

Performing Extended Pelvic Lymph Node Dissection Before Prostatectomy was Associated with Lower Apical Positive Surgical Margin Rates During Robot-Assisted Radical Prostatectomy: A Single-Centre Retrospective Cohort Study

Robot Yardımlı Radikal Prostatektomi Sırasında Prostatektomi Öncesi Uygulanan Genişletilmiş Pelvik Lenf Nodu Diseksiyonu, Daha Düşük Apikal Pozitif Cerrahi Sınır Oranları ile İlişkilidir: Tek Merkezli Retrospektif Kohort Çalışması

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ABSTRACT

Objective: Positive surgical margins remain clinically relevant after robot-assisted radical prostatectomy (RARP). Whether performing extended pelvic lymph node dissection (ePLND) before, rather than after, prostatectomy is associated with lower apical positive surgical margin (PSM) rates has not been evaluated with adjusted comparative data.

Materials and Methods: We performed a retrospective cohort study of 250 consecutive patients who underwent primary RARP with ePLND at a single tertiary centre. Patients were classified by operative sequence as ePLND-first (n = 121) or prostatectomy-first (n = 129). The primary multivariable analyses were conducted in the full 250-patient cohort with nerve-sparing intent coded as a 3-level categorical variable; a pre-specified subgroup analysis was conducted in the 188 patients undergoing any form of nerve-sparing surgery. The primary endpoint was apical PSM. Because apical PSM events were sparse, the adjusted analysis used Firth penalised logistic regression.

Results: Baseline characteristics were similar between groups. Apical PSM occurred in 6 of 121 patients (5.0%; 95% confidence interval [CI] 2.3% to 10.4%) in the ePLND-first group and 13 of 129 (10.1%; 95% CI 6.0% to 16.5%) in the prostatectomy-first group. In the primary multivariable analysis of the full 250-patient cohort, ePLND-first sequencing was associated with lower adjusted odds of apical PSM (adjusted OR 0.38; 95% CI 0.14 to 1.03; $p = 0.056$); in the pre-specified nerve-sparing subgroup (n = 188), the adjusted association was stronger (OR 0.19; 95% CI 0.04 to 0.97; $p = 0.046$; unadjusted 1.2% vs 8.8%, Fisher's exact $p = 0.023$). Total operative time was shorter in the ePLND-first group (195.2 vs 202.9 min; $p = 0.029$). Lymph node yield and major complication rates were similar between groups.

Conclusion: In this retrospective cohort, performing ePLND before prostatectomy was associated with directionally

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lower adjusted odds of apical PSM during RARP in the full 250-patient cohort, with a stronger association in the pre-specified nerve-sparing subgroup analysis. For men undergoing nerve-sparing RARP with planned ePLND, sequence may represent a practical operative strategy associated with lower apical margin risk without an evident perioperative penalty.

Keywords: robot-assisted radical prostatectomy, extended pelvic lymph node dissection, positive apical surgical margin, prostate cancer

ÖZET

Amaç: Robot yardımcı radikal prostatektomi (RARP) sonrasında pozitif cerrahi sınırlar klinik önemini korumaktadır. Genişletilmiş pelvik lenf nodu diseksiyonunun (ePLND) prostatektomiden önce yapılmasının, daha düşük apikal pozitif cerrahi sınır oranları ile ilişkili olup olmadığı karşılaştırmalı verilerle değerlendirilmemiştir.

Gereç ve Yöntemler: Ocak 2022 ile Ocak 2025 tarihleri arasında tek bir üçüncü basamak merkezde primer RARP ve ePLND uygulanan ardışık 250 hastayı içeren retrospektif bir kohort çalışması yapıldı. Hastalar önce ePLND sonra prostatektomi (n = 121) ve önce prostatektomi sonra ePLND (n = 129) yapılanlar olmak üzere 2 gruba ayrıldı. Birincil çok değişkenli analizler tüm 250 hastalık kohortta, sinir koruma niyetinin üç düzeyli kategorik değişken (yok, tek taraflı, iki taraflı) olarak kodlandığı modelle gerçekleştirildi; herhangi bir sinir koruma uygulanan 188 hastada önceden belirlenmiş bir alt-grup analizi yapıldı. Birincil sonlanım noktası apikal pozitif cerrahi sınırdı. Apikal pozitif cerrahi sınır olayları az olduğu için düzeltilmiş analizde Firth cezalandırılmış lojistik regresyon kullanıldı.

Bulgular: Gruplar başlangıç özellikleri açısından benzerdi. Apikal pozitif cerrahi sınır, önce ePLND yapılan 121 hastanın 6'sında (%5,0; %95 güven aralığı [GA] %2,3-%10,4), önce prostatektomi yapılan 129 hastanın ise 13'ünde (%10,1; %95 GA %6,0-%16,5) saptandı. Tam 250 hastalık kohortta birincil çok değişkenli analizde ePLND'nin prostatektomiden önce yapılması yönsel olarak daha düşük apikal pozitif cerrahi sınır olasılığı ile ilişkili bulundu (OR 0,38; %95 GA 0,14–1,03; $p = 0,056$); önceden belirlenmiş sinir koruma alt-grup analizinde ilişki daha güçlüydü (OR 0,19; %95 GA 0,04–0,97; $p = 0,046$; düzeltilmemiş 1/86 vs 9/102 = %1,2 vs %8,8, Fisher kesin $p = 0,023$). Toplam ameliyat süresi önce ePLND yapılan grupta daha kısaydı (195,2'ye karşı 202,9 dakika; $p = 0,029$). Lenf nodu sayısı ve majör komplikasyon oranları gruplar arasında benzerdi.

Sonuçlar: Bu retrospektif kohortta, ePLND'nin prostatektomiden önce yapılması, RARP sırasında daha düşük apikal pozitif cerrahi sınır olasılığı ile yönsel olarak ilişkili bulundu; sinyal sinir koruma yapılan önceden belirlenmiş alt-grupta daha güçlüydü. Sinir koruma uygulanan ve ePLND planlanan RARP olgularında, lenf nodu diseksiyonunun prostatektomiden önce yapılması, belirgin bir perioperatif dezavantaj oluşturmadan daha düşük apikal cerrahi sınır riski ile birlikte pratik bir teknik tercih olabilir.

Anahtar Kelimeler: robot yardımcı radikal prostatektomi, genişletilmiş pelvik lenf nodu diseksiyonu, pozitif apikal cerrahi sınır, prostat kanseri

INTRODUCTION

Robot-assisted radical prostatectomy (RARP) is a standard surgical treatment for localised prostate cancer (1). Positive surgical margins remain clinically relevant after RARP because they are associated with biochemical recurrence and may alter the use of adjuvant or salvage therapy (2–6). Site-specific patterns vary across series, but the apex is repeatedly among the most common locations of margin positivity (2,4,5).

Extended pelvic lymph node dissection (ePLND) remains the recommended nodal template when lymph node dissection is undertaken at radical prostatectomy (7). Williams and colleagues described performing ePLND before the prostatectomy to improve exposure of the deep hypogastric planes during RARP (8). That rationale is plausible. Other technical modifications that improve visualisation of the apex, including the puboprostatic open-collar

technique and synchronous retro-apical urethral transection, have been associated with lower apical PSM rates (9,10). The same principle underlies detailed descriptions of apical dissection in robotic prostatectomy (11). However, published reports on ePLND sequencing have been primarily technical or descriptive, not adjusted comparisons of oncological margin outcomes (8,12).

It therefore remains unknown whether performing ePLND before rather than after prostatectomy during RARP is associated with lower apical PSM rates. We used data from 250 consecutive patients treated at a single tertiary centre to compare apical PSM rates between ePLND-first and prostatectomy-first sequencing, and to evaluate differences in overall PSM, operative efficiency, nodal yield, complications, and early biochemical recurrence.

MATERIALS AND METHODS

Study design and cohort

We conducted a retrospective cohort study at Umraniye Training and Research Hospital, Istanbul, Türkiye. Between January 2022 and January 2025, 932 patients underwent radical prostatectomy. After exclusion of 12 patients treated with an open approach, 920 patients who underwent RARP were screened. Of these, 323 underwent RARP with ePLND and were assessed for eligibility. We included patients who underwent primary RARP with ePLND during the study period. We excluded salvage RARP ($n = 2$), prior neoadjuvant androgen deprivation therapy ($n = 10$), clinically node-positive disease (cN1; $n = 18$), conversion to open surgery ($n = 2$), non-adenocarcinoma histology ($n = 1$), and cases with incomplete data ($n = 40$): 30 patients lacked postoperative follow-up data and 10 lacked preoperative biopsy results. The final analytic cohort comprised 250 patients (Figure 1). Of the 250 patients, 188 underwent some form of nerve-sparing surgery (unilateral or bilateral) and were analysed as a pre-specified subgroup in addition to the primary full-cohort analysis. The study was approved by the Scientific Research Ethic Committee of Umraniye Training and Research Hospital, Istanbul, Türkiye (IRB-2025-470, Date: December 18, 2025).

Exposure definition

Patients were classified according to operative sequence. In the ePLND-first group ($n = 121$), bilateral ePLND was completed before prostatectomy. In the prostatectomy-first group ($n = 129$), prostatectomy was completed before lymph node dissection. The sequence reflected surgeon preference during the study period. Five surgeons performed all procedures. The study was approved by the institutional review board of Umraniye Training and Research Hospital (approval number: IRB-2025-470).

Surgical technique

All procedures were performed using the da Vinci Xi robotic platform (Intuitive Surgical, Sunnyvale, CA, USA). The ePLND template included the obturator, external iliac, internal iliac, and common iliac nodal packets bilaterally, consistent with current guideline-based extended dissection (7). Surgical approach (Retzius-sparing or standard anterior) and nerve-sparing strategy were determined by the operating surgeon on the basis of disease characteristics and intraoperative findings.

Outcomes

The primary endpoint was apical PSM, defined as tumour cells extending to the inked apical margin on final pathology. Secondary endpoints were overall PSM, site-specific margin rates, total operative time, console time, ePLND time, estimated blood loss, length of stay, catheter duration, lymph node yield, major complications within 90 days (Clavien-Dindo grade III or higher), symptomatic lymphocele, 90-day readmission, and biochemical recurrence (BCR). BCR was defined as two consecutive postoperative prostate-specific antigen values of 0.2 ng/mL or higher. Pathological reporting followed the 2014 International Society of Urological Pathology consensus recommendations (13).

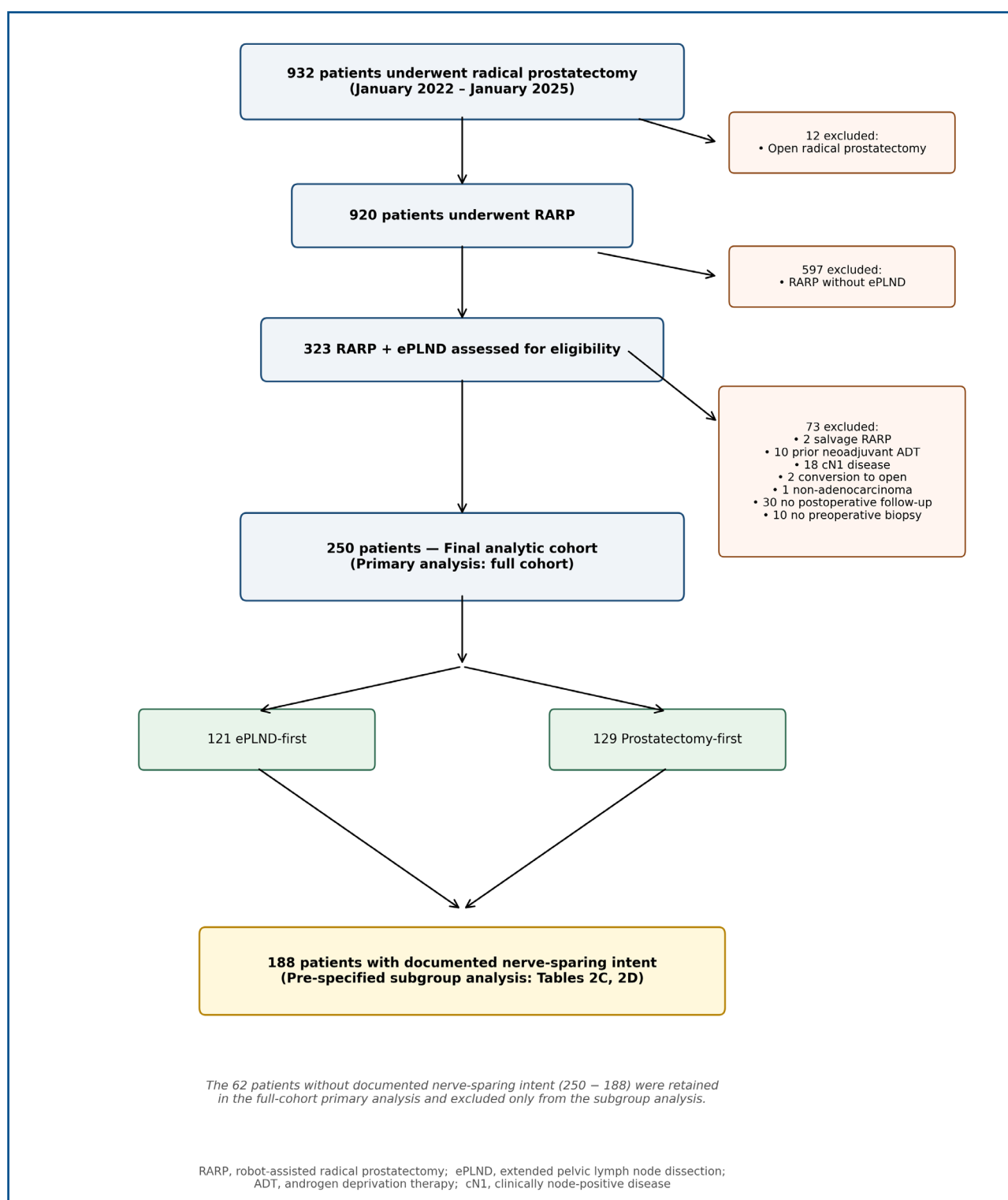


Figure 1. STROBE flow diagram of patient selection. Of 932 patients who underwent radical prostatectomy during the study period, 250 met all eligibility criteria and constituted the primary analytic cohort (full-cohort multivariable analysis: Tables 2A and 2B). Within this cohort, the 188 patients with documented bilateral or unilateral nerve-sparing intent comprised a pre-specified subgroup for the secondary analysis (Tables 2C and 2D); the 62 patients without nerve-sparing intent were retained in the full cohort and excluded only from the subgroup analysis. ePLND, extended pelvic lymph node dissection; RARP, robot-assisted radical prostatectomy; ADT, androgen deprivation therapy; PSM, positive surgical margin.

Statistical Analysis

Continuous variables are reported as mean standard deviation (SD) when approximately normally distributed and as median (interquartile range [IQR]) otherwise. Group comparisons used Welch's *t*-test or the Mann-Whitney *U* test for continuous variables, and the Chi-square test or Fisher's exact test for categorical variables. Proportions are reported with Wilson 95% confidence intervals (CIs), and absolute differences with Newcombe-Wilson 95% CIs.

All seven pre-specified covariates were entered simultaneously into a single multivariable model. Variable selection was specified a priori on clinical and anatomical grounds; no data-driven selection (e.g., stepwise or backward elimination) was applied. The univariable estimates presented alongside the multivariable results in Table 2 are reported for transparency, in line with STROBE recommendations, and were not used to select variables for the multivariable model. The primary adjusted analysis used Firth penalised logistic regression because apical PSM events were sparse relative to the number of candidate covariates. Firth penalisation reduces small-sample bias and addresses separation problems in logistic regression (14). Pre-specified covariates were operative sequence, cumulative surgeon experience, surgical approach, nerve sparing intent, prostate volume, biopsy Grade Group, and clinical T stage. We did not include postoperative pathological variables in the primary model because they may lie on the causal pathway between operative technique and margin status. For overall PSM, we used standard logistic regression with the same covariate set. A sensitivity analysis replaced clinical T stage with NCCN risk group to reduce concern about collinearity. The primary multivariable analyses were estimated in the full 250-patient cohort (19 apical PSM events; 44 overall PSM events) with nerve-sparing intent coded as a 3-level categorical variable (none, unilateral, bilateral; none as reference); the binary versus 3-level specification was compared by likelihood ratio testing, which favoured the 3-level coding ($p = 0.048$). A pre-specified subgroup analysis examined the 188 patients undergoing any form of nerve-sparing surgery (10 apical PSM events; 30 overall PSM events), motivated by the mechanistic basis of our hypothesis. All tests were 2-sided, and p values < 0.05 were considered statistically significant. Analyses were performed in Python 3.10 with NumPy 1.24 and custom routines implementing the Firth penalised likelihood with step-halving convergence control.

RESULTS

Baseline Characteristics

Baseline characteristics were generally similar between groups, with the exception of clinical T stage distribution (Table 1). Mean age was 65.5 ± 5.9 years in the ePLND-first group and 66.0 ± 5.8 years in the prostatectomy-first group ($p = 0.503$). Median preoperative PSA was 8.3 ng/mL (IQR 5.3–12.1) and 9.1 ng/mL (IQR 5.6–12.8), respectively ($p = 0.246$). Prostate volume, body mass index, Charlson comorbidity index, Briganti score, NCCN risk group, pathological T stage, and surgical approach were similar between groups. Clinical T stage distribution showed a borderline difference (overall $p = 0.055$): cT1c disease was more common in the ePLND-first group (46.3% vs 30.2%), whereas locally advanced disease was more common in the prostatectomy-first group (cT2c 19.4% vs 14.9%; cT3a 12.4% vs 8.3%; cT3b 7.0% vs 1.7%). Clinical T stage was included as an ordinal covariate in all multivariable models. The distribution of nerve-sparing intent (none, unilateral, bilateral) was similar between groups (overall $p = 0.265$; Table 1).

Apical Positive Surgical Margins

Apical PSM was less frequent in the ePLND-first group. The event rate was 6 of 121 patients (5.0%; 95% CI 2.3% to 10.4%) in the ePLND-first group and 13 of 129 (10.1%; 95% CI 6.0% to 16.5%) in the prostatectomy-first group ($p = 0.155$). The absolute risk difference was -5.1 percentage points (95% CI -12.1% to 1.7%).

In the primary multivariable analysis of the full 250-patient cohort, ePLND-first sequencing was associated with directionally lower adjusted odds of apical PSM (adjusted OR 0.38; 95% CI 0.14 to 1.03; $p = 0.056$; Table 2A and Figure 2). In the pre-specified subgroup analysis restricted to the 188 patients undergoing nerve-sparing surgery, apical

PSM occurred in 1 of 86 ePLND-first patients (1.2%) and 9 of 102 prostatectomy-first patients (8.8%; Fisher's exact $p = 0.023$), and the adjusted association was stronger (adjusted OR 0.19; 95% CI 0.04 to 0.97; $p = 0.046$; Table 2C). In a sensitivity analysis that replaced clinical T stage with NCCN risk group, the full-cohort point estimate was attenuated but directionally consistent (adjusted OR 0.44; 95% CI 0.17 to 1.16; $p = 0.098$). Within the nerve-sparing subgroup, the sensitivity estimate that replaced clinical T stage with NCCN risk group was similar to the primary subgroup result (adjusted OR 0.20; 95% CI 0.04 to 1.02; $p = 0.052$).

Table 1. Baseline Demographics and Clinical Characteristics

Variable	ePLND-first (n = 121)	Prostatectomy-first (n = 129)	p
Age, years, mean $\pm$ SD	65.5 $\pm$ 5.9	66.0 $\pm$ 5.8	0.503
BMI, kg/m ² , mean $\pm$ SD	28.2 $\pm$ 3.5	28.1 $\pm$ 3.4	0.751
PSA, ng/mL, median (IQR)	8.3 (5.3–12.1)	9.1 (5.6–12.8)	0.246
Prostate volume, mL, mean $\pm$ SD	44.5 $\pm$ 13.6	45.4 $\pm$ 12.3	0.612
Briganti score, %, mean $\pm$ SD	20.0 $\pm$ 9.3	20.6 $\pm$ 9.0	0.584
CCI, median (IQR)	1 (0–2)	1 (0–2)	0.196
Surgeon prior cases, median (IQR)	499 (228–829)	387 (210–715)	0.146
Clinical T stage, n (%)			0.055
cT1c	56 (46.3)	39 (30.2)	
cT2a	15 (12.4)	21 (16.3)	
cT2b	20 (16.5)	19 (14.7)	
cT2c	18 (14.9)	25 (19.4)	
cT3a	10 (8.3)	16 (12.4)	
cT3b	2 (1.7)	9 (7.0)	
Biopsy Grade Group, n (%)			0.563
1	12 (9.9)	10 (7.8)	
2	34 (28.1)	43 (33.3)	
3	31 (25.6)	39 (30.2)	
4	29 (24.0)	27 (20.9)	
5	15 (12.4)	10 (7.8)	
NCCN risk group, n (%)			0.759
Favorable intermediate	14 (11.6)	16 (12.4)	
Unfavorable intermediate	38 (31.4)	35 (27.1)	
High	69 (57.0)	78 (60.5)	
Approach, n (%)			0.570
Standard anterior	95 (78.5)	106 (82.2)	
Retzius-sparing	26 (21.5)	23 (17.8)	
Nerve-sparing intent, n (%)			0.265
None	35 (28.9)	27 (20.9)	
Unilateral	33 (27.3)	34 (26.4)	
Bilateral	53 (43.8)	68 (52.7)	
Pathological T stage, n (%)			0.926
pT2	74 (61.2)	77 (59.7)	
pT3a	33 (27.3)	35 (27.1)	
pT3b	14 (11.6)	17 (13.2)	

Abbreviations: BMI, body mass index; CCI, Charlson comorbidity index; IQR, interquartile range; NCCN, National Comprehensive Cancer Network; PSA, prostate-specific antigen; SD, standard deviation.

Table 2. Univariable and Multivariable Regression Analyses for Positive Surgical Margins

A. Primary analysis: Apical positive surgical margin in the full 250-patient cohort (19 events)

Variable	Univariable		Multivariable (Firth)	
	OR (95% CI)	p	OR (95% CI)	p
ePLND-first (vs Prostatectomy-first)	0.49 (0.18–1.29)	0.146	0.38 (0.14–1.03)	0.056
Surgeon prior cases (per case)	1.00 (1.00–1.00)	0.054	1.00 (1.00–1.00)	0.105
Retzius-sparing (vs Standard)	1.60 (0.56–4.53)	0.378	1.50 (0.53–4.27)	0.446
Unilateral nerve sparing (vs None)	0.55 (0.17–1.82)	0.329	0.33 (0.09–1.21)	0.094
Bilateral nerve sparing (vs None)	0.62 (0.24–1.58)	0.314	0.34 (0.12–0.99)	0.048
Prostate volume (per mL)	0.99 (0.96–1.03)	0.713	1.00 (0.97–1.04)	0.984
Biopsy Grade Group (per unit)	1.05 (0.70–1.58)	0.799	0.97 (0.65–1.46)	0.884
Clinical T stage (ordinal)	0.89 (0.65–1.20)	0.440	0.81 (0.59–1.11)	0.188

B. Primary analysis: Overall positive surgical margin in the full 250-patient cohort (44 events)

Variable	Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p
ePLND-first (vs Prostatectomy-first)	0.69 (0.36–1.34)	0.275	0.62 (0.31–1.23)	0.170
Surgeon prior cases (per case)	1.00 (1.00–1.00)	0.323	1.00 (1.00–1.00)	0.602
Retzius-sparing (vs Standard)	1.98 (0.94–4.15)	0.071	1.94 (0.91–4.17)	0.088
Unilateral nerve sparing (vs None)	1.03 (0.50–2.14)	0.938	0.75 (0.30–1.86)	0.528
Bilateral nerve sparing (vs None)	0.69 (0.36–1.34)	0.275	0.58 (0.25–1.35)	0.206
Prostate volume (per mL)	1.01 (0.98–1.03)	0.539	1.01 (0.98–1.04)	0.496
Biopsy Grade Group (per unit)	1.13 (0.85–1.50)	0.409	1.09 (0.80–1.47)	0.591
Clinical T stage (ordinal)	0.98 (0.80–1.21)	0.854	0.93 (0.75–1.16)	0.537

C. Pre-specified nerve-sparing subgroup analysis: Apical positive surgical margin (n = 188; 10 events)

Variable	Univariable		Multivariable (Firth)	
	OR (95% CI)	P	OR (95% CI)	P
ePLND-first (vs Prostatectomy-first)	0.17 (0.03–1.00)	0.050	0.19 (0.04–0.97)	0.046
Surgeon prior cases (per case)	1.00 (1.00–1.00)	0.052	1.00 (1.00–1.00)	0.079
Retzius-sparing (vs Standard)	1.28 (0.29–5.59)	0.745	1.14 (0.27–4.84)	0.861
Bilateral vs Unilateral nerve sparing	1.21 (0.33–4.49)	0.779	0.89 (0.24–3.27)	0.865
Prostate volume (per mL)	1.04 (0.99–1.09)	0.143	1.05 (0.99–1.10)	0.094
Biopsy Grade Group (per unit)	0.69 (0.38–1.27)	0.236	0.66 (0.36–1.21)	0.182
Clinical T stage (ordinal)	1.00 (0.68–1.47)	0.985	0.94 (0.64–1.37)	0.736

D. Pre-specified nerve-sparing subgroup analysis: Overall positive surgical margin (n = 188; 30 events)

Variable	Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p
ePLND-first (vs Prostatectomy-first)	0.45 (0.19–1.05)	0.063	0.46 (0.19–1.10)	0.081
Surgeon prior cases (per case)	1.00 (1.00–1.00)	0.193	1.00 (1.00–1.00)	0.350
Retzius-sparing (vs Standard)	2.66 (1.11–6.36)	0.028	2.60 (1.05–6.45)	0.040
Bilateral vs Unilateral nerve sparing	0.80 (0.36–1.78)	0.587	0.72 (0.31–1.69)	0.454
Prostate volume (per mL)	1.02 (0.99–1.05)	0.296	1.01 (0.98–1.05)	0.461
Biopsy Grade Group (per unit)	1.00 (0.69–1.44)	0.986	0.94 (0.64–1.38)	0.749
Clinical T stage (ordinal)	1.05 (0.82–1.34)	0.692	0.99 (0.76–1.27)	0.922

Abbreviations: CI, confidence interval; ePLND, extended pelvic lymph node dissection; OR, odds ratio; PSM, positive surgical margin. Panels A and B report the primary analyses estimated on the full 250-patient cohort (19 apical and 44 overall PSM events).

Panels C and D report pre-specified subgroup analyses estimated on the 188 patients undergoing any form of nerve-sparing surgery (10 apical and 30 overall PSM events). The univariable column reports each variable's unadjusted association with the outcome. The multivariable column reports adjusted estimates from a single model in which all seven pre-specified covariates were entered simultaneously. In each panel, the apical PSM model used Firth penalised logistic regression because of sparse events; the overall PSM model used standard logistic regression. Bold indicates $p < 0.05$.

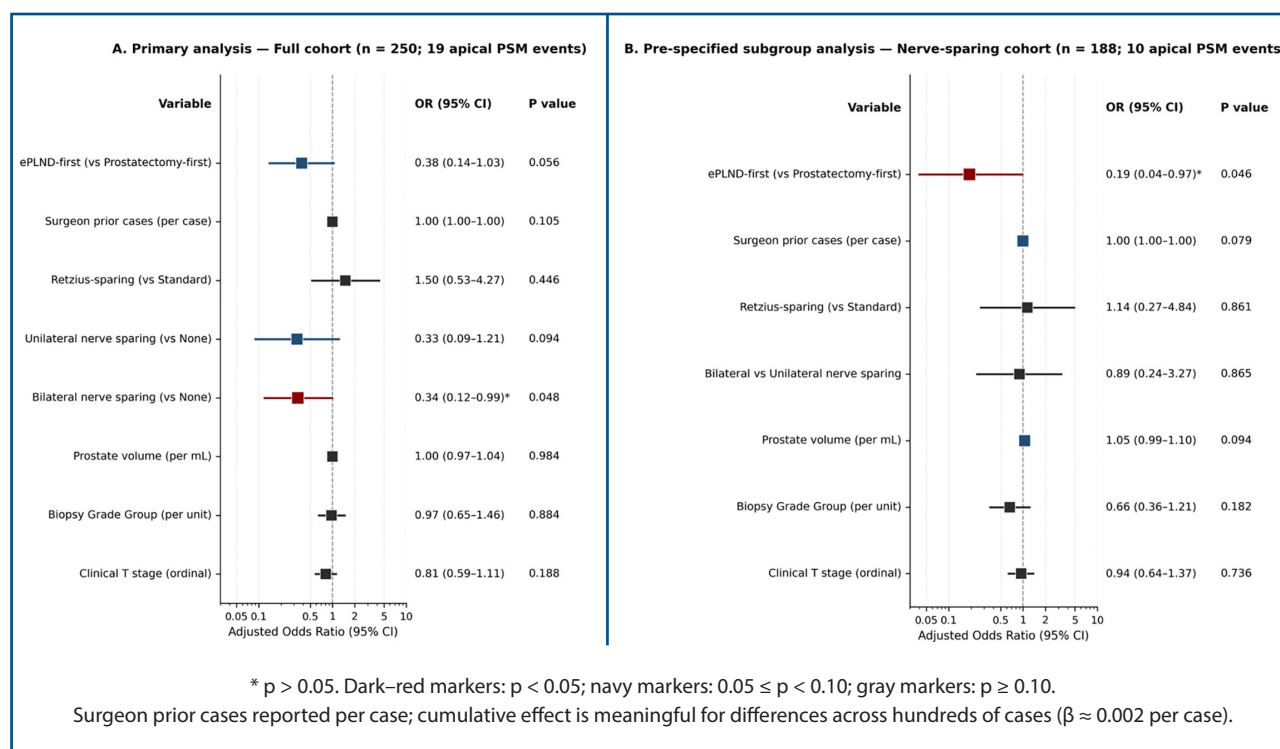


Figure 2. Forest plot of multivariable regression analyses for variables associated with apical positive surgical margin. (A) Primary analysis in the full 250-patient cohort (19 apical PSM events) with nerve-sparing intent coded as a 3-level categorical variable (none, unilateral, bilateral; none as reference). (B) Pre-specified subgroup analysis in the 188 patients undergoing any form of nerve-sparing surgery (10 apical PSM events) with nerve sparing coded as bilateral versus unilateral. Square markers represent adjusted odds ratio point estimates; horizontal bars denote 95% confidence intervals. The vertical reference line indicates an odds ratio of 1.0. Dark-red markers: $p < 0.05$; navy markers: $0.05 \leq p < 0.10$; gray markers: $p \geq 0.10$. Both analyses used Firth penalised maximum likelihood estimation.

Overall Positive Surgical Margins

Overall PSM was numerically lower in the ePLND-first group, but the difference was imprecise. Overall PSM occurred in 18 of 121 patients (14.9%; 95% CI 9.6% to 22.3%) in the ePLND-first group and 26 of 129 (20.2%; 95% CI 14.1% to 27.9%) in the prostatectomy-first group ($p = 0.320$). The absolute difference was -5.3 percentage points (95% CI -14.6% to 4.3%).

In the primary multivariable analysis of the full 250-patient cohort, ePLND-first sequencing was directionally associated with lower overall PSM but did not reach statistical significance (adjusted OR 0.62; 95% CI 0.31 to 1.23; $p = 0.170$; Table 2B). Retzius-sparing approach was associated with borderline higher overall PSM (adjusted OR 1.94; 95% CI 0.91 to 4.17; $p = 0.088$). In the pre-specified nerve-sparing subgroup, ePLND-first sequencing showed a similar directional association (adjusted OR 0.46; 95% CI 0.19 to 1.10; $p = 0.081$; Table 2D), and Retzius-sparing was significantly associated with higher overall PSM (adjusted OR 2.60; 95% CI 1.05 to 6.45; $p = 0.040$). Site-specific PSM rates outside the apex were low and similar between groups (Figure 3).

Perioperative Outcomes

Operative efficiency favoured the ePLND-first sequence (Table 3). Mean total operative time was 195.2 $\pm$ 27.4 minutes in the ePLND-first group and 202.9 $\pm$ 28.2 minutes in the prostatectomy-first group, a mean difference of -7.7 minutes (95% CI -14.7 to -0.8 ; $p = 0.029$). Console time was also shorter (153.4 vs 161.4 minutes; $p = 0.024$). The ePLND component itself took less time when performed first (42.3 $\pm$ 9.3 vs 46.5 $\pm$ 9.2 minutes; $p < 0.001$).

Estimated blood loss, length of stay, and lymph node yield were similar between groups. Catheter duration differed by 0.4 days (8.5 $\pm$ 1.3 vs 8.1 $\pm$ 1.4 days; $p = 0.045$), a finding of marginal statistical significance and doubtful clinical importance.

Complications and Biochemical Recurrence

Complication rates were similar. Major complications within 90 days occurred in 4 of 121 patients (3.3%) in the ePLND-first group and 6 of 129 (4.7%) in the prostatectomy-first group ($p = 0.750$). Symptomatic lymphocele rates were nearly identical (7.4% vs 7.0%; $p = 1.000$), and 90-day readmission rates did not differ significantly (9.1% vs 5.4%; $p = 0.330$).

Biochemical recurrence was less frequent in the ePLND-first group in unadjusted analysis: 2 of 121 patients (1.7%; 95% CI 0.5% to 5.8%) versus 12 of 129 (9.3%; 95% CI 5.4% to 15.6%; $p = 0.011$). Mean follow-up was similar between groups (28.6 $\pm$ 9.6 vs 27.1 $\pm$ 10.2 months; $p = 0.219$).

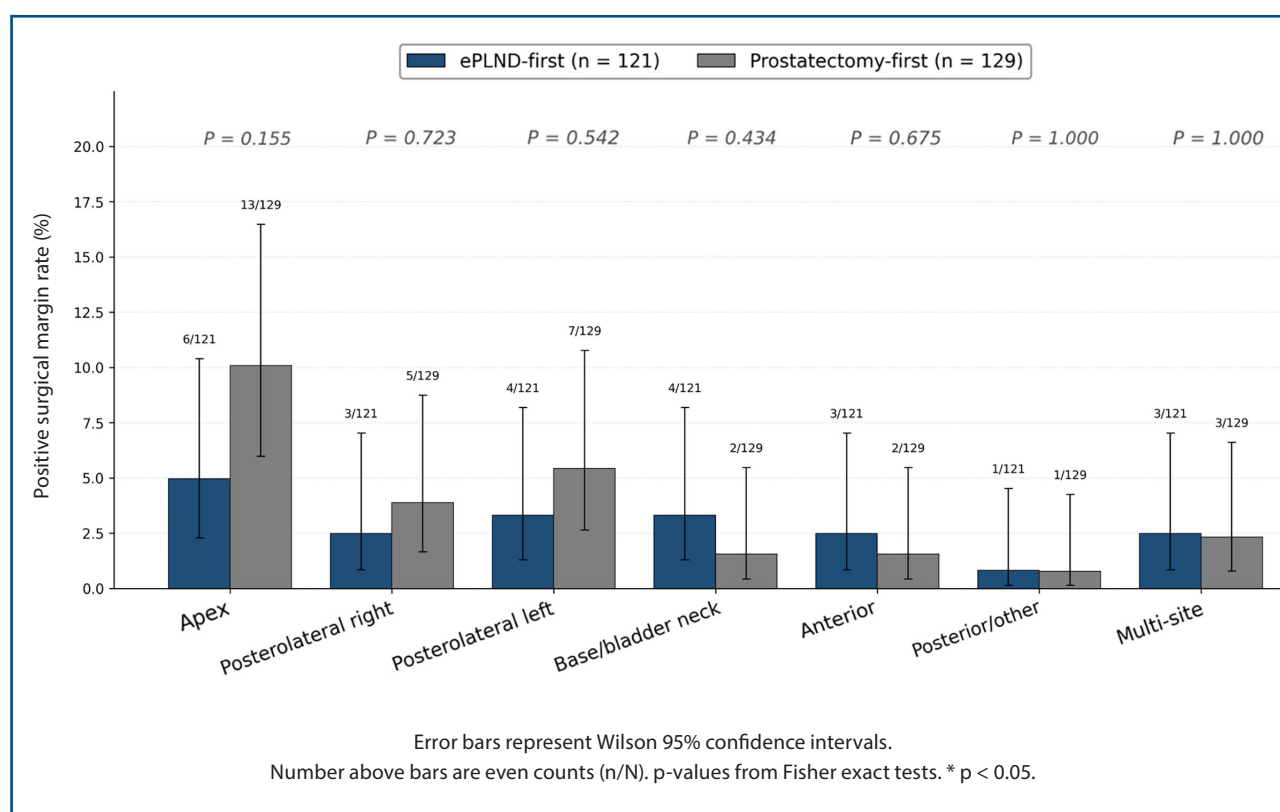


Figure 3. Site-specific positive surgical margin rates by surgical sequence group. Bars represent the proportion of patients with positive surgical margins at each anatomical site; error bars denote Wilson score 95% confidence intervals. Numbers above bars indicate event counts. The apex was the most common site of margin positivity in both groups, with a numerically lower rate in the ePLND-first group (5.0% vs 10.1%). Fisher's exact test P values: apex 0.155, posterolateral right 0.723, posterolateral left 0.542, base/bladder neck 0.434, anterior 0.675, posterior other 1,000, multi-site 1,000.

Table 3. Perioperative and Oncological Outcomes

Outcome	ePLND-first (n = 121)	Prostatectomy-first (n = 129)	p
Total operative time, min, mean $\pm$ SD	195.2 $\pm$ 27.4	202.9 $\pm$ 28.2	0.029
Console time, min, mean $\pm$ SD	153.4 $\pm$ 27.4	161.4 $\pm$ 28.2	0.024
ePLND time, min, mean $\pm$ SD	42.3 $\pm$ 9.3	46.5 $\pm$ 9.2	<0.001
EBL, mL, median (IQR)	161 (108–216)	166 (115–226)	0.345
LN yield, median (IQR)	22 (19–25)	22 (19–24)	0.363
LOS, days, median (IQR)	2 (2–3)	2 (2–3)	0.354
Catheter days, mean $\pm$ SD	8.5 $\pm$ 1.3	8.1 $\pm$ 1.4	0.045
Apical PSM, n (%)	6 (5.0)	13 (10.1)	0.155
Overall PSM, n (%)	18 (14.9)	26 (20.2)	0.320
EPE, n (%)	47 (38.8)	52 (40.3)	0.897
SVI, n (%)	14 (11.6)	17 (13.2)	0.848
Major complications, n (%)	4 (3.3)	6 (4.7)	0.750
Symptomatic lymphocele, n (%)	9 (7.4)	9 (7.0)	1.000
90-day readmission, n (%)	11 (9.1)	7 (5.4)	0.330
BCR, n (%)	2 (1.7)	12 (9.3)	0.011
Follow-up, months, mean $\pm$ SD	28.6 $\pm$ 9.6	27.1 $\pm$ 10.2	0.219

Abbreviations: BCR, biochemical recurrence; EBL, estimated blood loss; EPE, extraprostatic extension; ePLND, extended pelvic lymph node dissection; IQR, interquartile range; LN, lymph node; LOS, length of stay; PSM, positive surgical margin; SD, standard deviation; SVI, seminal vesicle invasion. Bold indicates $p < 0.05$.

DISCUSSION

In this cohort, performing ePLND before prostatectomy was associated with directionally lower adjusted odds of apical PSM during RARP (adjusted OR 0.38; 95% CI 0.14 to 1.03; $p = 0.056$ in the full 250-patient cohort), with a stronger signal in the pre-specified nerve-sparing subgroup (adjusted OR 0.19; 95% CI 0.04 to 0.97; $p = 0.046$; Fisher's exact 1/86 vs 9/102, $p = 0.023$). The ePLND-first sequence was also associated with shorter operative time, without an evident penalty in lymph node yield or perioperative safety.

Williams and colleagues described the ePLND-first sequence as a technical approach that clears the pelvic sidewall before the prostatectomy begins (8). Our findings extend that description by providing an adjusted comparison of sequence and apical margin status. Jarzowski and colleagues reported a combined laparoscopic approach to radical prostatectomy and lymphadenectomy, but did not compare sequence directly (12). The present study therefore addresses a specific question that, to our knowledge, had not previously been examined with multivariable adjustment.

The most plausible explanation is anatomical. Apical dissection is one of the most exacting steps in robotic prostatectomy (11). Prior technical modifications that improve exposure of the apical plane have been associated with lower apical margin rates. These include the puboprostatic open-collar technique and synchronous retro-apical urethral transection (9,10). ePLND-first sequencing may operate through the same principle. By removing the nodal packets before apical dissection, the surgeon may enter the deepest part of the operation with a cleaner field and less tissue crowding.

The association between operative sequence and apical PSM appeared to be concentrated in patients undergoing nerve-sparing surgery. Among the 188 patients with documented nerve-sparing intent, apical PSM occurred in 1

of 86 ePLND-first cases (1.2%) and 9 of 102 prostatectomy-first cases (8.8%; Fisher's exact $p = 0.023$). Among the 62 patients without nerve-sparing intent, apical PSM rates were nearly identical between sequence groups (5 of 35 versus 4 of 27; 14.3% versus 14.8%). This pattern is consistent with the proposed anatomical mechanism: in nerve-sparing cases, apical dissection follows a delicate plane where exposure quality may be most influential, whereas in non-nerve-sparing cases the apical dissection plane is intentionally wider for margin clearance and may be less dependent on pelvic sidewall exposure. The pattern may also reflect random variation given the sparse event count. Within the primary multivariable model, bilateral nerve sparing relative to no nerve sparing was itself independently associated with lower apical PSM (adjusted OR 0.34; 95% CI 0.12 to 0.99; $p = 0.048$; Table 2A). This pattern reflects disease selection in nerve-sparing cases: compared with patients undergoing nerve-sparing surgery, the non-nerve-sparing subgroup had a higher proportion of biopsy Grade Group ≥ 4 disease (45.2% vs 28.2%; $p = 0.020$), which explains part of the higher absolute apical PSM rate in non-nerve-sparing patients (14.5% vs 5.3%; Fisher's exact $p = 0.026$). The multivariable model adjusts for biopsy Grade Group, clinical T stage, prostate volume, and surgeon cumulative experience, but residual confounding from unmeasured anatomic features that may inform the nerve-sparing decision (for example, MRI tumour location, capsular contact, or apical lesion proximity) cannot be excluded.

Surgical margin length carries independent prognostic weight for biochemical recurrence, with a recently described 3.5 mm cut-off from a cohort at our institution (15). Among the 19 patients with an apical positive margin in the present study, the mean apical margin length was similar between sequence groups (2.85 mm in the ePLND-first group versus 2.87 mm in the prostatectomy-first group); margin length above the 3.5 mm threshold was present in 1 of 6 apical PSMs in the ePLND-first group and 4 of 13 in the prostatectomy-first group. These data suggest that ePLND-first sequencing was associated with a lower incidence of apical PSM rather than with shorter margin length conditional on margin presence.

Not every outcome moved in the same direction. Overall PSM was numerically lower in the ePLND-first group, but the confidence interval was wide and included no clear difference. We therefore interpret the main signal as site-specific rather than global. The operative time difference favored ePLND-first, but the magnitude was modest. That finding is supportive, not central. In our data, Retzius-sparing RARP was associated with borderline higher overall PSM in the primary full-cohort analysis (adjusted OR 1.94; 95% CI 0.91 to 4.17; $p = 0.088$) and with significantly higher overall PSM within the nerve-sparing subgroup (adjusted OR 2.60; 95% CI 1.05 to 6.45; $p = 0.040$). The association did not extend to apical PSM specifically (adjusted OR 1.14; 95% CI 0.27 to 4.84). One anatomical interpretation is that the Retzius-sparing approach modifies the anterior and basal dissection planes while leaving the apical plane comparatively less perturbed, potentially shifting margin risk to non-apical sites; this interpretation is speculative and not directly tested by the present data. Published comparative evidence on margin outcomes with Retzius-sparing surgery remains mixed, and current systematic review data have not resolved the issue (16).

The ePLND component itself can be performed using different technical approaches, including antegrade and retrograde sequences of nodal packet dissection. In the present cohort the institutional standard approach was used across all five surgeons, and technique-level variation within ePLND was not analysed. Differences in ePLND technique may modify the operative time advantage observed in the ePLND-first group.

The lower BCR rate in the ePLND-first group should be interpreted with several reservations. The comparison was unadjusted; median follow-up of 26 months is short for definitive recurrence ascertainment; the distributions of pathological T stage, Grade Group, and overall PSM did not differ markedly between sequence groups; and the absolute number of events was small (2 events in the ePLND-first group versus 12 in the prostatectomy-first group). Plausible explanations include mediation through reduced apical PSM, chance aggregation given the sparse event count, or unmeasured biological factors. We do not infer a direct causal relationship between operative sequence and biochemical control.

This study has limitations. Operative sequence was determined by surgeon preference rather than randomisation, so residual confounding cannot be excluded; we adjusted for cumulative surgeon experience and ran a sensitivity analysis substituting NCCN risk group for clinical T stage, but unmeasured differences between groups may persist. Among measured baseline variables, clinical T stage distribution showed a borderline imbalance, with more locally advanced disease in the prostatectomy-first group (Table 1; overall $p = 0.055$); the multivariable model included clinical T stage as an ordinal covariate (Table 2A: adjusted OR 0.81; 95% CI 0.59 to 1.11; $p = 0.188$), and the sensitivity analysis substituting NCCN risk group for clinical T stage yielded a directionally consistent estimate (adjusted OR 0.44; 95% CI 0.17 to 1.16; $p = 0.098$), so the estimated effect of operative sequence was not driven by this imbalance. Apical PSM events were sparse, with 19 events in the full cohort and 10 in the nerve-sparing subgroup, yielding events-per-variable ratios of 2.7 and 1.4 respectively; Firth penalisation mitigates small-sample bias but does not eliminate wide confidence intervals, and the adjusted estimates are exploratory. Sequence assignment varied across the five participating surgeons (Supplementary Table S1), and surgeon-level clustering of operative practice could not be fully separated from the sequence-effect estimate. The nerve-sparing subgroup analysis examines the population in which our mechanistic hypothesis applies most directly; the weaker signal in the full cohort reflects attenuation by patients without nerve-sparing intent, in whom the apical dissection plane is intentionally wider. The study is retrospective and confined to a single centre; the 40 patients excluded for incomplete data (30 without follow-up, 10 without preoperative biopsy) reflect absence of essential outcome or covariate variables rather than selective dropout.

CONCLUSION

Performing extended pelvic lymph node dissection before prostatectomy was associated with directionally lower apical positive surgical margin rates in the full 250-patient cohort and significantly lower rates in the pre-specified nerve-sparing subgroup. The signal is consistent with the anatomical hypothesis that improved pelvic exposure facilitates the delicate apical dissection required for neurovascular bundle preservation. Where ePLND is planned during nerve-sparing radical prostatectomy, performing the lymph node dissection first is a practical operative strategy with no evident perioperative penalty.

Supplementary Table S1. Surgeon-level distribution of operative sequence and apical positive surgical margin events.

Surgeon	ePLND-first, n (apical PSM events)	Prostatectomy-first, n (apical PSM events)	Total cases
Surgeon 1	37 (1)	26 (1)	63
Surgeon 2	22 (1)	30 (2)	52
Surgeon 3	32 (1)	28 (1)	60
Surgeon 4	22 (3)	34 (6)	56
Surgeon 5	8 (0)	11 (3)	19
Total	121 (6)	129 (13)	250

Apical PSM event counts are shown in parentheses. No surgeon used exclusively one sequence.

Abbreviations

BCR, biochemical recurrence; BMI, body mass index; CCI, Charlson comorbidity index; CI, confidence interval; EBL, estimated blood loss; ePLND, extended pelvic lymph node dissection; IQR, interquartile range; ISUP, International Society of Urological Pathology; NCCN, National Comprehensive Cancer Network; OR, odds ratio; PSA, prostate-specific antigen; PSM, positive surgical margin; RARP, robot-assisted radical prostatectomy; SD, standard deviation.

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Informed Consent Statement: The requirement for informed consent was waived because of the retrospective design and the use of de-identified data.

Data Availability Statement: The data presented in this study are available from the corresponding author on reasonable request.

Ethical Approval: The study was conducted in accordance with the Declaration of Helsinki and approved by the Scientific Research Ethic Committee of Umraniye Training and Research Hospital, İstanbul, Türkiye (IRB-2025-470, Date: December 18, 2025).

Author Contributions

Conceptualization: A.İ., H.S.G., N.M.Ş.; Methodology: A.İ., H.S.G., A.T.; Data curation: A.İ., B.Ö., M.E.T., S.S.; Formal analysis: A.İ., H.S.G., A.E.; Investigation: A.İ., H.S.G., C.E.Y.; Writing - original draft: A.İ., N.M.Ş.; Writing - review and editing: R.S., E.V.K., H.S.G., F.Y.S., M.B. All authors read and approved the manuscript.

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