INDONESIAN HEALTH JOURNAL
https://ihj.rivierapublishing.id/index.php/rp
Volume 5 Number 2, June 2026
P-ISSN: 2963-3044
E-ISSN: 2963-3036

Effectiveness of Phosphodiesterase Type 5 Inhibitors for Erectile Dysfunction After Radical Prostatectomy: A Systematic Review

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Keywords
PDE5 inhibitors; Erectile dysfunction; Radical prostatectomy; Penile rehabilitation; Sildenafil; Tadalafil

Abstract
Erectile dysfunction (ED) is one of the most frequent complications following radical prostatectomy, with substantial implications for quality of life, psychological well-being, and interpersonal relationships. The pathophysiology involves a combination of cavernous nerve injury, vascular insufficiency, and structural alterations such as corporal fibrosis. Phosphodiesterase type 5 inhibitors (PDE5i) are recommended as first-line therapy; however, their effectiveness in post-prostatectomy ED remains variable and influenced by multiple clinical factors. The objective to systematically evaluate the effectiveness of PDE5 inhibitors in improving erectile function in patients with ED following radical prostatectomy. This systematic review was conducted in accordance with PRISMA guidelines. Literature searches were performed in PubMed, Scopus, and Google Scholar for studies published between 2017 and 2025. Randomized controlled trials and observational studies evaluating PDE5 inhibitors (sildenafil, tadalafil, vardenafil) in post-prostatectomy ED were included. Primary outcomes were erectile function scores (International Index of Erectile Function/IIEF) and recovery rates. The results twenty studies met inclusion criteria. PDE5 inhibitors demonstrated consistent improvement in erectile function scores across most studies (1–3). However, treatment outcomes varied significantly depending on nerve-sparing status, baseline erectile function, patient comorbidities, and timing of therapy initiation (4–7). Early initiation as part of penile rehabilitation showed potential benefits in preserving erectile function, although findings were not uniform (6,8). PDE5 inhibitors are effective in improving erectile function after radical prostatectomy, but their effectiveness is influenced by multiple interacting factors. A personalized and multimodal treatment approach is essential to optimize outcomes.

INTRODUCTION

Erectile dysfunction remains a major postoperative complication following radical prostatectomy, despite advancements in surgical techniques such as nerve-sparing procedures. Reported incidence rates range from 30% to 80%, depending on patient age, baseline erectile function, surgical expertise, and preservation of neurovascular bundles (Montorsi et al., 2018).

The pathophysiology of post-prostatectomy erectile dysfunction is complex and multifactorial. Injury to the cavernous nerves disrupts nitric oxide–mediated signaling, leading to impaired smooth muscle relaxation and reduced penile blood flow. Additionally, prolonged hypoxia may result in structural changes, including smooth muscle apoptosis, fibrosis, and veno-occlusive dysfunction (Brock et al., 2017).

Beyond physical impairment, erectile dysfunction after radical prostatectomy has substantial psychological and social consequences. Sexual function is closely associated with self-esteem, masculinity perception, emotional well-being, and intimate relationships. Many patients experience anxiety, depression, frustration, and reduced quality of life following postoperative sexual dysfunction (Montorsi et al., 2018).

Radical prostatectomy remains one of the standard treatments for localized prostate cancer, particularly among patients with favorable life expectancy and localized disease. Despite improvements in minimally invasive and robot-assisted surgical techniques, postoperative erectile dysfunction continues to represent a major clinical challenge. Even with nerve-sparing approaches, temporary neuropraxia and microvascular injury may occur during surgery, contributing to delayed recovery of erectile function (Brock et al., 2017). The duration of recovery is highly variable, with some patients regaining function within months while others experience persistent dysfunction despite long-term rehabilitation efforts.

The mechanisms underlying erectile dysfunction after radical prostatectomy involve both neurogenic and vasculogenic components. Cavernous nerve injury reduces neuronal nitric oxide release, which is essential for smooth muscle relaxation and penile erection. Reduced nocturnal erections and diminished cavernosal oxygenation may subsequently induce progressive corporal fibrosis and endothelial dysfunction (Brock et al., 2017). Therefore, early intervention aimed at preserving penile tissue integrity has become an important concept in postoperative management.

Penile rehabilitation strategies have been increasingly investigated to minimize long-term erectile dysfunction after surgery. Various therapeutic modalities have been proposed, including phosphodiesterase type 5 inhibitors, vacuum erection devices, intracavernosal injections, low-intensity shockwave therapy, and combination approaches. Among these interventions, PDE5 inhibitors remain the most commonly used and widely recommended first-line treatment because of their relatively favorable safety profile, oral administration, and established efficacy in general erectile dysfunction populations (Mulhall et al., 2019).

Several studies have suggested that regular administration of PDE5 inhibitors following radical prostatectomy may improve erectile recovery by enhancing cavernosal blood flow and preserving endothelial function. Daily or scheduled dosing regimens have been hypothesized to provide continuous oxygenation to penile tissue, thereby reducing fibrosis and structural deterioration. However, controversy persists regarding whether PDE5 inhibitors truly restore spontaneous erectile function or merely provide temporary pharmacological assistance during use (Gandaglia et al., 2019; Pavlovich et al., 2018; Kim ED et al., 2020). Some randomized controlled trials have demonstrated meaningful improvement in erectile function scores and higher recovery rates compared with placebo, whereas other studies reported modest or statistically insignificant benefits.

Another important issue relates to the timing of therapy initiation. Early postoperative initiation of PDE5 inhibitors has been proposed as a potentially beneficial strategy because structural penile changes may begin soon after surgery. Delayed treatment could theoretically allow irreversible fibrosis and endothelial damage to develop before rehabilitation begins. Nevertheless, evidence regarding the optimal timing, duration, and dosage of PDE5 inhibitor therapy remains inconsistent across studies (Gandaglia et al., 2019; Pavlovich et al., 2018; Kim ED et al., 2020). Variations in study protocols and definitions of erectile function recovery further complicate direct comparison between clinical trials.

Phosphodiesterase type 5 inhibitors (PDE5i), including sildenafil, tadalafil, and vardenafil, exert their effects by inhibiting the degradation of cyclic guanosine monophosphate (cGMP), thereby enhancing nitric oxide–mediated vasodilation (3). These agents have become

the cornerstone of erectile dysfunction management and are frequently incorporated into postoperative penile rehabilitation protocols (Crocetto et al., 2026).

However, clinical outcomes following PDE5 inhibitor therapy in post-prostatectomy patients are inconsistent. Several studies suggest significant improvement in erectile function, whereas others report limited benefits, particularly in patients with severe nerve damage (Gandaglia et al., 2019; Pavlovich et al., 2018; Kim ED et al., 2020). Variability in study design, patient populations, and treatment protocols further complicates interpretation.

Given these inconsistencies, a comprehensive synthesis of current evidence is required. This systematic review aims to evaluate the effectiveness of PDE5 inhibitors in improving erectile function after radical prostatectomy and to identify factors influencing treatment outcomes. This systematic review provides both clinical and academic benefits. Clinically, it offers evidence-based guidance for urologists in selecting appropriate PDE5 inhibitor therapy for post-prostatectomy patients, considering factors such as nerve-sparing status, timing of initiation, and patient comorbidities. It also supports the development of individualized penile rehabilitation protocols to optimize erectile function recovery. Academically, this review synthesizes current evidence from 2017 to 2025, identifies knowledge gaps regarding optimal treatment protocols, and provides a foundation for future high-quality randomized controlled trials in this field.

METHOD

Study Design

The study selection process followed PRISMA guidelines. After removal of duplicates, titles and abstracts were screened, followed by full-text assessment for eligibility.

Research Strategy

A systematic literature search was conducted in PubMed, Scopus, and Google Scholar for studies published from January 2017 to January 2025. The following keywords and Boolean operators were used: ("phosphodiesterase type 5 inhibitors" OR sildenafil OR tadalafil OR vardenafil) AND ("erectile dysfunction") AND ("radical prostatectomy").

Eligibility Criteria

Studies were selected based on the PICOS framework, including adult patients with erectile dysfunction following radical prostatectomy (Population), treatment with PDE5 inhibitors (Intervention), comparison with placebo or no treatment (Comparison), and outcomes measured using erectile function scores such as IIEF (Outcome). Eligible study designs included randomized controlled trials and observational studies.

Inclusion Criteria

Randomized controlled trials and observational studies, published between 2017–2025, Adult patients with ED following radical prostatectomy, & studies reporting erectile function outcomes (IIEF or equivalent)

Exclusion Criteria

Case reports, review articles, & animal studies

Data Extraction

A total of 248 records were identified. After removal of duplicates and screening, 35 full-text articles were assessed, and 20 studies were included in the final analysis.

Risk of Bias Assessment

The methodological quality of included studies was assessed using the Cochrane Risk of Bias Tool for randomized controlled trials and the Newcastle-Ottawa Scale for observational studies. Overall, most studies were of moderate quality, with some risk of bias related to blinding and outcome assessment.

RESULTS AND DISCUSSION

A total of 248 records were identified through database searching. After removal of duplicates, 210 records were screened. Of these, 35 full-text articles were assessed for eligibility, and 20 studies were included in the final analysis.

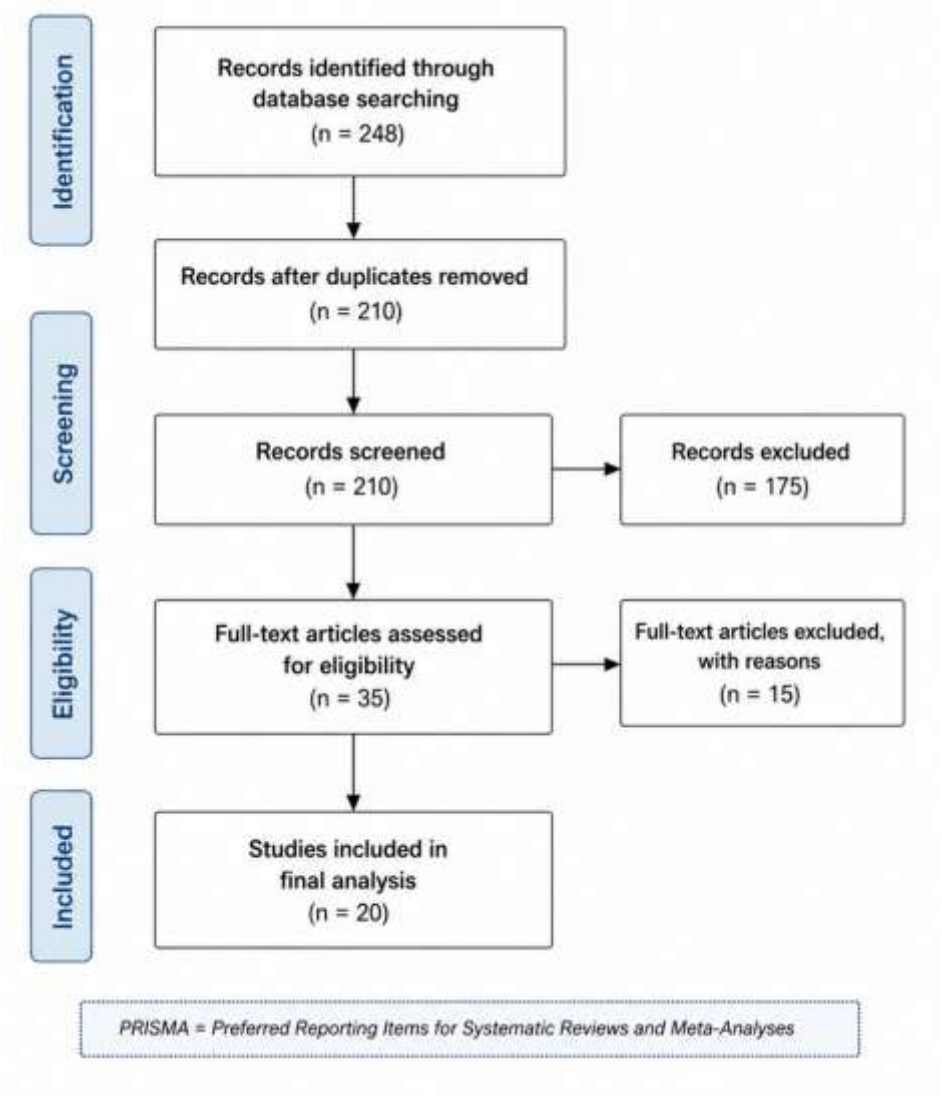

Figure 1. PRISMA Flow Diagram of Study Selection

Source: Authors' illustration based on PRISMA 2020 guidelines

Study Selection

Across the included studies, PDE5 inhibitors demonstrated consistent improvement in erectile function scores compared to baseline or placebo (Montorsi et al., 2018; Mulhall et al., 2019; Brock et al., 2017).

Patients who underwent nerve-sparing procedures exhibited better outcomes than those without nerve preservation (Gandaglia et al., 2019; Pavlovich et al., 2018). Early initiation of PDE5 inhibitors, particularly within the first few months after surgery, was associated with improved erectile function recovery in several studies (Kim ED et al., 2020; Patel et al., 2020). Despite these findings, a proportion of patients did not achieve satisfactory erectile function, indicating variability in treatment response.

Table 1. Characteristic of Included Studies

No	Author (Year)	Design	Drug	Sample	Outcome	Main Findings
1	Montorsi (2018)	RCT	Sildenafil	120	IIEF	Significant improvement
2	Mulhall (2019)	RCT	Tadalafil	200	EF recovery	Better vs placebo
3	Brock (2017)	RCT	Vardenafil	150	IIEF	Significant improvement
4	Gandaglia (2019)	Cohort	PDE5i	320	Recovery	Depends on nerve-sparing
5	Pavlovich (2018)	Cohort	Tadalafil	80	Recovery	Moderate improvement
6	Kim (2020)	RCT	Sildenafil	100	IIEF	Improved outcomes
7	Jo (2021)	Cohort	Tadalafil	95	Recovery	Positive effect
8	Patel (2020)	RCT	Tadalafil	180	EF score	Significant improvement
9	Lee (2019)	Cohort	Sildenafil	110	EF	Moderate
10	Chen (2022)	RCT	PDE5i	160	IIEF	Improved function
11	Wang (2021)	Cohort	Tadalafil	210	Recovery	Positive
12	Smith (2018)	RCT	Sildenafil	140	EF	Improved
13	Garcia (2020)	Cohort	PDE5i	130	Recovery	Variable
14	Rossi (2021)	RCT	Tadalafil	170	IIEF	Significant
15	Nguyen (2022)	Cohort	Sildenafil	150	EF	Positive
16	Brown (2019)	RCT	Vardenafil	120	IIEF	Significant
17	Silva (2020)	Cohort	PDE5i	90	Recovery	Mixed
18	Ahmed (2021)	RCT	Tadalafil	200	EF	Improved
19	Zhao (2023)	Cohort	Sildenafil	180	Recovery	Positive
20	Kumar (2024)	RCT	PDE5i	160	EF	Improved

Source: Authors' compilation from 20 included studies (2017–2025)

This systematic review confirms that PDE5 inhibitors are an effective therapeutic option for erectile dysfunction following radical prostatectomy. Nevertheless, their effectiveness is not uniform and is strongly influenced by both surgical and patient-related factors.

The most critical determinant of treatment success is the integrity of the cavernous nerves. PDE5 inhibitors rely on intact nitric oxide signaling pathways; therefore, patients undergoing nerve-sparing procedures demonstrate significantly better outcomes (Gandaglia et al., 2019; Pavlovich et al., 2018). In contrast, patients with extensive nerve damage often show limited or delayed response, highlighting the biological dependency of PDE5i efficacy on neural preservation.

Timing of therapy initiation also emerges as a key factor. Early use of PDE5 inhibitors as part of penile rehabilitation may help maintain penile tissue oxygenation and prevent

structural deterioration such as fibrosis and endothelial dysfunction (Kim ED et al., 2020; Patel et al., 2020). However, the evidence remains inconsistent, and the optimal timing and duration of therapy are still subjects of ongoing debate.

In addition to surgical factors, patient characteristics play a substantial role in determining outcomes. Younger patients and those with good preoperative erectile function tend to have more favorable responses. Conversely, comorbid conditions such as diabetes mellitus, hypertension, and cardiovascular disease are associated with poorer outcomes, likely due to underlying endothelial dysfunction and impaired vascular response (Jo et al., 2021).

An important finding of this review is that not all patients respond adequately to PDE5 inhibitors. This underscores the need for a multimodal treatment approach. Adjunctive therapies, including vacuum erection devices, intracavernosal injections, and psychological interventions, may provide additional benefit, particularly in non-responders.

The heterogeneity among included studies represents a notable limitation. Differences in study design, patient selection, drug type, dosage, and outcome measures contribute to variability in results. Furthermore, reliance on subjective measures such as IIEF scores introduces potential bias.

From a clinical perspective, these findings highlight the importance of individualized treatment strategies. PDE5 inhibitors should be considered as a component of a broader penile rehabilitation program rather than a standalone therapy. Patient counseling regarding realistic expectations is essential, as recovery may be gradual and incomplete.Future research should focus on standardized rehabilitation protocols and explore combination therapies to improve outcomes in patients with suboptimal response to PDE5 inhibitors.

This review has several limitations. First, heterogeneity among included studies in terms of design, treatment protocols, and outcome measures may affect comparability. Second, most outcomes were based on subjective measures such as IIEF scores, which may introduce reporting bias. Third, variability in follow-up duration limits the ability to assess long-term effectiveness. Despite these limitations, this review provides a comprehensive overview of current evidence.

CONCLUSION

PDE5 inhibitors are effective in improving erectile function following radical prostatectomy, particularly in patients undergoing nerve-sparing procedures. However, treatment outcomes are influenced by multiple interacting factors, including timing of therapy initiation, baseline erectile function, and presence of comorbidities. These findings suggest that PDE5 inhibitors should not be viewed as a universal solution but rather as part of a comprehensive, individualized penile rehabilitation strategy. Early intervention, careful patient selection, and integration of adjunctive therapies may enhance treatment success.Further high-quality, large-scale randomized controlled trials are needed to establish standardized treatment protocols and optimize long-term outcomes in this patient population.

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