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Original Article

Efficacy of neoadjuvant novel hormonal therapy combined with radical prostatectomy for high-risk prostate cancer and analysis of biochemical recurrence-free survival

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Abstract: Objective: To investigate the efficacy of neoadjuvant novel hormonal therapy (NHT) combined with radical prostatectomy (RP) in patients with high-risk prostate cancer (HRPCa), and identify independent influencing factors for 3-year biochemical recurrence-free survival (BCRFS). Methods: A total of 420 patients with HRPCa treated between 2017 and 2022 were enrolled and retrospectively analyzed. All patients were divided into training (n=294) and validation (n=126) sets at a 7:3 ratio. Each cohort was further subdivided into the combination group and the RP-alone control group. Relevant clinical data were collected, and Cox regression analysis, nomogram construction and receiver operating characteristic (ROC) curve analysis were performed. Results: Baseline data were well balanced between the sets and the groups (all P>0.05). The combination group presented significantly lower positive surgical margin rate (8.7% vs 31.9%), lymph node metastasis rate (10.7% vs 27.8%) and 3-year biochemical recurrence (BCR) rate (12.0% vs 30.6%, all P<0.001), as well as longer BCRFS (34.81±3.27 months vs 33.14±5.67 months, P=0.002). No significant difference was observed in postoperative complication rate between the two groups (4.0% vs 6.9%, P=0.266). Preoperative prostate-specific antigen ≥28.285 ng/mL, Gleason score ≥8.5, positive surgical margin and lymph node metastasis were independent risk factors for BCR (all P<0.003). The area under the ROC curve of the combined prediction model was 0.881 in the training cohort and 0.876 in the validation cohort. Conclusion: NHT combined with RP can improve clinical outcomes of HRPCa without increasing postoperative complications. The four above-mentioned indicators can effectively predict the 3-year BCR risk of patients.

Keywords: Neoadjuvant novel hormonal therapy, radical prostatectomy, Gleason score, positive surgical margin, biochemical recurrence-free survival

Introduction

Prostate cancer is a common male malignant tumor. Among them, high-risk prostate cancer (HRPCa) has large tumor volume, aggressive biological behavior and high postoperative biochemical recurrence (BCR) risk, which has always been the core difficulty and research hotspot in clinical treatment [1, 2]. At present, radical prostatectomy (RP) is the mainstream surgical treatment for HRPCa. Laparoscopic radical prostatectomy (LRP) has been widely applied due to its minimal invasiveness and rapid postoperative recovery [3]. However, LRP is technically demanding and accompanied by certain postoperative complication risks. Single RP treatment still has limitations such as high positive surgical margin rate and high lymph node metastasis risk, which lead to persistently elevated postoperative BCR rate and poor long-term therapeutic efficacy [4, 5]. Therefore, exploring optimized treatment regimens to reduce recurrence risk and improve long-term prognosis is of great clinical significance.

Existing studies have confirmed that neoadjuvant hormonal therapy can expand surgical indications and improve postoperative patho-

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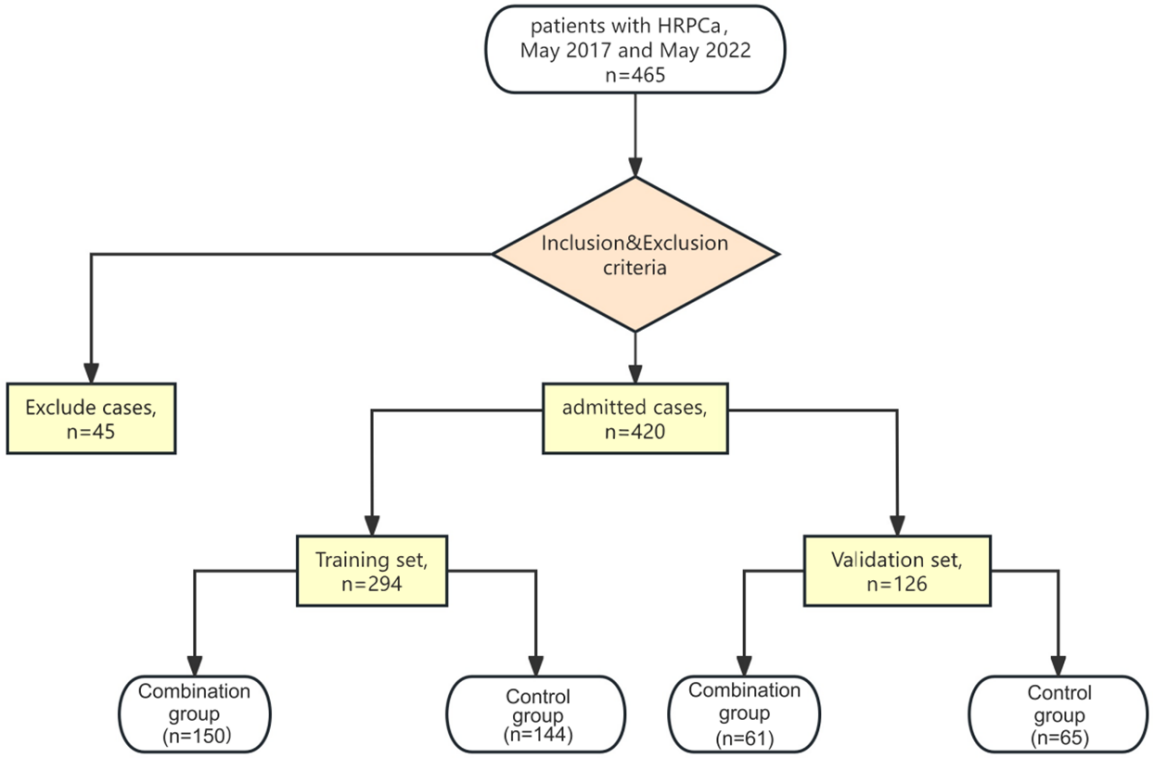

Figure 1. Flow diagram. Note: NHT: neoadjuvant hormonal therapy; HRPCa: high-risk prostate cancer.

logical grading results [6, 7]. In the treatment of prostate cancer, neoadjuvant novel hormonal therapy (NHT) combined with radical surgery can stably reduce androgen level, shrink tumor lesions, simplify surgical procedures and reduce surgical trauma, thereby optimizing survival prognosis and quality of life of patients [8, 9]. Although several studies have focused on NHT combined with RP for HRPCa treatment, the clinical value of standardized novel NHT combined regimen, especially its influence on 3-year BCRFS and related risk factors, has not been fully clarified. In addition, the currently available clinical prediction tools for postoperative BCR risk in HRPCa patients are insufficiently accurate, which restricts the formulation of individualized treatment and follow-up strategies.

On this basis, this study retrospectively analyzed clinical data of HRPCa patients to explore the clinical application value of NHT combined with RP. By establishing training and validation cohorts, we identified independent risk factors for BCR and constructed a nomogram prediction model, so as to realize quantitative prediction of 3-year postoperative BCR risk. This study compensates for the research deficiency regarding the prognostic influence of novel neoadjuvant endocrine therapy on HRPCa, and provides objective evidence for clinical treatment selection and postoperative recurrence risk assessment.

Materials and methods

Patients' selection

This study retrospectively collected clinical data of 465 patients diagnosed with HRPCa who were admitted to Baoji Gaoxin Hospital, Xianyang First People's Hospital, China-Japan Union Hospital of Jilin University and Affiliated Hospital of Northwest University from May 2017 to May 2022.

Inclusion criteria: (1) Prostatic acinar adenocarcinoma confirmed by systematic prostate core needle biopsy; (2) Preoperative serum prostate-specific antigen (PSA) >20 ng/mL and biopsy Gleason score ≥8; (3) Complete preoperative abdominopelvic imaging examination combined with whole-body bone scan or prostate-specific membrane antigen PET-CT exami-

Table 1. Baseline data of the training set and the validation set [n (%), $\bar{x}\pm sd$]

	Training set (n=294)	Validation set (n=126)	t/χ^2	P
Age (yr)	56.34±4.53	56.41±4.56	0.145	0.885
BMI (kg/m^2)	22.58±2.49	22.55±2.52	0.113	0.910
Hypertension			0.412	0.521
Yes	164 (55.8)	66 (52.1)		
No	130 (44.2)	60 (47.9)		
Hyperlipidemia			0.147	0.701
Yes	153 (52.0)	63 (50.0)		
No	141 (48.0)	63 (50.0)		
Education level			0.123	0.940
High school degree	31 (13.28)	14 (11.1)		
College degree	153 (56.25)	67 (53.2)		
Bachelor degree or above	110 (30.47)	45 (35.7)		
Prostate volume (ml)	46.59±5.08	49.61±5.09	0.037	0.971
Maximum tumor diameter (cm)	3.17±0.12	3.18±0.15	0.632	0.528
TNM staging			0.559	0.576
I-II	130 (44.2)	52 (41.3)		
III-IV	164 (55.8)	74 (58.7)		
PSA (ng/mL)	27.28±1.52	27.16±1.45	0.752	0.453
Gleason score	8.47±0.56	8.42±0.51	0.861	0.390

Note: NHT: neoadjuvant hormonal therapy; BMI: body mass index; PSA: prostate-specific antigen.

nation; (4) Newly diagnosed cases without previous anti-tumor treatment for prostate cancer; (5) Receiving standardized RP including laparoscopic, robot-assisted laparoscopic or open surgery; (6) Karnofsky Performance Status (KPS) score ≥80; (7) Complete clinical treatment data, perioperative pathological data and follow-up data.

Exclusion criteria: (1) Patients with severe cardiac, hepatic or renal insufficiency; (2) Combined with other malignant tumors; (3) Poor surgical tolerance or complicated conditions affecting surgical efficacy and prognosis; (4) Previous history of pelvic radiotherapy or systemic chemotherapy; (5) History of abdominopelvic and bladder surgery interfering with RP; (6) Incomplete clinical data or lost to follow-up.

The participant screening process is shown in **Figure 1**. Finally, 420 eligible patients were enrolled and divided into training and validation cohorts at a ratio of 7:3. The training cohort consisted of 294 patients (150 in the combination group, 144 in the RP-alone control group), and the validation cohort included 126 patients (61 in the combination group, 65 in the RP-alone control group). This study was approved by the Ethics Committee of Baoji Gaoxin Hospital.

Data extraction

Trained urological researchers independently extracted clinical data according to unified standard forms with consistent evaluation criteria. Any controversial data was reviewed and adjudicated by a senior chief urologist to ensure data authenticity and consistency. All data were imported into Excel database with double entry and logical error checking.

All patients in the control group received RP alone, while patients in the combination group received 3-month preoperative NHT intervention. The NHT regimen was as follows: oral enzalutamide 160 mg once daily combined with subcutaneous injection of luteinizing hormone-releasing hormone (LHRH) analogues (goserelin 3.6 mg or leuprorelin 3.75 mg) every 28 days. We collected baseline clinical data, postoperative pathological indicators, postoperative complication conditions and 3-year follow-up outcomes including BCR status and

Table 2. Baseline data of the two groups [n (%), $\bar{x}$±sd]

	Combination group (n=150)	Control group (n=144)	t/χ^2	P
Age (yr)	56.27±4.98	56.40±4.01	0.245	0.806
BMI (kg/m^2)	22.53±2.75	22.64±2.19	0.378	0.705
Hypertension			1.566	0.211
Yes	89 (59.3)	75 (52.1)		
No	61 (40.7)	69 (47.9)		
Hyperlipidemia			0.048	0.826
Yes	79 (52.7)	74 (51.4)		
No	71 (47.3)	70 (48.6)		
Education level			0.320	0.852
High school degree	17 (11.3)	14 (9.7)		
College degree	76 (50.7)	77 (53.5)		
Bachelor degree or above	57 (38.0)	53 (36.8)		
Prostate volume (ml)	46.47±5.61	46.72±4.49	0.421	0.674
Maximum tumor diameter (cm)	3.18±0.16	3.19±0.13	0.587	0.558
TNM staging			0.006	0.939
I-II	66 (44.0)	64 (44.4)		
III-IV	84 (56.0)	80 (55.6)		
PSA (ng/mL)	27.10±1.58	27.31±1.38	1.212	0.227
Gleason score	8.42±0.57	8.48±0.55	0.918	0.359

Note: NHT: neoadjuvant hormonal therapy; BMI: body mass index; PSA: prostate-specific antigen.

Table 3. Incidence of adverse reactions in both groups of patients [n (%)]

	Combination group (n=150)	Control group (n=144)	t/χ^2	P
Surgical margin			24.818	<0.001
Positive	13 (8.7)	46 (31.9)		
Negative	137 (91.3)	98 (68.1)		
Lymph node metastasis			13.951	<0.001
Yes	16 (10.7)	40 (27.8)		
No	134 (89.3)	104 (63.2)		
BCR in 3 year occurs			15.201	<0.001
Yes	18 (12.0)	44 (30.6)		
No	132 (88.0)	100 (69.4)		
BCRFS (months)	34.81±3.27	33.14±5.67	3.109	0.002

Note: NHT: neoadjuvant hormonal therapy; BCR: biochemical recurrence; BCRFS: biochemical recurrence-free survival.

BCRFS, and verified the consistency of all follow-up records, pathological reports and laboratory results.

Outcome measures

Primary outcomes: Postoperative adverse events were recorded in detail, including anastomotic leakage, urinary leakage, erectile dysfunction and urinary incontinence.

All patients were followed up for 3 years after discharge to record the occurrence of BCR. BCR was defined as sustained postoperative serum PSA elevation ≥0.2 ng/mL without spontaneous decline during reexamination.

Secondary outcomes: Baseline clinical indicators including age, body mass index (BMI), comorbidities, educational level, prostate volume, maximum tumor diameter, TNM stage, preoperative PSA level and Gleason score were collected. Postoperative pathological indicators including positive surgical margin status and lymph node metastasis status were recorded within one week after surgery. Positive

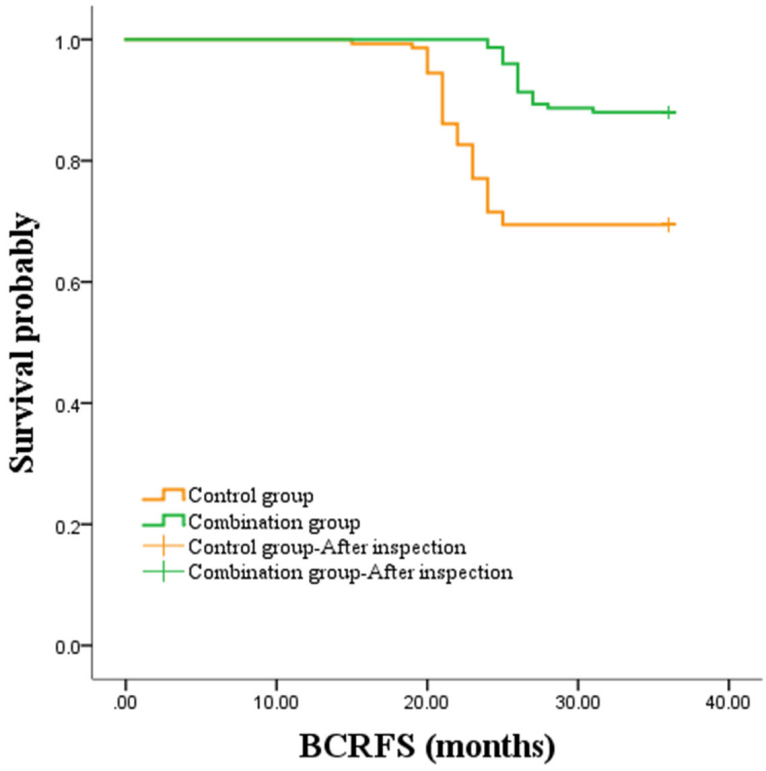

Figure 2. Kaplan-Meier curves for BCR in 3 year occurs in both groups of patients. Note: BCR: biochemical recurrence; BCRFS: biochemical recurrence-free survival; NHT: neoadjuvant hormonal therapy.

surgical margin was defined as tumor cells detected on the inked resection margin of postoperative specimens. Lymph node metastasis was confirmed by postoperative histopathological examination of resected pelvic lymph nodes.

Statistical analysis

Statistical analyses were performed using SPSS 20.0 software. The Shapiro-Wilk test was used for normality test. Normally distributed continuous data were expressed as mean ± standard deviation ($\bar{x}$±sd), and compared by independent-samples t test. Categorical data were expressed as cases (percentage) and compared via chi-square test. Kaplan-Meier method was adopted for survival analysis, and the log-rank test was used for inter-group comparison. Variables with P<0.1 in univariate analysis were included in multivariate Cox proportional hazards regression model, and forward stepwise regression was employed for variable screening (inclusion α=0.05, exclusion α=0.10). Nomogram prediction models were constructed and visualized using R software. Receiver operating characteristic (ROC) curves were utilized to assess the prognostic value of independent prognostic factors, and the DeLong test was applied to compare the areas under the ROC curves (AUCs) across different prediction models. A two-tailed P<0.05 was considered statistically significant.

Results

Comparison of baseline data between the training and validation sets

There were no significant differences in age, BMI, hypertension, hyperlipidemia, educational level, prostate volume, maximum tumor diameter, TNM staging, PSA level and Gleason score between the two cohorts (all P>0.05, **Table 1**).

Comparison of baseline data between the combination and control groups

No significant differences were found in all baseline clinical characteristics between the combination and control groups (all P>0.05, **Table 2**).

Comparison of positive surgical margin rate, lymph node metastasis rate and 3-year BCR rate between the combination and control groups

The positive surgical margin rate, lymph node metastasis rate and 3-year BCR rate in the combination group were 8.7% (13/150), 10.7% (16/150) and 12.0% (18/150) respectively, which were significantly lower than those in the control group [31.9% (46/144), 27.8% (40/144), and 30.6% (44/144)]. Meanwhile, the combination group achieved longer BCRFS than the control group (all P<0.05, **Table 3**; **Figure 2**).

Comparison of postoperative complication rate between the combination and control groups

No significant difference was detected in the overall postoperative complication rate between the two groups (P>0.05, **Table 4**).

Table 4. Incidence of adverse reactions in both groups of patients [n (%)]

Groups	n	Anastomotic leakage	Urinary leakage	Erectile dysfunction	Urinary incontinence	Incidence of complications
Combination group	150	3 (2.0)	3 (2.0)	0 (0.0)	0 (0.00)	6 (4.0)
Control group	144	4 (2.8)	3 (2.1)	1 (0.7)	1 (0.7)	10 (6.9)
t						1.238
P						0.266

Note: NHT: neoadjuvant hormonal therapy.

Table 5. Univariate analysis of factors affecting BCR occurring in HRPCa patients [n (%), $\bar{x}\pm sd$]

	BCR Group (n=62)	NBCR group (n=232)	t/χ^2	P
Age (yr)	56.32±4.59	56.34±4.52	0.031	0.975
BMI (kg/m^2)	22.63±2.42	22.57±2.51	0.168	0.866
Hypertension			1.263	0.261
Yes	32 (51.6)	132 (56.9)		
No	30 (48.4)	100 (44.1)		
Hyperlipidemia			0.044	0833
Yes	33 (53.2)	120 (51.7)		
No	29 (46.8)	112 (48.3)		
Education level			1.091	0.580
High school degree	8 (12.9)	23 (9.9)		
College degree	34 (54.8)	119 (51.3)		
Bachelor degree or above	20 (32.3)	90 (38.8)		
Prostate volume (ml)	46.77±5.02	46.54±5.11	0.316	0.752
Maximum tumor diameter (cm)	3.19±0.13	3.18±0.15	0.479	0.632
TNM staging			0.028	0.866
I-II	28 (45.2)	102 (44.0)		
III-IV	34 (54.8)	130 (56.00)		
PSA (ng/mL)	28.63±1.46	26.91±1.32	8.909	<0.001
Gleason score	8.94±0.51	8.34±0.50	8.358	<0.001
Surgical margin			43.883	<0.001
Positive	31 (50.0)	28 (12.1)		
Negative	31 (50.0)	204 (87.9)		
Lymph node metastasis			20.949	<0.001
Yes	29 (46.8)	27 (11.6)		
No	33 (53.2)	205 (88.4)		

Note: BCR: biochemical recurrence; HRPCa: high-risk prostate cancer; NHT: neoadjuvant hormonal therapy; BMI: body mass index; PSA: prostate-specific antigen.

Univariate analysis

Univariate analysis showed that age, BMI, comorbidities, prostate volume, maximum tumor diameter and TNM stage were not correlated with postoperative BCR (all P>0.05). By contrast, higher preoperative PSA level, higher Gleason score, positive surgical margin and lymph node metastasis were closely associated with increased BCR risk (all P<0.05, **Table 5**).

Multivariate Cox regression analysis

Significant variables screened by univariate analysis were included in multivariate Cox regression model after grouping assignment according to cutoff values of PSA and Gleason score (**Table 6**). The results confirmed that preoperative PSA ≥28.285 ng/mL, Gleason score ≥8.5, positive surgical margin and lymph node metastasis were independent risk factors for postoperative BCR in HRPCa patients (**Table 7**).

Table 6. Influencing factors assignment

Influencing Factors	Assignment
Surgical margin	0: Negative
	1: Positive
Lymph node metastasis	0: No
	1: Yes
PSA	0: <28.285 ng/mL
	1: ≥28.285 ng/mL
Gleason Score	0: <8.5
	1: ≥8.5

Note: PSA: prostate-specific antigen.

Nomogram analysis

The nomogram constructed based on the above four indicators showed that all variables had good predictive efficacy for postoperative BCR risk in both training and validation cohorts (**Figure 3A**, **3B**). Calibration curves verified favorable consistency between predicted value and actual outcome in both cohorts (training cohort: χ^2=6.823, P=0.559; validation cohort: χ^2=5.976, P=0.650, **Figure 3C**, **3D**).

ROC curve analysis

ROC curve analysis indicated that single clinical indicator had limited predictive value for 3-year BCR, while the combined prediction model possessed higher predictive accuracy in both cohorts (**Table 8**; **Figure 4**).

Discussion

HRPCa is characterized by strong invasive ability and high postoperative BCR risk. Most patients are diagnosed at high-risk stage without obvious early clinical symptoms, so its standardized treatment has always been a key research direction in urology [10, 11]. RP is a standard surgical treatment for HRPCa, but single surgical resection cannot completely eliminate latent tumor lesions, easily leading to high positive surgical margin rate and lymph node metastasis, and further inducing postoperative BCR [12]. This study retrospectively analyzed real clinical data to explore the clinical effect of NHT combined with RP and identify independent prognostic factors affecting 3-year BCR.

This study confirmed that compared with single RP treatment, preoperative NHT combined with RP can effectively reduce positive surgical margin rate, lymph node metastasis rate and 3-year BCR rate, prolong BCRFS, and will not increase postoperative complication risks. This conclusion is consistent with previous clinical research results [13, 14]. Mechanically, combined NHT regimen can effectively inhibit androgen signaling pathway, induce prostate cancer cell apoptosis, reduce tumor volume and invasiveness, and create favorable surgical conditions [15, 16]. Reduced tumor burden can also decrease intraoperative tumor cell dissemination and residual lesions, so as to lower local recurrence and distant metastasis risks [17, 18].

Multivariate Cox regression results verified that elevated preoperative PSA level, high Gleason score, positive surgical margin and lymph node metastasis are independent risk factors for postoperative BCR, which is consistent with previous research conclusions [19, 20]. PSA level directly reflects tumor load; higher value indicates stronger tumor invasiveness and higher recurrence probability [21]. Gleason score evaluates tumor differentiation degree, and higher score represents higher tumor malignancy [22]. Positive surgical margin suggests incomplete tumor resection, and residual microscopic tumor lesions are the direct cause of sustained PSA elevation and BCR [23]. Lymph node metastasis implies the occurrence of early tumor lymphatic diffusion, accompanied by potential occult distant micrometastases, which greatly increases long-term recurrence risk [24].

The established nomogram prediction model has good stability and discrimination ability in internal and external verification. Single indicator has inevitable clinical limitations: PSA elevation can also be caused by benign prostatic diseases [25]; biopsy Gleason score is prone to sampling bias [26]; postoperative pathological margin evaluation cannot detect microscopic residual lesions comprehensively [27]; routine lymph node dissection cannot rule out occult micrometastases completely [28]. The combined application of four indicators can make up for the defects of single index evaluation, and comprehensively judge postoperative recurrence risk from tumor load, malignancy degree, local resection status and metastatic potential [29-31]. Clinically, for HRPCa patients with multiple high-risk recurrence factors, preoperative 3-month NHT combined with RP is recommended, and individualized postopera-

Table 7. Multivariate Cox regression analysis of factors affecting BCR occurring in HRPCa patients

Factors	β	StdError	Wald x^2	P	HR	95% CI	
						Lower	Upper
Surgical margin: Positive	0.868	0.282	9.449	0.002	2.382	1.370	4.143
Lymph node metastasis: Yes	0.838	0.279	9.016	0.003	2.312	1.338	3.996
PSA ≥28.285 ng/mL	0.899	0.287	9.838	0.002	2.458	1.401	4.312
Gleason score ≥8.5	1.373	0.376	13.326	<0.001	3.946	1.888	8.246

Note: BCR: biochemical recurrence; HRPCa: high-risk prostate cancer; PSA: prostate-specific antigen; 95% CI: 95% confidence interval.

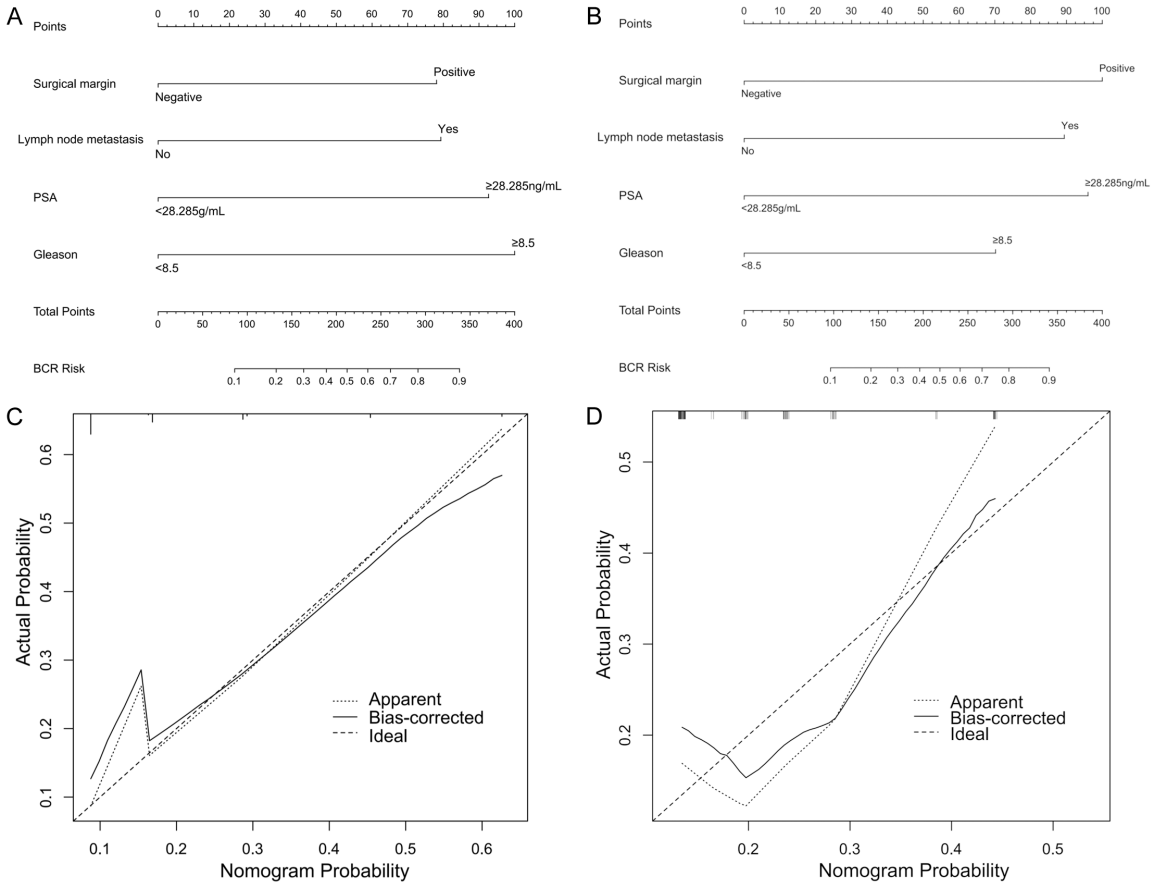

Figure 3. Construction and diagnostic performance evaluation of the nomogram model: (A) Nomogram for training set; (B) Nomogram for validation set; (C) Calibration curve for validating the nomogram of training set; (D) Calibration curve for validating the nomogram of validation set. Note: BCR: biochemical recurrence; PSA: prostate-specific antigen.

tive follow-up and adjuvant treatment strategies should be formulated to improve long-term prognosis.

This study has several limitations. First, the follow-up period was limited to 3 years, and long-term survival outcomes were not observed, so the long-term safety and efficacy of this combined regimen still need further verification. Second, this study did not explore the optimal intervention cycle and different drug matching schemes of neoadjuvant therapy. Third, the prediction model failed to incorporate genetic molecular markers and emerging imaging prognostic indicators, which may affect its predictive efficiency. In the future, we will carry out prospective randomized controlled trials to further optimize the clinical application scheme

Table 8. Results of ROC curves for assessing 3-year BCR occurrence based on various risk factors

	Training set			Validation set		
	AUC	95% CI	Delong test	AUC	95% CI	Delong test
Surgical margin	0.690	0.608-0.772	<0.001	0.691	0.563-0.818	<0.001
Lymph node metastasis	0.676	0.593-0.759	<0.001	0.701	0.576-0.826	<0.001
PSA	0.813	0.753-0.872	0.029	0.817	0.721-0.913	0.024
Gleason score	0.764	0.699-0.829	0.002	0.773	0.672-0.873	0.003
Combine	0.881	0.833-0.930	-	0.876	0.789-0.964	

Note: BCR: biochemical recurrence; PSA: prostate-specific antigen; AUC: area under the curve; 95% CI: 95% confidence interval.

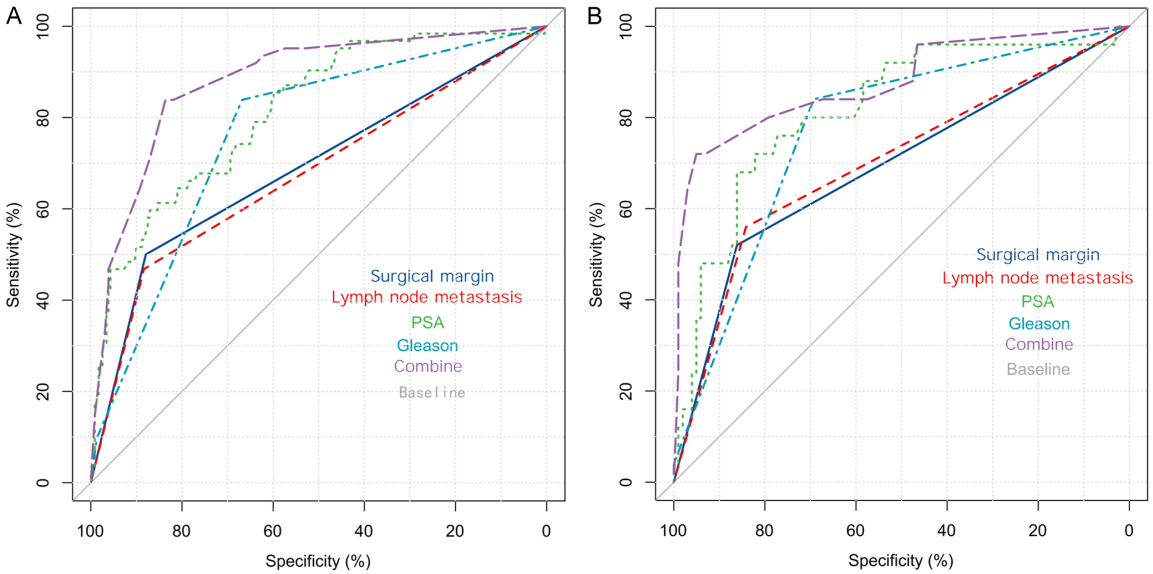

Figure 4. ROC curves predicting BCR in 3 year occurs for various risk factors: (A) Training set; (B) Validation set. Note: BCR: biochemical recurrence; PSA: prostate-specific antigen.

of NHT combined with RP, and enrich predictive variables to improve the clinical application value of the nomogram model.

In conclusion, NHT combined with RP can significantly reduce positive surgical margin rate, lymph node metastasis rate and 3-year BCR risk in HRPCa patients, and prolong BCRFS without increasing postoperative complications. Preoperative PSA level, Gleason score, surgical margin status and lymph node metastasis status are reliable independent predictors of 3-year postoperative BCR. The nomogram model established based on the above factors is worthy of clinical popularization and application.

Disclosure of conflict of interest

None.

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References

[1] Draulans C, Haustermans K, Pos FJ, van der Heide UA, De Cock L, van der Voort van Zyp J, De Boer H, Smeenk RJ, Kunze-Busch M, Monninkhof EM, De Roover R, Isebaert S and Kerkmeijer LGW. Stereotactic body radiotherapy with a focal boost to the intraprostatic tumor for intermediate and high risk prostate cancer: 5-year efficacy and toxicity in the hypo-FLAME trial. Radiother Oncol 2024; 201: 110568.

[2] Jin X, Tong W, Sun L, Lu S, Sun P, Li H and Liu Y. Association of composite dietary anti-

oxidant index with high risk of prostate cancer in middle-aged and elderly men: insights from NHANES. Front Immunol 2025; 16: 1530174.
[3] Shore N, Hafron J, Saltzstein D, Brown G, Belkoff L, Aggarwal P, Phillips J, Bhaumik A and McGowan T. Apalutamide for high-risk localized prostate cancer following radical prostatectomy (Apa-RP). J Urol 2024; 212: 682-691.
[4] Devos G, Tosco L, Baldewijns M, Gevaert T, Goffin K, Petit V, Mai C, Laenen A, Raskin Y, Van Haute C, Goeman L, De Meerleer G, Berghen C, Devlies W, Claessens F, Van Poppel H, Everaerts W and Joniau S. ARNEO: a randomized phase II trial of neoadjuvant degarelix with or without apalutamide prior to radical prostatectomy for high-risk prostate cancer. Eur Urol 2023; 83: 508-518.
[5] Gómez Rivas J, Ortega Polledo LE, De La Parra Sánchez I, Gutiérrez Hidalgo B, Martín Monterrubio J, Marugán Álvarez MJ, Somani BK, Enikeev D, Puente Vázquez J, Sanmamed Salgado N, Galante Romo MI and Moreno Sierra J. Current status of neoadjuvant treatment before surgery in high-risk localized prostate cancer. Cancers (Basel) 2024; 17: 99.
[6] Sun G, Liang Z, Jiang Y, Ma S, Chen S and Liu R. Clinical analysis of perioperative outcomes on neoadjuvant hormone therapy before laparoscopic and robot-assisted surgery for localized high-risk prostate cancer in a Chinese cohort. Curr Oncol 2022; 29: 8668-8676.
[7] Matsumoto K, Niwa N, Kosaka T, Takeda T, Yasumizu Y, Tanaka N, Morita S, Mizuno R, Shinojima T, Asanuma H and Oya M. Negative impact of neoadjuvant hormonal therapy on detecting biochemical recurrence after radical prostatectomy. Int J Clin Oncol 2021; 26: 1722-1728.
[8] Nakane K, Kawase M, Kato D, Iinuma K, Kawase K, Takeuchi S, Tobisawa Y, Ito T and Koie T. Combination approach using neoadjuvant therapy with radical prostatectomy for improving oncological outcomes of high-risk prostate cancer: a narrative review. Transl Cancer Res 2024; 13: 3889-3897.
[9] Arroyo-Rojas Y, Rodriguez-Sanchez L, Colandrea G, Otaola Arca H, Lanz C, Barret E, Sanchez-Salas R, Macek P and Cathelineau X. The role of androgen deprivation therapy prior to radical prostatectomy in high-risk prostate cancer: a systematic review. Minerva Urol Nephrol 2024; 76: 141-147.
[10] Triner D, Johnson K, Meah S, Daignault-Newton S, Vaishampayan N, Dhir A, Labardee C, Ferrante S, Ginsburg KB, Lane BR, George AK and Semerjian A. Recovery of social continence and sexual function in men with high-risk prostate cancer after radical prostatectomy: results from a statewide collaborative. Urology 2024; 193: 125-132.
[11] Bottillo I, Sciarra A, Bevilacqua G, Gentilucci A, Sciarra B, Santarelli V, Salciccia S, Bacigalupo F, Pastacaldi F, Ciccone MP, De Marchis L, Santini D, Magliocca FM, Merenda E, Forte F and Grammatico P. Early detection of the pathogenetic variants of homologous recombination repair genes in prostate cancer: critical analysis and experimental design. Biology (Basel) 2025; 14: 117.
[12] Fang AM, Jackson J, Gregg JR, Chery L, Tang C, Surasi DS, Siddiqui BA, Rais-Bahrami S, Bathala T and Chapin BF. Surgical management and considerations for patients with localized high-risk prostate cancer. Curr Treat Options Oncol 2024; 25: 66-83.
[13] Wang X, Qi M, Zhang J, Sun X, Guo H, Pang Y, Zhang Q, Chen X, Zhang R, Liu Z, Liu L, Hao X and Han B. Differential response to neoadjuvant hormonal therapy in prostate cancer: predictive morphological parameters and molecular markers. Prostate 2019; 79: 709-719.
[14] Tosco L, Laenen A, Briganti A, Gontero P, Karnes RJ, Albersen M, Bastian PJ, Chlosta P, Claessens F, Chun FK, Everaerts W, Gratzke C, Graefen M, Kneitz B, Marchioro G, Salas RS, Tombal B, Van den Broeck T, Moris L, Battaglia A, van der Poel H, Walz J, Bossi A, De Meerleer G, Haustermans K, Van Poppel H, Spahn M and Joniau S. The survival impact of neoadjuvant hormonal therapy before radical prostatectomy for treatment of high-risk prostate cancer. Prostate Cancer Prostatic Dis 2017; 20: 407-412.
[15] Freedland SJ, Davis M, Epstein AJ, Arondekar B and Ivanova JI. Real-world treatment patterns and overall survival among men with Metastatic Castration-Resistant Prostate Cancer (mCRPC) in the US Medicare population. Prostate Cancer Prostatic Dis 2024; 27: 327-333.
[16] Wang Z, Wang J, Li D, Wu R, Huang J, Ye L, Tuo Z, Yu Q, Shao F, Wusiman D, Cho WC, Koh SB, Xiong W and Feng D. Novel hormone therapies for advanced prostate cancer: understanding and countering drug resistance. J Pharm Anal 2025; 15: 101232.
[17] Farzat M, Weib P, Sukhanov I, Rosenbauer J, Tanislav C and Wagenlehner FM. Effect of neoadjuvant hormonal therapy on the postoperative course for patients undergoing robot-assisted radical prostatectomy. J Clin Med 2023; 12: 3053.
[18] Yang J, Xiong X, Zheng W, Liao X, Xu H, Yang L and Wei Q. Combining novel hormonal therapies with a poly (ADP-Ribose) polymerase inhibitor for metastatic castration-resistant prostate cancer: emerging evidence. Curr Oncol 2023; 30: 10311-10324.

[19] Wang H, Xue W, Yan W, Yin L, Dong B, He B, Yu Y, Shi W, Zhou Z, Lin H, Zhou Y, Wang Y, Shi Z, Ren S, Gao X, Wang L and Xu C. Extended focal ablation of localized prostate cancer with high-frequency irreversible electroporation: a non-randomized controlled trial. JAMA Surg 2022; 157: 693-700.

[20] Preisser F, Heinze A, S Abrams-Pompe R, Budäus L, Chun FK, Graefen M, Huland H and Tilki D. Impact of positive surgical margin length and Gleason grade at the margin on oncologic outcomes in patients with nonorgan-confined prostate cancer. Prostate 2022; 82: 949-956.

[21] Tosoian JJ, Zhang Y, Xiao L, Xie C, Samora NL, Niknafs YS, Chopra Z, Siddiqui J, Zheng H, Herron G, Vaishampayan N, Robinson HS, Arivoli K, Trock BJ, Ross AE, Morgan TM, Palapattu GS, Salami SS, Kunju LP, Tomlins SA, Sokoll LJ, Chan DW, Srivastava S, Feng Z, Sanda MG, Zheng Y, Wei JT and Chinnaiyan AM. Development and validation of an 18-gene urine test for high-grade prostate cancer. JAMA Oncol 2024; 10: 726-736.

[22] Ning J, Spielvogel CP, Haberl D, Trachtova K, Stoiber S, Rasul S, Bystry V, Wasinger G, Baltzer P, Gurnhofer E, Timelthaler G, Schlederer M, Papp L, Schachner H, Helbich T, Hartenbach M, Grubmüller B, Shariat SF, Hacker M, Haug A and Kenner L. A novel assessment of whole-mount Gleason grading in prostate cancer to identify candidates for radical prostatectomy: a machine learning-based multiomics study. Theranostics 2024; 14: 4570-4581.

[23] Guo H, Zhang L, Shao Y, An K, Hu C, Liang X and Wang D. The impact of positive surgical margin parameters and pathological stage on biochemical recurrence after radical prostatectomy: a systematic review and meta-analysis. PLoS One 2024; 19: e0301653.

[24] Xin S, Liu X, Li Z, Sun X, Wang R, Zhang Z, Feng X, Jin L, Li W, Tang C, Mei W, Cao Q, Wang H, Zhang J, Feng L and Ye L. ScRNA-seq revealed an immunosuppression state and tumor microenvironment heterogeneity related to lymph node metastasis in prostate cancer. Exp Hematol Oncol 2023; 12: 49.

[25] Sanli Y, Kuyumcu S, Sanli O, Buyukkaya F, İribaş A, Alcin G, Darendeliler E, Ozluk Y, Yildiz SO and Turkmen C. Relationships between serum PSA levels, Gleason scores and results of 68Ga-PSMAPET/CT in patients with recurrent prostate cancer. Ann Nucl Med 2017; 31: 709-717.

[26] Akkaya H, Dilek O, Özdemir S, Taş ZA, Öztürk İS and Gülek B. Can the Gleason score be predicted in patients with prostate cancer? A dynamic contrast-enhanced MRI, ((68))Ga-PSMA PET/CT, PSA, and PSA-density comparison study. Diagn Interv Radiol 2023; 29: 647-655.

[27] Mallikarjunappa SS and Osunkoya AO. Radical prostatectomy findings in patients with locally aggressive Grade group 5 prostatic adenocarcinoma and negative limited or extended pelvic lymph node dissection. Pathol Res Pract 2023; 244: 154415.

[28] Yamada Y, Fujii Y, Kakutani S, Kimura N, Sugimoto K, Hakozaki Y, Sugihara T, Takeshima Y, Kawai T, Nakamura M, Kamei J, Taguchi S, Akiyama Y, Sato Y, Yamada D, Urabe F, Miyazaki H, Enomoto Y, Fukuhara H, Nakagawa T, Fujimura T and Kume H. Development of risk-score model in patients with negative surgical margin after robot-assisted radical prostatectomy. Sci Rep 2024; 14: 7607.

[29] Höti N, Lih TS, Dong M, Zhang Z, Mangold L, Partin AW, Sokoll LJ, Kay Li Q and Zhang H. Urinary PSA and serum PSA for aggressive prostate cancer detection. Cancers (Basel) 2023; 15: 960.

[30] Shiota M, Takamatsu D, Matsui Y, Yokomizo A, Morizane S, Saito R, Miyake M, Tsutsumi M, Yamamoto Y, Tashiro K, Tomida R, Narita S, Edamura K, Yamaguchi T, Hashimoto K, Kato M, Kasahara T, Yoshino T, Akamatsu S, Kaneko T, Matsukawa A, Matsumoto R, Joraku A, Saito T, Kato T, Kato M, Enokida H, Sakamoto S, Terada N, Kanno H, Nishiyama N, Kimura T, Kitamura H and Eto M. Prognostication in lymph node-positive prostate cancer with no PSA persistence after radical prostatectomy. Ann Surg Oncol 2024; 31: 3872-3879.

[31] Kroon LJ, Remmers S, Busstra MB, Gan M, Klaver S, Rietbergen JBW, van der Slot MA, Hollemans E, Kweldam CF, Bangma CH, Roobol MJ and van Leenders G. Centralized prostatectomy with intraoperative NeuroSAFE margin assessment improves surgical margin control. Histopathology 2024; 85: 760-768.