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ORIGINAL RESEARCH

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# The value of the magnetic resonance apparent diffusion coefficient in predicting Gleason grouping upgrading after radical prostatectomy

Chao Zhong[1], Jun-Guang Wang[1,*]

[1]Department of Radiology, Ningbo Yinzhou NO. 2 Hospital, 315000 Ningbo, Zhejiang, China

***Correspondence**
tsjunguang@163.com
(Jun-Guang Wang)

## Abstract

**Background**: This study aims to evaluate the predictive value of apparent diffusion coefficient (ADC) measurements in identifying cases where Gleason grade grouping is upgraded following radical prostatectomy (RP). Accurate preoperative assessment of prostate cancer (PCa) aggressiveness remains a critical challenge, particularly in anticipating discrepancies between biopsy-based and post-surgical Gleason grading. **Methods**: A retrospective analysis was conducted on clinical and MRI data from 135 patients with PCa who underwent both biopsy and RP. Patients were categorized into two groups based on whether their Gleason grade group was upgraded postoperatively. Variables showing significant differences between the Gleason grade upgrade (GGU) and non-Gleason group upgrade (non-GGU) groups were included in a multivariable logistic regression analysis to identify independent predictors of GGU following laparoscopic radical prostatectomy. Receiver operating characteristic (ROC) curves were generated for each independent predictor to evaluate their diagnostic performance in detecting GGU. Clinical decision curve analysis was performed to assess the clinical net benefit of ADC value, body mass index (BMI) and percentage of positive needles. **Results**: The univariate analysis indicated statistically significant differences among groups in terms of BMI, ADC, prostate imaging and data reporting system (PI-RADS) v2.1 and so on ($p < 0.05$). Multivariable logistic regression analysis showed BMI, percentage of positive needles, and ADC as independent risk factors for GGU in PCa ($p < 0.05$). ROC curve analysis showed that the best threshold for predicting GGU in PCa was ADC $\geq 0.75 \times 10^{-3}$ mm$^2$/s. The clinical decision curve analysis demonstrated that the ADC value, BMI, and the percentage of positive biopsy cores provided greater net clinical benefits in predicting GGU. **Conclusions**: Based on the 2014 International Society of Urological Pathology (ISUP) grading criteria, this study found that ADC value, BMI and percentage of positive biopsy cores demonstrated the strongest diagnostic performance in predicting GGU in PCa.

## Keywords

Prostate cancer; Apparent diffusion coefficient; Gleason group; Body mass index

## 1. Introduction

Prostate cancer (PCa) is one of the most common malignant tumors in men, and has the second-highest incidence rate in men [1]. Currently, the grading of prostate biopsy and radical prostatectomy (RP) specimens follows the revised Gleason grading system introduced by the International Society of Urological Pathology (ISUP) in 2014, which provides an effective framework for stratifying PCa risk [2, 3]. A study reported that about 20–30% of RP specimens were higher than those of prostate needle biopsy specimens [4]. Multiparametric magnetic resonance imaging (mpMRI) is considered the best imaging method for preoperative diagnosis and evaluation of PCa. Furthermore, it has a significant role in the treatment and prognosis of patients [5, 6]. The European Society of Genitourinary Radiology further standardized prostate imaging by introducing the Prostate Imaging Reporting and Data System version 2.1 (PI-RADS v2.1), which enhances the detection and risk stratification of prostate lesions [7]. The precise relationship between PI-RADS v2.1 guidelines and pathological Gleason grade upgrade (GGU) in PCa remains unclear. To address this gap, the present study incorporated clinical parameters, imaging findings and preoperative biopsy results to assess the diagnostic performance of each factor in predicting GGU. The ultimate goal was to support clinicians with more reliable diagnostic tools, therefore minimizing the risks of overdiagnosis and inaccurate diagnosis in patients with PCa.

## 2. Materials and methods

### 2.1 Patient information

The clinical data of 135 patients who underwent mpMRI and ultrasound-guided prostate biopsy before RP at Ningbo Urology and Nephrology Hospital between September 2018 and May 2024, were retrospectively analyzed. The ISUP pathological grade from the postoperative RP specimens served as the reference standard.

Inclusion criteria were as follows:

(1) No previous endocrine therapy, radiotherapy, or chemotherapy before the mpMRI examination;

(2) Completion of ultrasound-guided systematic prostate biopsy following mpMRI;

(3) An interval of no more than one month between mpMRI and RP;

(4) Availability of complete postoperative pathological data.

Exclusion criteria included:

(1) Poor-quality MRI images that hindered accurate diagnosis or measurement;

(2) Incomplete clinical data.

Refer to Fig. 1 for detailed patient characteristics.

### 2.2 Instruments and methods

MRI examinations were conducted using a GE SIGNA Voyager 1.5T superconducting scanner (Boston, Massachusetts, USA) equipped with an abdominal phased-array coil for signal reception. Before imaging, patients were instructed to empty their bowels to minimize gas-related artifacts in the intestinal lumen and to moderately fill the bladder for optimal visualization. During positioning, the coil was centered over the pubic symphysis and secured with a strap to reduce motion artifacts caused by respiration.

The scanning range included the entire prostate and bilateral seminal vesicles. The imaging protocol comprised axial T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI), and dynamic contrast-enhanced T1-weighted imaging (T1WI). For contrast-enhanced imaging, gadolinium diethylenetriamine pentaacetic acid (Gd-DTPA) was administered intravenously at a dose of 0.1 mmol/kg body weight via the cubital vein at a flow rate of 2.5 mL/s.

### 2.3 MRI analysis and data measurement

Two radiologists, with 10 and 20 years of experience in genitourinary MRI diagnosis, respectively, independently evaluated the tumors according to the PI-RADS v2.1 guidelines. They documented parameters including prostate volume, tumor apparent diffusion coefficient (ADC) values, tumor contact length (TCL), and enhancement curve characteristics. Any discrepancies in their assessments were resolved through discussion to reach a consensus.

### 2.4 Puncture and gross pathology interpretation

The Gleason score 6 was defined as group 1, 7 (3 + 4) as group 2, 7 (4 + 3) as group 3, 8 (4 + 4, 3 + 5, 5 + 3) as group 4, and 9–10 (4 + 5, 5 + 4, 5 + 5) as group 5 based on the 2014 ISUP grouping system [8]. According to the presence of GGU after the operation, patients were divided into the GGU group and the non-GGU group. All pathological diagnoses were read by two senior pathologists to obtain the results.

### 2.5 Statistical analysis

Data analysis was performed using SPSS 21.0 (IBM Corp., Armonk, NY, USA), MedCalc 22.001 (MedCalc software Ltd, Oostende, Belgium), and Stata version 17.0 (StataCorp LLC., Austin, TX, USA) statistical software. Normally distributed continuous variables were presented as mean ± standard deviation ($\bar{x} \pm SD$), while non-normally distributed continuous

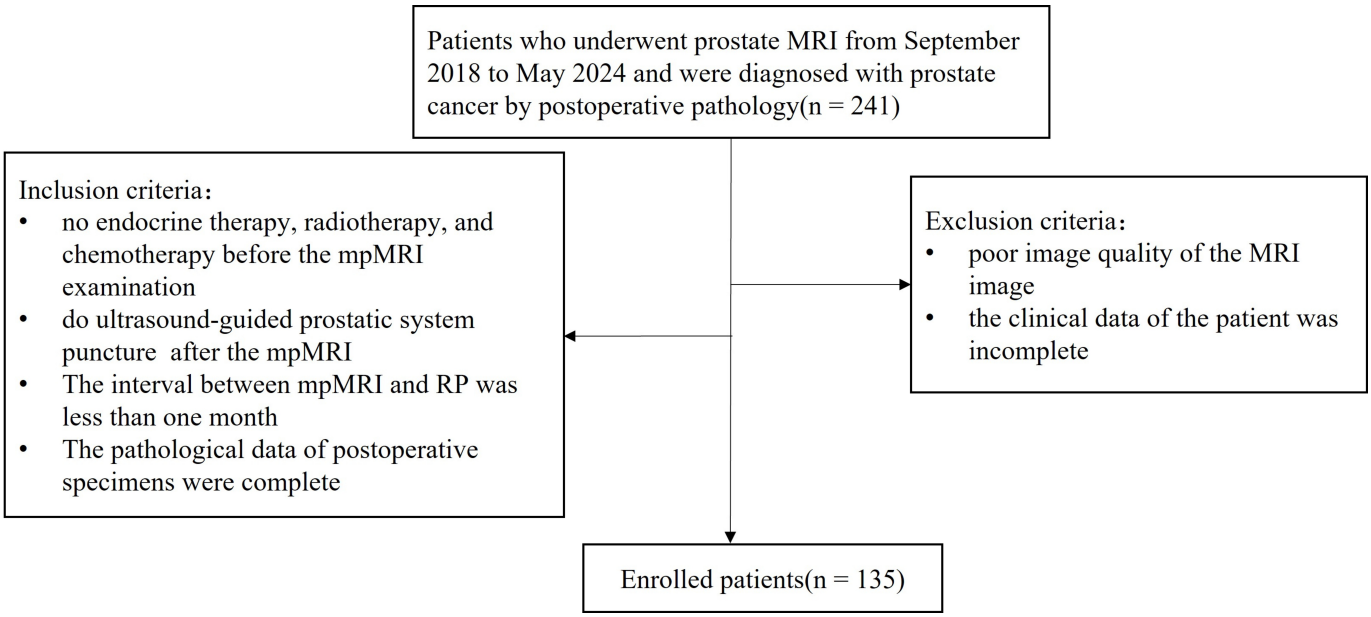


**FIGURE 1. Flow chart of patient enrollment.** MRI: magnetic resonance imaging; mpMRI: Multiparametric magnetic resonance imaging.

variables were expressed as median with interquartile range. Categorical variables were summarized using frequencies and percentages.

For the univariate analysis of GGU, comparisons between categorical variables were conducted using the chi-square ($\chi^2$) test, and continuous variables were compared using the independent samples *t*-test. Variables with a significance level of $p < 0.05$ in univariate analysis were entered into a multivariable logistic regression model, with $p < 0.05$ indicating statistical significance.

Receiver operating characteristic (ROC) curves were generated, and the area under the curve (AUC) was calculated to evaluate the diagnostic performance of imaging parameters and GGU predictors. Interobserver agreement was assessed using the Kappa statistic, with values greater than 0.80 indicating excellent consistency.

## 3. Results

### 3.1 Descriptive statistics

The agreement between the two physicians evaluating PCa using T2WI, DWI and other sequences was strong, with a Kappa value exceeding 0.80.

In this study, a total of 135 radical prostatectomies were successfully performed, with 50 patients classified into the GGU group and 87 patients in the non-GGU group. Table 1 summarizes the changes in the 2014 ISUP grade groups between biopsy specimens and RP specimens. The number of cases exhibiting GGU across ISUP groups 1, 2, 3 and 4 was 31 (23.0%), 14 (10.4%), 3 (2.2%) and 2 (1.5%), respectively.

### 3.2 Clinicopathological and multiparameter magnetic resonance imaging factors associated with GGU

The univariate analysis results are presented in Table 2. Comparison between the GGU and non-GGU groups demonstrated statistically significant differences in body mass index (BMI), prostate-specific antigen (PSA) levels, percentage of positive biopsy cores, prostate volume, ADC value, TCL, enhancement curve patterns, and PI-RADS v2.1 scores ($p < 0.05$).

### 3.3 Multivariable analysis and receiver operating characteristic analysis for GGU

The BMI, percentage of positive biopsy cores, and ADC value were included in the multivariable logistic regression analysis (Table 3). These factors were identified as independent predictors of GGU in PCa ($p < 0.05$).

The ROC curves for ADC value, BMI and percentage of positive cores in predicting GGU are shown in Fig. 2. The AUC values were 0.711 (95% CI (confidence interval): 0.626–0.785), 0.606 (95% CI: 0.518–0.689), and 0.713 (95% CI: 0.628–0.787), respectively, indicating good diagnostic performance. An ADC value threshold of $>0.75 \times 10^{-3}$ mm$^2$/s was identified as the optimal cutoff for predicting GGU in PCa.

### 3.4 Clinical decision curves of the ADC value, BMI and percentage of positive needles

Analysis of clinical decision curves across various risk thresholds showed that the curves for GGU based on ADC value,BMI and percentage of positive biopsy cores were positioned in the upper right quadrant, between the ALL and None curves. This placement indicates that these factors provide relatively net clinical benefits (Fig. 3).

## 4. Discussion

Occasional discrepancies, including underestimation or overestimation, between Gleason scores obtained from prostate needle biopsy and those from RP specimens can greatly affect the diagnosis, treatment decisions and prognosis of PCa patients. The 2014 ISUP grading system, which represents an enhancement of the traditional Gleason system, has been shown to more accurately predict PCa—specific survival and the risk of biochemical recurrence following RP [3, 9].

We developed a predictive model to assess the diagnostic accuracy of ISUP pathological upgrading following RP. This approach addresses two key points: first, the postoperative pathological grade often exceeds that determined by biopsy, and second, it aims to guide the optimal diagnosis and treatment strategy for patients. In this study, 50 out of 135 cases (37.1%) experienced Gleason grade upgrading, a rate slightly lower than that reported by Liu A *et al.* [10], potentially due

**TABLE 1. 2014 ISUP group distribution of puncture pathology and pathology after radical prostatectomy in patients with prostate cancer.**

| Puncture pathological ISUP grouping based on biopsy specimen assessment | Pathological ISUP grouping after radical prostatectomy | | | | | Total |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | |
| 1 | 4 (3.0%) | 17 (12.6%) | 14 (10.4%) | - | - | 35 (25.9%) |
| 2 | - | 15 (11.1%) | 14 (10.4%) | - | - | 29 (21.5%) |
| 3 | - | 9 (6.7%) | 13 (9.6%) | 2 (1.5%) | 1 (0.7%) | 25 (18.5%) |
| 4 | - | 4 (3.0%) | 20 (14.8%) | 1 (0.7%) | 2 (1.5%) | 27 (20.0%) |
| 5 | - | 2 (1.5%) | 4 (3.0%) | 2 (1.5%) | 11 (8.1%) | 19 (14.1%) |
| Total | 4 (3.0%) | 47 (34.8%) | 65 (48.1%) | 5 (3.7%) | 14 (10.4%) | 135 (100.0%) |

*ISUP: International Society of Urological Pathology.*

**TABLE 2. Comparison of clinicopathological data between the GGU group and the non-GGU group after radical prostatectomy.**

| Project | GGU group (n = 50) | Non-GGU group (n = 85) | *p* value |
|---|---|---|---|
| Age (yr) | 68.7 ± 5.8 | 70.4 ± 5.5 | 0.091 |
| BMI (kg/m$^2$) | 24.21 ± 3.00 | 23.02 ± 3.15 | 0.034 |
| PSA (ng/mL) | 14.56 (4.19, 43.14) | 18.41 (4.11, 125.17) | 0.006 |
| percentage of positive needles (%) | 0.26 ± 0.18 | 0.45 ± 0.27 | <0.001 |
| PI-RADS v2.1 | | | |
| 3 | 34 | 33 | |
| 4 | 13 | 32 | 0.002 |
| 5 | 3 | 20 | |
| ADC ($\times 10^{-3}$ mm$^2$/s) | 0.84 ± 0.11 | 0.73 ± 0.17 | <0.001 |
| TCL (mm) | 16.54 ± 8.2 | 22.79 ± 14.22 | 0.006 |
| Enhancement curve | | | |
| Type III | 14 (10.3) | 39 (28.9) | 0.031 |
| Type I, II | 36 (26.7) | 46 (34.1) | |
| PV classification (mL) | | | |
| ≤30 | 27 | 34 | |
| 30–60 | 17 | 48 | 0.029 |
| ≥60 | 6 | 3 | |

*GGU: Gleason grade upgrade; BMI: body mass index; PSA: prostate-specific antigen; PI-RADS: Prostate Imaging Reporting and Data System; ADC: apparent diffusion coefficient; TCL: tumor contact length; PV: prostate volume.*

**TABLE 3. Multivariable logistic regression analysis of independent risk factors for GGU after prostate cancer surgery.**

| Parameter terms | B value | Standard error | Wald value | *p* value | OR value | 95% CI |
|---|---|---|---|---|---|---|
| BMI | 0.143 | 0.069 | 4.316 | 0.038 | 1.153 | (1.008, 1.320) |
| ADC value | 3.979 | 1.638 | 5.902 | 0.015 | 53.481 | (2.157, 1325.818) |
| percentage of positive needles | −2.299 | 1.019 | 5.090 | 0.024 | 0.100 | (0.014, 0.740) |

*OR: Odds ratio; CI: confidence interval; BMI: body mass index; ADC: apparent diffusion coefficient.*

to the smaller sample size. However, this rate was somewhat higher than findings from another study in the US [11], which might be attributed to racial differences.

Currently, DWI is the only non-invasive MRI technique that captures the movement of water molecules within living tissues. The degree of water molecule restriction in the cellular microenvironment correlates directly with tissue cell density. The ADC value derived from DWI serves as a crucial pathological marker for distinguishing between benign and malignant lesions, as well as for tumor staging. This information aids in the early diagnosis, pathological classification, and prognosis evaluation of PCa [12–14]. This study confirmed that the ADC value was an independent risk factor for GGU ($p$ = 0.007), as the AUC of predicting GGU was 0.711, indicating a high diagnostic value of the ADC value for predicting GGU. Further, the optimal threshold was $>0.75 \times 10^{-3}$ mm$^2$/s, indicating that the greater the ADC value, the greater the possibility of pathological escalation after RP. These findings align with those reported by Abreu-Gomez *et al.* [15], who demonstrated a strong correlation between ADC values and pathological outcomes in PCa patients. However, while this study focused on the association between ADC values and pathological progression, Abreu-Gomez *et al.* [15] specifically examined the relationship between ADC values and seminal vesicle invasion in PCa. Previous research has also highlighted the significance of ADC measurements in evaluating tumor differentiation and predicting risk grades in PCa. Furthermore, ADC values were found to be inversely correlated with the 2014 ISUP grade groups [16, 17], a finding that was also observed in this study. It was further noted that lesions with postoperative pathological grade upgrading generally exhibited lower ADC values compared to those without upgrading. Lower ADC values corresponded to higher lesion specificity. Moreover, cases with higher pathological grades identified in biopsy specimens tended to match the postoperative pathology. This pattern may be explained by the fact that higher ISUP grades reflect more aggressive tumors with poorer cell differentiation and greater atypia, resulting in a higher nuclear-to-cytoplasm ratio. As a result, this leads to increased cell density, tighter cellular arrangement and reduced extracellular space, all of which restrict water molecule diffusion. Therefore, a lower ADC value is indicative of a greater likelihood that pre-

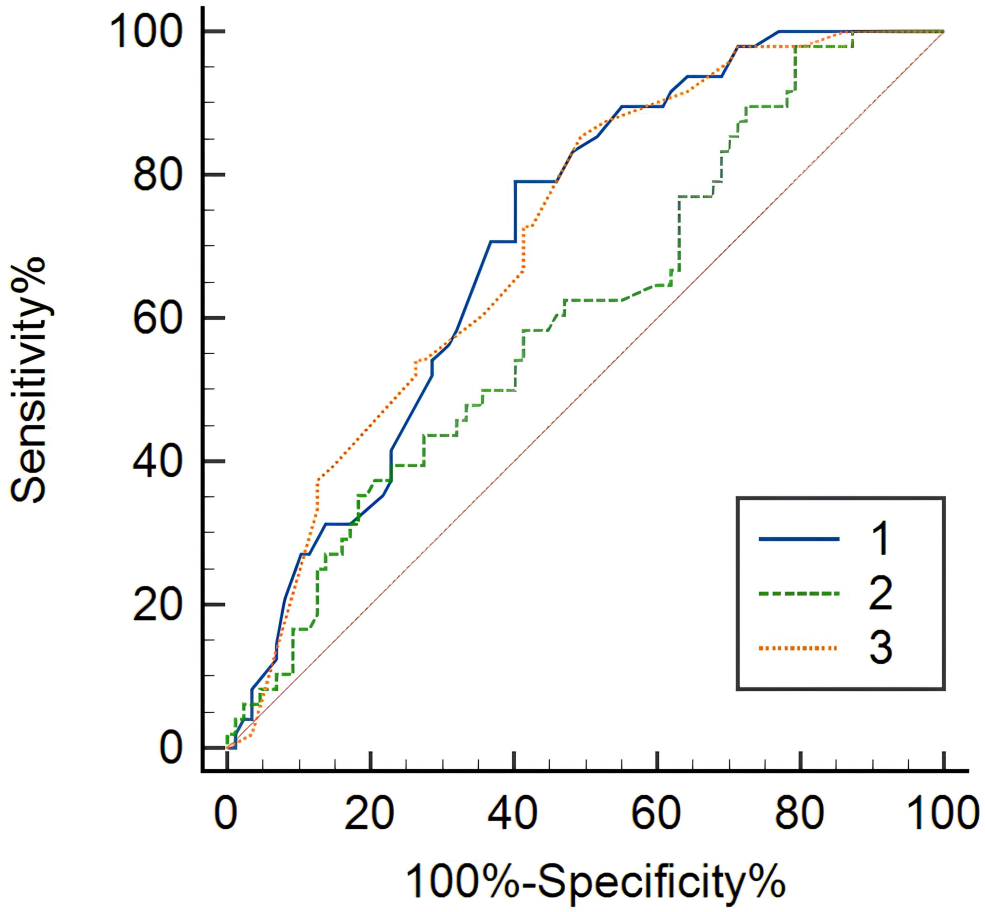


**FIGURE 2. ROC curves of BMI, ADC value and percentage of positive needles predicting GGU after prostate cancer surgery.** Explanatory note: 1: ADC value; 2: BMI; 3: percentage of positive needles.

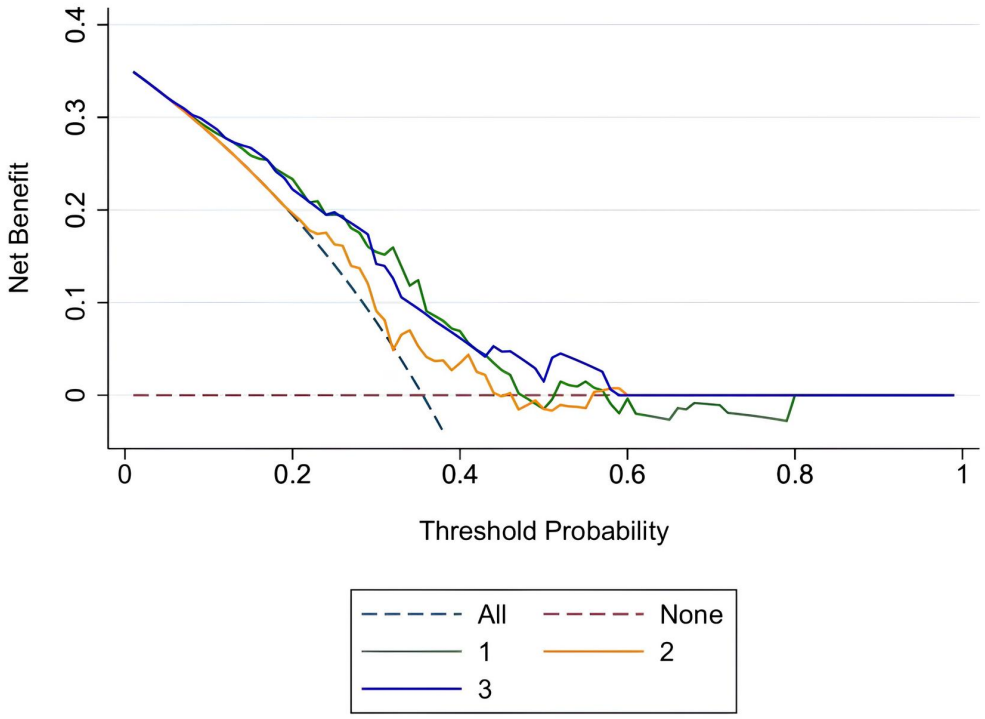


**FIGURE 3. Decision curves of the ADC value, BMI and percentage of positive needles.** Explanatory note: 1: ADC value; 2: BMI; 3: percentage of positive needles; All: full intervention; None: full non-intervention.

operative biopsy grading will be consistent with postoperative pathological findings. In comparison, prostate cancers with lower malignancy tend to exhibit more cystic changes and less cellular atypia. This increases the likelihood of sampling normal tissue during biopsy, which can result in significant discrepancies between the biopsy findings and the postoperative pathological grade, often leading to apparent grade upgrading after surgery.

The multivariable analysis in this study identified the ratio of positive biopsy cores as an independent risk factor for postoperative pathological upgrading, demonstrating strong predictive value for GGU (AUC = 0.713). The proportion of positive cores reflects tumor volume and burden [18]. A lower ratio of positive cores increases the likelihood of sampling normal tissue during biopsy, which may lead to underestimation of the Gleason score and a higher chance of pathological upgrading after surgery. This phenomenon may also be linked to hormone levels involved in prostate growth and differentiation.

Previous research has identified BMI as a predictor of postoperative pathological upgrading [10, 19]. Consistent with these findings, this study also demonstrated that BMI is an independent risk factor for predicting GGU, aligning with results from both domestic and international cohorts. Obesity is associated with reduced androgen levels, and lower testosterone may contribute to the progression of PCa. In this study, the ROC curve for BMI predicting GGU yielded an AUC of 0.606, indicating a moderate diagnostic value.

This study has several limitations. First, its retrospective design and relatively small sample size may introduce selection bias. Second, variability in biopsy techniques and operator practices among patients could also contribute to selection bias. Third, although two experienced radiologists jointly evaluated the PI-RADS v2.1 scores and other MRI measurements, some degree of subjectivity remains, which may result in classification bias. Finally, the study used postoperative pathological grade as the primary endpoint, rather than more direct clinical outcomes such as biochemical recurrence or patient survival, limiting the assessment of the prognostic value of the clinical parameters for guiding treatment decisions.

## 5. Conclusions

In conclusion, the final pathological grading of PCa patients, according to the 2014 ISUP classification, can be more accurately predicted by integrating the analysis of ADC values, BMI and the proportion of positive biopsy cores. Notably, higher ADC values are linked to an increased likelihood of pathological upgrading following RP compared to initial biopsy results.

### AVAILABILITY OF DATA AND MATERIALS

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

### AUTHOR CONTRIBUTIONS

CZ and JGW—designed the research study. CZ—performed the research; analyzed the data; wrote the manuscript. JGW—provided help and advice on the data collection. Both authors contributed to editorial changes in the manuscript. Both authors read and approved the final manuscript.

### ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study involved humans, and thus was approved by Ningbo Yinzhou No. 2 Hospital Medical Ethics Committee (NO. 2025036). The study was conducted following the local legislation and institutional requirements. The ethics committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because it was deemed unnecessary due to the retrospective design of the study. Written informed consent was not obtained from the individuals for the publication of any potentially identifiable images or data included in this article because our ethics committee supported our retrospective study without the need for informed consent.

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### CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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