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Original Article

Robot-assisted radical prostatectomy reduces biochemical recurrence risk and improves urinary continence recovery compared with laparoscopic approach in high-risk localized prostate cancer after neoadjuvant therapy: a real-world propensity score-matched analysis

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Abstract: This retrospective study compared the oncological and functional outcomes of robot-assisted radical prostatectomy (RARP) versus laparoscopic radical prostatectomy (LRP) in 523 patients with high-risk localized prostate cancer (HR-LPC) receiving neoadjuvant therapy (NAT). After 1:1 propensity score matching (PSM), 218 patients per group were included. Multivariate Cox regression confirmed that RARP was independently associated with a significantly lower biochemical recurrence (BCR) risk compared with LRP (after PSM: HR=0.626, 95% CI 0.471-0.833, P=0.001), a finding that remained robust across all sensitivity analyses. Subgroup analyses identified significant BCR protection by RARP in patients with preoperative PSA ≥20 ng/mL (P=0.001), pathological T stage pT2-pT3a (P=0.002), biopsy ISUP grade 4 (P=0.005), negative lymph nodes (P<0.001), ADT monotherapy (P=0.007), and age ≥65 years (P=0.002), with no significant heterogeneity across subgroups (all P-interaction >0.05). RARP also demonstrated perioperative advantages over LRP, including less intraoperative blood loss (median 239.5 vs. 399.5 mL, P<0.001), lower transfusion rate (4.59% vs. 12.39%, P=0.003), and shorter hospital stay (median 7 vs. 9 days, P<0.001), while pathological outcomes were comparable between groups (all P>0.05). Regarding functional recovery, RARP achieved significantly higher urinary continence rates at postoperative months 1 (33.5% vs. 21.1%, P=0.005), 3 (53.2% vs. 38.5%, P=0.003), 6 (74.8% vs. 60.6%, P=0.002), and 12 (84.9% vs. 73.9%, P=0.006), with a median continence recovery time of 3 months versus 6 months in the LRP group (P<0.001). These findings suggest that RARP offers meaningful oncological and functional advantages over LRP in HR-LPC patients undergoing NAT.

Keywords: Prostate cancer, neoadjuvant therapy, robot-assisted radical prostatectomy: laparoscopic radical prostatectomy, propensity score matching, biochemical recurrence-free survival, urinary continence recovery

Introduction

Prostate cancer (PC), among the most prevalent male-specific malignancies worldwide, exhibits a rising global incidence and mortality. According to the latest global cancer statistics, PC was newly diagnosed in about 1.46 million new cases globally in 2022, with nearly 390,000 deaths, ranking second in the incidence of male malignancies [1]. China has also reported an obviously increasing PC incidence in recent years, closely related to the aging population, lifestyle changes, and the increasingly popularized prostate-specific antigen (PSA) screening [2]. In clinical practice, high-risk localized prostate cancer (HR-LPC) is usually defined according to D'Amico risk stratification or international guidelines, which mainly include PSA >20 ng/mL, Gleason score ≥8, or clinical stage ≥T2c [3, 4]. In such patients, the

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tumor presents with a more aggressive biological behavior that significantly increases the risk of local progression and distant metastasis, with a high incidence of postoperative biochemical recurrence (BCR) even after radical prostatectomy (RP) [5]. BCR, defined as two consecutive postoperative serum PSA levels ≥0.2 ng/mL, is not merely a laboratory finding but a clinically meaningful harbinger of disease progression. Studies have demonstrated that BCR is independently associated with a substantially elevated risk of distant metastasis and cancer-specific mortality, with the interval from BCR to metastasis averaging 8 years in high-risk patients [5]. Moreover, patients experiencing early BCR (within 2 years of surgery) or with rapid PSA doubling time (<3 months) face particularly poor oncological prognoses. Therefore, reducing BCR risk remains one of the most critical goals in the surgical management of HR-LPC, and the choice of surgical technique may play an important independent role in achieving this objective.

Against this background, neoadjuvant therapy (NAT) has gradually become an important research direction in perioperative HR-LPC management. Androgen deprivation therapy (ADT), the core of neoadjuvant endocrine therapy (NET), works theoretically by decreasing tumor load, reducing tumor volume, and improving surgical resection conditions by inhibiting the androgen receptor (AR) signaling [6]. With the emergence of novel AR pathway inhibitors, NAT strategies combining drugs such as Abiraterone, Enzalutamide, and Apatamide with ADT have attracted growing clinical interest [7]. Recent evidence has demonstrated the ability of neoadjuvant intensive endocrine therapy to increase the postoperative organ-confined proportions, reduce surgical margin positivity rates, and significantly elevate pathologic response rates [8]. For example, the randomized phase II trial ARNEO showed that neoadjuvant Degarelix with Apalutamide could obtain better pathological responses than ADT alone [9]. However, there remains a dearth of high-quality evidence regarding whether NAT can improve long-term oncological outcomes, and the optimal timing and surgical approach after NAT remains a subject of intense debate [10]. Critically, NAT-induced periprostatic tissue fibrosis, inflammatory changes, and increased pelvic adhesion not only blur anatomical planes but also substantially elevate surgical difficulty. These local changes may specifically compromise the quality of key operative steps, including neurovascular bundle preservation (NVBP), precise apical dissection, and urethrovesical anastomosis, which are directly linked to both oncological clearance and postoperative functional recovery. Urinary incontinence, one of the most debilitating complications following radical prostatectomy, significantly impairs patients' quality of life and is reported to affect up to 20-40% of patients at 12 months post-surgery [11]. Given that NAT may further compromise the integrity of the sphincteric complex and surrounding supportive structures, the choice of surgical technique in this setting may have amplified implications for continence recovery outcomes.

In terms of surgical techniques, radical prostatectomy has undergone a technological evolution from open surgery to laparoscopic and then to robot-assisted. Compared with traditional open surgery, laparoscopic radical prostatectomy (LRP) excels in reducing surgical trauma and shortening recovery time; however, its two-dimensional vision and restricted equipment movement limit its applications in complex anatomical operations [11]. Robot-assisted radical prostatectomy (RARP) relies on three-dimensional (3D) high-definition visual field, tremor filtering, and the multi-degree-of-freedom mechanical arm system, which allows the operator to manipulate more precisely and stably in key steps such as prostate apex treatment, NVBP, and urethrovesical anastomosis [12]. A number of randomized controlled studies and meta-analyses have shown that RARP has some advantages over LRP in perioperative indices (e.g., blood loss, blood transfusion rate, hospitalization time) and early functional recovery, though with similar or marginally improved oncological outcomes [12, 13]. However, the vast majority of these studies were conducted in patients who did not receive NAT. The post-NAT surgical environment, characterized by distorted tissue planes, increased fibrosis, and heightened pelvic adhesion, may fundamentally alter the relative technical merits of these two approaches, potentially magnifying the precision-related advantages of the robotic platform in ways not observed in the standard surgical setting [14].

At present, comparative investigations into the surgical methods of HR-LPC patients after NAT

are rather limited. Most of the existing evidence is based on small-sample single-center retrospective studies with short follow-up duration, frequently involving fewer than 100 patients per group and median follow-up periods under 24 months, failing to comprehensively evaluate the impact of different surgical techniques on long-term oncological outcomes [14]. Additionally, given that surgical modality selection in real-world clinical practice is often influenced by factors like patient baseline characteristics, tumor load, and operator experience, traditional retrospective research is prone to selection bias. Through propensity score matching (PSM), the between-group difference in baseline data can be effectively balanced in observational studies, thus improving the reliability and credibility of comparison among different treatment groups [15].

In this context, the present study addresses a critical and underexplored clinical question by systematically comparing RARP and LRP in HR-LPC patients following NAT, using a large real-world cohort with rigorous PSM-based confounding control. Several features distinguish this study from existing literature and underscore its innovative value. First, to our knowledge, this represents one of the largest single-center real-world comparative analyses specifically focused on the post-NAT surgical setting, with 523 consecutive patients and a follow-up extending to 5 years. Second, beyond the primary oncological endpoint of BCR-free survival (BRFS), this study simultaneously evaluates urinary continence recovery as a key functional outcome, providing a more comprehensive assessment of treatment efficacy. Third, the robustness of the conclusions is rigorously validated through multiple sensitivity analyses and prespecified subgroup analyses, addressing the methodological limitations of prior studies. These efforts aim to provide a high-quality evidence base to guide individualized surgical decision-making in this challenging patient population, ultimately contributing to optimized comprehensive treatment strategies for HR-LPC patients undergoing NAT.

Methods and materials

Sample size calculation

BRFS, the primary endpoint of this study, was analyzed using the Cox's proportional hazards (PH) model. Hence, sample size computation was conducted by employing the Schoenfeld's formula, $d = \frac{(z_{\alpha/2} + z_{\beta})^2}{(\ln HR)^2}$, where d represents the number of required end-point events, HR stands for the expected hazard ratio (HR), Zα/2 indicates the standard normal distribution value corresponding to the two-tailed significance level α, and Zβ denotes the standard normal distribution value corresponding to the power. Referring to a multi-center study of post-NAT radical prostatectomy for high/very high risk PC patients (Nezasa et al. [16]), the BCR incidence was about 31.4%-40.7% at a median follow-up of 47 months, and the expected HR was around 0.70 according to the between-group difference. With two-tailed α=0.05 (Z=1.96) and power of 0.80 (1-β=0.80, Z=0.84) for substitution into the formula, the required number of end-point events was about 62. Based on a mean BCR rate of approximately 36% reported in the reference study, the total sample size required was estimated to be 172 cases. Factoring in a ~10% attrition rate, the final minimum sample size was approximately 190 cases. This study actually included 416 eligible patients. After PSM at a 1:1 ratio, 218 cases were included in each group, which met the power threshold (Figure S1).

Research participants

Consecutive HR-LPC patients (n=523) who underwent radical prostatectomy following NAT in Sir Run Run Shaw Hospital, affiliated with Zhejiang University School of Medicine from January 2019 to June 2025 were retrospectively included. Allocation was based on surgical techniques employed, which assigned patients to an RARP group and an LRP group. The Sir Run Run Shaw Hospital, affiliated with Zhejiang University School of Medicine Medical Ethics Committee has reviewed and approved the research protocol. The Helsinki Declaration [17] principles were followed throughout. This study was conducted as a retrospective observational study; therefore, treatment allocation was not randomized. The choice of surgical technique (RARP or LRP) was not assigned by the investigators but was determined through shared decision-making between the treating urologist, the patient, and their family members. Prior to surgery, all patients and their guardians were fully informed of the potential benefits, limitations, associated costs, and

possible complications of each surgical approach. The final treatment decision was made voluntarily based on the patient's and family's preferences, financial circumstances, and overall clinical condition. To minimize the selection bias inherent in this non-randomized design, propensity score matching (PSM) was employed to balance baseline characteristics between the two groups.

Patient selection criteria

Fulfilling all of the following requirements means study inclusion: Patients were eligible if all of the following criteria were met: male patients with histologically confirmed prostate adenocarcinoma via prostate biopsy; meeting the diagnostic criteria for HR-LPC (preoperative PSA >20 ng/mL, Gleason score ≥8 [ISUP grade ≥4], or clinical stage ≥cT2c); preoperative receipt of NET, including ADT monotherapy or ADT combined with novel ARTAs, for a minimum of 3 months prior to surgery; underwent either LRP or RARP as definitive surgical treatment; ECOG performance status of 0-1; and complete preoperative, intraoperative, pathological, and follow-up data available for endpoint evaluation.

Exclusion is based on the fulfillment of any of the conditions stated below: Patients were excluded if any of the following were present: distant metastasis at diagnosis (cM1), including bone or visceral metastasis; prior pelvic radiotherapy, HIFU, TURP, or previous prostate surgery; histological subtypes other than conventional prostate adenocarcinoma (e.g., neuroendocrine or small cell carcinoma); concurrent or prior malignancies within 5 years before enrollment; receipt of systemic anti-tumor treatments other than the specified NAT regimen prior to surgery; severe cardiopulmonary, hepatic, or renal dysfunction contraindicating major surgery; and missing key clinical or pathological data precluding primary endpoint assessment.

Treatment methods

All patients received NET preoperatively. The NAT included ADT monotherapy or ADT combined with novel ARTAs for intensive endocrine therapy. In ADT, gonadotropin-releasing hormone (GnRH) agonists or antagonists, including Leuprorelin, Goserelin, or Degarelix, were used. For some patients, novel ARTAs, like Abiraterone, Enzalutamide, or Apalutamide, were added on the basis of ADT. NAT duration was determined according to the clinical condition, typically lasting for 3-6 months or ≥6 months. Following NAT, all patients underwent either RARP or LRP, with the operations performed by experienced urological surgeons. The decision on NVBP (non-preservation, unilateral, or bilateral) was made comprehensively by integrating preoperative imaging evaluation and intraoperative conditions. Pelvic lymph node (LN) dissection (PLND), covering the scope of the obturator formamen and internal/external iliac LNs, was performed for clinically high-risk patients or those with imaging-evidenced higher risk of lymph node metastasis.

Clinical data collection

Patients' clinical data were collected retrospectively through the hospital electronic medical record system, including demographics, baseline tumor characteristics, NAT-associated data, operation-related data, perioperative outcomes, pathological findings, and follow-up data.

Demographics and basic clinical data: The data covered age, body mass index (BMI), Eastern Cooperative Oncology Group (ECOG) performance status score [18], American Society of Anesthesiologists (ASA) classification [19], as well as history of hypertension, diabetes, cardiovascular disease, and abdominal surgery.

Baseline tumor characteristics and NAT-associated data: This included preoperative PSA level, biopsy ISUP grading, perineural invasion (PNI), lymphovascular invasion (LVI), number of positive cores, positive biopsy core rate, clinical T staging (cT staging), clinical N staging (cN staging), NAT regimen, and NAT duration.

Operation-related and perioperative data: Information on surgical technique, NVBP approaches, operation time (OT), intraoperative blood loss (IBL), intraoperative blood transfusion, intraoperative conversion to open surgery, LN yield, duration of urinary catheterization, postoperative hospital stay, 30-day readmission rate, 30-day reoperation rate, and postoperative complications (POCs) was retrieved. POCs were evaluated according to the Clavien-Dindo grading system.

Pathological findings and follow-up data: The data collected included postoperative pathological T staging (ypT staging), pathological downstaging, surgical margin positivity rate, LN involvement, positive LN count, postoperative pathological Gleason score changes, postoperative PNI and LVI status, specimen weight, and pathologic response to NAT. Also, PSA testing data at each postoperative time point and urinary continence recovery-associated follow-up data were gathered.

Measurement methods

Laboratory tests: Pre- and post-operatively, serum PSA levels (in ng/mL) were measured by electrochemiluminescence immunoassay (ECLIA) using the UniCel DxI 800 full-automatic immunoassay analyzer manufactured by Beckman Coulter. BCR was defined as two consecutive serum PSA levels ≥0.2 ng/mL post-operation.

Imaging evaluation: Clinical evaluations were based on the results of pelvic multiparametric magnetic resonance imaging (mpMRI), computed tomography (CT), and whole-body bone scanning.

Pathological evaluation: All biopsy and surgical specimens were evaluated by pathologists with professional qualifications in urological pathology, and diagnosed and graded according to the World Health Organization (WHO) classification criteria of prostate tumors.

Functional score: Urinary continence was evaluated by the International Consultation on Incontinence Questionnaire Short-Form (ICIQ-SF) [20]. Urinary continence recovery was defined as no need to use safety pads (0 pad) post-operation. Follow-up evaluation was performed at postoperative months 1, 3, 6, and 12.

Outcome measures

Primary endpoint: Biochemical recurrence-free survival (BRFS), defined as the time interval from the date of surgery to the first confirmed BCR event (two consecutive serum PSA levels ≥0.2 ng/mL) or the date of last follow-up. PSA levels were measured at each scheduled post-operative follow-up visit.

Secondary endpoints: Perioperative outcomes (recorded intraoperatively and during the immediate postoperative period): operation time (OT), intraoperative blood loss (IBL), intraoperative blood transfusion rate, rate of intraoperative conversion to open surgery, postoperative complication rate (graded according to the Clavien-Dindo classification), duration of urinary catheterization, postoperative hospital stay, 30-day readmission rate, and 30-day reoperation rate.

Pathological outcomes (assessed from surgical specimens by qualified urological pathologists following surgery): postoperative pathological T staging (ypT staging), pathological downstaging rate (defined as ≥cT3 downstaged to ypT2), overall surgical margin positivity rate, lymph node (LN) involvement rate, positive LN count, postoperative pathological Gleason score variation, postoperative pathological PNI and LVI status, specimen weight, and pathologic response to NAT evaluated by Miller-Payne grading (MPG).

Functional outcomes (evaluated at postoperative months 1, 3, 6, and 12): urinary continence recovery rate, defined as no requirement for safety pads (0 pad) as assessed by the International Consultation on Incontinence Questionnaire Short-Form (ICIQ-SF), and time to urinary continence recovery.

Statistical analysis

All statistical analyses were performed with R (Version 4.5.1; mainly including MatchIt, survival, survminer, and mice) and SPSS (Version 27.0). Continuous variables, shown as the median and interquartile range (IQR), and categorical variables, expressed by frequencies and percentages (n, %), were examined by the Mann-Whitney U test and the χ^2 test or Fisher's exact test for inter-group differences. To reduce baseline difference-induced selection biases, the 1:1 nearest-neighbor PSM method was used with a caliper of width equal to 0.2. The matching quality was evaluated by the standardized mean difference (SMD). Concerning survival, BRFS was visualized by Kaplan-Meier (KM) curves and compared between groups with the Log-rank test. Furthermore, BCR-associated independent determinants were pinpointed by univariate and multivariate Cox's

PH regression models, with HRs and 95% confidence intervals (CIs) reported. The model's PH assumption was evaluated by the Schoenfeld residuals test, and multicollinearity was tested by the variance inflation factor (VIF) and the Spearman correlation matrix. Prespecified sensitivity analyses (full-cohort analysis, complete-case analysis, multiple imputation analysis, and restrictive analysis excluding patients with NAT <6 months), as well as subgroup analyses, were also carried out. All statistical tests were two-tailed and performed at a significance level of P<0.05.

Results

Baseline feature comparison

Before PSM, 523 patients were included, including 268 patients in the RARP group and 255 patients in the LRP group. The groups were statistically different in age composition (P= 0.023), NAT regimen (P=0.008), and positive biopsy core rate (P=0.012). Conversely, statistical significance was absent in BMI, ECOG score, ASA grading, preoperative PSA, biopsy ISUP grading, PNI, LVI, clinical T/N staging, NAT duration, hypertension/diabetes/cardiovascular disease history, abdominal surgery history, and NVBP approaches (P>0.05; **Table 1**).

Baseline characteristic comparison post-PSM

Following PSM, 218 patients were included in each group, totaling 436 cases. The baseline characteristics were well balanced across the groups, evidenced by non-significance in age, BMI, ECOG score, ASA grading, preoperative PSA, biopsy ISUP grading, PNI, LVI, clinical T/N staging, NAT regimen/duration, history of hypertension/diabetes/cardiovascular disease/abdominal surgery, NVBP approaches, and positive biopsy core rate (P>0.05; **Table 2**; **Figure 1**).

Comparison of perioperative outcomes

218 cases per group were included post-PSM. The RARP group showed lower rates of intraoperative blood transfusion and intraoperative conversion to open surgery than the LRP group, with less IBL, shorter urinary catheterization and postoperative hospitalization durations, but extended OT (all P<0.05). Non-significant between-group differences were identified regarding 30-day readmission, 30-day reoperation, complication classification, ≥II POCs, postoperative bleeding/hematoma, surgical wound/pelvic infection, anastomotic leakage/urinary fistule, lymphocyst, deep venous thrombosis/pulmonary embolism, or LN yield (all P>0.05; **Table 3**).

Pathological outcomes

The study cohorts were consistent in the overall pathological outcomes pre- and post-PSM. 218 cases per group were included after matching, with 436 cases in total. The groups did not differ statistically in pathological T staging, pathological downstaging, surgical margin positivity, LN involvement, postoperative Gleason score changes, postoperative pathological PNI/LVI, pathologic response to NAT, specimen weight, and positive LN count (all P>0.05), suggesting that the two surgical methods contributed to no significant differences in pathological outcomes (**Table 4**).

BRFS outcomes

KM survival analysis showed superior BRFS outcomes in RARP-treated patients compared to LRP-managed cases before and after PSM (both P<0.05). Before PSM, BRFS was longer in the RARP group versus the LRP group at each follow-up timeline from 1 to 5 years. This trend remained consistent following PSM, with extended BRFS observed in the RARP group at 1, 2, 3, 4, and 5 years compared to the LRP group (**Figure 2A-H**).

Factors influencing BCR by univariate Cox regression analysis

Before PSM, surgical approach (RARP vs. LRP, P=0.008), preoperative PSA level (P<0.001), biopsy ISUP grading (P<0.001), surgical margin positivity (P<0.001), lymph node involvement (P<0.001), postoperative pathological PNI (P<0.001), pathological T staging (ypT3b: P=0.010; ypT4: P<0.001), and Miller-Payne grading (MPG; Grade 3: P=0.015; Grade 4: P=0.028) of pathological response to NAT were identified by the univariate Cox regression analysis as significant correlates of the BCR risk (**Table 5**).

Following PSM, surgical technique (P<0.001), preoperative PSA (P=0.006), biopsy ISUP grad-

Table 1. Inter-group comparison before propensity score matching (n=523)

Variable	Total	LRP group (n=255)	RARP group (n=268)	Statistic	P
Age				χ^2=5.198	0.023
<65	194 (37.09%)	82 (32.16%)	112 (41.79%)		
≥65	329 (62.91%)	173 (67.84%)	156 (58.21%)		
BMI				χ^2=0.704	0.402
<24	220 (42.07%)	112 (43.92%)	108 (40.30%)		
≥24	303 (57.93%)	143 (56.08%)	160 (59.70%)		
ECOG score				χ^2=0.231	0.631
0	358 (68.45%)	172 (67.45%)	186 (69.40%)		
1	165 (31.55%)	83 (32.55%)	82 (30.60%)		
ASA grading				χ^2=0.065	0.798
I	194 (37.09%)	96 (37.65%)	98 (36.57%)		
II	329 (62.91%)	159 (62.35%)	170 (63.43%)		
Preoperative PSA				χ^2=3.553	0.059
<20	192 (36.71%)	104 (40.78%)	88 (32.84%)		
≥20	331 (63.29%)	151 (59.22%)	180 (67.16%)		
Biopsy ISUP grading				χ^2=3.585	0.058
Grade 4	210 (40.15%)	113 (44.31%)	97 (36.19%)		
Grade 5	313 (59.85%)	142 (55.69%)	171 (63.81%)		
PNI				χ^2=0.291	0.590
Yes	322 (61.57%)	154 (60.39%)	168 (62.69%)		
No	201 (38.43%)	101 (39.61%)	100 (37.31%)		
LVI				χ^2=0.155	0.693
Yes	156 (29.83%)	74 (29.02%)	82 (30.60%)		
No	367 (70.17%)	181 (70.98%)	186 (69.40%)		
Clinical T staging				χ^2=0.710	0.871
cT2	59 (11.28%)	31 (12.16%)	28 (10.45%)		
cT3a	280 (53.54%)	138 (54.12%)	142 (52.99%)		
cT3b	153 (29.25%)	71 (27.84%)	82 (30.60%)		
cT4	31 (5.93%)	15 (5.88%)	16 (5.97%)		
Clinical N staging				χ^2=0.002	0.961
cN0	425 (81.26%)	207 (81.18%)	218 (81.34%)		
cN1	98 (18.74%)	48 (18.82%)	50 (18.66%)		
NAT regimen				χ^2=7.019	0.008
ADT	252 (48.18%)	138 (54.12%)	114 (42.54%)		
ADT+novel endocrine therapy	271 (51.82%)	117 (45.88%)	154 (57.46%)		
NAT duration				χ^2=1.286	0.257
<6 months	144 (27.53%)	76 (29.80%)	68 (25.37%)		
≥6 months	379 (72.47%)	179 (70.20%)	200 (74.63%)		
Hypertension history				χ^2=0.629	0.428
Yes	280 (53.54%)	132 (51.76%)	148 (55.22%)		
No	243 (46.46%)	123 (48.24%)	120 (44.78%)		
Diabetes history				χ^2=0.028	0.866
Yes	100 (19.12%)	48 (18.82%)	52 (19.40%)		
No	423 (80.88%)	207 (81.18%)	216 (80.60%)		
Cardiovascular disease history				χ^2=0.001	0.973
Yes	70 (13.38%)	34 (13.33%)	36 (13.43%)		
No	453 (86.62%)	221 (86.67%)	232 (86.57%)		
History of abdominal operation				χ^2=1.975	0.160
Yes	94 (17.97%)	52 (20.39%)	42 (15.67%)		
No	429 (82.03%)	203 (79.61%)	226 (84.33%)		
Neurovascular bundle preservation approaches				χ^2=2.520	0.284
Non-preservation	306 (58.51%)	158 (61.96%)	148 (55.22%)		
Unilateral	132 (25.24%)	60 (23.53%)	72 (26.87%)		
Bilateral	85 (16.25%)	37 (14.51%)	48 (17.91%)		
Positive biopsy core rate (%)	63.64 [50.00, 81.53]	60.00 [50.00, 77.78]	66.67 [50.00, 83.33]	Z=2.512	0.012

Note: LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; ASA, American Society of Anesthesiologists; PSA, prostate-specific antigen; ISUP, International Society of Urological Pathology; PNI, perineural invasion; LVI, lymphovascular invasion; ADT, androgen deprivation therapy.

Table 2. Baseline feature comparison following PSM

Variable	Total	LRP group (n=218)	RARP group (n=218)	Statistic	P
Age				χ^2=0.361	0.548
<65	154 (35.32%)	74 (33.94%)	80 (36.70%)		
≥65	282 (64.68%)	144 (66.06%)	138 (63.30%)		
BMI				χ^2=0.085	0.771
<24	185 (42.43%)	94 (43.12%)	91 (41.74%)		
≥24	251 (57.57%)	124 (56.88%)	127 (58.26%)		
ECOG score				χ^2=0.094	0.760
0	293 (67.20%)	148 (67.89%)	145 (66.51%)		
1	143 (32.80%)	70 (32.11%)	73 (33.49%)		
ASA grading				χ^2=0.485	0.486
I	159 (36.47%)	83 (38.07%)	76 (34.86%)		
II	277 (63.53%)	135 (61.93%)	142 (65.14%)		
Preoperative PSA				χ^2=0.156	0.693
<20	166 (38.07%)	85 (38.99%)	81 (37.16%)		
≥20	270 (61.93%)	133 (61.01%)	137 (62.84%)		
Biopsy ISUP grading				χ^2=0.150	0.698
Grade 4	184 (42.20%)	94 (43.12%)	90 (41.28%)		
Grade 5	252 (57.80%)	124 (56.88%)	128 (58.72%)		
PNI				χ^2=1.648	0.199
Yes	271 (62.16%)	129 (59.17%)	142 (65.14%)		
No	165 (37.84%)	89 (40.83%)	76 (34.86%)		
LVI				χ^2=0.395	0.530
Yes	130 (29.82%)	62 (28.44%)	68 (31.19%)		
No	306 (70.18%)	156 (71.56%)	150 (68.81%)		
Clinical T staging				χ^2=0.291	0.962
cT2	45 (10.32%)	22 (10.09%)	23 (10.55%)		
cT3a	235 (53.90%)	116 (53.21%)	119 (54.59%)		
cT3b	129 (29.59%)	67 (30.73%)	62 (28.44%)		
cT4	27 (6.19%)	13 (5.96%)	14 (6.42%)		
Clinical N staging				χ^2=0.236	0.627
cN0	352 (80.73%)	178 (81.65%)	174 (79.82%)		
cN1	84 (19.27%)	40 (18.35%)	44 (20.18%)		
NAT regimen				χ^2=0.330	0.565
ADT	218 (50.00%)	112 (51.38%)	106 (48.62%)		
ADT+novel endocrine therapy	218 (50.00%)	106 (48.62%)	112 (51.38%)		
NAT duration				χ^2=0.395	0.530
<6 months	130 (29.82%)	68 (31.19%)	62 (28.44%)		
≥6 months	306 (70.18%)	150 (68.81%)	156 (71.56%)		
Hypertension history				χ^2=0.009	0.923
Yes	237 (54.36%)	119 (54.59%)	118 (54.13%)		
No	199 (45.64%)	99 (45.41%)	100 (45.87%)		
Diabetes history				χ^2=0.220	0.639
Yes	92 (21.10%)	44 (20.18%)	48 (22.02%)		
No	344 (78.90%)	174 (79.82%)	170 (77.98%)		
Cardiovascular disease history				χ^2=0.309	0.578
Yes	60 (13.76%)	28 (12.84%)	32 (14.68%)		
No	376 (86.24%)	190 (87.16%)	186 (85.32%)		
History of abdominal operation				χ^2=0.142	0.706
Yes	77 (17.66%)	40 (18.35%)	37 (16.97%)		
No	359 (82.34%)	178 (81.65%)	181 (83.03%)		
Neurovascular bundle preservation approaches				χ^2=2.165	0.339
Non-preservation	259 (59.40%)	136 (62.39%)	123 (56.42%)		
Unilateral	107 (24.54%)	52 (23.85%)	55 (25.23%)		
Bilateral	70 (16.06%)	30 (13.76%)	40 (18.35%)		
Positive biopsy core rate (%)	62.50 [50.00, 80.00]	60.00 [50.00, 77.78]	62.50 [50.00, 80.00]	Z=0.034	0.973

Note: PSM, propensity score matching; LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; ASA, American Society of Anesthesiologists; PSA, prostate-specific antigen; ISUP, International Society of Urological Pathology; PNI, perineural invasion; LVI, lymphovascular invasion; ADT, androgen deprivation therapy.

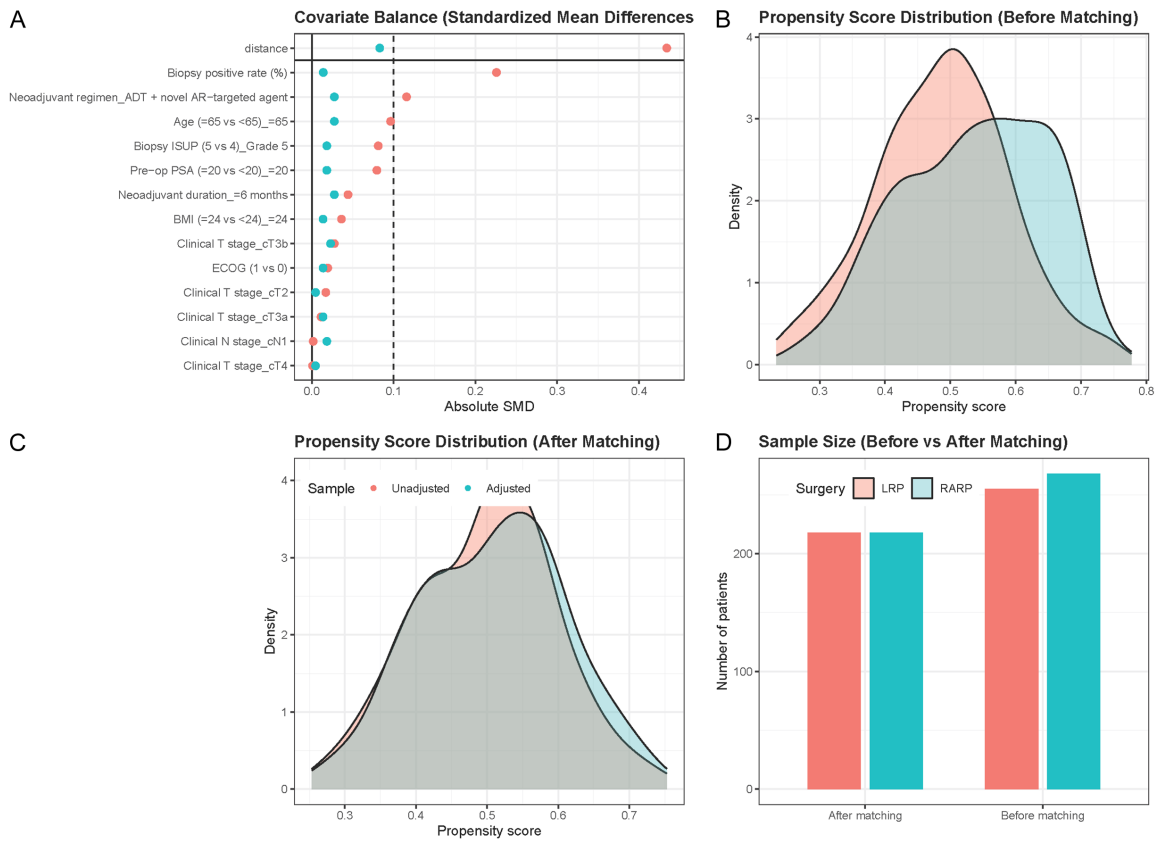


Figure 1. Covariate balance and sample distribution before and after PSM. A: SMD comparison of covariates before and after matching (Love plot), with the dotted line representing the SMD=0.1 threshold; B: Propensity score distributions of the two groups before matching; C: Propensity score distributions of the two groups after matching; D: Sample size changes of the two groups before and after matching. Note: PSM, propensity score matching; SMD, standardized mean difference; ADT, androgen deprivation therapy; AR, androgen receptor; ISUP, International Society of Urological Pathology; PSA, prostate-specific antigen; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy.

ing (P<0.001), surgical margin positivity (P< 0.001), lymph node involvement (P<0.001), postoperative pathological PNI (P=0.003), and pathological T staging (ypT3b: P=0.024; ypT4: P<0.001) remained to be significantly related to the risk of BCR (**Table 5**). Age, PNI, postoperative pathological LVI, NAT regimen/duration, clinical T staging, pathological T stage ypT3a, pathologic response to NAT (MPG score), and positive biopsy core rate did not show statistical significance before and after PSM (all P>0.05; **Table 5**).

Multivariate Cox regression model diagnostics

Before constructing the multivariate Cox's PH regression model, all candidate variables were tested for multicollinearity and PH assumption. In the VIF analysis, all variables exhibited a VIF of <5 (pre-PSM mean: ~1.07; post-PSM mean: ~1.05) and a tolerance of >0.85, suggesting no obvious multicollinearity among the included variables (**Figure 3B** and **3E**). According to the Spearman correlation matrix, the absolute values of the maximum correlation coefficients between variables before and after PSM were 0.165 and 0.146, respectively, with weak correlations between variables, further excluding serious collinearity issues (**Figure 3A** and **3D**).

The results of the PH assumption test (Schoenfeld residuals) indicated *P* values under 0.001 in the global test before and after PSM, suggesting the overall model's violation of the PH assumption. Further analysis revealed that preoperative PSA, pathological T staging, surgical margin positivity, and LN involvement did not meet the PH assumption before and after PSM (preoperative PSA: P<0.001 both before and after PSM; pathological T staging: P<0.001

Table 3. Between-group comparison of perioperative outcomes before and after PSM

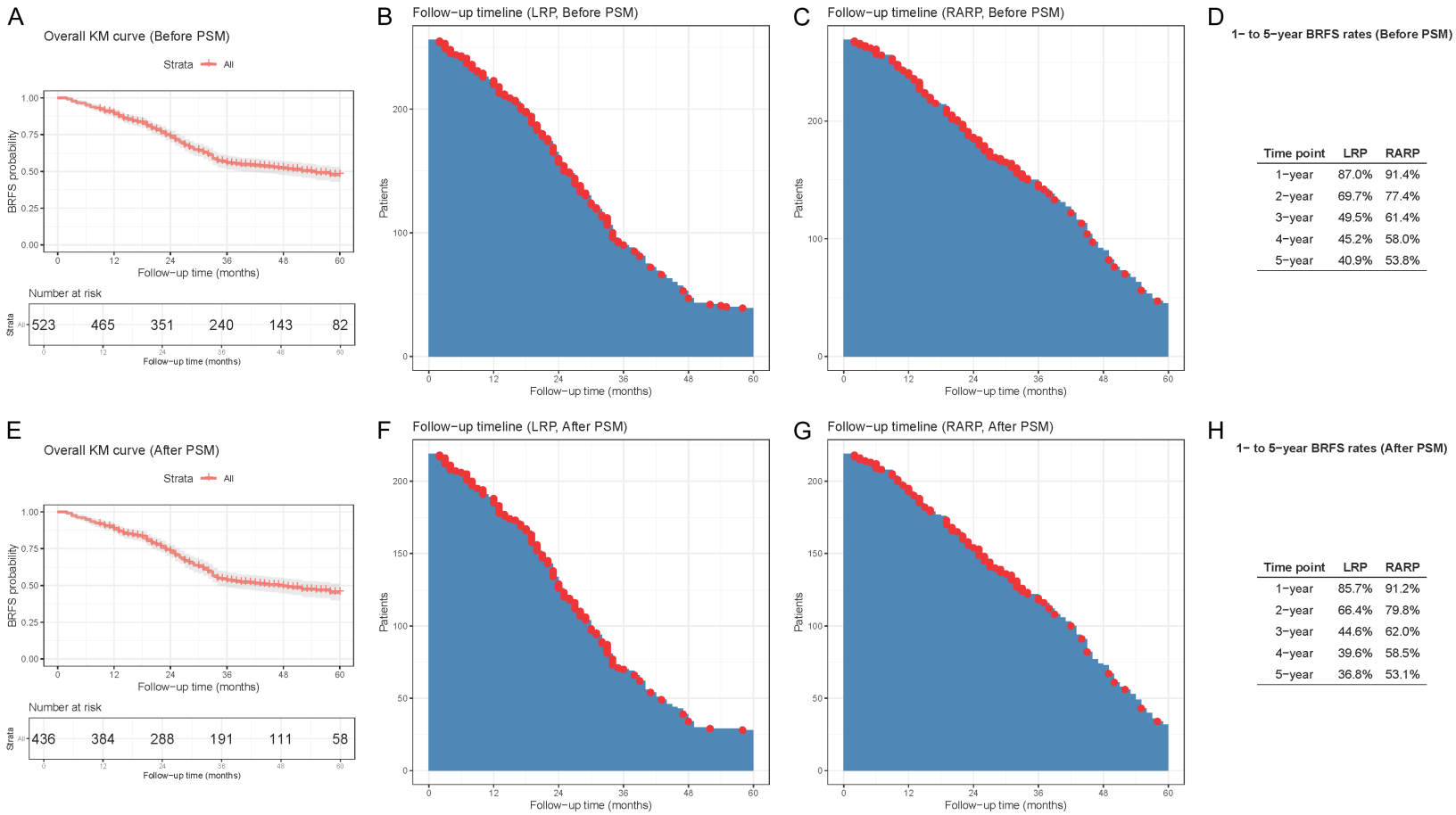
Variable	Before PSM			After PSM		
	LRP group (n=255)	RARP group (n=268)	Statistic/P	LRP group (n=218)	RARP group (n=218)	Statistic/P
Intraoperative blood transfusion			χ^2=11.048; P≤0.001			χ^2=8.535; P=0.003
Yes	32 (12.55%)	12 (4.48%)		27 (12.39%)	10 (4.59%)	
No	223 (87.45%)	256 (95.52%)		191 (87.61%)	208 (95.41%)	
Intraoperative conversion to open surgery			χ^2=4.382; P=0.036			χ^2=4.084; P=0.043
Yes	8 (3.14%)	1 (0.37%)		8 (3.67%)	1 (0.46%)	
No	247 (96.86%)	267 (99.63%)		210 (96.33%)	217 (99.54%)	
30-day readmission			χ^2=2.362; P=0.124			χ^2=1.606; P=0.205
Yes	22 (8.63%)	14 (5.22%)		20 (9.17%)	13 (5.96%)	
No	233 (91.37%)	254 (94.78%)		198 (90.83%)	205 (94.04%)	
30-day reoperation			χ^2=0.405; P=0.525			χ^2=0.714; P=0.398
Yes	8 (3.14%)	6 (2.24%)		8 (3.67%)	5 (2.29%)	
No	247 (96.86%)	262 (97.76%)		210 (96.33%)	213 (97.71%)	
Clavien-Dindo classification of complications			χ^2=4.028; P=0.133			χ^2=2.760; P=0.252
No	174 (68.24%)	200 (74.63%)		153 (70.18%)	159 (72.94%)	
I	28 (10.98%)	30 (11.19%)		21 (9.63%)	27 (12.39%)	
≥II	53 (20.78%)	38 (14.18%)		44 (20.18%)	32 (14.68%)	
≥II complications (total)			χ^2=3.967; P=0.046			χ^2=2.295; P=0.130
Yes	53 (20.78%)	38 (14.18%)		44 (20.18%)	32 (14.68%)	
No	202 (79.22%)	230 (85.82%)		174 (79.82%)	186 (85.32%)	
Postoperative hemorrhage/hematoma			χ^2=3.702; P=0.054			χ^2=2.992; P=0.084
Yes	22 (8.63%)	12 (4.48%)		19 (8.72%)	10 (4.59%)	
No	233 (91.37%)	256 (95.52%)		199 (91.28%)	208 (95.41%)	
Surgical wound/pelvic infection			χ^2=0.345; P=0.557			χ^2=0.343; P=0.558
Yes	10 (3.92%)	8 (2.99%)		7 (3.21%)	5 (2.29%)	
No	245 (96.08%)	260 (97.01%)		211 (96.79%)	213 (97.71%)	
Anastomotic leakage/urinary fistule			χ^2=1.248; P=0.264			χ^2=1.371; P=0.242
Yes	10 (3.92%)	6 (2.24%)		8 (3.67%)	4 (1.83%)	
No	245 (96.08%)	262 (97.76%)		210 (96.33%)	214 (98.17%)	
Lymphocyst			χ^2=2.035; P=0.154			χ^2=2.696; P=0.101
Yes	14 (5.49%)	8 (2.99%)		13 (5.96%)	6 (2.75%)	
No	241 (94.51%)	260 (97.01%)		205 (94.04%)	212 (97.25%)	
Deep venous thrombosis/pulmonary embolism			χ^2=0.159; P=0.690			χ^2=0.454; P=0.501
Yes	6 (2.35%)	4 (1.49%)		6 (2.75%)	3 (1.38%)	
No	249 (97.65%)	264 (98.51%)		212 (97.25%)	215 (98.62%)	
Operation time (min)	170.00 [138.00, 198.00]	189.00 [161.25, 216.00]	Z=4.919; P≤0.001	166.50 [134.25, 194.75]	188.00 [159.75, 214.00]	Z=4.876; P≤0.001
Intraoperative blood loss (mL)	401.00 [279.50, 510.00]	230.00 [156.75, 316.00]	Z=11.416; P≤0.001	399.50 [269.75, 505.75]	239.50 [167.00, 317.00]	Z=9.821; P≤0.001
Lymph node yield	17.00 [11.00, 21.00]	17.00 [13.00, 22.00]	Z=1.825; P=0.068	16.00 [10.25, 21.00]	17.00 [13.00, 22.00]	Z=1.848; P=0.065
Duration of urinary catheterization (days)	10.00 [8.00, 12.00]	9.00 [7.00, 11.00]	Z=4.117; P≤0.001	10.00 [8.00, 12.00]	9.00 [7.00, 11.00]	Z=3.960; P≤0.001
Postoperative hospital stay (days)	9.00 [7.00, 12.00]	7.00 [5.00, 9.00]	Z=7.331; P≤0.001	9.00 [7.00, 12.00]	7.00 [5.00, 9.00]	Z=6.382; P≤0.001

Note: PSM, propensity score matching; LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy.

Table 4. Comparison of pathological outcomes between LRP and RARP before and after PSM

Variable	Before PSM			After PSM		
	LRP group (n=255)	RARP group (n=268)	Statistic/P	LRP group (n=218)	RARP group (n=218)	Statistic/P
Pathological T staging (ypT)			χ^2=1.826; P=0.609			χ^2=4.994; P=0.172
ypT2	62 (24.31%)	78 (29.10%)		49 (22.48%)	66 (30.28%)	
ypT3a	104 (40.78%)	106 (39.55%)		90 (41.28%)	89 (40.83%)	
ypT3b	68 (26.67%)	62 (23.13%)		58 (26.61%)	50 (22.94%)	
ypT4	21 (8.24%)	22 (8.21%)		21 (9.63%)	13 (5.96%)	
Pathological downstaging (≥cT3→ypT2)			χ^2=2.260; P=0.133			χ^2=1.184; P=0.277
Yes	42 (16.47%)	58 (21.64%)		38 (17.43%)	47 (21.56%)	
No	213 (83.53%)	210 (78.36%)		180 (82.57%)	171 (78.44%)	
Surgical margin positivity (overall)			χ^2=0.542; P=0.462			χ^2=0.752; P=0.386
Yes	70 (27.45%)	66 (24.63%)		62 (28.44%)	54 (24.77%)	
No	185 (72.55%)	202 (75.37%)		156 (71.56%)	164 (75.23%)	
Lymph node involvement			χ^2=0.520; P=0.471			χ^2=1.908; P=0.167
Yes	52 (20.39%)	48 (17.91%)		44 (20.18%)	33 (15.14%)	
No	203 (79.61%)	220 (82.09%)		174 (79.82%)	185 (84.86%)	
Postoperative pathological Gleason score variation			χ^2=0.123; P=0.940			χ^2=0.194; P=0.907
Downgraded	52 (20.39%)	58 (21.64%)		47 (21.56%)	46 (21.10%)	
Unchanged	172 (67.45%)	178 (66.42%)		146 (66.97%)	144 (66.06%)	
Upgraded	31 (12.16%)	32 (11.94%)		25 (11.47%)	28 (12.84%)	
Postoperative pathological PNI			χ^2=0.357; P=0.550			χ^2=0.084; P=0.772
Yes	138 (54.12%)	152 (56.72%)		124 (56.88%)	121 (55.50%)	
No	117 (45.88%)	116 (43.28%)		94 (43.12%)	97 (44.50%)	
Postoperative pathological LVI			χ^2=0.212; P=0.645			χ^2=0.000; P=1.000
Yes	64 (25.10%)	72 (26.87%)		55 (25.23%)	55 (25.23%)	
No	191 (74.90%)	196 (73.13%)		163 (74.77%)	163 (74.77%)	
Pathologic response to NAT (MPG)			χ^2=1.654; P=0.647			χ^2=1.691; P=0.639
Grade 1 (pCR)	10 (3.92%)	14 (5.22%)		8 (3.67%)	9 (4.13%)	
Grade 2 (>95% tumor regression)	38 (14.90%)	46 (17.16%)		30 (13.76%)	37 (16.97%)	
Grade 3 (50%-95% regression)	96 (37.65%)	104 (38.81%)		85 (38.99%)	89 (40.83%)	
Grade 4 (<50% regression)	111 (43.53%)	104 (38.81%)		95 (43.58%)	83 (38.07%)	
Specimen weight (g)	54.00 [42.00, 70.00]	54.50 [43.00, 68.25]	Z=0.494; P=0.621	56.50 [42.00, 70.75]	54.50 [41.00, 68.00]	Z=0.942; P=0.346
Positive LNs (positive LN count, positive cases)	3.00 [1.00, 4.00]	2.00 [2.00, 4.00]	Z=0.784; P=0.433	3.00 [1.00, 4.00]	2.00 [2.00, 3.00]	Z=0.936; P=0.349

Note: PSM, propensity score matching; LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy; PNI, perineural invasion; LVI, lymphovascular invasion; MPG, Miller-Payne grading; pCR, pathological complete response.



Time point	LRP	RARP
1−year	87.0%	91.4%
2−year	69.7%	77.4%
3−year	49.5%	61.4%
4−year	45.2%	58.0%
5−year	40.9%	53.8%

Time point	LRP	RARP
1−year	85.7%	91.2%
2−year	66.4%	79.8%
3−year	44.6%	62.0%
4−year	39.6%	58.5%
5−year	36.8%	53.1%

Figure 2. Survival analysis of BRFS in the LRP and RARP groups before and after PSM. A: Overall KM survival curves of the two groups before PSM; B: Follow-up timelines of the LRP group before PSM; C: Follow-up timelines of the RARP group before PSM; D: 1-to-5-year BRFS rates of the two groups before PSM; E: Overall KM survival curves of the two groups after PSM; F: Follow-up timelines of the LRP group after PSM; G: Follow-up timelines of the RARP group after PSM; H: 1-to-5-year BRFS rates of the two groups after PSM. Note: BRFS, biochemical recurrence-free survival; LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy; PSM, propensity score matching; KM, Kaplan-Meier.

Table 5. Univariate Cox proportional hazards regression analysis of factors associated with biochemical recurrence before and after PSM

Variable name	Before PSM			After PSM		
	β	P	HR_95CI	β	P	HR_95CI
Surgical technique						
LRP (reference)						
RARP	-0.350	0.008	0.705 (0.545-0.911)	-0.496	<0.001	0.609 (0.461-0.805)
Age						
≥65 (reference)						
<65	-0.167	0.225	0.846 (0.646-1.108)	-0.141	0.344	0.868 (0.648-1.163)
Preoperative PSA						
≥20 (reference)						
<20	-0.471	<0.001	0.624 (0.472-0.825)	-0.414	0.006	0.661 (0.493-0.886)
Biopsy ISUP grading						
Grade 5 (reference)						
Grade 4	-0.687	<0.001	0.503 (0.379-0.667)	-0.668	<0.001	0.513 (0.381-0.690)
PNI						
No (reference)						
Yes	-0.137	0.300	0.872 (0.672-1.131)	-0.200	0.158	0.818 (0.620-1.081)
Surgical margin positivity (overall)						
No (reference)						
Yes	0.534	<0.001	1.706 (1.300-2.239)	0.616	<0.001	1.851 (1.387-2.469)
Lymph node involvement						
No (reference)						
Yes	0.829	<0.001	2.291 (1.717-3.057)	0.775	<0.001	2.171 (1.573-2.997)
Postoperative pathological PNI						
No (reference)						
Yes	0.506	<0.001	1.658 (1.271-2.163)	0.436	0.003	1.547 (1.163-2.057)
Postoperative pathological LVI						
No (reference)						
Yes	0.166	0.256	1.180 (0.887-1.571)	0.198	0.209	1.219 (0.895-1.661)
NAT regimen						
ADT (reference)						
ADT+novel AR-targeted agents	-0.002	0.991	0.998 (0.773-1.290)	0.044	0.753	1.045 (0.794-1.375)
NAT duration						
≥6 months (reference)						
<6 months	-0.153	0.311	0.858 (0.638-1.154)	-0.105	0.502	0.900 (0.662-1.224)
Clinical T staging						
cT2 (reference)						
cT3a	0.102	0.643	1.107 (0.721-1.700)	0.216	0.383	1.242 (0.764-2.018)
cT3b	0.143	0.539	1.153 (0.732-1.818)	0.158	0.547	1.171 (0.700-1.961)
cT4	-0.238	0.510	0.788 (0.388-1.601)	-0.219	0.576	0.804 (0.374-1.729)
Pathological T staging (ypT)						
ypT2 (reference)						
ypT3a	-0.064	0.717	0.938 (0.662-1.328)	-0.077	0.684	0.926 (0.639-1.342)
ypT3b	0.461	0.010	1.585 (1.114-2.256)	0.437	0.024	1.548 (1.060-2.261)
ypT4	1.147	<0.001	3.148 (1.999-4.958)	1.177	<0.001	3.244 (1.963-5.362)
Pathologic response to NAT (MPG)						
Grade 1 (pCR) (reference)						
Grade 2 (>95% tumor regression)	0.930	0.052	2.535 (0.991-6.484)	1.006	0.058	2.735 (0.965-7.752)

Grade 3 (50%-95% regression)	1.115	0.015	3.050 (1.241-7.492)	0.970	0.058	2.637 (0.967-7.192)
Grade 4 (<50% regression)	1.010	0.028	2.747 (1.118-6.750)	0.948	0.064	2.580 (0.946-7.038)
Positive biopsy core rate (%)	0.005	0.125	1.005 (0.999-1.011)	0.006	0.079	1.006 (0.999-1.013)

Note: PSM, propensity score matching; HR, hazard ratio; CI, confidence interval; LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy; PSA, prostate-specific antigen; ISUP, International Society of Urological Pathology; PNI, perineural invasion; LVI, lymphovascular invasion; ADT, androgen deprivation therapy; AR, androgen receptor; MPG, Miller-Payne grading; pCR, pathological complete response.

before PSM and P=0.002 after PSM; surgical margin positivity: P<0.001 both before after PSM; LN involvement: P=0.011 before PSM and P=0.013 after PSM). The other variables all followed the PH assumption (all P>0.05; **Figure 3C** and **3F**).

Optimization of handling strategies for variables violating the PH assumption

For the four variables that did not meet the PH assumption (preoperative PSA, pathological T staging, surgical margin positivity, and LN involvement), 27 handling strategies were constructed and compared systematically. As indicated by the Akaike information criterion (AIC) comparison results, the AIC value of the "all 4 (S09)" strategy was the lowest before and after PSM (1519 and 1251, respectively), suggesting that this handling strategy was the best-fit model (**Figure 4A** and **4B**).

In the re-verification of the global PH assumption, the S09 strategy passed the global PH test before and after PSM (P=0.5651 before PSM and P=0.4979 after PSM). Additionally, the "PSA+PSM (S12)" strategy showed a pre- and post-PSM *P*-value of 0.0623 and 0.0636, respectively, in the global PH test, which also reached an acceptable level. However, the global PH test of other major stratification strategies failed tp reach the statistical significance threshold (**Figure 4E**).

Under different handling strategies, the HR of surgical techniques for BCR was generally stable. Among the main strategies, the HR of surgical approaches was about 0.607-0.651 before PSM and 0.599-0.636 after PSM, with the protective effect of RARP relative to LRP being statistically significant in all strategies (all P<0.05), suggesting that the research conclusion had good robustness against the PH assumption handling methods (**Figure 4C** and **4D**). Based on AIC and PH assumption test results, combined with the model's interpretability, the "All 4 (S09)" strategy was finally selected as the optimal modeling scheme for multivariate Cox regression.

Multivariate Cox's PH regression analysis

Using preoperative PSA level and surgical margin status for stratified sampling, the final multivariate Cox's PH regression model was constructed. In the global Schoenfeld residuals test, the final model showed a *P* value of 0.062 before PSM and 0.064 after PSM, suggesting no significant violation of the overall PH assumption. Further testing showed a certain deviation of pathological T staging and LN involvement from the PH assumption in the final model; hence, the two indices should be explained with caution in the result interpretation (**Figure 5A** and **5B**).

In the multivariate analysis, surgical approach before and after PSM was an independent protective factor for BCR, with the RARP procedure significantly reducing BCR risk compared with LRP (before PSM: HR=0.648, 95% CI: 0.491-0.853, P=0.002; after PSM: HR=0.626, 95% CI: 0.471-0.833, P=0.001). Furthermore, biopsy ISUP grade 5 (before PSM: HR=1.789, P<0.001; after PSM: HR=1.739, P<0.001), LN involvement (before PSM: HR=1.980, P<0.001; after PSM: HR=1.782, P<0.001), postoperative pathological PNI (before PSM: HR=1.590, P=0.001; after PSM: HR=1.463, P=0.012), and pathological T stage ≥pT3b (before PSM: HR=1.592, P<0.001, after PSM: HR=1.603, P=0.001) were all independent risk factors for BCR before and after PSM Age, NAT regimen/duration, postoperative pathological LVI, and positive biopsy core rate differed non-significantly before and after PSM (all P>0.05; **Figure 5C** and **5D**).

When assessing the model's discrimination ability, the pre-PSM C-index of the final model was 0.6728, which changed to 0.6712 post-

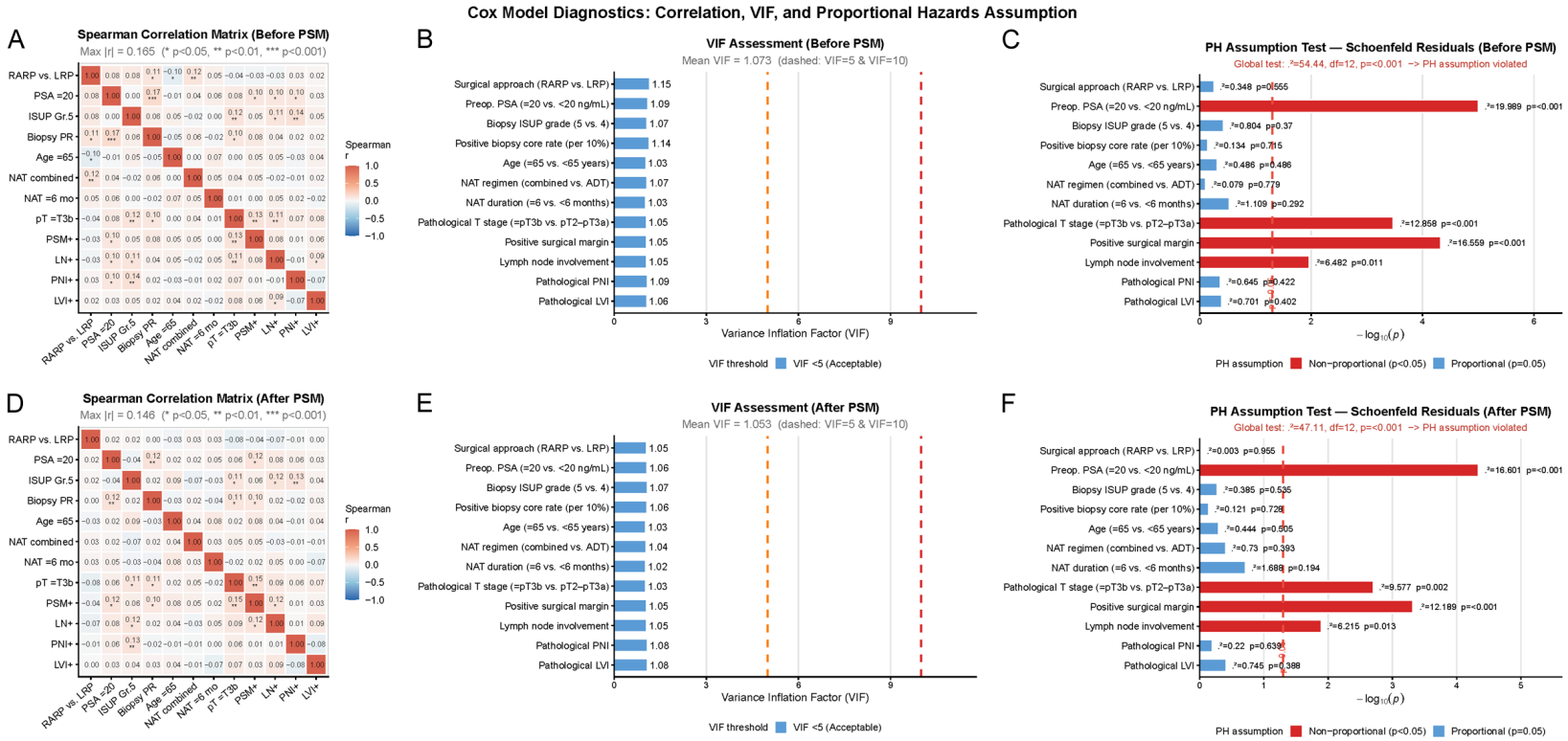


Figure 3. Multivariate Cox regression model diagnostics: Spearman correlation matrix, VIF, and PH assumption test. A: Spearman correlation matrix between variables before PSM; B: VIF evaluation of variables before PSM; C: Proportional hazards assumption test (Schoenfeld residuals) before PSM; D: Spearman correlation matrix between variables after PSM; E: VIF evaluation of variables after PSM; F: Proportional hazards assumption test (Schoenfeld residuals) after PSM. Note: VIF, variance inflation factor; PH, proportional hazards; PSM, propensity score matching; LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy; PSA, prostate-specific antigen; ISUP, International Society of Urological Pathology; NAT, neoadjuvant therapy; ADT, androgen deprivation therapy; PSM+, positive surgical margin; LN+, lymph node involvement; PNI, perineural invasion; LVI, lymphovascular invasion.

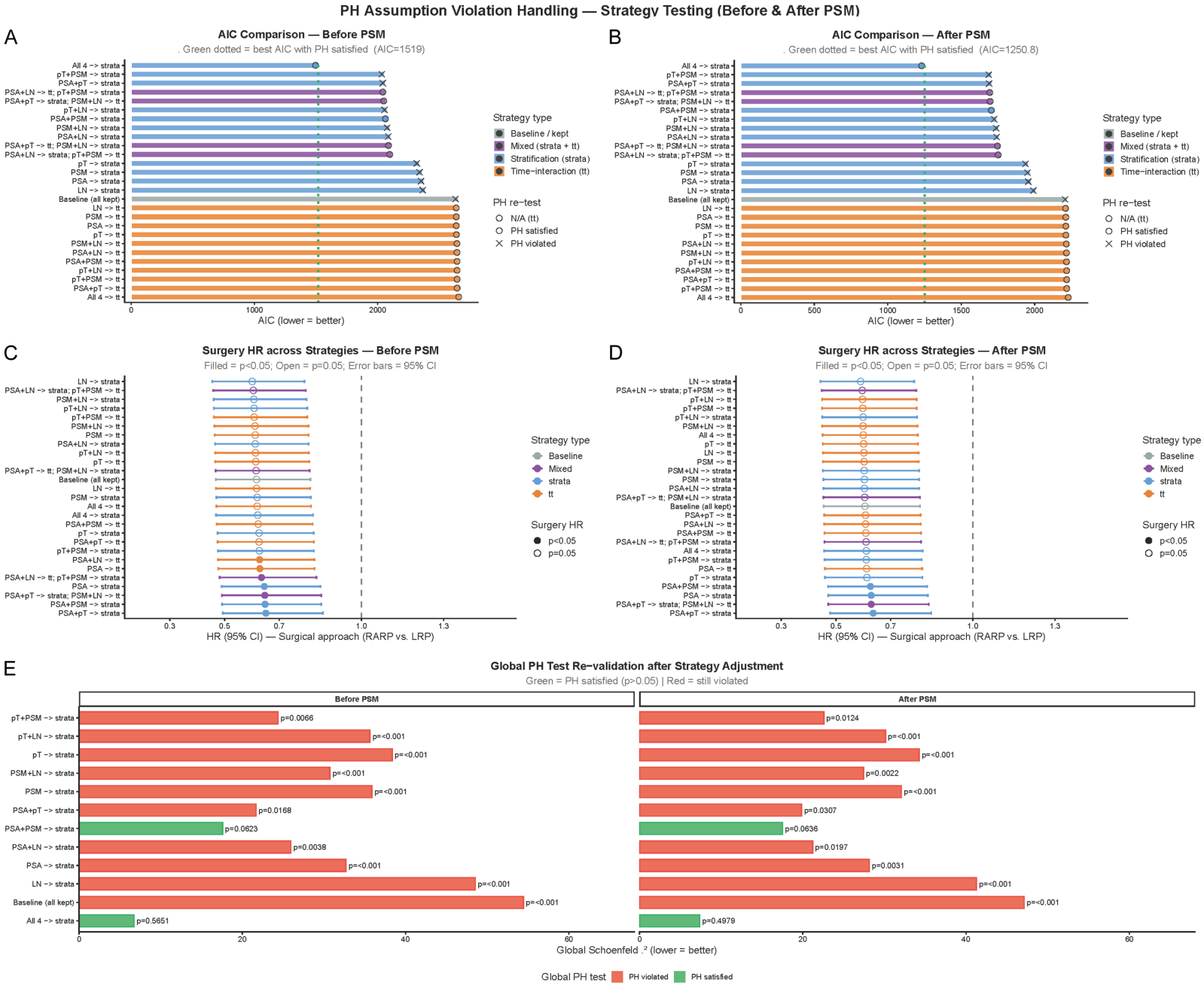

PH Assumption Violation Handling — Strategy Testing (Before & After PSM)
A
AIC Comparison — Before PSM
. Green dotted = best AIC with PH satisfied (AIC=1519)
All 4 ~> strata
pT+PSM ~> strata
PSA+pT ~> strata
PSA+LN ~> tt; pT+PSM ~> strata
PSA+pT ~> strata; PSM+LN ~> tt
pT+LN ~> strata
PSA+PSM ~> strata
PSM+LN ~> strata
PSA+LN ~> strata
PSA+pT ~> tt; PSM+LN ~> strata
PSA+LN ~> strata; pT+PSM ~> tt
pT ~> strata
PSM ~> strata
PSA ~> strata
LN ~> strata
Baseline (all kept)
LN ~> tt
PSM ~> tt
PSA ~> tt
pT ~> tt
PSM+LN ~> tt
PSA+LN ~> tt
PSA+PSM ~> tt
pT+LN ~> tt
pT+PSM ~> tt
PSA+pT ~> tt
All 4 ~> tt
0
1000
2000
AIC (lower = better)
Strategy type
Baseline / kept
Mixed (strata + tt)
Stratification (strata)
Time−interaction (tt)
PH re−test
N/A (tt)
PH satisfied
PH violated
B
AIC Comparison — After PSM
. Green dotted = best AIC with PH satisfied (AIC=1250.8)
0
500
1000
1500
2000
AIC (lower = better)
C
Surgery HR across Strategies — Before PSM
Filled = p<0.05; Open = p=0.05; Error bars = 95% CI
0.3
0.5
0.7
1.0
1.3
HR (95% CI) — Surgical approach (RARP vs. LRP)
Strategy type
Baseline
Mixed
strata
tt
Surgery HR
p<0.05
p=0.05
D
Surgery HR across Strategies — After PSM
E
Global PH Test Re−validation after Strategy Adjustment
Green = PH satisfied (p>0.05) | Red = still violated
Before PSM
After PSM
p=0.0066
p=<0.001
p=<0.001
p=<0.001
p=<0.001
p=0.0168
p=0.0623
p=0.0038
p=<0.001
p=<0.001
p=<0.001
p=0.5651
p=0.0124
p=<0.001
p=<0.001
p=0.0022
p=<0.001
p=0.0307
p=0.0636
p=0.0197
p=0.0031
p=<0.001
p=<0.001
p=0.4979
0
20
40
60
Global Schoenfeld .² (lower = better)
Global PH test
PH violated
PH satisfied

Figure 4. Systematic testing of the handling strategies for PH-violated variables: AIC comparison, surgery HR robustness, and global PH assumption re-validation. A: AIC comparison of various strategies before PSM; B: AIC comparison of various strategies after PSM; C: Forest plot of surgery HR across strategies before PSM; D: Forest plot of surgery HR across strategies after PSM; E: Global PH assumption re-validation after strategy adjustment (before and after PSM). Note: PH, proportional hazards; AIC, Akaike information criterion; HR, hazard ratio; PSM, propensity score matching; PSA, prostate-specific antigen; LN+, lymph node involvement; tt, time-varying interaction; PSM+, positive surgical margin; CI, confidence interval; LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy.

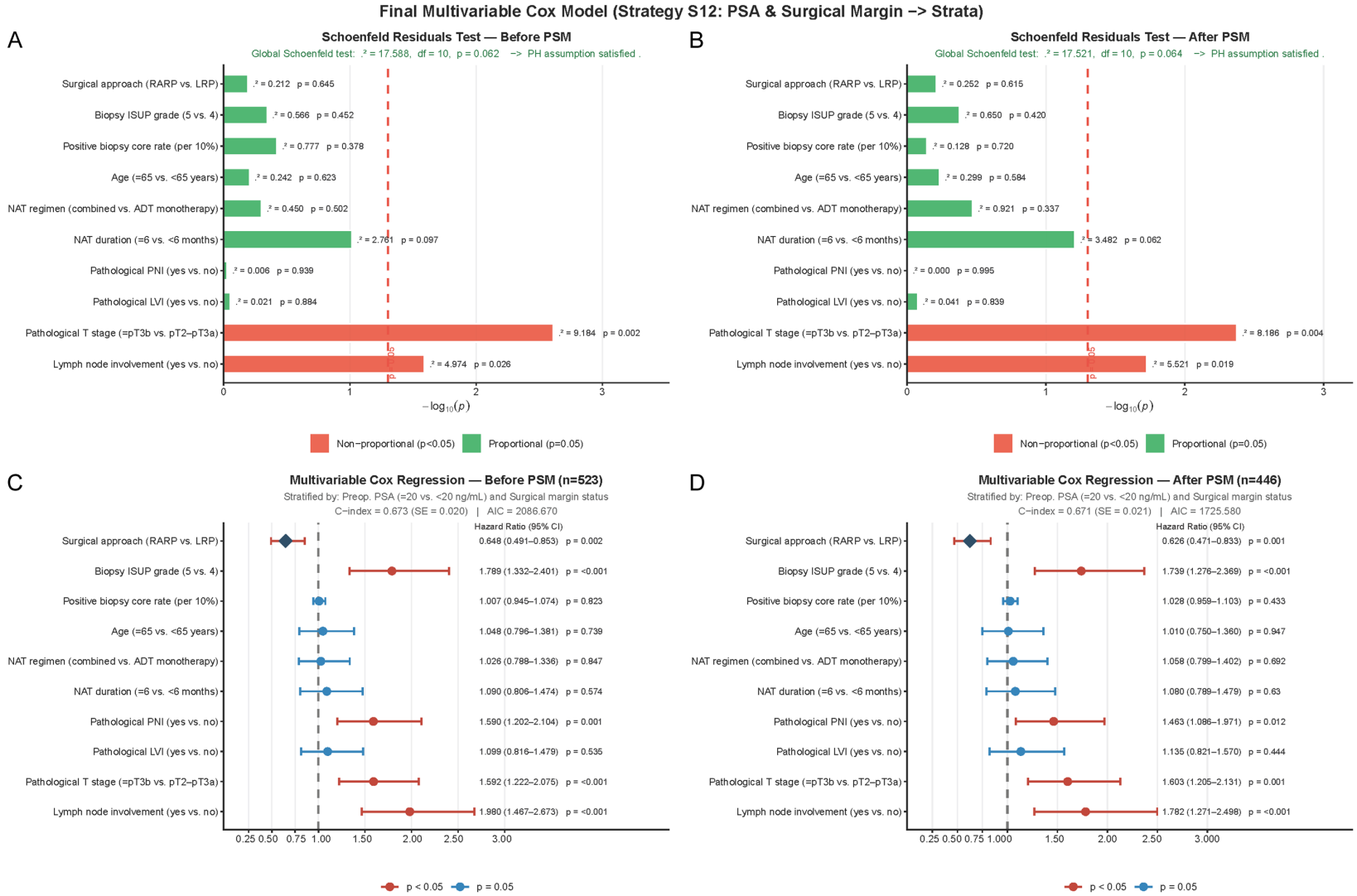


Figure 5. PH assumption validation of the final multivariate Cox PH regression model and the Forest plot. A: PH assumption test (Schoenfeld residuals) of the final model before PSM; B: PH assumption test (Schoenfeld residuals) of the final model after PSM; C: Forest plot of the HRs of various multivariate Cox regression variables before PSM; D: Forest plot of the HRs of various multivariate Cox regression variables after PSM. Note: PH, proportional hazards; PSM, propensity score matching; LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy; ISUP, International Society of Urological Pathology; NAT, neoadjuvant therapy; ADT, androgen deprivation therapy; PNI, perineural invasion; LVI, lymphovascular invasion; C-index, concordance index; AIC, Akaike information criterion; HR, hazard ratio; CI, confidence interval.

PSM, indicating the model's favorable discriminating power.

Sensitivity analysis

To check the robustness of the influence of surgical approaches on BCR, four sensitivity analyses were carried out. Pre- and post-PSM, the results of each sensitivity analysis were consistent with the main analysis. The independent protective effect of RARP compared with LRP on BCR was statistically significant in different analysis protocols (all P<0.05; **Figure 6A** and **6B**).

Specifically, in the main analysis (full cohort), RARP was significantly correlated with a reduced BCR risk before and after PSM (before PSM: HR=0.648, 95% CI 0.491-0.853, P= 0.002; after PSM: HR=0.626, 95% CI 0.471-0.833, P=0.001). Excluding patients with insufficient NAT duration (<6 months), the protective effect of RARP was found to be further enhanced (before PSM: HR=0.592, 95% CI 0.426-0.823, P=0.002; after PSM: HR=0.556, 95% CI 0.395-0.784, P<0.001), indicating that the difference between the two surgical techniques may be more pronounced in patients with an adequate NAT course.

The complete-case analysis results completely mirrored those of the main analysis (before PSM: HR=0.648, 95% CI 0.491-0.853, P= 0.002; after PSM: HR=0.626, 95% CI 0.471-0.833, P=0.001). Multiple imputation findings (m=20) also showed consistency with the main analysis results. Further testing indicated no missing values in the model variables included in this study, which meant that multiple imputation analysis is essentially equivalent to complete case analysis. Generally speaking, the point estimates for HRs and 95% CIs of surgical approaches were highly overlapped in the sensitivity analysis before and after PSM, demonstrating good consistency (**Figure 6C**). Therefore, the research conclusion demonstrates good robustness across different analytical strategies and sample selections.

Urinary continence recovery outcomes

Postoperative use of 0 safety pads (ICIQ-SF criteria) was defined as urinary continence recovery. The urinary continence recovery rate was notably higher in RARP-managed cases compared to LRP-treated counterparts across all time points before and after PSM. In the RARP group, the pre-PSM continence recovery rates at postoperative months 1, 3, 6, and 12 months were 31.3%, 52.2%, 73.1% and 85.1%, respectively, all higher than the corresponding rates in the LRP group (22.7%, 40.8%, 62.7%, and 74.5%; P=0.035, 0.011, 0.014, 0.004). The above differences persisted following PSM, with higher continence recovery rates across all postoperative timelines in the RARP group versus the LRP group (1 month: 33.5% vs. 21.1%, P=0.005; 3 months: 53.2% vs. 38.5%, P=0.003; 6 months: 74.8% vs. 60.6%, P=0.002; 12 months: 84.9% vs. 73.9%, P=0.006; **Figure 7A** and **7B**).

According to the KM curve of cumulative continence recovery, the time to continence recovery was markedly shortened in the RARP group relative to the LRP group before and after PSM (P<0.001 in the Log-rank test). Both pre- and post-PSM, the median time to continence recovery in the RARP group was 3 months (95% CI 3-6 months), compared to 6 months (95% CI 6-6 months) in the LRP group, suggesting that the RARP technique helped recover continence approximately 3 months earlier than the LRP procedure (**Figure 7C** and **7D**).

Subgroup analysis

Subgroup analyses were performed to evaluate the consistency of the association between surgical approach and BCR-free survival across clinically relevant strata before and after propensity score matching (PSM) (**Figure 8**). Before

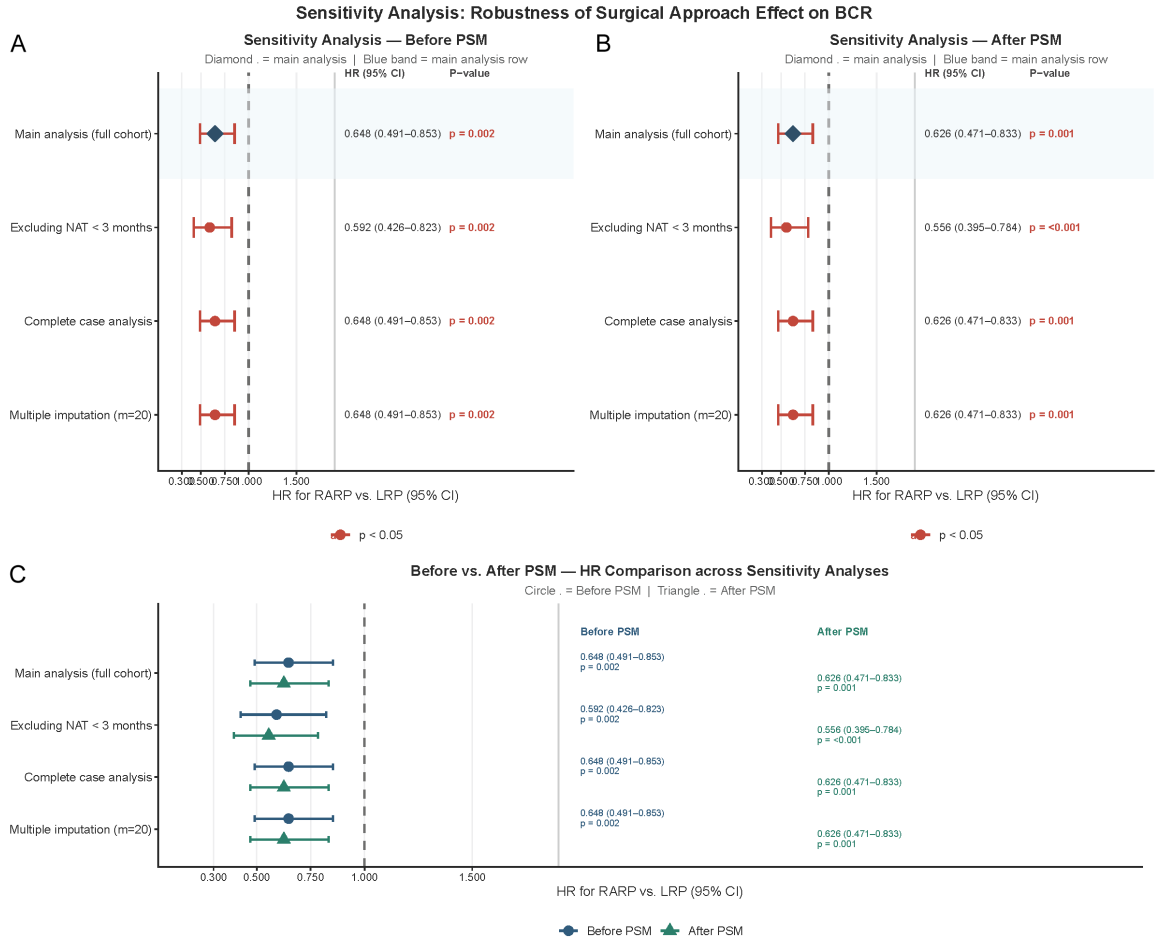


Figure 6. Sensitivity analysis of the influence of surgical approaches on BCR: HR-based robustness validation across various analytical strategies. A: Forest plot with HRs based on various sensitive analyses of surgical approach effect on BCR before PSM; B: Forest plot with HRs based on various sensitive analyses of surgical approach effect on BCR after PSM; C: Comparison diagram of HRs based on sensitivity analyses before and after PSM. Note: BCR, biochemical recurrence; HR, hazard ratio; PSM, propensity score matching; CI, confidence interval; NAT, neoadjuvant therapy; LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy; MI, multiple imputation.

PSM, RARP was associated with significantly improved BCR-free survival in patients with PSA≥20 ng/mL (HR 0.571, 95% CI 0.409-0.798; P=0.001), pT2-pT3a disease (HR 0.565, 95% CI 0.390-0.817; P=0.002), ISUP grade 4 disease (HR 0.499, 95% CI 0.296-0.841; P=0.009), lymph node-negative disease (HR 0.558, 95% CI 0.406-0.768; P<0.001), ADT monotherapy (HR 0.587, 95% CI 0.389-0.885; P=0.011), and age ≥65 years (HR 0.603, 95% CI 0.428-0.849; P=0.004).

After PSM, the favorable association between RARP and BCR-free survival remained significant in the same subgroups, including patients with PSA≥20 ng/mL (HR 0.561, 95% CI 0.395-0.798; P=0.001), pT2-pT3a disease (HR 0.552, 95% CI 0.378-0.806; P=0.002), ISUP grade 4 disease (HR 0.475, 95% CI 0.281-0.802; P=0.005), lymph node-negative disease (HR 0.561, 95% CI 0.405-0.775; P<0.001), ADT monotherapy (HR 0.557, 95% CI 0.363-0.855; P=0.007), and age ≥65 years (HR 0.573, 95% CI 0.401-0.817; P=0.002).

In contrast, the association between RARP and BCR-free survival did not reach statistical significance in patients with PSA<20 ng/mL, ≥pT3b disease, ISUP grade 5 disease, lymph node-positive disease, ADT plus novel androgen receptor-targeted therapy, or age <65 years, either before or after PSM. No significant interactions were observed across the reported subgroup variables before or after PSM, sug-

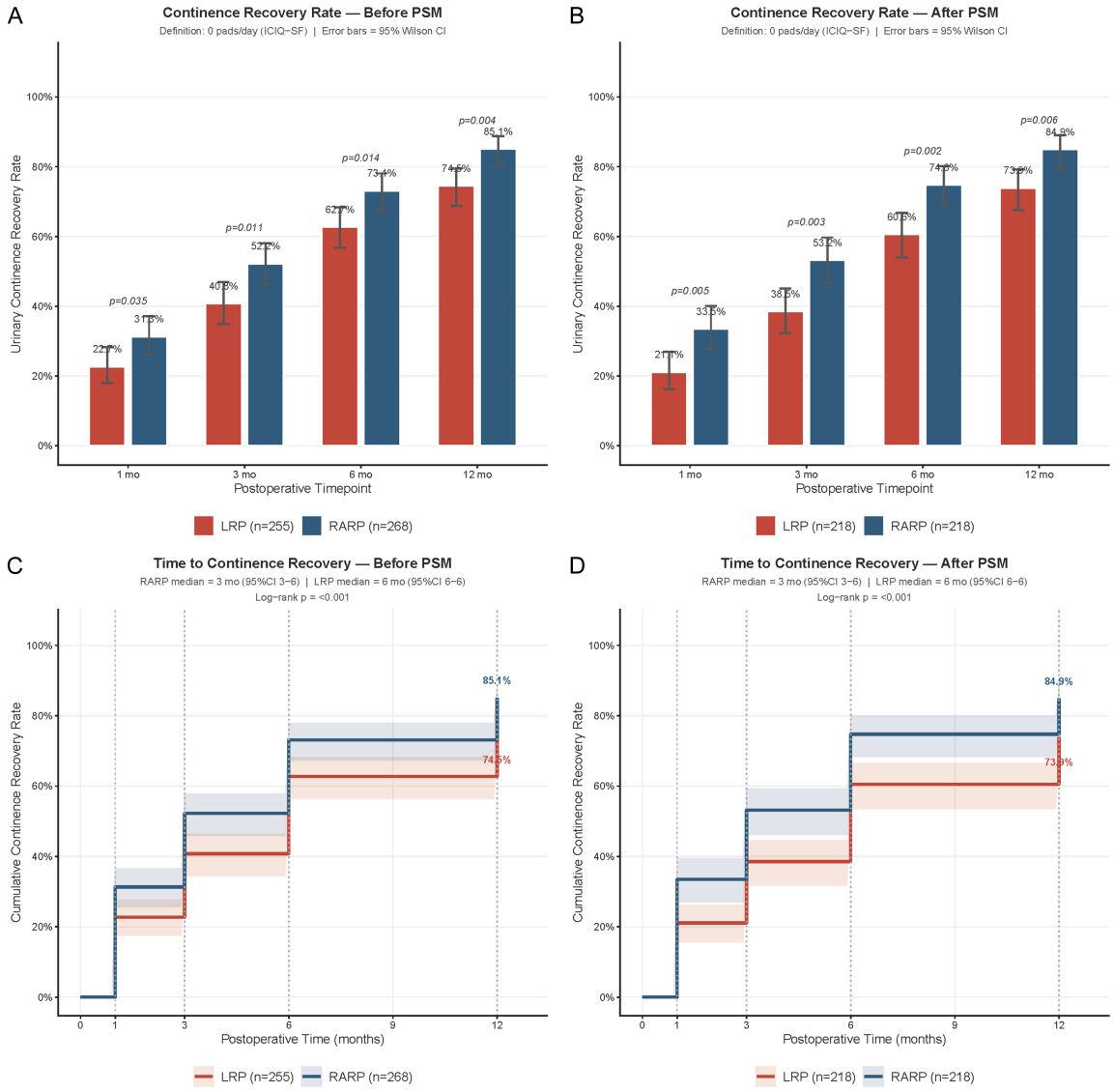


Figure 7. Comparison of continence recovery between LRP and RARP groups across various postoperative time points before and after PSM. A: Histogram of continence recovery rates of the two groups at each time point before PSM; B: Histogram of continence recovery rates across time points after PSM; C: KM curve of cumulative continence recovery before PSM; D: KM curve of cumulative continence recovery after PSM. Note: LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy; PSM, propensity score matching; KM, Kaplan-Meier; ICIQ-SF, International Consultation on Incontinence Questionnaire-Short Form; CI, confidence interval.

gesting no clear evidence of effect modification by pathological T stage, ISUP grade, lymph node status, neoadjuvant therapy regimen, or age.

Discussion

Based on real-world clinical data, this study compared the perioperative, pathological, and oncological outcomes of HR-LPC patients who received either RARP or LRP after NAT, with baseline confounders controlled through PSM. The results supported the superiority of RARP to LRP in some perioperative indices and functional recovery. Multivariate Cox's PH regression analysis further strongly linked RARP to a lower BCR risk.

In recent years, the application of NAT in HR-LPC has garnered growing clinical attention. The ADT-novel ARTA combination has been shown to demonstrate a favorable pathological

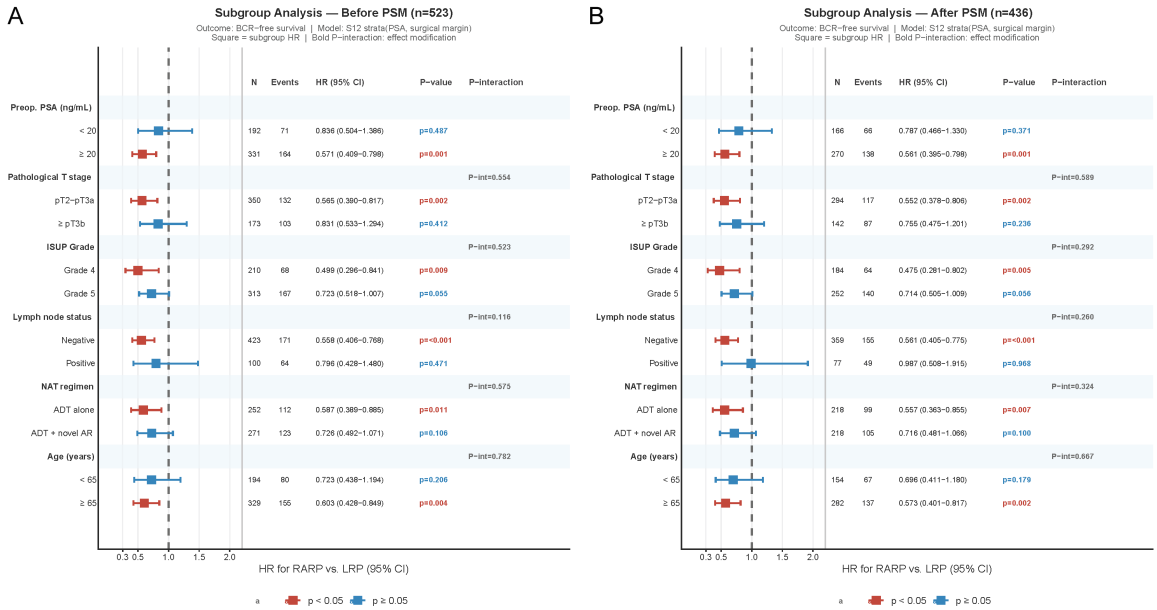


Figure 8. Subgroup analysis of the effect of surgical approaches on BCR: heterogeneity test of treatment effect before and after PSM. A: Forest plot showing HRs associated with the effect of surgical approaches on BCR in each subgroup before PSM; B: Forest plot showing HRs associated with the effect of surgical approaches on BCR across various subgroups after PSM. Note: BCR, biochemical recurrence; PSM, propensity score matching; PSA, prostate-specific antigen; ISUP, International Society of Urological Pathology; NAT, neoadjuvant therapy; ADT, androgen deprivation therapy; AR, androgen receptor; HR, hazard ratio; CI, confidence interval; LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy.

response rate in multiple Phase II studies [21]. However, there is no phase III data to support its use as a standard treatment, and the field is still in the evidence accumulation phase. Mechanistically, the core of NAT lies in reducing tumor load and reducing tumor volume by inhibiting AR signaling, thus ameliorating local surgical conditions. Concerning neoadjuvant intensive endocrine therapy, the randomized phase II trial ARNEO by Devos et al. [9] showed a reduction of the minimal residual disease (MRD) rate from 9.1% to 38% (P=0.002) by Apalutamide+Degarelix Acetate compared with ADT alone, providing a strong evidence-based basis for intensive combined endocrine strategies. A meta-analysis of the STAMPEDE platform [22] confirms that Abiraterone plus ADT can improve 6-year metastasis-free survival rates among high-risk non-metastatic PC patients from 69% to 82%, which supports its use as a new standard treatment scheme for this population. Furthermore, McKay et al. [23] and Zhang et al. [24] reported the pathological reaction of AAPL/APL combined regimen and Darolutamide+ADT, respectively, demonstrating the certain effectiveness and safety of both therapies, thus further enriching the drug options for NAT. In a phase II study (FAST-PC) [25], the NAT prrotocol combining Fuzuloparib, a PARP inhibitor, and abiraterone elevated the pCR/MRD rate to 46%, suggesting that multi-target combined strategies hold great promise for further exploration. However, NAT may also lead to pathologic change such as periprostatic tissue fibrosis, inflammatory reaction, and pelvic adhesion, which further blur anatomical layers and potentially increases surgical difficulty. In this context, a robotic surgical system with 3D high-definition vision, multi-degree-of-freedom manipulator, and a tremor filtering function may theoretically be more feasible for fine operation in complex anatomical environments, which can exert a more obvious impact on perioperative and long-term outcomes.

In terms of perioperative outcomes, this study observed the statistical advantages of RARP in several indicators: the RARP group exhibited less IBL, lower rates of intraoperative blood transfusion and conversion to open surgery, as well as shorter catheterization duration and postoperative hospital stay. In their retrospective study on the high-risk PC population in

China, Sun et al. [26] noted that NHT contributed to significant OT and blood loss reductions during the LRP procedure; however, this effect was relatively insignificant in the RARP cohort. It suggests that surgical modalities may, to some certain extent, independently adjust the influence of NAT on perioperative outcomes, consistent with the difference observed between the two surgical approaches in this study. In patients with non-low-risk PC, neoadjuvant ADT has been indicated to be effective in ameliorating core perioperative indices, like OT, blood loss, blood transfusion rate, and hospitalization time [27], which further supports the feasibility of post-NAT surgery in terms of perioperative safety. Of note, RARP was associated with significantly extended OT than LRP in this study (post-PSM median: 188 min vs. 166.5 min, P<0.001). Farzat et al.'s research [28] shows no marked rise in serious complications and 30-day readmission rate after RARP in patients receiving NHT, suggesting guaranteed overall safety of robot-assisted surgery in patients after NAT despite prolonged OT. The prolonged OT may be related to the installation and debugging of the robotic system, the more meticulous anatomical operation of the operator in the complex adhesion environment, and the learning curve effect. Nevertheless, the comprehensive advantages of RARP in core perioperative parameters (e.g., blood loss, hospitalization time) still hold clinical significance. The absence of statistical inter-group difference in the rates of POCs, 30-day readmission, and 30-day reoperation indicates basically equivalent safety of the two surgical techniques.

Regarding pathological outcomes, the two groups did not differ statistically in positive surgical margins, pathological downgrading rate, LN involvement, postoperative pathological PNI, LVI, and pathologic response to NAT before and after PSM, suggesting comparable outcomes of the two surgical methods in terms of tumor pathology. Wang et al. [29] reported found that the incidence of positive surgical margins of LRP patients receiving neoadjuvant hormonal therapy (NHT) shifted significantly from the apex (68.8%) to the fundus (57.7%), with pT staging, LN status, and LVI being independent risk factors for positive surgical margins post-NHT. It indicates that local anatomical changes following NAT may balance the difference in margin control between the two surgical methods, thus partially explaining the non-significant difference in pathological outcomes in this study. Also, NAT may have improved the surgical resection conditions of both groups to some extent by reducing the tumor load and tumor volume, and consequently weakened the influence of different surgical techniques on pathological outcomes. The non-significance can also be partially justified by the relatively limited sample size of this study, resulting in sufficient statistical power to detect subtle between-group differences in pathological outcomes. Therefore, this negative result should be interpreted with caution. It cannot be ruled out that there are yet undiscovered differences in the pathological aspects between the two surgical methods.

As far as oncological outcomes are concerned, KM analysis confirmed superior BRFS in RARP-treated patients compared to LRP-managed cases. After controlling for the potential confounding factors using the multivariate Cox model, RARP remained significantly related to a lower risk of BCR (before PSM: HR=0.648, 95% CI 0.491-0.853, P=0.002; after PSM: HR=0.626, 95% CI 0.471-0.833, P=0.001). Nezasa et al.'s multicenter PSM study [16] reported that the BCR incidence in RARP patients after NHT stood at 31.4%-40.7% at a median follow-up of 47 months, which is at a similar order of magnitude to the results of this study. Meanwhile, their study suggests that NHT with ADT alone can not significantly improve BRFS, which partially highlights the potential importance of the choice of surgical methods for oncological outcomes in the context of NAT. It is noteworthy that the groups showed no statistical difference in the surgical margin positivity rate, whereas RARP exhibited an independent protective effect on BCR risk. Literature shows [30] that while local positive margins are related to a significantly increased BCR risk in high-risk PC patients, factors other than the margin, including the fine anatomical separation of the prostate apex and the area around the neurovascular bundle, may play an independent role in long-term oncological outcomes. Besides, RARP following neoadjuvant chemohormonal therapy is indicated to significantly reduce the incidence of positive surgical margins and LVI (P<0.05), lowering the BCR rate from 29.5% to 15.8% (P=0.010) [31],

which hints at a possible synergy between NAT and surgical modalities. Thanks to the stable 3D vision and fine manipulation ability of the robotic system, higher quality tumor resection in complex anatomical areas may be achieved, though its exact mechanism needs further research and validation at the pathological and molecular levels.

Sensitivity analyses drew consistent conclusions under various analysis strategies, including restrictive analysis excluding patients with insufficient NAT (<6 months), complete case analysis, and multiple imputation analysis. The estimated HR of RARP and the 95% CI in each strategy were highly overlapped, suggesting the robustness of the research conclusions. Importantly, the protective effect of RARP was found to be enhanced after excluding patients with insufficient NAT course (post-PSM HR=0.556, 95% CI 0.395-0.784, P<0.001). It suggests that patients with relatively sufficient NAT may derive greater benefits from RARP, possibly due to a more thoroughly altered local anatomical environment under adequate NAT that amplifies the differences in the technical characteristics of the two surgical methods.

According to subgroup analyses, RARP showed significant BCR protection in the subgroups featuring preoperative PSA ≥20 ng/mL, pathological T stage pT2-pT3a, biopsy ISUP grade 4, negative LNs, ADT monotherapy, and age ≥65 years. Conversely, in subgroups characteristic of PSA<20 ng/mL, ≥pT3b, biopsy ISUP grade 5, LN involvement, ADT+novel ARTAs, and age <65, the difference was not statistically significant. Remarkably, since preoperative PSA has been treated as a stratification variable in the main model, no formal interaction test was conducted for the subgroup results of this variable, which is different from the analysis framework of other subgroup variables. For the remaining subgroups, no significant heterogeneity of surgical approach effects was found in the interaction test (all P>0.05), suggesting consistent protective effects of RARP across clinical subgroups, with no obvious effect modifications found. The non-significant differences in some subgroups (e.g., positive LNs, biopsy ISUP grade 5) can possibly be justified by the small sample size and insufficient statistical power of the specific subgroups, or that the technical differences in surgical methods have a more limited impact relative to the biological characteristics of the tumor itself in patients with a higher tumor burden or stronger biological invasiveness.

From the functional outcome perspective, this study systematically evaluated postoperative continence recovery. After PSM, higher continence recovery (defined as using 0 safety pad) rates were determined in the RARP group (33.5%, 53.2%, 74.8%, 84.9%) versus the LRP group (21.1%, 38.5%, 60.6%, 73.9%) across all postoperative recovery timelines (1, 3, 6, and 12 months), all reaching statistical significance (P<0.05). KM analysis further revealed a three-month earlier recovery of continence in the RARP group (median: 3 months, 95% CI 3-6 months) compared to the LRP group (median: 6 months, 95% CI 6-6 months), with the between-group difference being statistically significant in the Log-rank test (P<0.001). In a PSM analysis of locally advanced PC patients who received NHT [32], the continence recovery was improved to 42.86%, 62.34%, and 83.12% at 1, 3, and 12 months post-operation by NVBP in RARP, which was significantly higher than that of the non-preservation group. This finding supports the key role of fine neuroprotection in continence recovery, which is highly consistent with our observations. The evaluation criteria for continence recovery defined by the use of 0-1 pads have been widely applied in recent high-quality randomized controlled studies [33]. The postoperative recovery of urinary continence function has become an important dimension for the comprehensive evaluation of the therapeutic effect of PC surgeries. Early and targeted intervention is conducive to accelerating continence function recovery, which further highlights the clinical significance of promoting early functional recovery. The potential mechanism of RARP's advantages in continence recovery may be related to the technical characteristics of the robotic system in fine NVBP, the preservation of structural integrity of the external urethral sphincter, and accurate urethrovesical anastomosis. With smaller local tissue injury and tension, RARP could possibly help accelerate urinary continence recovery.

Still, several limitations in this study should be acknowledged. First, given the single-center retrospective research design, potential unmeasured confounding biases (e.g., differenc-

es in operator experience, surgical technique preferences in different institutions) can not be completely eliminated, despite the employment of PSM to control for the confounders observed. Another limitation is the limited sample size that can possibly lead to insufficient power. Additionally, as this study mainly evaluates BCR, an intermediate endpoint, extended follow-up periods are warranted to assess long-term oncology endpoints (metastatic survival, cancer-specific survival, etc.). Furthermore, given the certain heterogeneity among NAT regimens, the influence of different drug combinations and courses of treatment on surgical difficulty and oncological outcomes needs further detailed analysis. Finally, this study lacks a systematic evaluation of sexual function and other important functional outcomes, requiring the inclusion of more comprehensive quality-of-life-associated indicators in future research.

To sum up, in post-NAT HR-LPC patients, RARP has certain advantages over LRP in some core perioperative indices and is significantly related to a lower risk of BCR and earlier recovery of urinary continence function, though the two surgical methods are equivalent in overall pathological outcomes. The above findings demonstrate certain strengths of RARP in the comprehensive treatment strategy of this population. However, the conclusion needs further validation in multi-center and large-sample prospective studies, so as to provide more reliable evidence for the formulation of individualized treatment plans for high-risk PC patients.

Disclosure of conflict of interest

None.

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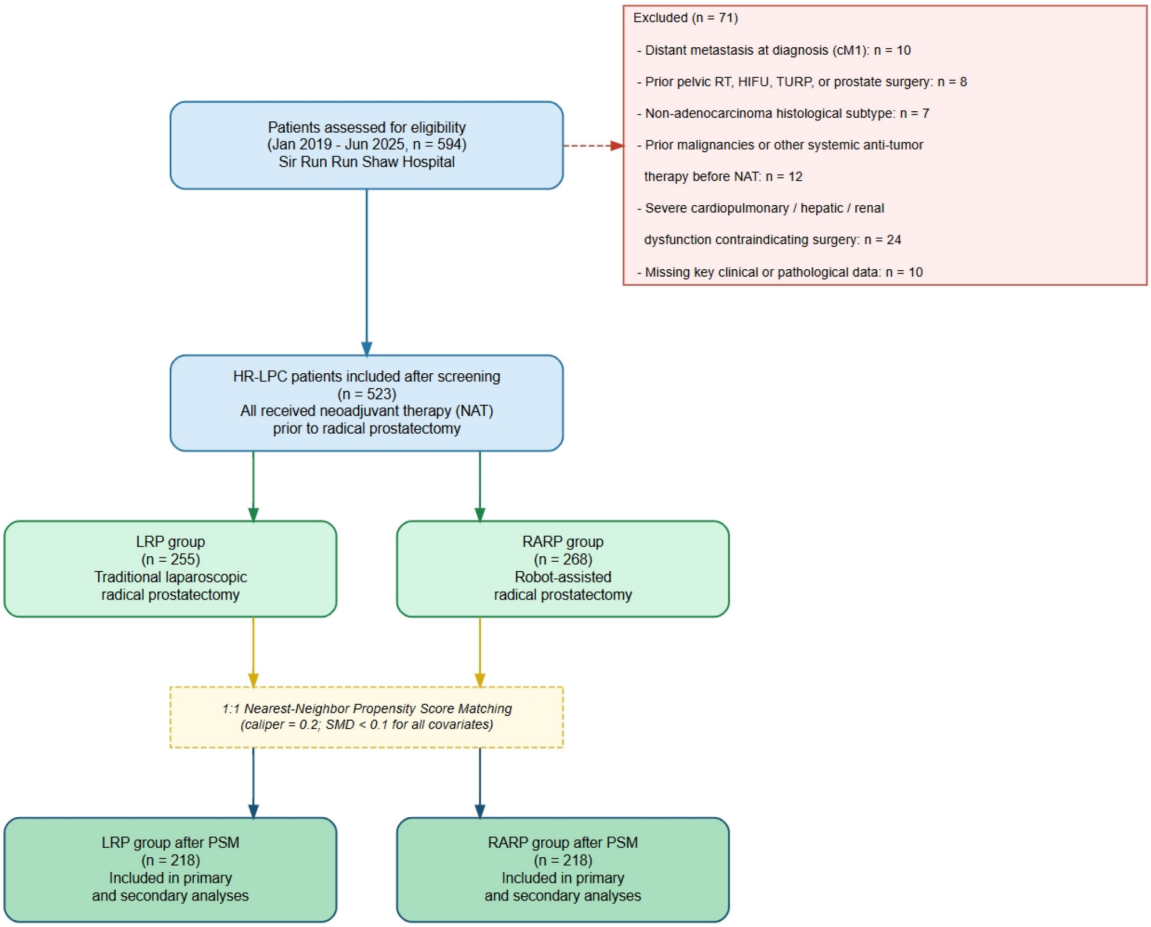

Figure S1. Flowchart.