# A nomogram to predict the upgrading rate of ISUP grades of RP in patients undergoing transrectal prostate biopsy and transperineal prostate biopsy

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**Research**

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# Abstract

**Backgroud:** This study was aimed to develop and internally validate a nomogram for risk of upgrade of ISUP (International Society of Urology Pathology) grade group from biopsy tissue to RP (radical prostatectomy) final histology.

**Methods:** 166 patients with prostate cancer were retrospectively analyzed and divided into two groups based on ISUP upgrade status from needle biopsy to radical prostatectomy specimen, these being the 'ISUP upgrade' group and the 'no ISUP upgrade' group. Logistic regression analysis was used to predict the significant independent factors for ISUP upgrade. A nonogram was then developed based on these independent factors, which would predict risk of ISUP upgrade. The C-index, calibration plot, and decision curve analysis were used to assess the discrimination, calibration, and clinical usefulness of the predicting model. Internal validation was evaluated by using the bootstrapping validation.

**Results:** There were 47 patients in the ISUP upgrade group and 119 patients in the no ISUP upgrade group respectively. Patients in the ISUP upgrade group tended to be of younger age, smaller PV (prostate volume), lower GS (Gleason score) of PB (prostate biopsy) tissue than the no ISUP upgrade group (p=0.043, p=0.041, p < 0.001, p =0.04, respectively). Multivariate logistic regression analysis showed that GS ≤6 (OR=14.236, P=0.001), prostate biopsy approach (TB-SB (transperineal prostate systematic biopsy) VS TR-SB (transrectal prostate systematic biopsy), OR=0.361, P=0.03) and number of positive cores < 10 (OR=0.396, P=0.04) were the independent risk factors for ISUP upgrade. A prediction nomogram model of ISUP upgrade was built based on these significant factors above, the area under the receiver operating characteristic (AUC) curve of which was 0.802. The C-index for the prediction nomogram was 0.798 (95%CI: 0.655–0.941) and the nomogram showed good calibration. High C-index value of 0.772 could still be reached in the interval validation. Decision curve analysis also demonstrated that the threshold value of RP-ISUP upgrade risk was 3% to 67%.

**Conclusion:** A novel nomogram incorporating PSA, GS of PCa, ways of prostate biopsy and number of positive cores was built with a relatively good accuracy to assist clinicians to evaluate the risk of ISUP upgrade in the RP specimen, especially for the low-risk prostate cancer diagnosed by TR-SB.


# Introduction

Prostate cancer (PCa) is a common malignant cancer in middle-aged and elderly men. With the aging process and the popularity of early screening for prostate cancer at home and abroad, the incidence of prostate cancer is on the rise at present [1]. The diagnosis of prostate cancer still depends on histopathology obtained by prostate biopsy, which is the gold standard for the diagnosis of prostate cancer. The Gleason score reported from prostate needle biopsy is considered an important factor in assessing prognosis for prostate cancer and therefore in guiding treatment decisions. However, many studies have shown poor correlation of GS at needle biopsy and that of the corresponding RP specimen. The concordance rate of them was only 28%-58%: 27% ~ 60% for low GS, and 8% ~ 32% for high GS [2]. In

2014, the improved GS system put forward by the International Society of Urology Pathology (ISUP) was the latest and most accurate grade system for prostate cancer[3, 4],which was widely used to assess the malignant degree of prostate cancer, at the same time, the new ISUP grade system evaluated better to guide the next treatment and assess the prognosis of patients with prostate cancer than the previous GSs system. However, even based on the 2014 ISUP grade system, the pathology grade of RP specimens was still higher than that of prostate biopsy tissues with an incidence of 20% ~ 30%[5, 6].

At present, few studies focus on the ISUP upgrade risk from prostate biopsy tissue to RP specimen, so we analyzed the risk factors of ISUP upgrade after RP compared with biopsy tissue, and a nomogram was established based on the significant risk factors, which could assist clinicians with an important reference when drawing up treatment plans for prostate cancer patients based on the clinical results of prostate biopsy.

# Patients And Methods

### Patients

This study retrospectively analyzed 736 patients with suspected prostate cancer admitted to the Affiliated Hospital of Qingdao University from May 2019 to May 2020, who underwent transrectal or transperineal prostate biopsy to diagnose prostate cancer, and 353 patients were identified to be with prostate cancer.

Exclusion criteria: (1). Patients without RP after prostate biopsy (54 cases); (2). Patients with ADT therapy and other treatments (35 cases); (3). Patients with chronic or acute inflammatory reaction (20 cases); (4). Patients combined with other malignant tumors (17 cases); (5). Patients with incomplete data (61 cases). This study included 166 patients at last, whose data were complete and detailed, the changes of ISUP grade in biopsy and RP were compared so as to identify the predictive factors of ISUP upgrade. This study was approved by the ethics committee of the Affiliated Hospital of Qingdao University.

### Methods

The WHO/ISUP 2014 classification system were divided into five groups, which were group 1: GS 3+3=6/10; Group 2: GS 3+4=7/10; Group 3: GS 4+3=7/10; Group 4: Gleason total score 8 and Group 5: Gleason total score 9-10 [3]. The ISUP upgrade group was defined as the increase grade of ISUP in RP specimen compared with prostate biopsy tissue. Then the patients were divided into the ISUP upgrade group (n= 47) and the ISUP non-upgrade group (n=119) according to the postoperative ISUP grade, and the independent factors for the prediction of ISUP elevation were analyzed. All pathologic diagnosis were identified by at least 2 pathologists. All patients were informed about the procedure of prostate biopsy and written informed consent were obtained.The prostate biopsy approaches included transrectal ultrasound (TRUS)-guided prostate systematic biopsy (TR-SB) and transperineal systematic biopsy (TB-SB). RP was performed in patients diagnosed with prostate cancer after biopsy.

All patients underwent mpMRI on a 1.5-T MRI or 3.0-T MRI, and patients had at least three sequences-triplanar T2 weighted, diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC), region of interest was identified on MRI by our surgeon during preoperative preparation.

### Biopsy

Transrectal prostate systematic biopsy (TR-SB): Systematic biopsy include 12slices was obtained from apex, apex lateral, mid, mid lateral, base and base lateral of right and left prostatic lobes of prostate[7], the biopsy number might vary according to the prostate volume or additional suspicious transrectal ultrasound findings. Biopsy tissue were fixed in a separate glass bottle containing 10% formaldehyde solution.

Transperineal prostate systematic biopsy (TB-SB): Systematic biopsy was typically 12 cores collected in the medial and lateral aspects of the apical, mid, and base of the prostate on the left and right side. Biopsy tissue were also fixed in a separate glass bottle containing 10% formaldehyde solution.

### Data collection

Preoperative and postoperative clinical characteristics and histopathological results were evaluated for each patient. Upgrade of ISUP and no ISUP upgrade of the tumor from biopsy to final pathology were recorded for each patient. Patient's records including age, PSA, PV, PSAD, Prostate biopsy, Total biopsy cores, Number of positive cores, Biopsy tumor percentage, T stage, GS of PCa and PSM (positive surgical margin) were retrieved from the hospital database for retrospective analysis.

### Statistics

Data was analyzed by IBM SPSS Statistics ver. 22.0 (IBM Corp., Armonk, NY, USA) and R 4.0.2 (formerly AT&T, now Lucent Technologies). Continuous variables were analyzed by using Student t test in variables with normal distribution. Categorical variables were compared using Chi-square test and Mann-Whitney U test. Uni and multiply logistic regression model for analyzing the effects of patients' clinical characteristics between ISUP Upgrade and No ISUP upgrade. The independent factors for the prediction of pathological escalation were identified and a nomogram model was established. The prediction of nomogram was evaluated by ROC curve (receive operating characteristic) and AUC (area under the curve). Bootstrap resampling was used to verify the model, at the same time, the calibration curve and DCA (decision curve analysis) were draw to evaluate the model. All P values were two-sided, and a difference of $P<0.05$ was considered statistically significant.

## Results

166 patients were evaluated in our study, comprising 47 patients in the ISUP upgrade group and 119 patients in the no ISUP upgrade group based on the change of ISUP grade. The mean age of patients was 68.99 ± 7.61, and the mean PSA of patients was 37.93 ± 50.77. The patient's clinical and histopathologic

characteristics were demonstrated in Table 1. As shown in the table, patients in the ISUP upgrade group showed younger age, smaller PV and lower GS scores than the no ISUP upgrade group ($p = 0.043$, $p = 0.041$, $p < 0.001$, $p = 0.04$, respectively), in addition, more patients in the TR-SB group inclined to the ISUP upgrade group than the TB-SB group ($P = 0.007$).

There were 66 patients and 100 patients underwent TB-SB and TR-SB, respectively. Table 2 showed the GS of PCa patients in the two ways of prostate biopsy groups. It demonstrated that TB-SB found more csPCa of patients (GS $\geq$ 7) than the group of TR-SB (44.8%VS38.8%, $P = 0.112$), but there were no significant differences in the detection rate of csPCa and PCa between the two prostate biopsy ways.

Table 3 and Fig. 1 showed the differences between the pathology ISUP of preoperative biopsy and pathological specimen, 47 of 166 patients were found with the ISUP group upgrade, whereas no ISUP upgrade was observed in the remaining 119 patients. The distribution of ISUP group of pathological specimen were 13 patients in Group 1, 39 patients in Group 2, 25 patients in Group 3, 24 patients in Group 4, 65patients in Group 5, respectively. The concordance from PB-ISUP group to RP-ISUP group was highest for GR5 (89.36%) and lowest for GR1 (39.4%), and 34.78% of patients in the biopsy GR 2, 38.46% patients in GR3 and 32.43% patients in GR 4 were upgraded respectively.

The results of the univariate and multivariate logistic regression analysis were displayed on the Table 4. A younger age, a higher preoperative PSA level, a smaller PV, a higher PSAD, ways of prostate biopsy, a fewer number of positive biopsy cores as well as percentage of cores, and PB-GS predicted ISUP upgrade in the univariable analysis. In the multivariable analysis, GS $\leq$ 6 (OR = 14.236, $P = 0.001$), prostate biopsy approach (TB-SB VS TR-SB, OR = 0.361, $P = 0.03$) and number of positive cores < 10 (OR = 0.396, $P = 0.04$) were found as the independent predictors to the RP-ISUP upgrade.

Based on the results of independent prognostic factors obtained by multivariate logistic regression analysis, a predicted model that incorporated the above independent predictors was constructed to predict the probability of postoperative ISUP upgrade of the specimen, which was developed and presented as the nomogram (Fig. 2).

The calibration curve of this RP-ISUP upgrade risk nomogram for the prediction of ISUP upgrade in prostate biopsy patients could well demonstrate the risk of ISUP upgrade after RP (Fig. 3), which displayed a high consistency between predicted and measured values. The C-index for the prediction nomogram was 0.798 (95%CI: 0.655–0.941) for our patients, moreover, the prediction nomogram was evaluated by ROC curve (Fig. 4), and the AUC (area under curve) of the ROC was 0.802. The predicted value of the nomogram was in further certified to be 0.772 through bootstrapping validation.

Figure 5 showed the decision curve of the predicted nomogram, and a positive net benefit was obtained in the range of threshold probabilities ranging from 0.03 to 0.67 in the model, using this RP-ISUP upgrade nomogram in the current study to predict RP-ISUP upgrade risk adds more benefit than the intervention-all-patients scheme or the intervention-none scheme.

# Discussion

Prostate cancer is the second most common cancer in males worldwide and continues to be a major cause of cancer deaths [8, 9]. Although patients were diagnosed to be prostate cancer by prostate biopsy, some patients were usually underestimated or overestimated for some subjective and objective reasons, which could result in delayed treatment or overtreatment. Biopsy sample could not reflect the overall pathological characteristics of the disease, and previous studies have reported the inconsistency in GS between prostate biopsy tissues and radical specimens [10]. Epstein and colleagues reported a significant incidence of both upgrading and downgrading of GS from prostate biopsy to RP [11]. It has been reported that almost 30% of patients with low-risk prostate cancer had aggressive features in their RP specimens [12]. The potential for under-treatment or overtreatment due to incorrect grading is a concern. In November 2014 the International Society of Urological Pathology (ISUP) proposed a contemporary Gleason group grading system as an update to the traditional 2005 system, Studies have confirmed that the 2014 ISUP group grading system could more accurately predict cancer-specific survival for prostate cancer as well as the rate of biochemical recurrence after RP [12, 13]. This was accepted by the World Health Organisation in 2016. In addition, The 2014 ISUP grouping system could reduce the incidence of postoperative pathological upgrading, although 19.5% of patients still had clinically significant grade upgrade[14]. The 'ISUP upgrade' group in our study represented 28.3% of the total patients, in comparison to Brassetti and colleagues who found that 41.4% of patients in their European center were upgraded on RP specimen[15], This higher proportion may be due to multifocal growth of prostate cancer with high heterogeneity [16]. Similarly, different methods of prostate biopsy will also influence the discrepancy in pathological grade between biopsy and RP.

In recent years, some predictive models and clinical parameters including PSA, biopsy and clinical stage have been used to assess the postoperative pathological escalation risk of prostate cancer[17–20], but there were no widely accepted models. The ability of these models to predict upgrading of pathology remains limited at present and they rarely incorporated the different prostate biopsy approaches into the models. In this current study, clinical and pathological parameters that may result in ISUP grade group upgrading were analyzed. Significant factors influencing ISUP grade group upgrade were found to be: GS, prostate biopsy approach and number of positive cores. A nomogram to predict risk of ISUP grade group upgrading was built based on the above independent factors incorporating PSA. The nomogram was found to have good discrimination and calibration power, based on internal validation in this cohort, as well as a high C-index and AUC which demonstrate that the nomogram could be widely accepted and used in the clinic-setting. Compared with previous research[20], this study included more predictive factors, which ensured that the prediction model established in this study was more accurate and credible.

In general, RP is not required at diagnosis for patients with low-risk PCa as these patients are safely managed with active surveillance (AS) protocols. However, some authors have pointed out that postoperative pathological upgrading does exist in these patients, with other literature reporting that this is more often seen in younger patients with PCa[21]. Therefore, accurate examination results before

surgery and precise prediction of postoperative pathological results were of great significance to the decisions of further treatment. It was reported that postoperative pathological upgrade was related to younger age patients with prostate cancer [21]. In the current study, although age was not an independent risk factor for ISUP-upgrade, the mean age in the ISUP-upgrade group was significantly younger than the no-ISUP-upgrade group (p = 0.043).

Serum PSA is an important component in risk stratifying patients with PCa, which is supported by research from local and foreign authors that found PSA positively correlated with GS on RP specimens [22, 23]. Although the current study similarly found that patients with PSAs ≥ 20 tended to have more aggressive PCa than those with lower PSAs, ISUP group of those patients did not show to tend to upgrade in our study.

GS of PCa, ways of prostate biopsy and number of positive cores were associated with greater odds of ISUP upgrade, who underwent subsequent biopsies as part of AS (active surveillance), and we found that these three factors were all related with the prostate biopsy, results showed that the TB-SB were more accurate in the ISUP of prostate biopsy tissue than the TR-SB, systemic prostate biopsy guided by transrectal ultrasound were the most common prostate biopsy to diagnose prostate cancer[24]. However, literature has shown that transrectal systematic prostate biopsy is less sensitive in detecting more aggressive PCa than TP-SB, patients with low-risk PCa who undergo TR-SB show a 25–30% rate of pathological upgrade from biopsy to RP. This is especially seen in patients with anterior tumors and large prostates [25], and the current study showed that TP-SB detects more csPCa than TR-SB (44.8% vs 38.8%,P = 0.112),although there was no significant difference, this demonstrated that transpereal prostate biopsy will likely reduce the probability of upgrading ISUP group grade in RP specimens, which could not only improve the detection rate of csPCa, but also reduce the probability of pathology escalation after radical surgery. It could provide clinicians with more accurate information in order to make the most suitable treatment for patients.

Therefore, accurate prognostic assessment would assist doctors to reevaluate the patients with ISUP disparities and take timely interventions to prevent testing in low-risk situations, which could also avoid delays or discontinuity in treatment when there was a high probability of a favorable net benefit. The prediction model was very conducive to the accurate assessment of the disease for the low-risk prostate cancer patients with active monitoring and simple conservative treatment. Moreover, the prediction model of this study included many significant clinical factors, which had strong predictive value through internal verification.

Limitations of this study include it being retrospective and conducted in a single center. Clinical outcomes such as CSS and biochemical recurrence were not assessed for patients within the two groups (ISUP upgrade and no ISUP upgrade), therefore the impact of this nomogram on outcomes is not known. In addition, although the overall accuracy of this model is higher than that of previous models, this nomogram needs to undergo external validation.

# Conclusion

This novel nomogram shows good accuracy in assisting clinicians to evaluate the risk of ISUP upgrading from prostate biopsy to radical prostatectomy. The nomogram is best used in patients with low-risk prostate cancer, where it can assist in clinical decision-making. This study also showed good correlation between the ISUP grade group reported from transperineal prostate biopsies compared to the respective radical prostatectomy specimens. Further research and external validation of this nomogram are recommended to assess its accuracy.

# Declarations

**Ethics approval**: This study was approved by the Ethic Committee of the Affiliated Hospital of Qingdao University.

**Consent to participate:** Informed consent was obtained in both written and verbal format from patients or guardian for participants under 16 years old to participate.

**Informed consent:** Not applicable.

**Availability of data and material:** Records and data pertaining to this study are in the patient's secure medical records in the Affiliated Hospital of Qingdao University

**Disclosure of potential conflicts of interest:** Not applicable.

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# Tables

Table 1. Patient Characteristics

| Characteristics | ISUP Upgrade | No ISUP upgrade | p |
|---|---|---|---|
| Cases (n) | 47(28.3%) | 119(71.7%) | |
| Age(year) | | | |
| Mean±s.d | 68.68±7.98 | 69.12±7.49 | 0.74 |
| 60 | 8(17%) | 8(6.7%) | 0.043 |
| ≥60 | 39(83%) | 111(93.3%) | |
| PSA (ng ml−1) | | | |
| ≤10 | 3(6.4%) | 27(22.7%) | 0.07[a] |
| 10-20 | 18(38.3%) | 38(31.9%) | |
| ≥20 | 26(55.3%) | 54(45.4%) | |
| PV (ml) | | | |
| 50 | 37(78.7%) | 74(62.2%) | 0.041 |
| ≥50 | 10(21.3%) | 45(37.8%) | |
| PSAD | | | |
| 0.20 | 2(4.3%) | 20(16.8%) | 0.058 |
| ≥0.20 | 45(95.7%) | 99(83.2%) | |
| T stage | | | |
| ≤T2a | 10(21.3%) | 26(21.8%) | 0.378[a] |
| T2b | 10(21.3%) | 13(10.9%) | |
| ≥T2c | 27(57.4%) | 80(67.3%) | |
| Gleason score of PCa | | | |
| ≤6 | 20(42.6%) | 13(10.9%) | 0.001 |
| ≥7 | 27(57.4%) | 106(89.1%) | |
| PB | | | |
| TR-SB | 36(76.6%) | 64(53.8%) | 0.007 |
| TB-SB | 11(23.4%) | 55(46.2%) | |
| Number of positive cores | | | |
| 10 | 33(70.2%) | 77(64.7%) | 0.499 |
| ≥10 | 14(29.8%) | 42(35.3%) | |
| Total biopsy cores | | | |
| ≤12 | 28(59.6%) | 51(42.9%) | 0.052 |
| 12 | 19(40.4%) | 68(57.1%) | |
| Total core percentage | | | |
| ≤5% | 9(19.1%) | 8(6.7%) | 0.093[a] |
| 5%-20% | 5(10.6%) | 15(12.6%) | |
| ≥20% | 33(70.3%) | 96(80.7%) | |
| PSM | | | |
| Y | 24(51%) | 48(40.3%) | 0.209 |
| N | 23(49%) | 71(59.7%) | |

a: Mann-Whitney U; PSA: prostate antigen; PV: prostate volume; PSAD: prostate antigen density; GS: gleason score; PB: prostate biopsy; TR-SB: transrectal biopsy; TB-SB: transperineal biopsy; PSM: positive surgical margin; ISUP: International Society of Urologic Pathology;

**Table 2.** DR of PCa and csPCa (clinical significant prostate cancer) between TB-SB and TR-SB

| DR GS,n(%) | TB-SB | TR-SB | P |
|---|---|---|---|
| DR | 135/270(50%) | 218/466(46.8%) | 0.4 |
| 7 | 14/135(10.4%) | 37/218(17.0 %) | 0.086 |
| Percent of ≥7 | 121/135(89.6%) | 181/218(83%) | 0.086 |
| DR of csPCa ≥7 | 121/270(44.8%) | 181/466(38.8%) | 0.112 |

TR-SB: transrectal systematic biopsy; TB-SB: transperineal systematic biopsy; csPCa: clinical significant prostate cancer

Table 3. Difference between preoperative needle biopsy ISUP and pathological specimen ISUP

| Preoperative needle biopsy ISUP grade | Pathological specimen ISUP grade 1 | 2 | 3 | 4 | 5 | Total |
|---|---|---|---|---|---|---|
| 1 | 13 | 14 | 4 | 1 | 1 | 33 |
| 2 | 0 | 15 | 5 | 2 | 1 | 23 |
| 3 | 0 | 5 | 11 | 1 | 9 | 26 |
| 4 | 0 | 3 | 4 | 18 | 12 | 37 |
| 5 | 0 | 2 | 1 | 2 | 42 | 47 |
| Total | 13 | 39 | 25 | 24 | 65 | 166 |

ISUP: International Society of Urologic Pathology

Table 4. Uni- and multivariable logistic regression to predict (a) ISUP upgrade from biopsy to radical prostatectomy

| Characteristics | β, OR (95% CI), P | β, OR (95% CI), P |
|---|---|---|
| Age(year) | | |
| <60VS≥60 | 1.046,2.846(1-8.098),0.050 | 0.142,1.153(0.313-4.244),0.83 |
| PSA (ng ml−1) | | |
| ≤10 | | |
| 10-20VS<10 | 1.45,4.263(1.141-15.928),0.031 | 1.028,2.796(0.528-14.798),0.227 |
| ≥20VS<10 | 1.466,4.333(1.203-15.605),0.025 | 1.504,4.499(0.793-25.541),0.09 |
| PV (ml) | | |
| <50VS≥50 | 0.811,2.25(1.02-4.961),0.044 | 0.863,2.371(0.851-6.605),0.099 |
| PSAD | | |
| <0.20VS≥0.20 | -1.514,0.220(0.049-0.982),0.047 | -0.28,0.756(0.103-5.529),0.783 |
| T stage | | |
| ≤T2a | | |
| T2bVS≤T2a | 0.693,2(0.665-6.013),0.217 | |
| ≥T2cVS≤T2a | -0.131,0.878(0.375-2.053),0.763 | |
| Gleason score of PCa | | |
| ≤6VS≥7 | 1.798,6.04(2.67-13.661),0.001 | 2.656,14.236(3.502-57.873),0.001 |
| PB | | |
| TB-SB VSTR-SB | -1.034,0.356(0.165-0.764),0.008 | -1.02,0.361(0.143-0.908),0.03 |
| Total biopsy cores | | |
| ≤12VS<12 | 0.675,1.965(0.989-3.904),0.054 | |
| Number of positive cores | | |
| <10VS≥10 | -0.820,0.441(0.222-0.876),0.019 | -0.925,0.396(0.164-0.96),0.04 |
| Total core percentage | | |
| ≤5% | | |
| 5%-20%VS≤5% | -1.216,0.296(0.074-1.189),0.086 | -0.165,0.848(0.132-5.427),0.861 |
| ≥20%VS≤5% | -1.186,0.306(0.109-0.857),0.024 | 0.33,1.391(0.25-7.734),0.706 |
| PSM | | |
| YVSN | 0.434,1.543(0.783-3.044),0.210 | |

PSA: prostate antigen; PV: prostate volume; PSAD: prostate antigen density; GS: gleason score; PB: prostate biopsy; TR-SB: transrectal biopsy; TB-SB: transperineal biopsy; PSM: positive surgical margin; ISUP: International Society of Urologic Pathology;

# Figures

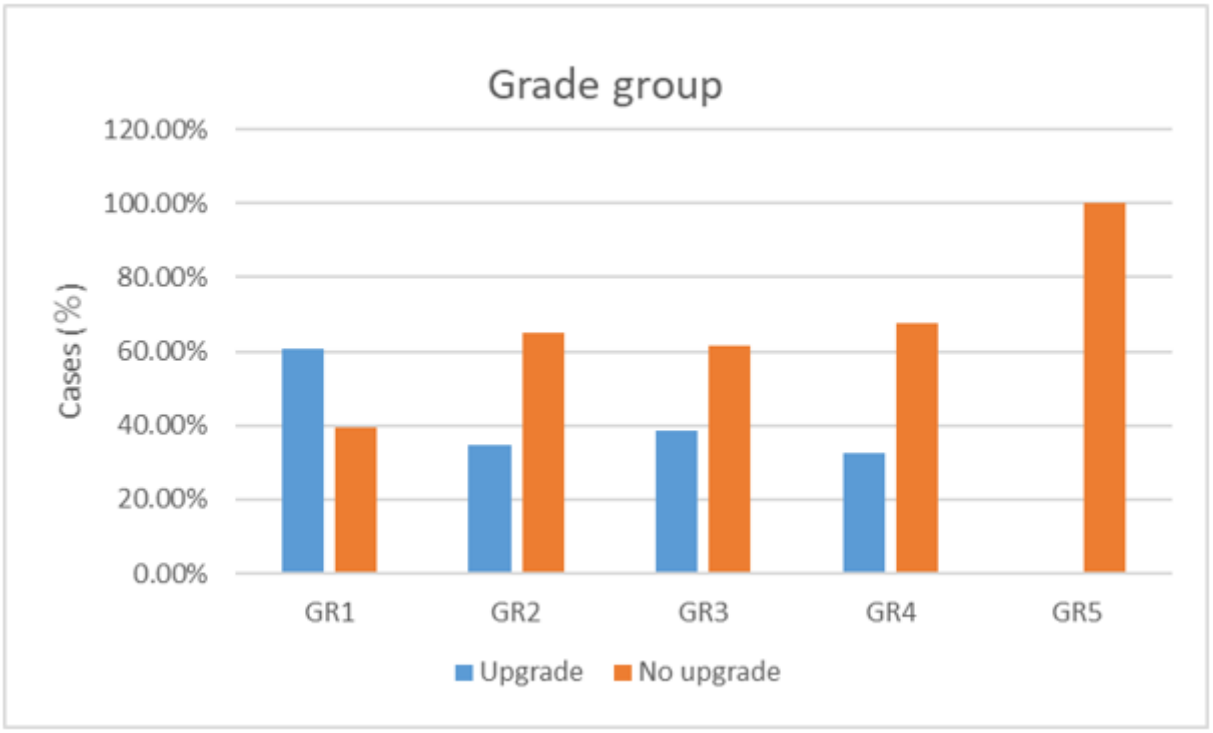
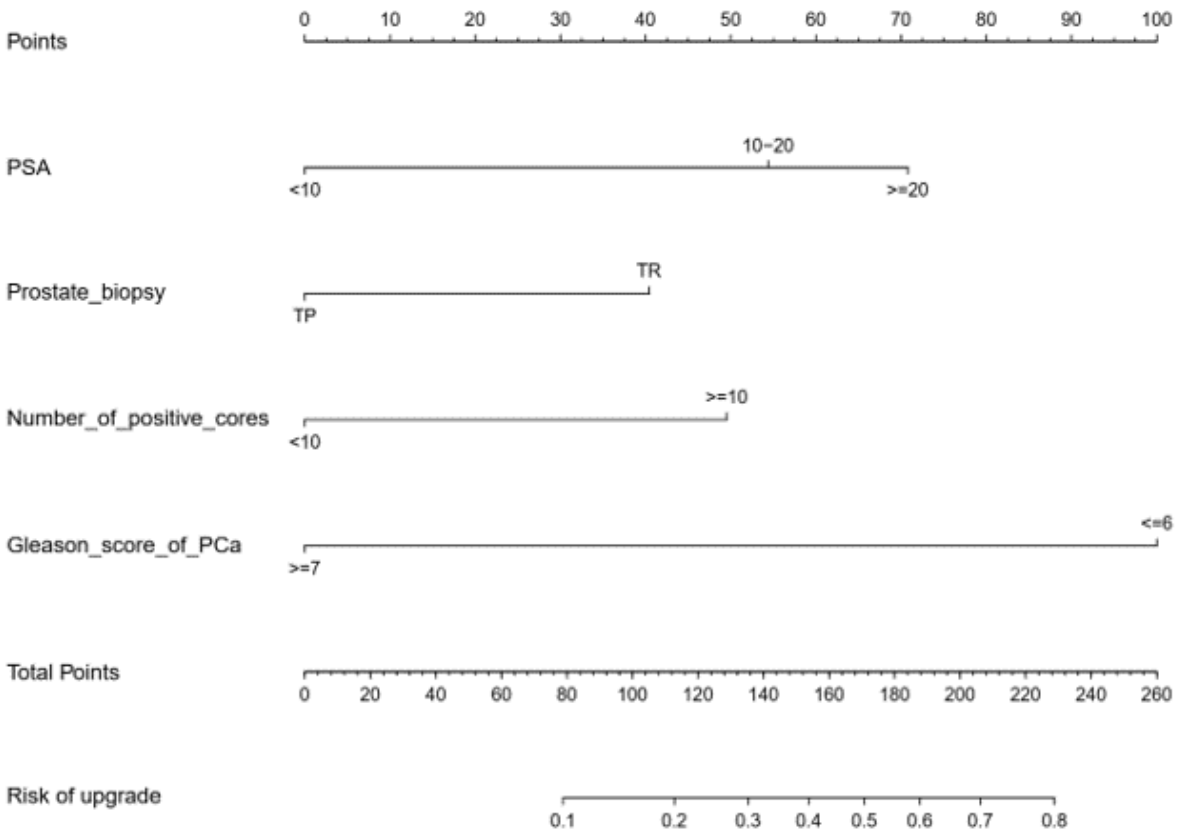


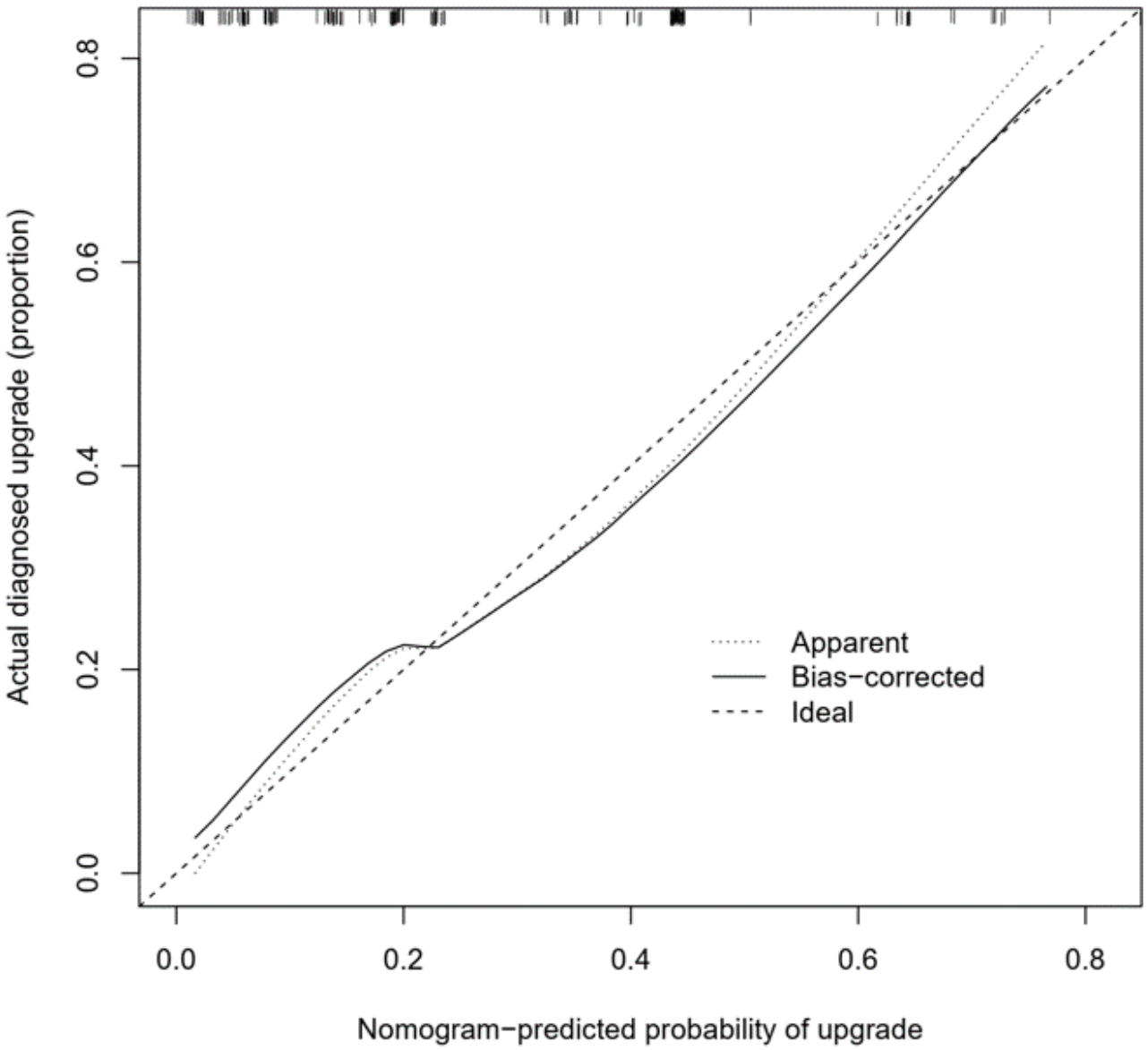

**Figure 1**

Concordance for individual ISUP grade groups 1–5 from biopsy to radical prostatectomy.



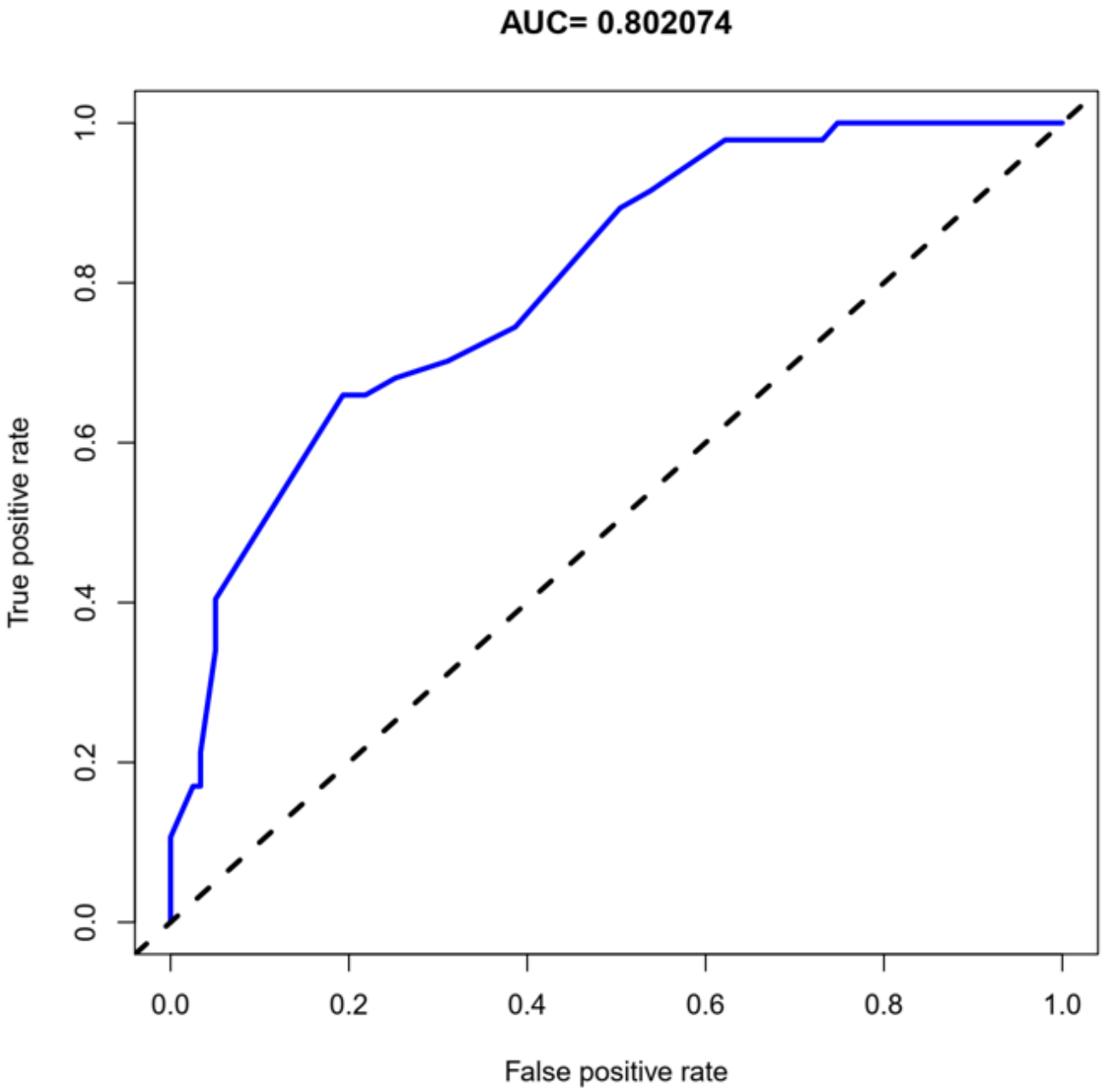

## Figure 2

RP-ISUP upgrade nomogram Note: The RP-ISUP upgrade nomogram was developed in the cohort, with the use of PSA, Prostate biopsy, Number of positive cores, GS of PCa. Abbreviations: PSA: prostate antigen; GS: gleason score; PB: prostate biopsy; ISUP: International Society of Urologic Pathology;



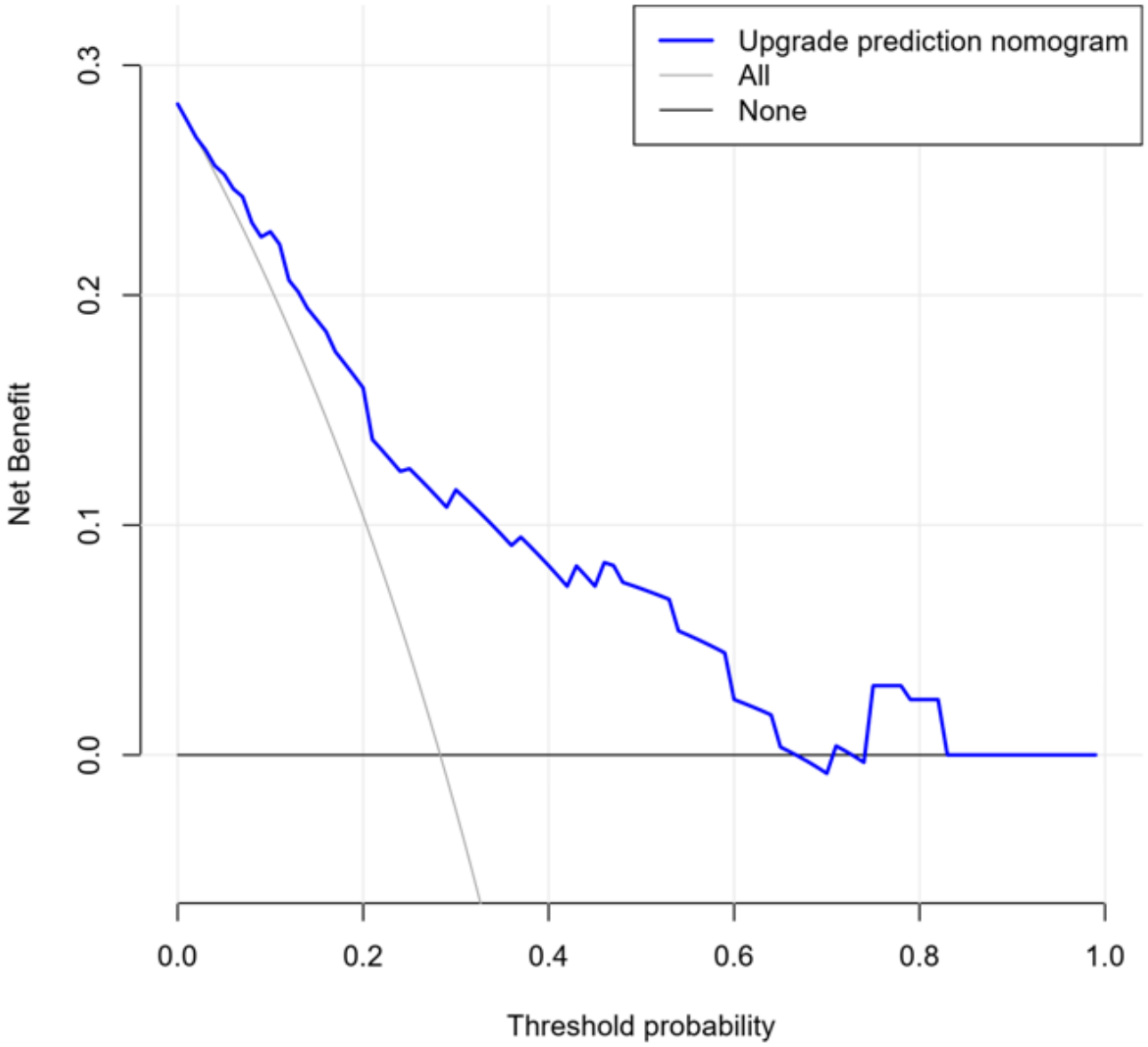

## Figure 3

Calibration curves of the RP-ISUP upgrade nomogram prediction in the cohort. Notes: The x-axis represents the predicted RP-ISUP upgrade risk. The y-axis represents the actual diagnosed RP-ISUP upgrade proportion. The diagonal dotted line represents a perfect prediction by an ideal model. The solid line represents the performance of the nomogram, of which a closer fit to the diagonal dotted line represents a better prediction.




## Figure 4

The ROC curve of the Nomogram model to predict the RP-ISUP upgrade.




## Figure 5

Decision curve analysis for the RP-ISUP upgrade nomogram. Notes: The y-axis measures the net benefit. The dotted line represents the RP-ISUP upgrade risk nomogram. The thin solid line represents the assumption that all patients are RP-ISUP upgrades. The thick solid line represents the assumption that no patients are no upgrade to RP-ISUP. The decision curve showed that the threshold value of RP-ISUP upgrade risk is 3%to 67%, using this RP-ISUP upgrade nomogram in the current study to predict RP-ISUP upgrade risk adds more benefit than the intervention-all-patients scheme or the intervention-none scheme.