# Independent Surgical Validation of the New Prostate Cancer Grade Grouping System

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**ABSTRACT**

OBJECTIVE: To report the independent prognostic impact of the new prostate cancer grade grouping system in a large external validation cohort of patients treated with radical prostatectomy.

Subjects/patients: Between 1994 and 2013, 3,694 consecutive men were treated by radical prostatectomy at a single institution. To investigate the performance of and validate the grade-grouping system, biochemical recurrence-free survival (bRFS) rates were assessed using Kaplan Meier tests, Cox-regression modeling, and discriminatory comparison analyses. Separate analyses were performed based on biopsy and prostatectomy grade.

RESULTS: Median follow-up was 52.7 months. The 5-year actuarial bRFS for biopsy grade-groups 1-5 were 94.2%, 89.2%, 73.1%, 63.1%, and 54.7%, respectively ($p<0.0001$). Similarly, the 5-year actuarial bRFS based on surgical grade groups was 96.1%, 93.0%, 74.0%, 64.4%, and 49.9% for grade groups 1-5, respectively ($p<0.0001$). The adjusted hazard ratios for bRFS relative to biopsy grade group 1 were 1.98, 4.20, 5.57, and 9.32 for groups 2, 3, 4, and 5, respectively ($p<0.0001$), and for surgical grade groups were 2.09, 5.27, 5.86, and 10.42 ($p<0.0001$). The five-grade group system had a higher prognostic discrimination compared to the commonly used 3-tier system (Gleason score 6 vs 7 vs 8-10).

CONCLUSIONS: In an independent surgical cohort, we have validated the prognostic benefit of the new prostate cancer grade grouping system with respect to bRFS, and demonstrated that the benefit is maintained after adjusting for important clinicopathologic variables. The greater

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predictive accuracy of the new system will improve risk stratification in the clinical setting and aid in patient counseling.

## INTRODUCTION

Since its introduction in the 1960s, Gleason score has been one of the most important predictors of adverse outcomes in prostate cancer.[1] The Gleason grading system has undergone significant modifications since its inception; however, issues still exist with the current system. The reporting of Gleason scores 2-5 has become virtually extinct,[2] and men with Gleason score 6 cancer may misinterpret their disease as intermediate-cancer on a 2-10 scale. Several risk-stratification schemas, including the D'Amico and National Comprehensive Cancer Network (NCCN) classifications, place patients into risk-groups based in part on a 3-tier Gleason grouping (6, 7, and 8-10), yet heterogeneity exists within these risk-groups. Patients with Gleason score 7 cancer are deemed intermediate-risk, however this is a heterogeneous group with Gleason score 4+3=7 tumors portending a worse prognosis than Gleason 3+4=7 tumors.[3-6] Similarly, patients with Gleason score 8-10 cancer are deemed high-risk, but multiple studies have demonstrated that the presence of Gleason pattern 5 disease is associated with worse clinical outcomes.[7-9] The granularity of what was initially a system consisting of 25 possible combinations of primary and secondary patterns has been largely reduced to three risk groups.

To address these concerns, a new grading system was proposed by the group from Johns Hopkins Hospital in 2013 that placed patients into five distinct grade groups: Grade group 1 (Gleason score ≤6), group 2 (Gleason score 3+4=7), group 3 (Gleason score 4+3=7), group 4 (Gleason score 8), and group 5 (Gleason score 9–10).[10] This system was validated by Epstein et al.in a large, multi-institutional analysis that demonstrated significant prognostic differences between the new grade groups for predicting biochemical recurrence (BCR), and this classification demonstrated slightly higher prognostic discrimination when compared against alternative Gleason grade categorizations.[11] As a result, this grading system was recently endorsed by the International Society of Urological Pathology (ISUP).[11]

Despite overwhelming endorsement, this proposal was validated primarily from institutions that had previously reported significant differences in some of these groups—for example, between groups 2 and 3 (Gleason score 3+4 vs 4+3).[5,6,12-14] Thus, independent validation from a distinct cohort may provide further corroboration of this new system.

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Furthermore, the follow-up of the primary study was short (~2 years). In the current study, we sought to assess the validity of the new grading system in an external cohort of surgical patients treated at a single-institution.

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## MATERIALS AND METHODS

### Patients

Under an Institutional Review Board approved protocol, we performed a retrospective review of the medical records of 3,715 consecutive men treated by radical prostatectomy for clinically localized prostate cancer from 1994-2013 at a single institution. Patients were excluded if they did not have both a biopsy and prostatectomy grade, yielding 3,694 patients that formed the study cohort. All biopsy and prostatectomy specimens were assigned a traditional biopsy Gleason score during routine pathologic evaluation performed by board-certified anatomic pathologists. The highest Gleason score sampled in biopsy samples was used to assign the biopsy grade. Tertiary Gleason score was not routinely collected and was not included in any analyses. The majority of cases were signed-out by pathologists with subspecialty training in genitourinary pathology.

Pre-operative prostate-specific antigen (PSA) levels were obtained for all patients, and post-operative follow-up included routine PSA monitoring approximately every 3-6 months. Clinical, pathological, and long term oncologic data were collected prospectively and were supplemented by medical record review.

In order to assess the new grade grouping system, patients were categorized according to Gleason grade as previously described ($\leq$6, 3+4=7, 4+3=7, 4+4=8, and 9-10) and assigned to groups 1-5, respectively.[10] Separate analyses were performed using biopsy grade and prostatectomy grade for group assignment.

### Statistical Analysis

The primary outcome was biochemical recurrence-free survival (bRFS) defined from the time of surgery to BCR or last follow-up. BCR was defined as two consecutive post-operative serum PSA levels >0.2 ng/mL. For the primary analyses, univariable and multivariable Cox regression were performed to evaluate the association between the grade groupings and bRFS. All significant variables in the univariable analysis were included in the multivariable analysis.

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The covariates in the biopsy multivariable model included grade groupings (1-5), clinical T-stage (T1c/T2a, T2b/c, T3-T4), pre-operative PSA (<10, 10-20, >20), and year of treatment (before and after 2005). The covariates in the prostatectomy multivariable model were the same as in the biopsy model with the exception of pathologic T-stage (T2a, T2b/T2c, T3-T4), which was used in place of clinical staging.

Kaplan-Meier analysis with the log-rank test was also used to determine the biochemical recurrence-free survival (bRFS) among the grade-groupings. Unadjusted and adjusted Kaplan-Meier curves were constructed to illustrate the differences in bRFS between groups. The adjusted Kaplan-Meier curves were adjusted using the same covariates as in the respective multivariable Cox regression analysis. Using both biopsy and prostatectomy specimens, the estimated area under the receiver operating characteristic curves (AUC) was determined for the new grade groupings (1-5), and the conventional three-grouped stratification schema (6 vs. 7 vs 8-10). This was performed for the entire cohort, with subsequent stratification by date of treatment (pre-2005 vs post-2005) due to the change in Gleason grading at that time (ISUP).[15] For all statistical analyses, two-tailed P values of $\leq$0.05 were considered statistically significant. Statistical analyses were performed using IBM SPSS version 21.0(SPSS Inc., Chicago, IL USA).

## RESULTS

### Clinical Characteristics

Across 3,715 consecutive men treated by radical prostatectomy from 1994-2013, the median follow-up of the cohort was 52.7 months. The median age of our cohort was 60 years (range, 34-83 years, **Table 1**). Half of the cohort (49.8%) was treated pre-2005, and the remaining patients were treated from 2005 until 2013. Almost all patients were either NCCN low risk (41.2%) or intermediate risk (50.2%), while only 8.6% were high risk. Similarly, most patients were clinical stage T1c/T2a (88.9%) and had pre-treatment PSA levels <10 ng/ml (84.1%). Distribution of biopsy and prostatectomy grade groupings are shown in **Table 1**.

### Biopsy Grade Groupings

The 5-year actuarial bRFS for biopsy grade-groups 1-5 were 94.2%, 89.2%, 73.1%, 63.1%, and 54.7%, respectively (p<0.0001, **Figure 1a**). All comparisons between groups were significant with the exception of groups 4 with group 5 (p=0.067, **Table 2**). On univariable

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analysis, biopsy grade group, clinical T-stage, pre-operative PSA, and year of treatment were significant predictors of bRFS, while age was not. Biopsy grade grouping had an incremental increase in the hazard for biochemical recurrence; relative to biopsy grade-group 1, the hazard ratios (HR) were 2.1, 4.8, 6.9, and 10.6 for groups 2, 3, 4, and 5, respectively (p <0.0001 for all).

On multivariable analysis after adjusting for clinical T-stage, pre-operative PSA and year of treatment, there was a statistically significant increase in the adjusted hazard ratio (aHR) for BCR across all grade groupings. The adjusted hazard ratios relative to biopsy grade-group 1 were 1.98, 4.20, 5.57, and 9.32 for groups 2, 3, 4, and 5, respectively (p <0.0001 for all), **Table 3**). Additionally, an increase in clinical T-stage (T1c/T2a as the reference) was significantly associated with an increased aHR for biochemical recurrence; T2b/T2c (aHR 1.52 [95%CI 1.27-1.82], p<0.0001), and T3-4 (aHR 2.27 [95%CI 1.00-5.17], p=0.050). Pre-operative PSA was also significantly associated with an increase in aHR for biochemical recurrence as was year of treatment. Adjusted Kaplan-Meier curves of the 5 biopsy grade groupings after adjustment for clinical T-stage, pre-operative PSA and year of treatment are shown in **Supplementary Figure 1a**.

Prostatectomy Grade Groupings

The 5-year actuarial bRFS for prostatectomy grade-groups 1-5 were 96.1%, 93.0%, 74.0%, 64.4%, and 49.9%, respectively (p<0.0001), **Figure 1b**). All comparisons between groups were significant (**Table 2**). On univariable analysis, prostatectomy grade group, pathologic T-stage, pre-operative PSA, and year of treatment were significant predictors of bRFS, while age was not. Grade group was associated with an incremental increase in the hazard for BCR; relative to biopsy grade-group 1, the HRs were 2.3, 7.3, 10.4, and 18.9 for groups 2, 3, 4, and 5, respectively (p <0.0001 for all).

On multivariable analysis after adjusting for clinical T-stage, pre-operative PSA and year of treatment, there was a statistically significant increase in the adjusted hazard ratio for biochemical recurrence across all grade groupings (p<0.0001). The adjusted hazard ratios relative to prostatectomy grade-group 1 were 2.09, 5.27, 5.86, and 10.42 for groups 2, 3, 4, and 5, respectively (**Table 4**). Additionally, an increase in pathological T-stage (T2a as the reference) was significantly associated with an increased aHR for biochemical recurrence; T2b/T2c (AHR 1.44 [95%CI 1.06-1.96], p=0.02), and T3-4 (aHR 3.38 [95%CI 2.47-4.64], p<0.0001). Pre-

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operative PSA was also significantly associated with an increase in aHR for biochemical recurrence as was year of treatment. Adjusted Kaplan-Meier curves of the 5 prostatectomy grade groupings after adjustment for pathologic T-stage, pre-operative PSA and year of treatment are shown in **Supplementary Figure 1b**.

Discrimination analyses

To compare the discriminatory power of the new grade grouping system to the commonly used 3-tier Gleason groupings (6 vs 7 vs 8-10), AUC analyses were performed (**Table 5**). There was an improvement in the AUC for bRFS for both the biopsy (0.65 vs 0.67) and the prostatectomy (0.66 vs. 0.72) samples. These findings held true when analyzing pre-2005 patients before the ISUP update occurred (biopsy 0.67 vs 0.68, and prostatectomy 0.68 vs 0.73). However, this was most prominent post-2005 (biopsy 0.72 vs 0.76, prostatectomy 0.70 vs. 0.80). The prostatectomy grade consistently had more discriminatory power than biopsy grade using the new grade grouping system.

## DISCUSSION

In 1966, Donald Gleason first proposed criteria for grading prostate cancer based on architectural patterns[16] and subsequently demonstrated that the sum of the primary and secondary histological patterns (Gleason score) was strongly correlated with mortality.[17] Since this time, Gleason score has remained one of the strongest predictors of long-term outcomes in prostate cancer, including PSA recurrence and disease-specific mortality.[18-20]

While the essence of this original system is still largely used today, the clinical practice and presentation of prostate cancer has changed dramatically over the past 50 years. In the late 1960s, there was no PSA screening, digital rectal screening was not routinely performed, and biopsy techniques were more limited.[21] Consequently, men presented with more advanced disease.[17] In 2005, the ISUP convened a consensus conference to address controversial issues relating to the Gleason system, which had been largely unchanged for 40 years. This conference resulted in many modifications, but perhaps the largest change was the refinement of different histologic categories that limited the definition of pattern 3 while widening the scope of pattern 4 disease.[15] These modifications improved prognostication: In a study by Dong et al, patients with original (pre-2005) Gleason 6 disease that were upgraded to modified Gleason 7 or 8 disease had

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worse bRFS and metastasis-free survival compared to patients with original and modified Gleason 6 disease.[22]

Despite the improved prognostication, significant stage migration occurred as a result of the modified system. Gleason 6 cancers are now a more homogeneous group with an artificially improved prognosis due to the reclassification of higher risk patients out of this group, in line with the "Will Rogers phenomenon."[23] The diagnosis of Gleason $\leq$6 has become less common, as demonstrated by a large SEER and NCDB analysis from 2004-2011.[24] The 2005 modifications also limited the clinical use of low-grade patterns, recommending against the diagnosis of Gleason score 1+1=2, and declaring that the diagnosis of Gleason scores 3-4 should be made "rarely, if ever" on needle biopsy. The first recommendation for Gleason scores 2-4 not to be made on biopsy was from an editorial by Epstein in 2000 which was adopted in the consensus conference in 2005.[25] Helpap et al. reported that the percent of prostatectomy specimens with Gleason scores 2-5 decreased from 6.3 to 0% when comparing original and modified grading criteria.[2] Thus, the reporting of Gleason scores 2-5 has become virtually extinct in modern practice. The current Gleason scoring system may lead patients to incorrectly perceive "grade 6" as intermediate-risk on a 10-point scale, which may potentially contribute to disease overtreatment.[26] This is in stark contrast to the low probability of BCR at 5 years for patients with Gleason 6 disease (94.2% and 96.1% 5-year actuarial bRFS for biopsy and prostatectomy grade, respectively). A label of "grade-group 1" may more accurately reflect the relatively low-risk nature of this group.

There have been multiple studies demonstrating the prognostic differences between Gleason score 3+4 and Gleason 4+3 disease, the former associated with increased bRFS,[3,6,12] lower rates of distant metastases,[3,12] and higher disease-specific survival.[3,12] However, current clinical practice guidelines, including the NCCN guidelines, incorporate the overall Gleason score into their risk-stratification schemas with no formal role for the primary Gleason pattern. As such, patients with Gleason scores 3+4 and 4+3 are both labeled "intermediate-risk" despite their prognostic differences. We demonstrate significant differences in bRFS for patients 3+4 vs. 4+3 disease (89.2% vs. 73.1% biopsy 5-year actuarial BCR, $p<0.0001$; 93.0% vs 74% prostatectomy 5 year-actuarial BCR, $p<0.0001$).

In addition, most risk-stratification schemas classify patients with Gleason scores 8-10 as high-risk, without discrimination between Gleason 8 vs. Gleason 9-10. However, multiple

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studies have demonstrated significantly worse outcomes in patients with Gleason pattern 5 (GP5).[8,9,27] Sabolch et al. assessed the impact of GP5 in patients treated with dose-escalated radiation therapy and demonstrated that patients with GP5 had significantly lower freedom from metastasis ($p < 0.002$), cause-specific survival ($p < 0.0001$), and overall survival ($p < 0.0001$).[8] Nanda et al. also demonstrated significant differences in PSA recurrence for men with Gleason 8 disease compared to those with Gleason scores 9-10.[27] Our analysis confirms bRFS differences for patients with Gleason 8 vs. Gleason 9-10 disease (63.1% vs. 54.7% biopsy 5-year actuarial bRFS; 64.4% vs 49.8% prostatectomy 5 year-actuarial bRFS).

This new grading system was recently endorsed by the ISUP and has been accepted by the World Health Organization.[11] Our study provides an independent external validation of this new grading schema from a distinct surgical cohort. To our knowledge, this is the first to demonstrate a difference in adjusted biochemical recurrence-free survival based on these grade groupings.

As a retrospective study, our analysis has important limitations. Although multiple clinical variables were included in our models, it is possible that there are additional unmeasured cofounders that may have affected the results. We attempt to control for stage migration by including the year of treatment in our analysis. 0ne-half of the patients in this study preceded 2005 when grading was different than what is currently recommended. It should also be emphasized that although the new grade group system was accurate in the pre-2005 cohort, it was more accurate following 2005 in support that the post-2005 grading better correlates with prognosis. Additionally, biochemical recurrence, rather than metastases or cancer specific survival, was used as the primary end-point of our study because 1) to validate the similar endpoint of prior studies, and 2) due to the rarity of these other outcomes in a localized surgical cohort. Lastly, submission of the entire prostate for histopathologic evaluation at prostatectomy is not routinely performed at our institution, however this would be expected to impact cases equally across grade groups.

In conclusion, we provide independent validation of the new grading system. We demonstrate a step-wise, increased risk of BCR in these groupings based on both biopsy and prostatectomy grade. Additionally, the grade groupings demonstrated higher prognostic discrimination when compared against the more-traditional Gleason grade categorization. This new system may allow for improved prognostication, and these results support their clinical

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implementation. Future work is needed to understand the clinical impact the new grade grouping system has on patient decision making.

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**Figure Legends:**

**Figure 1**: Unadjusted Kaplan-Meier Analyses of Biochemical Recurrence-Free Survival for (**A**) biopsy grade and (**B**) prostatectomy grade.

**Table 1**: Baseline Characteristics

Abbreviations: PSA-prostate specific antigen

**Table 2**: Pairwise Log Rank Comparisons of Biopsy and Prostatectomy Grade Groupings for bRFS.

Abbreviations: bRFS-biochemical recurrence-free survival

**Table 3**: Multivariate analysis for bRFS based on pre-operative features (biopsy grade grouping and clinical T-stage).

Abbreviations: bRFS-biochemical recurrence-free survival, CI-confidence interval, HR-hazard ratio, PSA-prostate specific antigen

**Table 4**: Multivariate analysis for bRFS based on post-operative features (prostatectomy grade grouping and pathologic T-stage).

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Abbreviations: bRFS-biochemical recurrence-free survival, CI-confidence interval, HR-hazard ratio, PSA-prostate specific antigen

**Table 5**: Results of receiver-operating curve discriminatory analysis for the entire cohort, those treated pre-2005, and post-2005 for the classical 3-tier Gleason grouping (6, 7, and 8-10) and the new 5-tier grade grouping system.

Abbreviations: AUC-area under the curve, bRFS-biochemical recurrence-free survival

**Supplementary Figures:**

**Supplementary Figure 1**: Adjusted Kaplan-Meier Analyses of Biochemical Recurrence-Free Survival for (**A**) biopsy grade and (**B**) prostatectomy grade.

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Table 1

| Variable | | n | % |
|---|---|---|---|
| **Age (years)** | | | |
| | *Median (range)* | 60 | (34-83) |
| **Year of Treatment** | | | |
| | *<2005* | 1838 | 49.8 |
| | *>2005* | 1856 | 50.2 |
| **NCCN Risk Group** | | | |
| | *Low* | 1521 | 41.2 |
| | *Intermediate* | 1854 | 50.2 |
| | *High* | 319 | 8.6 |
| **Biopsy Grade Group** | | | |
| | *1 (3+3=6)* | 1824 | 49.4 |
| | *2 (3+4=7)* | 1249 | 33.8 |
| | *3 (4+3=7)* | 387 | 10.5 |
| | *4 (8)* | 148 | 4.0 |
| | *5 (9-10)* | 86 | 2.3 |
| **Clinical T-stage** | | | |
| | *T1c/T2a* | 3283 | 88.9 |
| | *T2b/T2c* | 399 | 10.8 |
| | *T3a* | 8 | 0.2 |
| | *T3b* | 4 | 0.1 |
| **Baseline PSA (ng/mL)** | | | |
| | *<10* | 3108 | 84.1 |
| | *10-20* | 486 | 13.2 |
| | *>20* | 100 | 2.7 |
| **Prostatectomy Grade Group** | | | |
| | *1 (3+3=6)* | 1084 | 29.3 |
| | *2 (3+4=7)* | 1723 | 46.6 |
| | *3 (4+3=7)* | 637 | 17.2 |
| | *4 (8)* | 123 | 3.3 |
| | *5 (9-10)* | 127 | 3.4 |

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| | | | |
|---|---|---|---|
| **Pathologic T-stage** | | | |
| | *T2a* | 741 | 20.1 |
| | *T2b/T2c* | 2306 | 62.4 |
| | *T3a* | 470 | 12.7 |
| | *T3b* | 165 | 4.5 |

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**Table 2. Pairwise Log Rank Comparisons of Biopsy and Prostatectomy Grade Groupings for bRFS**

| **Biopsy Grade Groupings** | **1** | **2** | **3** | **4** | **5** |
|---|---|---|---|---|---|
| **1** | - | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| **2** | <0.0001 | - | <0.0001 | <0.0001 | <0.0001 |
| **3** | <0.0001 | <0.0001 | - | 0.024 | <0.0001 |
| **4** | <0.0001 | <0.0001 | 0.024 | - | 0.067 |
| **5** | <0.0001 | <0.0001 | <0.0001 | 0.067 | - |
| **Prostatectomy Grade Groupings** | **1** | **2** | **3** | **4** | **5** |
| **1** | - | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| **2** | <0.0001 | - | <0.0001 | <0.0001 | <0.0001 |
| **3** | <0.0001 | <0.0001 | - | 0.028 | <0.0001 |
| **4** | <0.0001 | <0.0001 | 0.028 | - | 0.006 |
| **5** | <0.0001 | <0.0001 | <0.0001 | 0.006 | - |

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Table 3. Pre-operative multivariable model for bRFS

| | bRFS | | | |
|---|---|---|---|---|
| | | 95.0% CI | | |
| **Variable** | **HR** | **Lower** | **Upper** | **P-value** |
| **Biopsy Grade Group** | | | | |
| Grade Group 1 | Reference | - | - | |
| Grade Group 2 | 1.98 | 1.58 | 2.48 | <0.0001 |
| Grade Group 3 | 4.20 | 3.26 | 5.40 | <0.0001 |
| Grade Group 4 | 5.57 | 4.02 | 7.72 | <0.0001 |
| Grade Group 5 | 9.32 | 6.41 | 13.54 | <0.0001 |
| **Clinical T-stage** | | | | |
| T1c/T2a | Reference | - | - | |
| T2b/c | 1.52 | 1.27 | 1.82 | <0.0001 |
| T3-T4 | 2.27 | 1.00 | 5.17 | 0.050 |
| **Pre-operative PSA** | | | | |
| PSA <10 | Reference | - | - | |
| PSA 10-20 | 2.31 | 1.89 | 2.83 | <0.0001 |
| PSA >20 | 3.17 | 2.32 | 4.34 | <0.0001 |

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Table 4. Prostatectomy findings multivariable model for bRFS

| | bRFS | | | |
|---|---|---|---|---|
| | | 95.0% CI | | |
| **Variable** | **HR** | **Lower** | **Upper** | **P-value** |
| **Prostatectomy Grade Group** | | | | |
| Grade Group 1 | Reference | - | - | |
| Grade Group 2 | 2.09 | 1.54 | 2.82 | <0.0001 |
| Grade Group 3 | 5.27 | 3.86 | 7.19 | <0.0001 |
| Grade Group 4 | 5.86 | 3.91 | 8.78 | <0.0001 |
| Grade Group 5 | 10.42 | 7.09 | 15.32 | <0.0001 |
| **Pathologic T-stage** | | | | |
| T2a | Reference | - | - | |
| T2b/c | 1.44 | 1.06 | 1.96 | 0.02 |
| T3-T4 | 3.38 | 2.47 | 4.64 | <0.0001 |
| **Pre-operative PSA** | | | | |
| PSA <10 | Reference | - | - | |
| PSA 10-20 | 1.80 | 1.46 | 2.21 | <0.0001 |
| PSA >20 | 2.17 | 1.58 | 2.99 | <0.0001 |

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Table 5. Results of receiver-operating curve discriminatory analysis

| | Discrimination (AUC) | |
|---|---|---|
| | **Biopsy bRFS** | **Prostatectomy bRFS** |
| **Entire Cohort (n=3694)** | | |
| Gleason 3 Groups (6 vs. 7 vs. 8-10) | 0.65 | 0.66 |
| New Grade Groups (6 vs 3+4 vs 4+3 vs 8 vs 9=10) | 0.67 | 0.72 |
| **Pre-2005 (n=1838)** | | |
| Gleason 3 Groups (6 vs. 7 vs. 8-10) | 0.67 | 0.68 |
| New Grade Groups (6 vs 3+4 vs 4+3 vs 8 vs 9=10) | 0.68 | 0.73 |
| **Post-2005 (n=1856)** | | |
| Gleason 3 Groups (6 vs. 7 vs. 8-10) | 0.72 | 0.70 |

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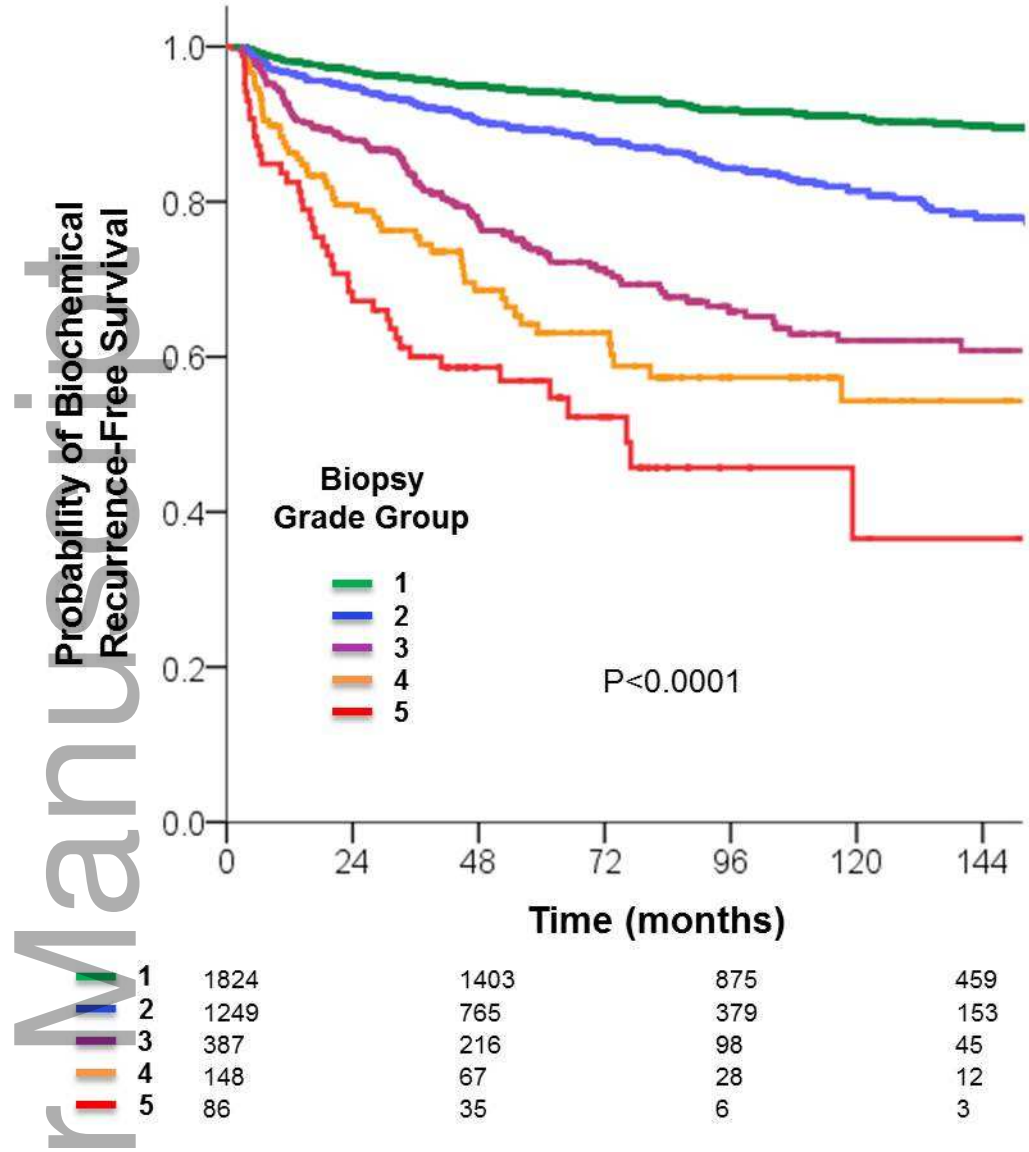


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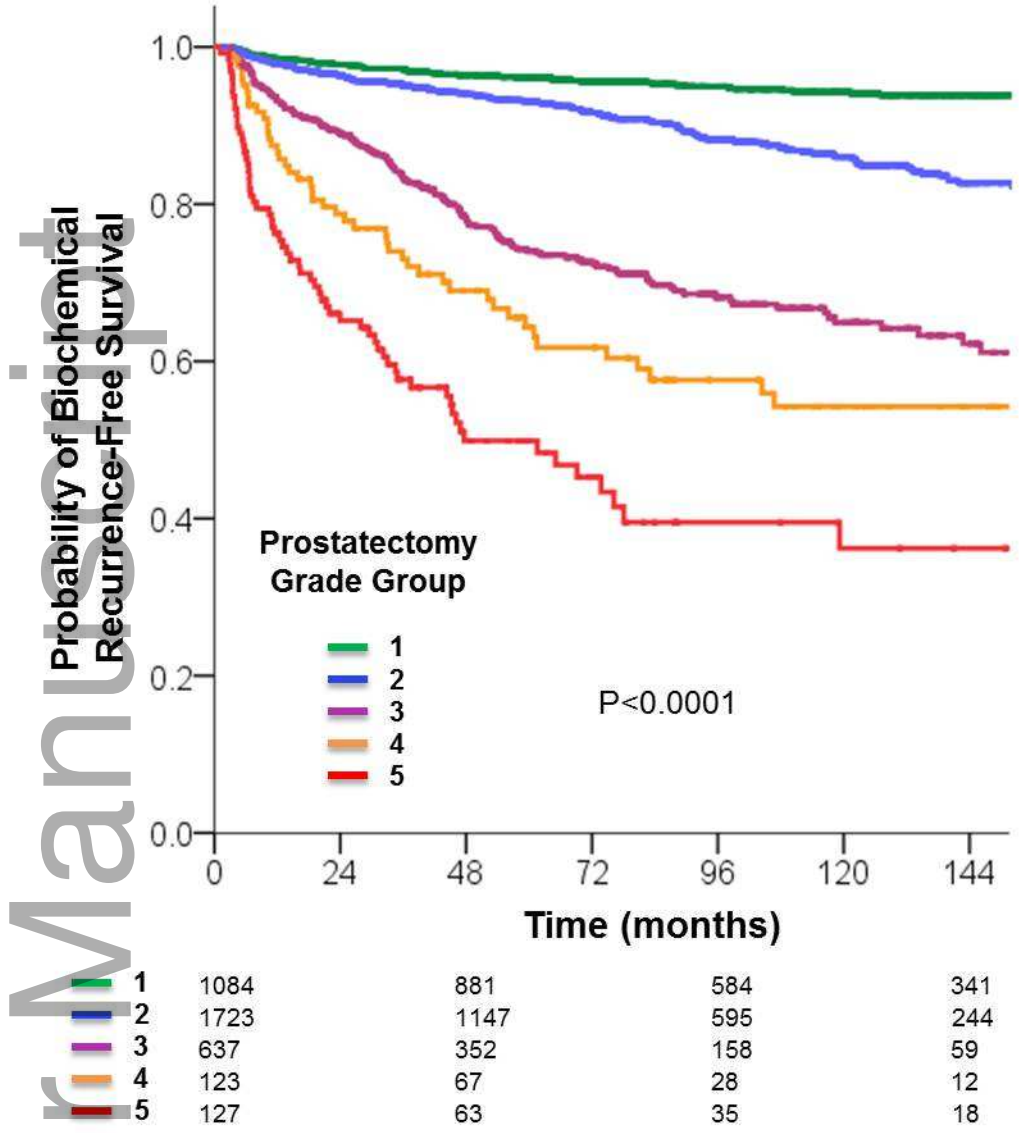


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