DOI: 10.4081/aiua.2025.13639

ORIGINAL PAPER

Recovery of functional outcomes after robot assisted radical prostatectomy (RaRP): Impact of vacuum therapy compared to PDE5 inhibitors alone

Pier Paolo Prontera [1], Francesca Romana Prusciano [2, 1], Marco Lattarulo [1], Arman Tsaturyan [3, 4], Carmine Sciorio [5], Francesco Saverio Grossi [1]

[1] Department of Urology, "S.S. Annunziata" Hospital, Taranto, Italy;
[2] Division of Urology, Hospital "Valle D'Itria", Martina Franca (TA), Italy;
[3] Department of Urology, Yerevan State Medical University after Mkhitar, Heratsi, Yerevan, Armenia;
[4] Department of Urology Erebouni Medical Center, Yerevan, Armenia;
[5] Department of Urology, "Alessandro Manzoni" Hospital of Lecco, Italy.

Summary

***Objective:** This study evaluated the primary efficacy of vacuum therapy combined with phosphodiesterase type 5 inhibitors (PDE5i) versus PDE5i alone in improving erectile function recovery, assessed via the International Index of Erectile Function (IIEF) questionnaire, after robotic-assisted radical prostatectomy (RARP). A secondary objective was to assess the impact of the combined therapy on continence outcomes, including pad usage and continence scores. The study also explored predictors of rehabilitation success and the potential synergistic effects of the combined approach.*

***Materials and methods:** A retrospective analysis of 101 patients who underwent RARP (2021-2023) was conducted. Patients were divided into Group 1 (PDE5i only, n = 70) and Group 2 (PDE5i + vacuum therapy, n = 31). Vacuum therapy was started within 20 days postoperatively and performed daily under specialist supervision. All data were completely anonymous. Primary outcomes included IIEF-5 scores for erectile function and continence recovery (pad usage, continence scores based on three levels: 0 - complete incontinence, 1 - stress incontinence and 2 - full continence). Predictive factors were analysed using repeated measures ANOVA and multivariate regression.*

***Results:** Group 2 showed significantly higher mean IIEF-5 scores at 12 months (10.2 vs. 2.5, p < 0.001) and earlier continence recovery, with better scores at 3 and 6 months (p < 0.05). Vacuum therapy and PDE5i accelerate continence recovery during the early postoperative period, with fewer pads required, compared with patients treated with PDE5i alone, at 6 months (1.32 vs. 1.62; p = 0.358) and 9 months (0.54 vs. 1.08; p = 0.034). Key predictors of recovery included age, BMI, nerve-sparing status, and preoperative continence levels.*

***Conclusions:** This study demonstrates the benefits of combining vacuum therapy with PDE5i for improving erectile function and early continence recovery after RARP, highlighting the importance of early, individualized rehabilitation. Vacuum therapy enhances oxygenation, reduces fibrosis and complements PDE5i effects. Further research is needed to refine predictive factors for success and explore the impact of intraoperative blood loss on erectile recovery, enabling optimized, tailored strategies for post-RARP rehabilitation.*

***KEY WORDS:** Prostate cancer; Urinary continence; Erectile dysfunction; IIEF; Robot-Assisted Radical Prostatectomy; Functional outcomes.*

Submitted 16 January 2025; Accepted 30 March 2025

INTRODUCTION

Robotic-assisted radical prostatectomy (RARP) has emerged as a gold standard for the surgical management of localized prostate cancer, offering superior oncological outcomes and reduced perioperative morbidity compared to traditional open surgery, confirming the advantages of minimally invasive techniques compared to traditional surgery, as in the case of laparoscopic radical prostatectomy (1). However, the procedure often results in significant postoperative complications, including *erectile dysfunction* (ED) and urinary incontinence, which can profoundly impact patients' quality of life (2). The pathophysiological mechanisms underlying these complications include cavernosal hypoxia, structural changes in penile tissue, and neurovascular injury (3, 4). Early penile rehabilitation protocols employing vacuum devices have been shown to counteract these effects by improving cavernosal oxygenation and reducing fibrosis (4, 5). Studies also suggest that vacuum therapy can preserve penile length and stimulate tissue remodeling, mitigating the adverse effects of extended hypoxia (5, 6).

Erectile dysfunction, a common consequence of RARP, stems from intraoperative injury to the neurovascular bundles, cavernosal hypoxia, and fibrosis.

Histopathological studies reveal that post-RARP penile tissue undergoes significant degenerative changes, including fibrosis and smooth muscle atrophy, primarily due to reduced oxygenation and extended denervation. This fibrosis is marked by an upregulation of pro-fibrotic cytokines, such as transforming growth factor-beta (TGF-β), which leads to an irreversible loss of elasticity and compliance in the cavernosal tissue (7). As *Djavan et al.* (2011) highlighted, these pathological changes compromise the structural integrity of penile tissue, necessitating early and effective intervention (8).

The pathogenesis of post-operative ED involves a multifaceted interplay of neurogenic, vascular, and psychological factors. Neurovascular bundle injury, even in nerve-sparing surgeries, can lead to axonal degeneration, impairing the signalling required for erectile function. Additionally, reduced endothelial *nitric oxide* (NO) production exacerbates cavernosal vasoconstriction and hypoxia, further fuelling the cycle of fibrosis (9).

The effectiveness of *phosphodiesterase type 5 inhibitors* (PDE5i) lies in their ability to enhance and restore normal erectile physiology by targeting the NO-*cyclic guanosine monophosphate* (cGMP) pathway. During sexual stimulation, nitric oxide is released from endothelial cells and non-adrenergic, non-cholinergic neurons, activating guanylate cyclase in the smooth muscle cells of the corpus cavernosum. This leads to increased cGMP levels, resulting in smooth muscle relaxation and subsequent cavernosal blood engorgement. PDE5i, such as tadalafil or sildenafil, inhibit the breakdown of cGMP by phosphodiesterase type 5, prolonging its vasodilatory effects and improving erectile function (7, 8).

Furthermore, the synergistic use of PDE5i and vacuum therapy has demonstrated promising outcomes in enhancing erectile recovery. The combined approach optimizes penile hemodynamics and structural integrity, facilitating a faster return to spontaneous erections compared to monotherapy (4-6). The role of patient-specific factors, including baseline erectile function and metabolic health, highlights the need for individualized rehabilitation strategies (4, 5).

Vacuum therapy complements the action of PDE5i by directly addressing cavernosal hypoxia and structural changes. By creating negative pressure around the penis, vacuum devices induce blood flow into the corpus cavernosum, counteracting ischemia and promoting oxygenation. Enhanced cavernosal oxygenation mitigates the risk of fibrosis and preserves smooth muscle integrity. Additionally, repeated mechanical stretching through vacuum use stimulates angiogenesis and tissue remodeling, which are critical for long-term recovery of erectile function.The role of vacuum in reducing oxidative stress and enhancing endothelial repair was elucidated, further supporting its application in post-RARP rehabilitation (9, 10).

RARP nerve-sparing techniques aim to preserve the integrity of the neurovascular bundles, mitigating the severity of ED. These techniques can be classified into full, partial, or minimal nerve-sparing approaches, each varying in the degree of tissue preservation. *Patel et al.* (2015) demonstrated that bilateral full nerve-sparing RARP significantly improves postoperative erectile function outcomes compared to unilateral or non-nerve-sparing procedures. However, the success of nerve-sparing also depends on preoperative factors, including patient age, baseline erectile function, and tumor location (7).

Urinary incontinence, another debilitating consequence of RARP, arises primarily from sphincteric dysfunction and pelvic floor weakness. The intricate balance between the internal and external urinary sphincters is disrupted during prostatectomy, leading to stress incontinence. Additionally, detrusor overactivity due to denervation may further exacerbate urinary symptoms. Studies, including those by *Preisser et al.* in 2019, have emphasized the role of meticulous surgical technique and early pelvic floor muscle rehabilitation in facilitating continence recovery (11). The role of vacuum therapy in this context remains underexplored but holds potential due to its capacity to enhance pelvic floor vascularization and support tissue regeneration (10).

The combined use of PDE5i and vacuum device has shown promising results in enhancing erectile function recovery. In 2018, *Salciccia et al.* demonstrated that patients undergoing integrated rehabilitation protocols experienced a significant improvement in *International Index of Erectile Function-5* (IIEF-5) scores, with outcomes superior to those achieved with PDE5 inhibitors alone (2). Similarly, Preisser et al. emphasized the role of multimodal approaches, particularly the synergistic effects of pharmacological and mechanical interventions, in accelerating functional recovery post-RARP (11).

While erectile function recovery has been the primary focus of most studies, urinary incontinence remains another prevalent and debilitating postoperative challenge. Existing evidence suggests that factors influencing continence recovery are multifactorial, involving age, surgical technique, and baseline pelvic floor function. PDE5 inhibitors are not directly related to continence outcomes, vacuum therapy may offer indirect benefits. *Du et al.* highlighted the potential of vacuum in promoting pelvic floor vascularization, which could facilitate faster continence recovery (10). However, systematic reviews, such as those conducted by *Califano et al.* (2021), have noted limited data directly addressing vacuum's role in continence improvement, pointing to a critical gap in literature (12).

Furthermore, systematic reviews and trials have consistently highlighted the multifactorial nature of recovery following RARP. A review by Preisser et al. highlighted the importance of tailoring rehabilitation strategies based on individual patient profiles, including age, preoperative IIEF scores, and surgical complexity (11). Trials such as Protect-T have also emphasized the need for early intervention and consistent adherence to rehabilitation protocols to optimize outcomes (13).

This study aims to evaluate the comparative efficacy of PDE5 inhibitors alone *versus* PDE5 inhibitors combined with vacuum therapy in the context of andrological rehabilitation post-RARP. Specifically, it focuses on primary endpoints, such as improvement in erectile function (assessed through IIEF-5 scores), and secondary endpoints, including the impact of vacuum on continence recovery. By leveraging statistical analyses and insights from the literature, this work seeks to contribute to the optimization of rehabilitation strategies following radical prostatectomy. Moreover, it addresses critical gaps identified in previous research, providing a comprehensive assessment of the benefits and limitations of combined rehabilitation protocols.

Materials and methods

A total of 153 patients who underwent *robotic-assisted radical prostatectomy* (RARP) at our institution between 2021 and 2023 were evaluated. Of these, 101 patients met specific inclusion and exclusion criteria and were enrolled in the study. Eligible patients had localized *prostate cancer* (PCa), were ≤ 75 years old, exhibited good performance status, and were either not suitable candidates for or not motivated toward active surveillance. Patients were excluded if they had a history of deprivation hormonal therapy, prior pelvic surgery or radiotherapy, or histological diagnoses performed at external institutions.

This study employed a retrospective design to evaluate the outcomes of patients who underwent radical prostatecto-

	PDE5i	PDE5i + Vacuum	P value
Age (years)	68 (54-75)	69.7 (63-76)	0.07
Height (mt)	1.73 (1.65-1.88)	1.77 (1.7-1.9)	0.29
Weight (kg)	81.7 (56-105)	71 (60-97)	1.96
Waist circumference (cm)	90.9 (70-110)	86.25 (78-94)	0.0004
BMI	27.2 (19.52-35.3)	23.34 (20.8-29.76)	1.41
Prostate volume (ml)	53.96 (20-142)	45.6 (27-85)	0.08
Pre-operative Total PSA (ng/ml)	9.4 (5.5-31.5)	8.86 (5-13.5)	0.50
Total cholesterol (mg/dl)	180.7 (112-263)	179.6 (101-269)	0.89
HDL (mg/dl)	51.27 (35-104)	48.6 (40-75)	0.24
Triglycerides (mg/dl)	111.34 (56-371)	120.5 (58-169)	0.20
Glycemia (mg/dl)	100.22 (78-172)	100.1 (73-141)	0.88
Pre-operative IIEF5 score	13 (0-25)	15 (2-24)	0.14
Pre-operative IPSS voiding score	6 (0-14)	7 (2-13)	0.12
Pre-operative IPSS storage score	4 (0-12)	4 (0-11)	0.79
Pre-operative QoL score	4 (0-10)	3 (0-8)	0.02
Risk of extracapsular invasion (MRKCC score)	52.5 (11-98)	49.6 (15-90)	0.58

Table 1.
Pre-operative Characteristics of Patients: PDE5i Alone vs. PDE5i Combined with Vacuum: Comparison of preoperative demographic, clinical, and biochemical characteristics between patients treated with PDE5 inhibitors (PDE5i) alone and those treated with PDE5i combined with vacuum therapy.
Data are presented as median (range), and p-values indicate statistical comparisons between the two groups.

my and subsequent andrological rehabilitation using either PDE5 inhibitors (PDE5i) alone or PDE5i combined with vacuum therapy. A total of 101 patients were included, divided into two treatment groups: Group 1 (PDE5i only, n = 70) and Group 2 (PDE5i + vacuum, n = 31). Patients in the vacuum therapy group (Group 2) performed vacuum-gymnastics under specialist guidance, dedicating at least 20 minutes daily to the therapy to ensure proper use of the device and adherence to the protocol. Both rehabilitation therapies were started within 45 days of surgery, with a mean start time of 20 days postoperatively. The primary endpoints were improvements in erectile function, measured through IIEF-5 scores and continence recovery.

Histological diagnosis was obtained via standard transrectal ultrasound-guided *trans-perineal prostate biopsy* (TRUS-SBx) or MRI/ultrasound fusion-guided *trans-perineal biopsy* (TBx+SBx). Fifty patients underwent fusion-guided biopsy, while 51 received a standard biopsy. All procedures were performed by an experienced operator. Fusion biopsy was indicated for patients with clinically significant PIRADS lesions (PIRADS ≥ 3) and included both targeted cores [based on the number and size of *regions of interest* (ROI)] and 12-16 systematic cores from a prostatic template covering the base, mid-gland, and apex bilaterally. When *multiparametric MRI* (mpMRI) was unavailable or no significant PIRADS lesions were identified, a standard 16-core TRUS-guided trans-perineal biopsy was performed according to institutional protocol, systematically sampling the base, mid-gland, apex, and transition zones bilaterally.

Preoperative staging was performed for all patients using contrast-enhanced total-body CT and total-body bone scintigraphy. All patients subsequently underwent RARP using the Da Vinci Xi (Intuitive) multiport robotic system. The procedures were performed by two surgeons, both employing the same standardized surgical technique, which included an anterograde extraperitoneal approach and a double-layer running anastomosis with posterior plate reinforcement using a 2-0 barbed suture. When indicated, a nerve-sparing technique was performed.

Histopathological analysis of surgical specimens was performed by an expert pathologist. Catheter removal was performed on the seventh postoperative day, only after excluding active peri-anastomotic urinary leakage through retrograde and voiding cystourethrography. All patients, after hospital discharge, underwent pelvic floor rehabilitation under the guidance of an experienced physiotherapist. Data collected included demographics (age, height, weight, waistline, BMI), preoperative factors (preoperative total PSA, plasma levels of total cholesterol, HDL, triglycerides, and glucose, preoperative IIEF-5, preoperative IPSS-QoL, risk of extracapsular extension calculated with the *Memorial Sloan Kettering Cancer Center* (MSKCC) nomogram) (Table 1), perioperative metrics (operative time, estimated blood loss, white blood cell changes up to 24 hours after surgery, nerve-sparing rates, pre-operative and post-operative Gleason score, pre-operative and post operative ISUP grade) (Tables 2-4), oncological outcomes (positive surgical margins, postoperative PSA levels at 3, 6, 9, and 12 months), and postoperative functional outcomes. Urinary continence was evaluated at 3, 6, 9, and 12 months using a continence score based on three levels (0 - complete incontinence, 1 - stress incontinence

Table 2.
Intraoperative and Pathological Outcomes: PDE5i vs PDE5i plus Vacuum Groups: Comparison of operative time and pathological outcomes, including positive surgical margins, nerve-sparing rates, and incidences of perineural and vascular invasion, between patients treated with PDE5 inhibitors (PDE5i) alone and those treated with PDE5i combined with vacuum therapy. Data are presented as median (range) or percentages, with p-values indicating statistical significance.

	PDE5i	PDE5i + Vacuum	P value
Operative time (min), mean (range)	205 (130-365)	200 (110-290)	0.62
Positive surgical margins (%)	32.86	3.39	0.0029
Nerve Sparing procedures (%)	35.71	19.35	0.158
Neural invasion (%)	71.43	51.61	0.087
Vascular invasion (%)	10	35.48	0.005

	Pre Operative Gleason (biopsy)		Post Operative Gleason (RaRP)	
Gleason, n°(%)	PDE5i	PDE5i + Vacuum	PDE5i	PDE5i + Vacuum
6 (3+3)	32 (45.71)	14 (45.16)	21 (30)	6 (19.35)
7 (3+4)	18 (25.71)	7 (22.58)	35 (50)	11 (35.48)
7 (4+3)	13 (18.57)	4 (12.9)	10 (14.29)	8 (25.81)
8 (4+4)	6 (8.57)	3 (9.68)	3 (4.29)	3 (9.68)
8 (3+5)		3 (9.68)		
8 (5+3)			1 (1.43)	3 (9.68)
9 (5+4)	1 (1.43)			

Table 3.
Comparison of Preoperative and Postoperative Gleason Scores in PDE5i vs. PDE5i Combined with Vacuum Therapy Groups: Distribution of Gleason scores from preoperative biopsy and postoperative robotic-assisted radical prostatectomy (RaRP) specimens in patients treated with PDE5 inhibitors (PDE5i) alone and those treated with PDE5i combined with vacuum therapy. Data are presented as the number of patients (n) and percentages (%).

	Pre Operative Gleason (biopsy)		Post Operative Gleason (RaRP)	
ISUP grade (%)	PDE5i	PDE5i + Vacuum	PDE5i	PDE5i + Vacuum
1	45.71	45.16	27.14	19.35
2	21.43	22.58	55.71	64.52
3	22.86	19.35	14.29	6.45
4	1.43	12.9	2.86	9.68
	Chi2 Statistic: 3.635 P value: 0.457		Chi2 Statistic: 3.940 P value: 0.268	

Table 4.
Comparison of Preoperative and Postoperative ISUP Grades in both PDE5i vs. PDE5i Combined with Vacuum Therapy Groups: Distribution of International Society of Urological Pathology (ISUP) grades from preoperative biopsy and postoperative robotic-assisted radical prostatectomy (RaRP) specimens in patients treated with PDE5 inhibitors (PDE5i) alone and those treated with PDE5i combined with vacuum therapy. Data are expressed as percentages (%), with Chi-squared statistics and p-values provided for comparisons: no significant differences were found.

	PDE5i	PDE5i + Vacuum	P value
Pre-operative IIEF	13.16 (0-25)	15.1 (0-22)	0.148
Post-operative IIEF 1 month, mean score (range)	1.1 (0-12)	4.4 (0-23)	0.012
Post-operative IIEF 3 months, mean score (range)	2.5 (0-16)	7.4 (0-23)	0.0001
Post-operative IIEF 6 months, mean score (range)	3.3 (0-16)	10.2 (0-25)	0.000
Post-operative IIEF 9 months, mean score (range)	2.5 (0-15)	10.2 (0-25)	0.000
Post-operative IIEF 12 months, mean score (range)	2.5 (0-15)	10.2 (0-25)	0.000

Table 5.
Comparison of IIEF Scores Between 'PDE5i + Vacuum' and 'Solo PDE5i' Groups: This table compares the mean IIEF scores and ranges (min-max) between the two treatment groups at each time point. P-values indicate the statistical significance of differences, with values below 0.05 considered significant.

	PDE5i	PDE5i + Vacuum	P value
PAD used at 1 month, mean number	3.32	3.87	0.410
PAD used at 3 months, mean number	2.67	2.54	0.813
PAD used at 6 months, mean number	1.62	1.32	0.358
PAD used at 9 months, mean number	1.08	0.54	0.034
PAD used at 12 months, mean number	0.55	0.38	0.413

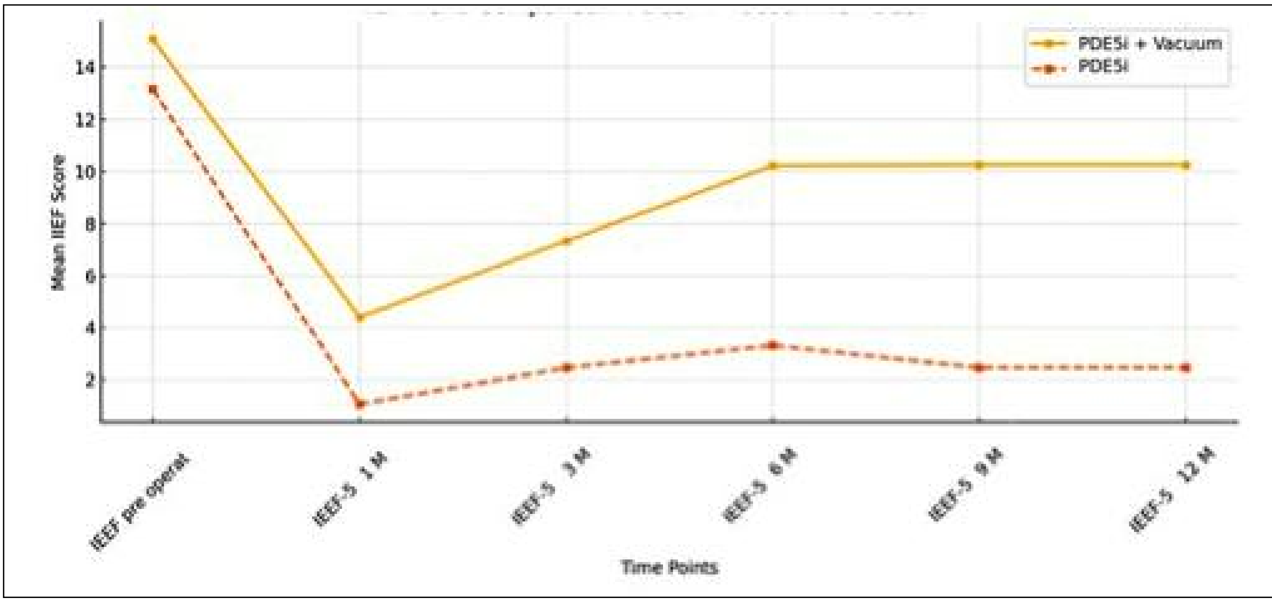
Table 6.
Comparison of Pad Usage Between PDE5i + Vacuum and Solo PDE5i Groups: This table presents the mean number of pads used daily at various time points (1, 3, 6, 9, and 12 months post-operatively) for each treatment group. P-values indicate the statistical significance of group differences.

and 2 - full continence). The variation in the number of daily pads used over the same time period was also calculated. Erectile function was assessed by the IIEF-5 at 3, 6, 9, and 12 months) (Tables 5, 6) (Figures 1, 2).
Statistical analyses were conducted using systematically collected and recorded data. Anthropometric parameters, biopsy types, prostate volumes, clinical stages, comorbidities, pre- and postoperative blood levels (including PSA and hemoglobin), operative times, histopathological findings, oncological and functional outcomes were included. Functional outcomes evaluated total PSA levels, urinary continence, and sexual potency at 1, 3, 6, 9, and 12 months post-procedure.
Comparative analyses included t-tests or Welch's t-tests for continuous variables and Chi-squared or Fisher's exact tests for categorical data. Repeated measures ANOVA and linear regression models were used to analyse trends in IIEF-5 scores and continence recovery at multiple time points. Multivariate analyses utilizing a Random Forest regression model assessed the predictive significance of variables such as age, BMI, PSA levels, and nerve-sparing status. A significance level of $p < 0.05$ was applied.

Results

A total of 101 patients were analysed, divided into Group 1 (PDE5i only, n=70) and Group 2 (PDE5i + vacuum, n = 31). Baseline characteristics, including age, BMI, preoperative IIEF-5 scores, and PSA levels, were comparable between the two groups. The mean age of participants was 68 years (range: 54-76), with a median BMI of 26.7 kg/m² (IQR: 24.5-28.3). Preoperatively, Group 2 exhibited a slightly higher median IIEF-5 score compared to Group 1 (15 *vs.* 13; p = 0.14), but this difference was not

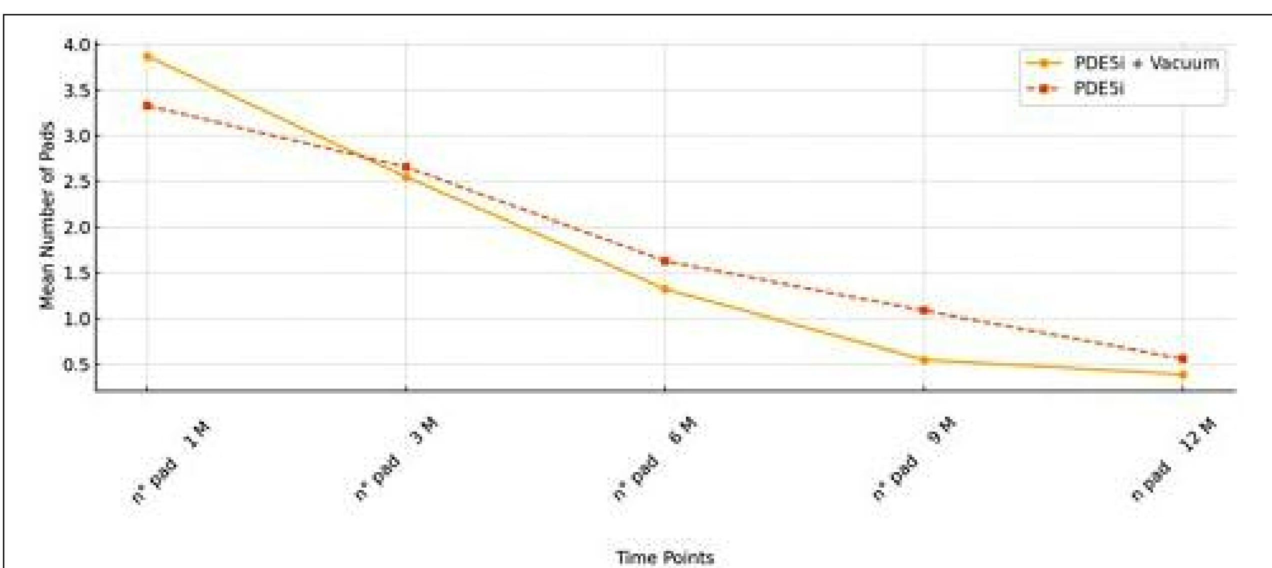
Figure 1.
IIEF Trend Comparison: PDE5i + Vacuum vs. PDE5i. This line graph compares the mean IIEF scores of the 'PDE5i + Vacuum' group and the 'PDE5i' group at six time points. Statistical significance is evident at multiple intervals, highlighting the superiority of combined treatment.



statistically significant. Similarly, no significant differences were observed in PSA levels (9.4 *vs.* 8.86 ng/mL; p = 0.50) or MSKCC-calculated extracapsular extension risk (52.5% *vs.* 49.6%; p = 0.58) (Table 1).
Postoperative erectile function recovery, as measured by IIEF-5 scores, demonstrated a marked improvement in Group 2 across all time points. At 12 months, the mean IIEF-5 score was significantly higher in Group 2 (10.2 vs. 2.5; p < 0.001). Early recovery trends were also more favorable in Group 2, with significant differences at 3 months (4.4 *vs.* 1.1; p = 0.012) and 6 months (10.2 *vs.* 3.3; p < 0.001) (Table 6, Figure 1).

Continence recovery, as assessed by the number of daily pads used and continence scores, showed earlier improvements in Group 2 compared to Group 1. At 3 and 6 months, continence scores were significantly higher in Group 2 (1.58 *vs.* 1.28; p = 0.025 and 1.58 *vs.* 1.21; p = 0.004, respectively). Pad usage trends mirrored these results, with fewer pads required in Group 2 at 6 months (1.32 *vs.* 1.62; p = 0.358) and 9 months (0.54 *vs.* 1.08; p = 0.034). By 12 months, no significant differences were observed between the groups in continence scores (1.14 vs. 1.26; p = 0.239) or pad usage (0.38 *vs.* 0.55; p = 0.413) (Tables 7, Figure 2).

Figure 2.
Pad Usage Over Time in PDE5i + Vacuum and PDE5i Groups. This line graph depicts the mean number of pads used daily by patients in each group across 12 months post-operatively, highlighting differences in recovery trajectories.combined treatment.



Multivariate analysis using Random Forest regression identified several factors influencing postoperative recovery. For erectile function, postoperative hemoglobin levels, age, nerve-sparing status, and BMI were the most significant predictors (Tables 7, 8). On the other hand, preoperative BMI, MSKCC-calculated extracapsular extension risk, and baseline continence scores primarily influenced continence recovery. Pre-operative metabolic markers (e.g., triglycerides, glucose) and hemoglobin levels are strong determinants of continence recovery and pad reduction (Table 9). The combination of pre-operative hemoglobin and post-operative hemoglobin shows a notable negative interaction coefficient (-0.322). This suggests that patients with lower pre-operative hemoglobin but better recovery post-operatively may benefit more in terms of pad usage. The regression models incorporating interaction terms achieved an R^2 of approximately 0.37, indicating that these interactions moderately explain the variance in recovery outcomes. Negative interaction coefficients imply counteracting effects, where the combined influence of two factors on pad usage diminishes their individual impacts. Recovery outcomes like pad usage are influenced not just by individual factors but also by their interplay (e.g., metabolic health and peri-operative recovery (Table 9). Postoperative PSA levels and operative time had limited impact on both outcomes.

Overall, the combination of PDE5 inhibitors with vacuum therapy resulted in significant improvements in erectile function recovery and earlier continence recovery. These benefits were particularly pronounced during the intermediate postoperative period, highlighting the potential of combined therapy to optimize functional outcomes following robotic-assisted radical prostatectomy.

Table 7.
Feature Importance Analysis for IIEF Recovery at 12 Months Using Random Forest: This table presents the relative importance of various pre-operative and peri-operative factors in predicting IIEF recovery at 12 months postoperatively. Feature importance was calculated using a Random Forest model, which accounts for non-linear relationships and interactions among variables.

Feature	Importance
Fasting Blood Glucose	0.307
Total colesterol	0.169
Prostatic volume	0.102
Post-operative Hb	0.064
Pre-operative PSA	0.061
Pre-operative Hb	0.043
QoL score	0.043
Triglyceridemia	0.039
HDL	0.037
IPSS storage score	0.032
IPSS voiding score	0.029
Operative time	0.028
Statin therapy	0.019
Age (years)	0.016
Therapy for hypertension	0.007

Table 8.
Partial Regression Analysis Results for IIEF Recovery at 12 Months: This table presents the results of partial regression analysis, showing the unique contribution of the top five most important factors identified by the Random Forest model. Partial $R2$ values indicate the proportion of variance in IIEF recovery at 12 months that can be attributed to each factor, independent of the others.

Feature	Partial R^2
Post-operative Hb (12 h)	0.029
Prostatic volume	0.026
Fasting Blood Glucose	0.021
Pre-operative PSA	0.011
Total colesterol	0.002

Table 9.
Most Significant Factors Influencing Continence and Pad Recovery: This table highlights the most significant factors based on their unique contributions (Max Partial R2) and interaction effects (Max Interaction Coefficient) on continence recovery and pad usage. Factors with high Partial R2 explain a larger portion of the outcome variance, while significant interaction coefficients indicate combined effects with other variables.

Factor	Max Partial R^2	Max Interaction Coefficient
Fasting blood glucose (mg/dl)	0.113	0.008
Post-operative Hb (entro 12 h)		0.057
triglyceridemia (mg/dl)	0.114	0.003
Antihypertensive therapy	0.191	
HDL (mg/dl)	0.156	
Operative time (min.)	0.204	
Pre-operative Hb (mg/dl)		0.057

Discussion

The early initiation of vacuum therapy has demonstrated a significant advantage in enhancing the recovery of erectile function. Patients who began vacuum therapy within a median of 20 days postoperatively exhibited superior IIEF-5 scores at all evaluated time points compared to those treated with PDE5i alone. This finding highlights the potential synergistic effect of combining pharmacological and mechanical interventions.

Moreover, the combination of vacuum therapy with PDE5i addresses both the structural and physiological facets of ED recovery. Clinical trials have consistently highlighted the efficacy of multimodal approaches in improving both IIEF scores and the rate of spontaneous erections (6-14).

Vacuum therapy likely exerts its benefits by improving cavernosal oxygenation and reducing oxidative stress, thereby mitigating fibrosis risk and promoting endothelial repair (9, 10).

The protective effects of vacuum therapy, mediated through antihypoxic and antifibrotic mechanisms, have been substantiated in both clinical and preclinical studies (4, 5).

The findings of this study align with existing literature on

the benefits of early initiation of penile rehabilitation. As demonstrated by Kohler et al., early use of VED therapy post-RARP significantly improves IIEF scores and prevents penile shortening (5).
The observed correlation between intraoperative blood loss and IIEF-5 recovery underscores the interplay of perioperative factors and functional outcomes. Patients with significant blood loss experienced greater reductions in hemoglobin levels, potentially impairing tissue oxygenation and delaying neurovascular recovery. Hypoxia, known to suppress *nitric oxide* (NO) synthesis and reduce *cyclic guanosine monophosphate* (cGMP)-mediated vasodilation, further compromises erectile function. These findings emphasize the importance of minimizing blood loss during surgery and ensuring optimal postoperative hemoglobin levels (7, 8).
Regarding continence recovery, vacuum therapy facilitated earlier improvements, particularly within the first six months postoperatively. Enhanced vascularization and tissue remodelling, as described by *Du et al.* (2018), likely contributed to accelerated healing of sphincteric and periurethral tissues. However, by 12 months, continence outcomes were comparable between groups, suggesting that vacuum therapy's primary benefit lies in promoting early recovery (10-12).
The timing of intervention plays a critical role, with studies indicating that early initiation within one month post-surgery yields superior outcomes compared to delayed protocols (5, 6).
Conversely, some studies have questioned the direct impact of vacuum therapy on continence, attributing outcomes primarily to factors such as preoperative BMI, baseline continence status, and surgical technique.
This perspective underscores the multifactorial nature of continence recovery and highlights the need for comprehensive patient assessments and individualized rehabilitation strategies (7-13).
The neuroprotective role of vacuum therapy is further corroborated by animal studies, which demonstrated its capacity to enhance eNOS expression, reduce apoptosis, and preserve smooth muscle integrity (4, 5). These findings suggest that vacuum therapy not only facilitates functional recovery but also contributes to long-term preservation of penile tissue architecture.
Additionally, patient satisfaction and adherence are critical for the success of rehabilitation protocols. Studies have noted that the empowerment derived from active participation in therapy, such as vacuum use, enhances patient compliance and psychological well-being (5-14).
Future research should explore the integration of emerging modalities, such as *low-intensity extracorporeal shockwave therapy* (LiESWT), alongside established therapies to further optimize recovery (4-14).
According to literature evidences, this study shows that early introduction of vacuum therapy in association to PED5i administration improves erectile function recovery and facilitating early continence restoration. Older patients and those with metabolic disorders may derive particular benefit from this approach due to their predisposition to slower recovery. While the physiological mechanisms underlying these benefits align with current evidence on cavernosal and pelvic floor rehabilitation, additional investigations are necessary to clarify the connection between perioperative factors and long-term functional outcomes, with particular attention to the correlation between intraoperative blood loss and the recovery of functional outcomes. A comprehensive, multimodal rehabilitation strategy tailored to individual patient profiles remains paramount in addressing the multifaceted challenges of post-RARP recovery.

Conclusions

This study highlights the significant benefits of combining vacuum therapy with PDE5i in the rehabilitation of functional outcomes following RARP. The findings underscore that early initiation of this multimodal approach facilitates improved recovery of erectile function, as evidenced by higher IIEF-5 scores, and accelerates continence recovery during the early postoperative period. Vacuum therapy enhances cavernosal oxygenation, reduces fibrosis, and promotes endothelial repair, complementing the pharmacological effects of PDE5 inhibitors.
The study also identifies critical factors influencing recovery, such as age, metabolic health, and perioperative vari-

Declarations

Ethical approval: *This study was approved by the Local Ethics Committee of Bari (BA), IRCCS Oncological Institute "Gabriella Serio" (Protocol number: 2112/CEL - Study "PrOPT").*

Availability of data and material: *The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request.*

Competing interests: *The authors declare no competing interests.*

Funding: *This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.*

Authors' contributions (according to http://www.icmje.org/#author): *1: P.P. Prontera - author corresponding Substantial contributions to the conception, design of the work, acquisition, analysis and interpretation of data for the work. Drafting the work, reviewing it critically for important intellectual content. Final approval of the version to be published. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; 2: F.R. Prusciano, F.S. Grossi: Substantial contributions to the conception, design of the work, acquisition, analysis and interpretation of data for the work. Drafting the work, reviewing it critically for important intellectual content. Final approval of the version to be published. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; 3: M. Lattarulo, A. Tsaturyan, F. Addabbo, C. Sciorio: Substantial contributions to the interpretation of data for the work. Reviewing it critically for important intellectual content. Final approval of the version to be published. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.*

Acknowledgments: *Not applicable.*

ables, emphasizing the importance of individualized rehabilitation protocols. While the combined therapy demonstrates clear advantages in improving functional outcomes, the results also reveal the importance of early intervention to optimize recovery trajectories.
Despite these promising findings, further research is warranted to strengthen the evidence regarding the predictive factors for the success of vacuum therapy, enabling a more tailored approach to treatment. Additionally, future studies should delve deeper into the correlation between intraoperative blood loss and delays in the recovery of erectile function, as measured by the IIEF-5, to optimize postoperative rehabilitation strategies further.
In conclusion, the synergistic effects of vacuum therapy and PDE5i provide a robust foundation for developing tailored, evidence-based strategies that address the multifaceted challenges of functional recovery post-RARP. This multimodal approach not only improves patient outcomes but also fosters greater satisfaction and adherence to rehabilitation, ultimately enhancing quality of life.

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Correspondence

Pier Paolo Prontera, MD (Corresponding Author)
pierpaolo.prontera@asl.taranto.it

Marco Lattarulo, MD
marco.lattarulo@asl.taranto.it

Francesco Saverio Grossi, MD, PhD
francescos.grossi@asl.taranto.it

Department of Urology, "S.S. Annunziata" Hospital
Via Bruno Francesco, 1 Street - 74010 Taranto (Italy)

Francesca Romana Prusciano, MD
francescaprusciano@gmail.com

Division of Urology, Hospital "Valle D'Itria", Martina Franca (TA), Italy

Arman Tsaturyan, MD, PhD
tsaturyanarman@yahoo.com

Department of Urology, Yerevan State Medical University after Mkhitar, Heratsi, Yerevan, Armenia

Carmine Sciorio, MD
carmine.sciorio@gmail.com

Department of Urology, "Alessandro Manzoni" Hospital of Lecco, 23900 (Italy)