



A comparative study of nerve-sparing techniques in open radical prostatectomy: Antegrade versus retrograde

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■ MAIN POINTS

- This study provides a direct comparison between antegrade and retrograde nerve-sparing techniques in open radical prostatectomy.
- The retrograde approach was associated with reduced operative time and shorter hospitalization.
- The antegrade approach resulted in lower intraoperative blood loss, indicating superior hemostatic control.
- Despite similar surgical margin rates, biochemical recurrence was more frequent in the antegrade group, likely due to a higher prevalence of high-grade tumors. Postoperative continence, erectile function, and anastomotic stricture rates were comparable between groups.
- Both techniques are safe and effective; surgical approach should be selected based on tumor characteristics and surgeon expertise.

■ ABSTRACT

Aim: To compare perioperative, oncological, and functional outcomes between antegrade and retrograde nerve-sparing techniques in open radical prostatectomy (ORP).

Materials and Methods: This retrospective study included 278 patients who underwent open radical prostatectomy (ORP) performed by a single surgeon between 2016 and 2025. Patients were divided based on the nerve-sparing approach: antegrade (n=90) or retrograde (n=188). Demographic characteristics, perioperative variables, pathological outcomes, biochemical recurrence (BCR), urinary continence, and erectile function were evaluated. Multivariable logistic regression analysis was used to determine independent predictors of BCR.

Results: Retrograde ORP demonstrated a shorter operative time compared with the antegrade technique (151.1 vs. 166.5 minutes, $p<0.001$), whereas the antegrade group was associated with lower intraoperative blood loss (437 vs. 517 mL, $p=0.047$). Biochemical recurrence was significantly higher in the antegrade group (33.3% vs. 18.8%, $p=0.008$). Postoperative functional outcomes, including urinary continence ($p=0.524$) and erectile function ($p=0.230$), were comparable between the groups. In multivariable logistic regression, the retrograde approach independently reduced the risk of biochemical recurrence (OR 0.38; 95% CI: 0.19–0.76; $p=0.0058$).

Conclusion: It is evident that both techniques are safe and effective in ORP. The retrograde approach was associated with more favourable oncological outcomes, whereas the antegrade technique provided better intraoperative hemostasis. The choice of surgical approach should be individualized based on tumor characteristics and surgeon expertise.

Keywords: Prostatectomy, Nerve-sparing, Prostate cancer, Open surgery, Biochemical recurrence

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■ INTRODUCTION

Radical prostatectomy (RP) remains a standard curative treatment for clinically localized prostate cancer, offering durable oncological control and long-term survival benefits [1]. Currently, RP can be performed through three main surgical modalities: open radical prostatectomy (ORP), laparoscopic radical prostatectomy (LRP), and robot-assisted laparoscopic prostatectomy (RALP). Minimally invasive approaches, particularly RALP, have gained popularity due to shorter recovery,

lower blood loss, and improved cosmesis. However, their adoption is limited by high costs, steep learning curves, and a lack of availability in low-resource settings [2,3]. Therefore, ORP remains a relevant and accessible surgical option, particularly in healthcare systems with limited access to advanced Technologies [4].

In this context, ORP continues to be a viable and widely performed surgical option. Despite technological advances, functional complications such as erectile dysfunction (ED)

and urinary incontinence remain major concerns following RP. Preservation of the neurovascular bundles (NVBs) is critical for maintaining postoperative continence and sexual function. Several factors influence functional outcomes, including nerve-sparing technique, surgeon experience, and patient-specific anatomy [5]. Two principal NVB preservation techniques have been described in ORP: the antegrade approach, which dissects from base to apex, and the retrograde approach, which proceeds in the opposite direction [6,7]. Both aim to minimize NVB trauma, but data comparing their relative efficacy is limited and inconclusive, particularly in open surgery.

Additionally, advances in surgical energy devices such as the Harmonic scalpel have improved hemostasis and reduced collateral tissue injury, potentially enhancing outcomes in nerve-sparing procedures [8]. Nonetheless, few studies have directly compared antegrade and retrograde nerve-sparing techniques using standardized surgical methods and instrumentation.

This study aims to compare the perioperative, oncological, and functional outcomes of antegrade versus retrograde nerve-sparing techniques in ORP. All procedures were performed with a consistent technique and energy device, minimizing confounding factors and enhancing the reliability of comparisons.

■ MATERIALS AND METHODS

Study design and surgical technique

This retrospective study analyzed a cohort of 278 patients who underwent open radical prostatectomy (ORP) at Atatürk Training and Research Hospital between 2016 and 2025. Patients were stratified into two groups based on the nerve-sparing technique employed: antegrade (n=90) or retrograde (n=188). To ensure procedural consistency, all operations were performed by a single urologist using a standardized surgical method and the Harmonic scalpel for hemostasis. During the study period, neither laparoscopic nor robotic-assisted radical prostatectomy was available, making ORP the exclusive surgical approach for all patients. The study protocol was approved by the Non-Interventional Clinical Research Ethics Committee of İzmir Kâtip Çelebi University Faculty of Medicine (Approval No: 2025/0172; Date: March 2025).

The nerve-sparing approach was chosen intraoperatively by the surgeon, based on anatomical factors such as prostate size, apical configuration, and vascular pattern. Therefore, the study was not randomized. Tumor grade and stage were not used to determine the surgical approach. This may introduce selection bias, but the use of a single surgeon, uniform technique, and consistent instrumentation minimizes variability and enhances comparability. This is discussed in the discussion section.

Patient selection and data collection

The inclusion criteria were as follows: prostate adenocarcinoma, radical prostatectomy performed at our institution, complete clinical and follow-up data, and a preoperative IIEF-5 score of at least 21. Exclusion criteria were prior pelvic surgery, metastatic disease, neoadjuvant therapy, or missing data.

Demographic and clinical variables recorded included age, body mass index (BMI), preoperative PSA, and presence of diabetes. Operative data included surgical technique, operative time, estimated blood loss, transfusion requirement, and length of hospital stay. Oncological parameters included biopsy and postoperative ISUP grade, Gleason score, surgical margin status, biochemical recurrence, duration of follow-up, and overall survival.

Since the present study compared the outcomes of two nerve-sparing techniques in patients who underwent nerve-sparing radical prostatectomy; the patients who received non-nerve-sparing surgery were excluded to ensure comparable results in terms of complications such as postoperative erectile function and incontinence.

Definitions and outcome measures

Urinary continence was defined as needing one protective pad per day. Erectile function was evaluated using the IIEF-5 questionnaire, with scores ≤ 12 indicating significant dysfunction. Biochemical recurrence (BCR) was defined as a PSA level ≥ 0.2 ng/mL confirmed by two consecutive measurements. Disease-free survival was defined as the interval from surgery to either BCR or the latest follow-up.

Statistical analysis

All statistical procedures were conducted using the IBM SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp.). The distribution of continuous variables was tested using the Kolmogorov–Smirnov test. Comparisons were made using the Mann–Whitney U test or independent samples t-test. Categorical variables were analyzed using Pearson's chi-square test. A p-value less than or equal to 0.05 was considered statistically significant.

Independent predictors of biochemical recurrence were identified using a multivariable logistic regression model. This included surgical approach (retrograde vs. antegrade), preoperative PSA, pathological ISUP grade, age, diabetes mellitus, and BMI. The model provided odds ratios (ORs) and 95% confidence intervals. All independent variables were entered simultaneously into the multivariable logistic regression model (enter method).

A post-hoc power analysis was conducted to confirm sufficient statistical power. This analysis used G*Power version 3.1, applying the Demidenko method for logistic regression. It found an observed OR of 0.38 for surgical approach, an event rate of 33%, and a total sample size of 278. The power was calculated as 0.86 ($\alpha = 0.05$).

Table 1. Demographic, operative, oncological, and functional outcomes in the nerve-sparing radical prostatectomy groups. Continuous variables are expressed as median (interquartile range) for non-normally distributed data or mean $\pm$ SD for normally distributed data. Categorical variables are presented as number of patients (percentage within group).

Parameter	Antegrade group (n = 90)	Retrograde group (n = 188)	p value
Demographic Data			
Age (years)	65.89 $\pm$ 5.70	65.79 $\pm$ 6.23	0.880
Body Mass Index (kg/m ²)	26.31 $\pm$ 2.89	25.74 $\pm$ 3.75	0.035
Preoperative PSA (ng/mL)	11.04 $\pm$ 9.54	12.13 $\pm$ 14.76	0.783
Diabetes Mellitus *	20 (22.20%)	24 (12.70%)	0.214
Operative Findings			
Operation Time (minutes)	160 (145-180)	148 (130-175)	<0.001
Intraoperative Blood Loss (mL)	430 (360-510)	510 (420-620)	0.047
Blood Transfusion required *	10 (11.10%)	30 (16.00%)	0.090
Hospital Stay (days)	7 (5-10)	6 (4-8)	0.042
Oncological Outcomes			
Positive Surgical Margin *	35 (38.90%)	63 (33.70%)	0.397
Biochemical Recurrence *	30 (33.30%)	35 (18.80%)	0.008
Overall Survival (alive) *	84 (93.30%)	176 (94.10%)	0.799
Functional Outcomes			
Urinary Incontinence *	35 (38.60%)	65 (34.50%)	0.524
Erectile Dysfunction *	87 (96.70%)	175 (93.10%)	0.230
Anastomotic Stricture *	20 (22.20%)	33 (17.60%)	0.354

* Variables analyzed by Chi-square test are indicated with an asterisk. Non-normally distributed continuous variables were compared using the Mann–Whitney U test. A p < 0.05 was considered statistically significant.

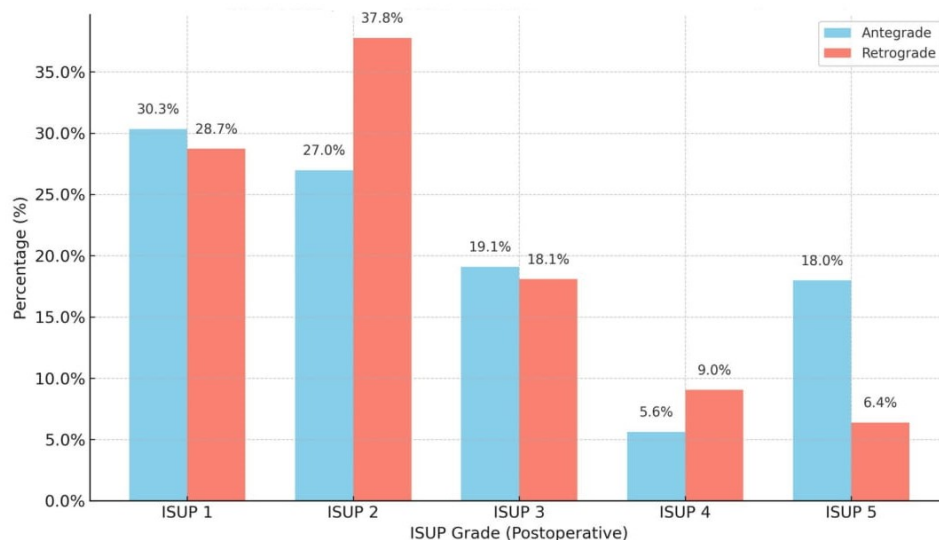


Figure 1. Postoperative pathological ISUP grade distribution in the antegrade (blue) and retrograde (red) groups. The chart depicts the percentage of patients in each group who had final pathology ISUP grades 1 through 5. A significantly higher fraction of tumors were ISUP grade 5 in the antegrade group, whereas the retrograde group had more grade 2 tumors (Chi-square p = 0.026). Data are expressed as percentages.

Prior to the multivariable logistic regression, multicollinearity among the independent variables was assessed. No significant collinearity was detected, and all variance inflation factor (VIF) values were below 2.5.

■ RESULTS

A total of 278 patients were included in the study, with 90 undergoing antegrade prostatectomy versus 188 undergoing ret-

rograde open radical prostatectomy. Demographic and baseline clinical characteristics were comparable between the two groups. The mean age was approximately 66 years, and preoperative PSA levels did not differ significantly. The retrograde group had a slightly lower BMI (25.74 vs. 26.31 kg/m², p = 0.035). The prevalence of diabetes mellitus was similar (22.2% vs. 12.7%, p = 0.214).

From a surgical perspective, the retrograde approach demon-

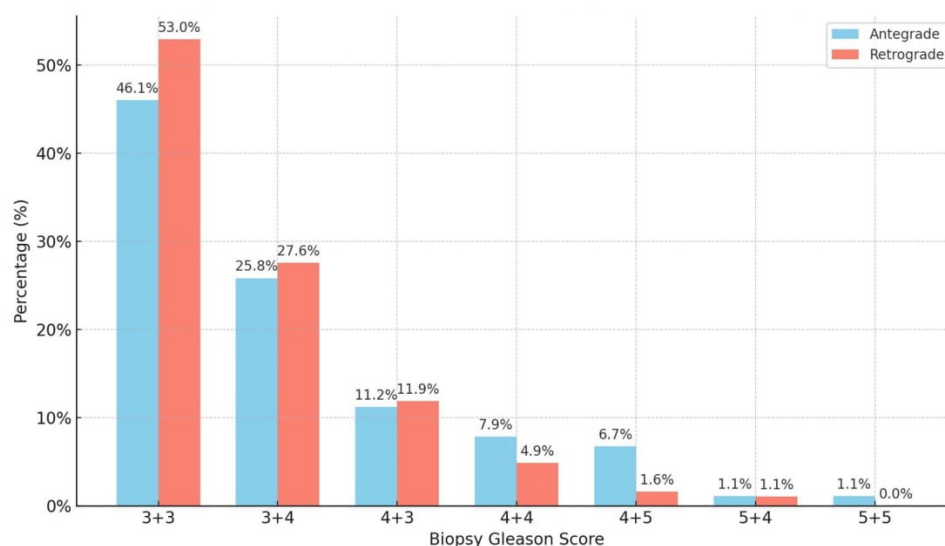


Figure 2. Distribution of biopsy Gleason scores in the antegrade (blue) and retrograde (red) groups. The percentage of patients with Gleason score 6, 7, 8, 9, or 10 on biopsy is shown for each surgical group. Both the antegrade and retrograde approaches yielded similar Gleason score distributions at diagnosis ($p > 0.20$), with over half of patients in each group having Gleason 6 disease on initial biopsy.

strated some advantages. It was associated with a shorter operative time (151.1 vs. 166.5 minutes, $p < 0.001$), although the antegrade approach resulted in lower intraoperative blood loss (437 vs. 517 mL, $p = 0.047$). There were more blood transfusions in the retrograde group (16.0% vs. 11.1%), but this was not significant ($p = 0.090$). The length of hospital stay was longer in the antegrade group (7.4 vs. 6.5 days, $p = 0.042$).

The median follow-up period was 62 months (range: 12–109) in the antegrade group and 59 months (range: 13–108) in the retrograde group. Oncological outcomes are summarised in Table 1. The rate of positive surgical margins was similar (38.9% vs. 33.7%, $p = 0.397$). However, more cases of biochemical recurrence occurred in the antegrade group (33.3% vs. 18.8%, $p = 0.008$). Overall survival was excellent and comparable (93.3% vs. 94.1%, $p = 0.799$).

Postoperative functional outcomes were similar (Table 1). The prevalence of urinary incontinence (≥ 2 pads/day) was 38.6% in the antegrade group and 34.5% in the retrograde group ($p = 0.524$). Erectile dysfunction rates were high in both groups (96.7% vs. 93.1%, $p = 0.230$). Anastomotic stricture occurred in 22.2% of the antegrade group and 17.6% of the retrograde group ($p = 0.354$).

Table 2 presents the distribution of biopsy and pathological Gleason and ISUP grades. Biopsy Gleason and ISUP grades did not differ significantly between groups ($p = 0.207$ and $p = 0.169$, respectively). In contrast, postoperative pathological ISUP scores demonstrated a significant difference ($p = 0.026$). The retrograde group had a higher proportion of intermediate-grade disease (notably ISUP 2), while the antegrade group exhibited a greater prevalence of high-grade tumors (notably ISUP 5) (Table 2 and Figure 1).

Similarly, the postoperative Gleason score distribution showed a non-significant trend toward higher grade tumors (scores 9–10) in the antegrade group ($p = 0.086$). These findings suggest that the retrograde technique may be associated with a more favorable pathological grade distribution despite comparable biopsy findings (Figure 2).

A multivariable logistic regression analysis was conducted to determine independent predictors of biochemical recurrence (Table 3). Pathological ISUP grade (OR = 2.01; 95% CI: 1.57–2.61; $p < 0.001$), preoperative PSA level (OR = 1.06; 95% CI: 1.03–1.09; $p = 0.0003$), and surgical approach (OR = 0.38; 95% CI: 0.19–0.76; $p = 0.0058$) were identified as significant predictors of recurrence. Age showed a borderline association (OR = 1.06; 95% CI: 0.99–1.11; $p = 0.052$), while diabetes mellitus and BMI were not associated with recurrence ($p = 0.45$ and $p = 0.57$, respectively). Notably, the surgical approach was coded as 0 = antegrade (reference) and 1 = retrograde; thus, the retrograde technique was associated with a 62% reduction in the odds of biochemical recurrence.

A post-hoc power analysis using G*Power version 3.1 (Demenko method for logistic regression) demonstrated an achieved power of 0.86 ($\alpha = 0.05$), based on an observed odds ratio of 0.38, an event rate of 33%, and a total sample size of 278, indicating sufficient statistical power for the observed effect.

DISCUSSION

This study offers a direct comparison between the antegrade and retrograde nerve-sparing techniques in open radical prostatectomy, an area with limited comparative data in the existing literature. Our results highlight that each technique

Table 2. Distribution of biopsy and postoperative Gleason scores and ISUP grades in antegrade and retrograde groups.

Score category	Antegrade group	Retrograde group
Biopsy Gleason Score		
Gleason 6 (3+3)	41 (46.10%)	98 (53.00%)
Gleason 7 (3+4)	23 (25.80%)	51 (27.60%)
Gleason 7 (4+3)	10 (11.20%)	22 (11.90%)
Gleason 8 (4+4)	7 (7.90%)	9 (4.90%)
Gleason 9 (4+5)	6 (6.70%)	3 (1.60%)
Gleason 9 (5+4)	1 (1.10%)	2 (1.10%)
Gleason 10 (5+5)	1 (1.10%)	0 (0.00%)
Biopsy ISUP Grade		
ISUP 1	40 (45.50%)	98 (52.40%)
ISUP 2	27 (30.70%)	53 (28.30%)
ISUP 3	9 (10.20%)	24 (12.80%)
ISUP 4	6 (6.80%)	9 (4.80%)
ISUP 5	6 (6.80%)	3 (1.60%)
Postoperative Gleason		
Gleason 6 (3+3)	27 (30.30%)	53 (28.60%)
Gleason 7 (3+4)	24 (27.00%)	71 (38.40%)
Gleason 7 (4+3)	17 (19.10%)	32 (17.30%)
Gleason 8 (3+5)	1 (1.10%)	0 (0.00%)
Gleason 8 (4+4)	2 (2.20%)	10 (5.40%)
Gleason 9 (4+5)	3 (3.40%)	7 (3.80%)
Gleason 9 (5+4)	11 (12.40%)	9 (4.90%)
Gleason 10 (5+5)	4 (4.50%)	3 (1.60%)
Postoperative ISUP		
ISUP 1	27 (30.30%)	54 (28.70%)
ISUP 2	24 (27.00%)	71 (37.80%)
ISUP 3	17 (19.10%)	34 (18.10%)
ISUP 4	5 (5.60%)	17 (9.00%)
ISUP 5	16 (18.00%)	12 (6.40%)

*ISUP: International Society of Urological Pathology. Percentages are calculated out of the number of patients with available data in each group. Denominators vary slightly across categories due to missing data. There were no significant between-group differences in biopsy Gleason or biopsy ISUP distributions ($p > 0.05$); the postoperative ISUP distribution differed significantly between groups ($p = 0.026$).

Table 3. Multivariate logistic regression model predicting biochemical recurrence.

Variable	Odds Ratio (OR)	95% Confidence Interval	p-value
Pathological ISUP	2.01	(1.57 – 2.61)	<0.001
Preoperative PSA	1.06	(1.03 – 1.09)	0.0003
Surgical Approach ¹	0.38	(0.19 – 0.76)	0.0058
Age	1.06	(0.89 – 1.00)	0.052
Diabetes Mellitus	0.73	(0.31 – 1.66)	0.45
BMI	0.97	(0.88 – 1.07)	0.57

presents distinct advantages and limitations across perioperative, oncologic, and functional outcomes.

The antegrade approach was associated with a significantly longer mean operative time (166.5 ± 32.2 vs. 151.1 ± 49.8 minutes, $p < 0.001$), potentially reflecting the careful dissection along anatomical planes and the stepwise vascular control that defines this technique, including early ligation of the prostatic pedicles and delayed division of the dorsal venous complex (DVC) [9–11]. Notably, the antegrade group ex-

hibited significantly less intraoperative bleeding compared to the retrograde group (437 ± 142 mL vs. 517 ± 188 mL, $p = 0.047$). While transfusion requirements did not reach statistical significance, they were numerically lower in the antegrade group (11.1% vs. 16.0%, $p = 0.090$). This may be attributed to earlier exposure and control of venous structures during antegrade dissection, facilitating more effective hemostasis in line with previous reports [12,13]. Despite improved bleeding control, patients in the antegrade group experienced a slightly longer hospital stay (7.4 ± 3.95 vs. 6.5 ± 2.75 days, $p = 0.042$). Although this difference is statistically significant, its clinical relevance may be minimal, possibly reflecting a marginally slower immediate recovery. Importantly, aside from a lower body mass index in the retrograde group (25.74 ± 3.75 vs. 26.31 ± 2.89 , $p = 0.035$), both groups were demographically similar, suggesting that perioperative differences likely stem from surgical technique rather than patient-related factors.

Oncologic efficacy appeared largely comparable between the two techniques. Positive surgical margin rates were similar (38.9% antegrade vs. 33.7% retrograde, $p = 0.397$), consistent with prior studies suggesting that nerve-sparing technique whether antegrade or retrograde does not compromise margin status or oncologic control [14,15]. However, the antegrade group showed a significantly higher rate of biochemical recurrence (33.3% vs. 18.8%, $p = 0.008$), despite similar margin positivity. This discrepancy may be explained by differences in tumor characteristics; the antegrade cohort had a higher proportion of high-grade tumors on final pathology, with ISUP grade 5 observed more frequently (18.0% vs. 6.4%, $p = 0.026$). Thus, the increased biochemical recurrence in the antegrade group may reflect a greater tumor burden rather than inadequate surgical clearance. Furthermore, the retrograde technique may allow for finer dissection near the prostatic apex and neurovascular bundles, enabling more complete excision of malignant tissue in anatomically challenging areas [14].

These findings indicate that both techniques remain viable options in the surgical management of localized prostate cancer, each with specific advantages: the antegrade technique offers better hemostasis, while the retrograde technique is associated with lower biochemical recurrence potentially due to enhanced apex dissection or a lower incidence of high-grade disease.

Rates of anastomotic stricture were comparable between groups, suggesting similar long-term safety. The equivalent stricture rates and survival outcomes support the notion that both nerve-sparing approaches are safe and oncologically sound when performed by experienced surgeons [16–18].

Postoperative functional outcomes were also similar between techniques, with no statistically significant differences in continence or erectile function. Urinary incontinence (defined as ≥ 2 pads/day) affected 38.6% of patients in the antegrade group and 34.5% in the retrograde group ($p = 0.524$), which

aligns with the wide variation in continence rates reported in the literature (ranging from 30–69%) (5). Erectile dysfunction was prevalent in both groups, as expected in this patient population. Clinically significant erectile dysfunction (IIEF-5 ≤ 12) was observed in 96.7% of antegrade and 93.1% of retrograde patients ($p = 0.230$), reflecting the inherent challenge of nerve preservation in open surgery and the strict definition employed. Nonetheless, a slight clinical trend favoring the retrograde group was observed in both continence and potency rates. This may be due to more delicate nerve-sparing at the apex with the retrograde technique, possibly facilitating better preservation of the neurovascular bundles and improved functional recovery.

Supporting this notion, Ko et al. found that a retrograde nerve-sparing technique in robotic prostatectomy yielded significantly better early potency recovery without affecting continence [15]. Likewise, de Carvalho et al. reported improved functional outcomes with a modified retrograde approach that preserved the dorsal vein complex during robotic prostatectomy [14]. Our findings are in line with these observations: although not statistically significant in our cohort, the retrograde technique appears at least equivalent and potentially advantageous when functional outcomes are a clinical priority.

Our multivariable analysis highlighted that both pathological ISUP grade and preoperative PSA level were significant predictors of biochemical recurrence. Notably, even after adjusting for these variables, the retrograde surgical approach remained independently protective, reducing the risk of recurrence by 62%, and thereby suggesting a potentially favorable oncologic impact. Although age demonstrated borderline significance, neither diabetes mellitus nor BMI were predictive. Furthermore, the robustness of these findings was supported by a post-hoc power analysis (power = 0.86, $\alpha = 0.05$), confirming the adequacy of the sample size for the observed effect.

All procedures were performed by an experienced surgeon using standardized techniques and consistent instrumentation, minimizing variability. Open surgery was chosen over laparoscopic or robotic approaches due to the surgeon's expertise and procedural consistency; robotic surgery was not available during the study period. The inclusion of a large number of cases from a high-volume center enhanced the study's ability to detect clinically meaningful differences between the techniques.

However, the retrospective design introduces potential bias, particularly due to the absence of randomization and potential differences in tumor characteristics. Intraoperative decisions may have been influenced by unmeasured confounders. The surgeon's experience likely improved over the nine-year period, and learning curve effects were not analyzed separately.

Functional outcomes were based on patient-reported measures (pad count, IIEF-5) without objective clinical valida-

tion. Although patients with IIEF-5 scores below 21 were excluded, documentation of preoperative erectile function was limited. Interpretation of postoperative functional outcomes particularly in older patients should therefore be made with caution.

Interaction effects between covariates (e.g., surgical technique and pathological grade) were not evaluated, which may limit interpretation of combined influences on recurrence risk.

Finally, the findings may not be generalizable, as all surgeries were performed by a single surgeon at a single center. While follow-up was adequate for assessing biochemical recurrence, longer-term data are needed to draw definitive conclusions regarding oncologic durability and late functional outcomes.

Conclusion

Both antegrade and retrograde nerve-sparing techniques in open radical prostatectomy represent safe and effective options for the treatment of organ-confined prostate cancer. The retrograde approach was associated with shorter operative time, lower rates of biochemical recurrence, and a trend toward improved functional outcomes, whereas the antegrade technique offered superior intraoperative hemostasis. The choice of surgical technique should be individualized based on patient and tumor characteristics, as well as surgeon expertise. These findings warrant further validation in prospective, multicenter trials.

A preliminary version of this study was delivered as an oral presentation at the Turkish Association of Urology Scientific Meeting, held at İzmir Kâtip Çelebi University Faculty of Medicine in March 2025.

Ethics Committee Approval: Ethical clearance for this research (approval code: 2025/0172) was obtained from the Non-Interventional Clinical Research Ethics Board of İzmir Kâtip Çelebi University, Faculty of Medicine.

Informed Consent: Not applicable, as the study was conducted retrospectively using anonymized patient data.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declare that they have no competing interests that could have influenced the outcomes of this study.

Author Contributions: Concept: H.T.; Design: H.T., E.M.Y.; Supervision: S.N.G.; Materials: H.T., S.Ö., O.K.; Data Collection and Processing: H.T., E.M.Y., S.Ö.; Analysis and Interpretation: H.T.; Literature Search: H.T., O.K.; Writing Manuscript: S.Ö.; Critical Review: S.N.G., Y.A.

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