Prostate Cancer

Prognostic Significance of Gleason Score Discrepancies between Needle Biopsy and Radical Prostatectomy

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Abstract

Objectives: Discordance between the Gleason score (GS) on needle biopsy (NB) and the GS of the radical prostatectomy (RP) specimen is a common finding. The objective of this study was to evaluate the prognostic significance of these discrepancies with respect to outcomes following RP.

Methods: In the study, 6625 men treated by RP were categorized as having NB=RP (68.8%), NB<RP (25.0%) or NB>RP (6.2%) GS, and stratified for analyses into RP GS groups. The Kaplan-Meier method was used to analyze differences in biochemical recurrence-free survival (BRFS), and multivariate Cox analyses were performed to estimate the independent relative risk of progression associated with GS discrepancies.

Results: Across multiple RP GS strata (3+4, 7, 8, 8–10), patients with a lower NB GS experienced significantly better BRFS than patients with equal NB and RP GS (all \( p < 0.05 \)). NB<RP GS was independently associated with better (pooled HR, 0.76, \( p = 0.001 \)) BRFS, within and across RP GS strata. Similarly, patients with NB>RP GS had poorer BRFS than patients with NB=RP GS across multiple RP GS strata (\(<3+3, 3+4, 7; \) all \( p < 0.05 \)). NB>RP GS was independently associated with worse (pooled HR, 1.91, \( p < 0.001 \)) BRFS probabilities, within and across RP GS strata.

Conclusions: Our data suggest that the GS of the NB adds additional prognostic value to the RP GS in a consistent manner that may be applicable to strategies of risk stratification and patient counseling after surgery.

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1. Introduction

Originally described in the 1960s, the Gleason score (GS) remains the most widely accepted grading system in the evaluation of adenocarcinoma of the prostate [1]. Given the inherent sampling error of diagnostic needle biopsy (NB) and the frequently multifocal nature of prostate cancer, discrepancy between the GS of NB and radical prostatectomy (RP) specimens is a common finding [2–15]. One review summarized 11 published series with over 2600 patients, in which an exact match in grading was seen in an average of only 42% of the time [16]. Inaccuracies in grade assignment on NB specimens have clear clinical relevance, to the extent that treatment decisions for patients with clinically localized disease may be guided in large part by the anticipated clinical behavior of the tumors detected.

A separate question that has received less critical study in the literature is whether these commonly seen discrepancies in grade assignment between NB and RP may in fact provide intrinsic prognostic information. It is generally accepted that the RP GS represents the “true” grade of the cancer, to the extent that the specimen is reviewed in its entirety. We evaluated the relationship between discrepancies between the GS on NB and RP and biochemical recurrence outcomes among men with clinically localized prostate cancer.

2. Materials and methods

2.1. Study population

We identified 6922 patients treated with anatomical RP for clinically localized prostate adenocarcinoma from 1982 to 2005 at the Johns Hopkins Hospital who had at least 1 yr of follow-up information available. Men treated with preoperative hormonal therapy (n = 116), radiation therapy (n = 3), or chemotherapy (n = 2) or postoperative adjuvant radiation therapy (n = 15) were excluded. Men with missing data for biopsy GS (n = 155) or prostatectomy GS (n = 6) were excluded. These exclusions resulted in a study population of 6625 men.

No patient received adjuvant radiation or hormonal therapy prior to biochemical progression, defined as a single prostate-specific antigen (PSA) ≥0.2 ng/ml. The needle biopsy GS reported in this study reflects our practice of in-house review of all diagnostic prostate biopsy material. The prostatectomy GS reported in this study is the GS of the dominant nodule, in line with the recommendations of the 2005 International Society of Urological Pathology Consensus Conference recommendations on Gleason scoring [17]. All pathological specimens were reviewed by members of our team of expert genitourinary pathologists. The prostatectomy specimens were sectioned as previously described [18]. Follow-up included PSA measure-

ments quarterly for year 1, semiannually for year 2, and yearly thereafter. All data were collected under an internal institutional review board–approved protocol in compliance with the Health Insurance Portability and Accountability Act.

2.2. Statistical analysis

For the purposes of the analyses in this study, patients were divided into three groups. Those with equal NB and RP GS, those with lower NB GS than RP GS, and those with higher NB GS than RP GS. The grade-discordant groups were separately compared with the reference of patients with consonant NB and RP GS, within each stratum of RP GS. This approach was used to evaluate the null hypothesis that the RP GS represents the “true” grade, and that a discrepant NB GS adds no additional prognostic information.

We explored differences in the distribution of clinical and pathological characteristics between patients in the three groups using rank-sum analysis for continuous variables and the chi-square test for categorical variables. The chance-corrected proportional agreement between NB and RP GS in these two eras was compared with the kappa statistic [19]. Time to biochemical progression was evaluated within RP GS strata: in men with NB-RP GS (RP GS < 3+3, 3+4, and 4+3) and those with NB-RP GS (RP GS 3+4, 4+3, 8, 8–10) with the use of Kaplan-Meier plots and the log-rank test. In addition, all patients with RP Gleason score 7 were pooled (not considering NB-RP GS discrepancies of 3+4 and 4+3) and analyzed for associations of upgrading and downgrading to Gleason score 7 and BRFS. To estimate the independent relative risk of progression associated with GS discrepancies within each RP GS stratum, we used multivariable Cox proportional hazards regression models adjusted for preoperative PSA (>10 ng/ml) as well as pathological variables (positive surgical margins, extraprostatic extension, seminal vesicle invasion, and lymph node metastasis). The concordance index was used to compare the predictive accuracy of Cox models with and without a covariate for Gleason score discrepancy [20]. Separate Cox models were run on patients treated in 1996 or later to account for the trend toward a lower frequency of grade discrepancies in patients treated in that era. All statistical analyses were performed with the use of STATA 9.0 (Stata Corp, College Station, TX, USA).

3. Results

Clinical and pathological characteristics of the patients in the three subgroups are presented in Table 1. Overall, 68.8% of patients had NB-RP GS, 25.0% had NB<RP GS, and 6.2% had NB-RP GS. Patients with discordant NB and RP GS had higher preoperative PSA concentrations and were more likely to have palpable disease, positive surgical margins, extraprostatic extension, seminal vesicle invasion, and lymph node metastasis (Table 1; all p < 0.01).

The proportions of patients with concordant, upgraded, and downgraded GS within NB and RP GS

strata are presented in Table 1. The majority of patients within high-grade RP GS groups were upgraded from a lower NB GS: 64.2% of RP GS 3+4, 71.9% of RP GS 4+3, and 66.9% of RP GS 8–10 (Table 1).

Median follow-up among men without biochemical progression was 4 yr (range, 1–23). Ten-year BRFS probabilities, stratified by NB and RP GS status, are presented in Table 2. NB < RP GS was associated with a significantly favorable BRFS probability relative to patients with NB=RP GS within RP GS strata (Fig. 1) and pooled across strata (log-rank p = 0.0003). The opposite association was again seen for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–0.89; p = 0.001). The opposite association was again seen in the multivariate models for patients with NB > RP GS within RP GS strata (3+3, 3+4; Table 4) and pooled across strata (HR, 1.91; 95%CI], 0.65–
95% CI, 1.49–2.43; \( p < 0.001 \). Consistent with the Kaplan-Meier analyses, neither lower nor higher NB GS was a significant effect modifier of risk of biochemical recurrence in crude or adjusted Cox analyses for patients with RP GS 4+3 (Tables 3 and 4).

We noted a significant trend in the proportion of patients with discrepant Gleason grade between NB and RP, with 38% of patients having discrepant grade prior to 1996 versus 28% of patients treated in 1996 or later (\( p \) trend < 0.001; Fig. 3). The chance-corrected proportional agreement between NB and RP GS in these two eras was in the “fair” range as defined by Landis and Koch (kappa [±SE] before 1996: 0.32 [0.01]; 1996 or later: 0.35 [0.01]) [19]. Separate Cox models including a term adjusting for year of surgery as a continuous variable were little different than the standard model (data not shown). To further study the effects of this trend, we ran additional separate Cox models restricted to patients treated in 1996 or later, a cut point chosen for its correspondence to an inflection in the proportion of patients with grade-discrepant cases (Fig. 3). The effect sizes and statistical significance of associations of NB<RP GS (Table 3) and NB>RP GS (Table 4) with the risk of PSA recurrence were similar in this more contemporary cohort. The concordance indices for models pooled across prostatectomy Gleason score strata for all patients with (0.58) and without (0.60) a covariate for NB/RP GS discrepancy were similar. However, in the more contemporary subgroup of the cohort (1996 or later), in which GS discrepancy was relatively less common, the addition of a term for NB/RP GS discrepancy resulted in improved predictive accuracy (0.70 vs. 0.52 for the model without a covariate for NB/RP GS discrepancy).

### 4. Discussion

Four decades after its initial description, the Gleason grade remains one of the most powerful prognostic predictors for adenocarcinoma of the prostate. In light of the inherent sampling error of needle biopsy and the frequently multifocal nature of prostate cancer, discordance in grade between biopsy and
prostatectomy specimens is a common finding, with rates of 32–73% reported in the literature [2–15]. Because the prostatectomy GS is based on review of the entire gland submitted for pathological evaluation, it is intuitive that this grade more accurately reflects the underlying biology of the disease. Indeed, when both the NB and RP GS are included in multivariate analyses to predict biochemical recurrence, RP GS has been shown to be a superior predictor of PSA outcome compared with the NB GS [5]. The preponderance of studies in the area of GS discrepancy have focused on strategies of predicting or potentially reducing the incidence of clinically significant upgrading [8,9]. Less clear however is what, if any, prognostic information might be obtained from NB specimens of lower or higher GS. For instance, if a patient with NB GS 3+3 is found to have RP GS 3+4, can he expect the same risk of recurrence as a patient who had GS 3+4 on NB and RP? We hypothesized that, among patients with a given RP GS (ie, RP GS 3+4), patients with a lower NB GS (ie, NB GS 3+3) or higher NB GS (ie, NB GS 4+3) would have correspondingly lower and higher risk, respectively, of biochemical recurrence after RP relative to patients with the same GS on NB and RP.

We examined the association between discordant NB and RP GS and biochemical progression after RP among over 6000 men treated by multiple surgeons at a tertiary referral center. This study constitutes the largest series addressing the issue of Gleason grade discrepancies and the first to systematically evaluate the prognostic significance of this phenomenon, across all Gleason score strata in era-specific analyses. Even after adjusting for PSA and pathological stage, we found consistently lower risks of PSA progression among patients with a lower NB GS and significantly increased risks of biochemical recurrence among men with a higher NB GS, within and across RP GS strata, relative to patients with equal NB and RP GS. In addition, we observed a highly significant trend toward a decreased frequency of grade-discordant cases in the past 10 yr. Although the prognostic significance of the observed phenomenon was attenuated somewhat in the higher-grade strata in this more contemporary era (Table 3), the overall associations

Fig. 2 – Biochemical recurrence–free survival in prostatectomy Gleason score groups stratified by equal (same grade) versus higher (downgraded) needle biopsy Gleason score.
remained robust and consistent. These data suggest that discrepancies in Gleason score between biopsy and prostatectomy may in fact illuminate a greater degree of precision in risk estimation models, underscoring the prognostic power of the Gleason grading system.

Other studies in the field shed light on potential explanatory hypotheses for GS discrepancies, including pathology error, borderline cases (in which an NB may be graded in two different, but not necessarily incorrect, ways), sampling error (in which a major component of the tumor in the RP is not present in the NB), and reverse sampling error (in which a minor component of tumor in the RP is sampled in NB) [6]. Pathology error is self-explanatory; consensus NB reading may reduce somewhat, but certainly not eliminate, the frequency of grade discrepancies [3,10]. Borderline cases are inherent to any grading system because grade is a continuum and there will inevitably be some cases in which the grade straddles two strata. Reverse sampling error can explain some cases of Gleason 3+4=7 or 4+3=7 on

Table 3 – Multivariate Cox proportional hazards regression of upgrade from biopsy to RP, within each RP grade

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
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<tbody>
<tr>
<td>RP Gleason 3+4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NB GS ≤3+3</td>
<td>0.70</td>
<td>0.54–0.91</td>
<td>0.007 (overall)</td>
</tr>
<tr>
<td>PSA &gt;10</td>
<td>1.68</td>
<td>1.30–2.18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SM</td>
<td>3.08</td>
<td>2.36–4.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LN</td>
<td>2.77</td>
<td>1.99–3.84</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>All RP Gleason 7</td>
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<tr>
<td>NB GS ≤3+3</td>
<td>0.62</td>
<td>0.51–0.75</td>
<td>&lt;0.001 (overall)</td>
</tr>
<tr>
<td>PSA &gt;10</td>
<td>1.79</td>
<td>1.47–2.18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LM</td>
<td>2.62</td>
<td>2.15–3.19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LN</td>
<td>2.83</td>
<td>2.23–3.60</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RP Gleason 4+3</td>
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| NB GS ≤3+4        | 0.88 | 0.63–1.24    | 0.479 (unadjusted)
|                    |      |              |       |
| RP Gleason 4+3 or |      |              |       |
| greater            |      |              |       |
| NB GS ≤3+4        | 0.72 | 0.52–0.95    | 0.001 (overall)
|                    | 0.80 | 0.58–1.10    | 0.184 (1996 or later)
| PSA >10           | 1.45 | 1.20–1.76    | <0.001 |
| SV                | 2.50 | 2.05–3.05    | <0.001 |
| Gleason 8–10      |      |              |       |
| NB GS ≤4+3        | 0.73 | 0.56–0.94    | 0.014 (overall)
|                    | 0.77 | 0.49–1.21    | 0.26 (1996 or later)
| SV                | 1.93 | 1.49–2.51    | <0.001 |
| CP                | 2.91 | 1.72–4.90    | <0.001 |
| Pooled across RP  |      |              |       |
| Gleason score strata: |      |              |       |
| NB=RP GS          | 0.76 | 0.65–0.89    | 0.001 (overall)
|                    | 0.75 | 0.59–0.95    | 0.016 (1996 or later)
| PSA >10           | 1.87 | 1.61–2.18    | <0.001 |

HR, hazard ratio; 95%CI, 95% confidence interval; RP, radical prostatectomy; NB GS, needle biopsy Gleason score; PSA, prostate-specific antigen; SM, positive surgical margins; LN, lymph node metastasis; SV, seminal vesicle invasion; CP, capsular penetration.

Table 4 – Multivariate Cox proportional hazards regression of downgrade from biopsy to RP, within each RP grade

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
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<tbody>
<tr>
<td>RP Gleason 3+3</td>
<td></td>
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</table>
| NB GS ≥3+4        | 3.13 | 2.08–4.72    | <0.001 (overall)
|                    | 3.67 | 2.02–6.61    | 0.006 (1996 or later)
| PSA >10           | 2.74 | 1.92–3.90    | <0.001 |
| LN                | 6.41 | 2.20–18.62   | 0.001 |
| RP Gleason 4+3    |      |              |       |
| NB GS ≥4+3        | 1.86 | 1.32–2.63    | <0.001 (overall)
|                    | 2.09 | 1.30–3.36    | 0.002 (1996 or later)
| PSA >10           | 2.56 | 1.78–3.69    | <0.001 |
| LN                | 3.02 | 1.92–4.75    | <0.001 |
| RP Gleason 4+3    |      |              |       |
| NB GS 8–10        | 1.30 | 0.77–2.00    | 0.322 (unadjusted)

HR, hazard ratio; 95%CI, 95% confidence interval; RP, radical prostatectomy; NB GS, needle biopsy Gleason score; PSA, prostate-specific antigen; SM, positive surgical margins; LN, lymph node metastasis; SV, seminal vesicle invasion; CP, capsular penetration.

* All models adjusted for preoperative PSA >10 ng/ml, SM, LN, SV, and CP. Hazard ratios are presented only for those terms that were statistically significant independent predictors of biochemical recurrence in each model.

† Hazard ratio for NB=RP GS relative to NB=RP GS for each RP GS stratum.

‡ The hazard ratios for grade discrepancy in patients treated in 1996 or later are presented after adjustment for the same pathological variables as in the full model.
needle biopsy in which the RP has such little pattern 4 that the RP GS is called 3+3=6 with tertiary pattern 4, resulting in an apparent discrepancy when the tertiary pattern is dropped in the simplified reporting of RP GS. Tumor location represents another potential cause of NB and RP GS discrepancy. Augustin et al [21] demonstrated that transition zone tumors have particularly poor concordance between pre- and postoperative GS.

Although we did not analyze tertiary RP Gleason patterns in this study, the phenomenon we observed cannot be completely accounted for by that convention. For example, we observed that patients with RP GS 3+4 and NB GS 3+3 were at significantly lower risk of progression compared with patients with NB and RP GS 3+4. We believe that the prognostic associations of GS changes we observed reflect an increase in the precision of describing the relative amounts of tumor with a given Gleason pattern in a given case. In the example above, the patient with NB GS 3+3 may likely have a greater proportion of pattern 3 in their RP, despite their ultimate RP GS 3+4, than the patient with RP GS 3+4 who initially had pattern 4 detected on NB.

Several small studies have supported the common sense conclusion that extended biopsy schemes offer improvements in grade accuracy relative to the historical 6-core sextant biopsy [11,14,15]. Although we did not analyze the effect of biopsy extent, the highly significant decreasing frequency of grade-discordant cases in our series in the contemporary era, with a sharp inflection in the distribution in the mid-1990s (Fig. 3) when extended biopsy schemes became widespread, suggest that this may explain at least part of the trend we observed.

In addition, a recent modernization of the Gleason scoring system may decrease the risk of upgrading and downgrading, and could affect the findings of this study [17].

The frequently multifocal nature of prostate cancer complicates the classification of architectural heterogeneity within and between tumor nodules. We did not specifically address the issue of multifocality because we could not tell whether our discrepancies were due to grade heterogeneity in a single-tumor nodule versus discrete tumor nodules. One series specifically examined this issue, finding the rate of upgrading to be twice as common among the over 80% of cases with heterogeneity in the topographical distribution of Gleason grades versus those cases with homogeneous grade [13].

Our group was the first to analyze the prognostic association of discordant GS and biochemical recurrence in patients with Gleason 7 disease on biopsy treated by a single surgeon [7]. The results of the present study are consistent with that earlier work, even with stricter definitions of the comparison groups to patients with consonant NB and RP GS, compared within and across multiple GS strata, and multivariate analyses adjusting for differences in PSA and pathological stage between the groups. More recently, Fitzsimons et al [22] found NB GS to be independently associated with biochemical progression after RP even after adjusting for the RP GS and other pathological features in a series of patients treated at multiple Veterans Affairs hospitals. Our overall findings are in line with that study, and the expanded cohort of our current study also provided the statistical power not only to detect a significant secular trend in grade discrepancies but also to test the significance of the observed phenomena in an era-specific manner.

This study has the limitations inherent to any retrospective study. Given the referral nature of our practice, we have incomplete data on any biopsies that may have been performed in addition to the index biopsy, the number of cores sampled in each case, and indices of the extent of involvement in particular cores. The volume of radical prostatectomy at our institution is too large for a single
pathologist to review all cases. Biopsy and prostatectomy Gleason were assigned by a small group of pathologists with extensive experience in genitourinary pathology; however, our database does not contain information on which pathologist read which case. The lack of information regarding the percent of biopsy cores or tissue with cancer represents one specific potential confounding factor previously demonstrated to have significance in the risk stratification of prostate cancer patients [23]; however, multiple studies have failed to demonstrate a significant relationship between tumor volume surrogates on NB and grade discrepancies [6,11,12]. In addition, this study exclusively analyzed biochemical progression and did not examine clinical outcomes of metastasis or death from prostate cancer, although earlier biochemical progression has been associated with greater risk of the development of distant metastases and prostate cancer-specific mortality [24,25].

5. Conclusions

Grade discrepancy between needle biopsy and prostatectomy is a very common finding. In light of the inherently more comprehensive sampling, the Gleason score of the surgical specimen is widely held to be the “true” pathological grade of surgically treated patients with prostate cancer. We found significant and consistent associations between upgrading or downgrading from preoperative Gleason score and biochemical recurrence–free survival after surgery, even after adjusting for differences in pathological stage and era of treatment. Our results suggest that, in the more contemporary era, this covariate may provide improved predictive accuracy in risk stratification models. These data underscore the validity and precision of the Gleason grading system for prostate cancer and support the inclusion of both pre- and postoperative Gleason score into models of risk stratification for surgically treated patients with adenocarcinoma of the prostate.

Conflicts of interest

The authors have nothing to disclose.

References


Editorial Comment on: Prognostic Significance of Gleason Score Discrepancies between Needle Biopsy and Radical Prostatectomy

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The Gleason grading system is a powerful tool to prognosticate and aid in the treatment of men with prostate cancer. The needle biopsy Gleason score correlates with virtually all other pathologic parameters, including tumor volume and margin status in radical prostatectomy specimens, serum prostate-specific antigen (PSA) levels, and many molecular markers. The Gleason score assigned to the tumor at radical prostatectomy is the most powerful predictor of progression following radical prostatectomy [1,2].

The study by Müntener et al investigated the prognostic significance of Gleason score discrepancies between needle biopsy and radical prostatectomy [3]. Grade discrepancy between needle biopsy and prostatectomy is a common finding. In general, adverse findings on needle biopsy accurately predict adverse findings in the radical prostatectomy specimen, whereas favorable findings on the needle biopsy do not necessarily predict favorable findings in the radical prostatectomy specimens in large part due to sampling error. In light of the inherently more comprehensive sampling, the Gleason score of the surgical specimen is widely held to be the “true” pathologic grade of surgically treated patients with prostate cancer [3].

Several papers have addressed the correlation between Gleason scores in needle biopsies and corresponding radical prostatectomy specimens [1,2,4–7]. Exact correlation of Gleason scores is found in 43% of cases and correlation plus or minus one Gleason score unit in 77% of cases. Undergrading of carcinoma in needle biopsy is the most common problem, occurring in 42% of all reviewed cases. Importantly, over-grading of carcinoma in needle biopsies may also occur, but this was only found in 15% of cases.

The following sources of discrepancy are identified [1,2]: (1) sampling error, (2) borderline cases, (3) pathology error, (4) pathologists’ education and experience, and (5) intraobserver and interobserver variability.

Perhaps the most important factor is sampling error, which relates to the small amount of tissue removed by thin core needle biopsies. The average 20-mm, 18-gauge core samples approximately 0.04% of the average gland volume (40 cc). The most common type of sampling error occurs when a higher grade component is present within the radical prostatectomy specimen and not sampled on needle biopsy. In some instances, undergrading results from an attempt to grade very tiny areas of carcinoma, so-called minimal or limited adenocarcinoma [6]. Scores of minimal adenocarcinoma in needle biopsies show a reasonably strong correlation with radical prostatectomy scores, but the Gleason scores do not have the same power to predict extraprostatic extension.
and positive margin status as they do in non-minimal carcinomas. Over-grading can result from sampling error in cases where the high-grade pattern is selectively represented in needle biopsy. It may only represent a very minor element in the radical prostatectomy specimen. Even the same cancer focus may have different grades depending on the area sampled.

Müntener et al [3] are the first to demonstrate that the Gleason score of the needle biopsy adds additional prognostic value to the radical prostatectomy Gleason score in a consistent manner that may be applicable to strategies of risk stratification and patient counseling after surgery. In particular, they found significant and consistent associations between up-grading or down-grading from pre-operative Gleason score and biochemical recurrence-free survival after surgery, even after adjusting for differences in pathologic stage and era of treatment. The group of authors suggest that, in the more contemporary era, this covariate may provide improved predictive accuracy in risk stratification models.

The data by Müntener et al [3] underscore the validity and precision of the Gleason grading system for prostate cancer and support the inclusion of both preoperative and postoperative Gleason score into models of risk stratification for surgically treated patients with adenocarcinoma of the prostate.

References


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