 2021	The research recruited individuals diagnosed with prostate carcinoma,	This research examines the oncological results of Extended Pelvic Lymph Node	Between May 2012 and December 2016, a total of 300 subjects were	The RCT demonstrates that EPLND improves pathological staging without

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[21]	meeting the criteria for RP and possessing a life expectancy of no less than a decade. Participants were mandated to exhibit negative lymph node metastases on clinical grounds and express their agreement through the execution of an informed consent document. Those with a medical history comprising substantial abdominal or pelvic surgeries, prior prostate surgeries, antecedent hormonal therapies or radiotherapies, bone metastases, or any other form of malignant neoplasm were deemed ineligible for inclusion in the study.	Dissection (EPLND) in contrast to Limited Pelvic Lymph Node Dissection (LPLND).	arbitrarily allocated to two cohorts: the LPLND cohort (consisting of 150 subjects who received surgical excision of the obturator nodes) and the EPLND cohort (comprising 150 subjects who underwent surgical excision of the obturator, external iliac, internal iliac, common iliac, and presacral nodes) bilaterally.	significantly affecting early oncological outcomes. Subgroup analysis indicates that patients with International Society of Urological Pathology (ISUP) grade groups 3-5 may experience benefits in terms of enhanced Biochemical recurrence-free survival (BCRFS). The study findings indicate that the extensive removal of lymph nodes did not achieve the expected reduction in biochemical recurrence for prostate cancer.
Kaushik *et al*. 2022 [22]	The research encompassed individuals between the ages of 30 and 80 who had received a confirmed recent diagnosis of localized prostate cancer via pathological examination or radiographic imaging and were slated for RP. The participants exhibited no concurrent active malignancies, were non-practitioners of yoga or meditation, possessed satisfactory pain management, and did not have any neurological or musculoskeletal ailments that could potentially hinder physical activity. Moreover, they expressed willingness to undergo randomization and blood sample collection, as well as the ability to provide informed consent. Individuals with an absolute contraindication to exercise or those suffering from psychotic disorders, addiction-related conditions, or significant cognitive impairments were excluded from the study.	This study endeavors to ascertain the efficacy of yoga in enhancing the QoL among individuals afflicted with prostate cancer by scrutinizing the accessible evidence.	A cohort consisting of 29 male individuals who have recently received a diagnosis of localized prostate cancer were randomly allocated into two groups: one receiving a 6-week yoga intervention (n=14), and the other receiving standard-of-care treatment (n=15). These interventions were administered prior to their undergoing RP.	Preoperative and postoperative yoga protocols enhanced the general state of wellness, fortified the immune system, and attenuated inflammation in male patients afflicted with prostate cancer. The incorporation of yoga within the perioperative milieu demonstrates feasibility.
Lane *et al*. 2022 [23]	Between 1999 and 2009, nine urology centers in the United Kingdom invited men aged 50-69 years to undergo PSA	This study aimed to evaluate the functional and QoL outcomes of various localized prostate cancer	Among the 2565 participants, 1135 men underwent active monitoring (AM), 750 underwent radical	Male individuals who remained under AM experienced gradual declines in both sexual and urinary function as they aged. In

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	testing at primary care practices.	treatments to guide treatment decision-making.	prostatectomy (RP), 603 received external-beam radiotherapy (EBRT) in combination with androgen-deprivation therapy (ADT), and 77 underwent low-dose-rate brachytherapy.	contrast, RP had immediate and sustained consequences on erectile dysfunction, which persisted in 85% of men after six years. Similarly, after EBRT, 69-74% of men reported experiencing ED, which was significantly higher compared to those in the AM group (P < 0.001). Following RP, 36% of men reported urinary leakage that necessitated the use of at least one pad per day, and this condition persisted in 20% of men after six years. However, there were no changes observed in men receiving EBRT or AM (P < 0.001). EBRT was associated with more severe bowel dysfunction and distress, such as bloody stools and fecal incontinence, in comparison to RP or AM (P < 0.001), with lesser effects observed after brachytherapy. Nonetheless, none of the treatments had an impact on the mental or physical QoL.

ACT-ED: acceptance and commitment therapy- erectile dysfunction; ADT: androgen deprivation therapy; AM: active monitoring; BCRFS: biochemical recurrence free survival; DFW: drug free washout; EBRT: external beam radiotherapy; ED: erectile dysfunction; EF: erectile function; EHS: erection hardness score; EM: enhanced monitoring; EPIC-CP: expanded prostate cancer index composite for clinical practice; EPLND: extended pelvic lymph node dissection; ICIQ-SF: international consultation on incontinence questionnaire- short form; IIEF-EF: international index of erectile function- erectile function; IPSS: international prostate symptom score; ISUP: international society of urological pathology; LI-ESWT: low intensity extracorporeal shockwave therapy; LPLND: limited pelvic lymph node dissection; MCID: minimum clinically significant improvement; Non-NSRP: non nerve sparing radical prostatectomy; NSRP: nerve sparing radical prostatectomy; PDE5-I: phosphodiesterase 5 inhibitors; PFM: pelvic floor muscle; PFM training: pelvic floor muscle training; PPI: post prostatectomy incontinence; PSA: prostate specific antigen; QoL: quality of life; RCT: randomized controlled trials; RP: radical prostatectomy; RTUS: real time ultrasound; SC: standard care; SEP3: sexual encounter profile question 3; UC: urinary continence; UI: urinary incontinence; VEDs: vaccum erection devices; WRNMM: walter reed national military medical centre.

Discussion

The restoration of penile function following treatment for prostate cancer has emerged as a crucial concern among urologists, given that procedures such as RP, radiation therapy, and hormone therapy can result in ED and negatively impact the patient's overall QoL. The main objective of PR is to minimize the detrimental effects of treatment on the ability to achieve erections and increase the chances of recovering EF to pre-treatment levels. Several approaches for PR have been proposed, including PDE5-I's, VEDs, intracavernosal injections (ICI), and penile prostheses [24].

PR endeavors to avert or mitigate the development of ED following prostate cancer treatment, aiming to enhance blood circulation to the penis and preserve the vitality of the erectile tissues. Several approaches to PR are available, including pharmacological therapies, VEDs, and penile injections [25–27].

Martins and Padma-Nathan [28] uncovered that among the 69 individuals who did not respond to ICI, 49% (34/69) exhibited veno-occlusive disease (VOD) either alone or in conjunction with arterial disease, which was the specific abnormality in blood flow that caused the lack of response to ICI. Furthermore, pure arterial insufficiency was detected in 16 out of 69 (23%) patients. Huang and Hsieh [28] conducted a study examining the vascular abnormalities observed in non-responders to sildenafil. They determined that 16 out of 38 (45%) individuals had VOD, a combination of VOD and arteriogenic condition in three cases (8%), purely arterial condition in nine cases (24%), and normal vascular parameters in nine cases (24%). The studies concluded that veno-occlusive ED was the most prevalent type among non-responders to sildenafil and was associated with inadequate penile rigidity.

For penile rehabilitation following NSRP, the utilization of intraurethral alprostadil and ICI therapy may be beneficial. Current data suggests that consistent use of these treatments can have a positive impact on EF. However, the available evidence is still insufficient to provide definitive recommendations. One trial has suggested that penile vibratory stimulation could be a potentially effective method for preserving and restoring EF after Non-NSRP, but further evidence is required to verify its efficacy [29].

Although some evidence suggests that immunophilin ligands, particularly tacrolimus, may exert a neuroprotective impact, RCTs have yet to validate this hypothesis [30]. Moreover, the efficacy of shockwave treatment for ED following prostate removal remains a topic of debate. Although certain investigations have suggested improved outcomes with the utilization of liESWT in conjunction with tadalafil, the results have not achieved statistical significance [31]. Furthermore, hyperbaric oxygen therapy has not exhibited a significant amelioration in EF post-prostatectomy [32]. This research is constrained by the limited availability of literature specifically focusing on RCTs, resulting in the inclusion of only 11 out of 517 records. Additionally, the studies exhibit considerable heterogeneity, further complicating the formulation of precise recommendations.

Conclusion

Management of prostate cancer can exert a profound and adverse influence on EF, resulting in substantial emotional and psychological ramifications for patients and their partners. PR signifies a promising therapeutic approach to prevent or reverse erectile dysfunction in men undergoing treatment for prostate cancer. PDE5-I, VEDs, and penile injections have displayed encouraging outcomes in fostering EF subsequent to prostate cancer treatment. Nevertheless, the most optimal PR tactic remains uncertain, necessitating additional high-caliber RCTs to evaluate the enduring effectiveness and safety of these interventions. With the ongoing progress in medical research and technology, there is a hopeful anticipation that more efficacious and personalized PR strategies will be devised to aid men in reclaiming their EF and augmenting their overall QoL following prostate cancer treatment.

Ethics approval

Not required.

Acknowledgments

None.

Competing of interest

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available in the article.

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