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Original contribution

Biopsy characteristics in men with a preoperative diagnosis of prostatic adenocarcinoma with high Gleason score (8-10) predict pathologic outcome in radical prostatectomy☆,☆☆

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Summary Even if limited to one biopsy core, most urologists and radiation oncologists use the highest Gleason score (GS) to guide therapy. To evaluate the suitability of using biopsy characteristics to predict tumor characteristics at radical prostatectomy (RP) in men with high biopsy GS (BGS) cancer to better select men who will most benefit from various local therapies, we retrospectively reviewed the biopsy and RP findings of 144 men with a BGS 8-10. One hundred six and 38 patients with a BGS of 8 and 9-10, respectively, were included. Forty-eight percent of cases were downgraded to a final GS of 7 at RP, including 54% of BGS 8, and 32% of BGS 9-10 group. Overall, 31% had pT2 disease at RP. Multiple biopsy features, including the GS, the number of positive cores, the number of cores with high-GS cancer, and the maximum volume of high-grade cancer per core (MVPC) consistently predicted final GS and RP tumor stage. Multivariate analysis showed that biopsy GS and MVPC were independent predictors of final GS, while MVPC was also an independent predictor for final pT stage. Patients with high BGS are not a homogeneous group in terms of local tumor characteristics. In addition to BGS (9-10 being worse than 8), other biopsy findings, especially the number of involved cores, number of cores with high-BGS cancer, and MVPC are important predictors of findings at RP that should be incorporated in the decision treatment planning. Most patients with only one core BGS 8 cancer harbor GS 7 cancer.

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1. Introduction

Prostate cancer (PCa) is the most prevalent cancer and the second leading cause of cancer death in men worldwide [1]. While the majority of tumors have an indolent behavior and remain localized to the prostate, a significant minority have an aggressive behavior and progress to systemic metastases and a fatal course. In order to better predict the clinical outcome and guide treatment, multiple clinical and pathologic prognostic variables have been identified and incorporated into predictive models and nomograms. Among them, Gleason score (GS) is one of the most important prognostic factor [2,3]. The D'Amico risk group classification, uses biopsy GS (BGS, 6 *vs*. 7 *vs*. 8-10), pre-operative prostate-specific antigen (PSA), and clinical stage to predict histologic findings at radical prostatectomy (RP), and to stratify patients into different risk categories based on clinical outcome. The assignment of different risk groups dictates the treatment modality of choice. While surgery is considered to be a standard treatment option for low- and intermediate-risk patients, its role in the high-risk group, especially in cases showing a BGS of 8-10, remains controversial due to the potential risk of treatment failure. Compared to low-risk PCa, RP in high-risk PCa has been shown to carry a 3.5-fold relative risk of recurrence, and 11-fold relative risk of systemic progression and cancer-specific mortality [4]. Thus, many have adopted a non-surgical approach in treating high-risk patients using combined radiation therapy and hormonal therapy, which is reflected in a decline in the rates of RPs from 34% between 1987 and 1992 to 14% between 1999 and 2003 in high-risk patients [5]. Moreover, with respect to radiation therapy, the presence of BGS 8-10 is an indication for combined modality therapy of radiation therapy and adjuvant androgen ablation, with its added morbidity.

In 2003, Kunz et al [6] reported that the presence of high-BGS cancer (BGS = 8-10), even if limited to one biopsy core, predicted high GS and tumor stage at RP [6]. Patients with a BGS of 4 + 4 = 8 and Gleason pattern grade 3 in other cores had a higher overall grade on RPs than those with pure GS of 4 + 3 = 7. This study advocated using the highest BGS rather than the overall biopsy GS for risk stratification, regardless of the number of cores harboring high-BGS PCa. Surprisingly, this has since become the common practice of many if not most urologists and radiation oncologists. Using this approach, a patient with one core of BGS 8 cancer and other cores with cancer GS <8 would be considered as having BGS 8 and would be stratified to the high-risk category similar to another patient who has BGS 8-10 in multiple cores. While this may be justified in some cases, the theoretical risk of such an approach is in over-assigning some patients who would have a final RP GS of 7 to the high-risk category simply because one core happens to sample an area with a predominance of Gleason pattern 4. This may result in choosing radiation and hormonal therapy as the main treatment in some patients. Recent studies have challenged this practice by showing that a significant proportion of men with high-BGS cancer have organ-confined disease (31%-45%), and/or GS of 7 (34%-56%) on RP, with a 5-year biochemical recurrence-free survival ranging from 32%-40% [4,7–12].

In the current multicentric study, we aimed to evaluate the suitability of using biopsy characteristics to predict local tumor characteristics at RP in men with high-BGS cancer, in order to better categorize risk and select appropriate treatment options.

2. Materials and methods

2.1. Cohort characteristics

The study was approved by the institutional review board. 144 men with PCa of GS 8-10 in any core who subsequently underwent RP between 1997 and 2013 were included. Seventy-seven cases were from the database of McGill University Health Centre and the Jewish General Hospital (Montreal, QC, Canada), 40 from Hopital H Mondor (Créteil, France), and 34 from Beth Israel Deaconess Medical Center (Boston, MA). All histologic slides of the biopsies and RPs were reviewed by three genitourinary pathologists (F.B., H.Y., and L.S.) independently using the International Society of Urological Pathology 2005 system (Fig.) [13] and American Joint Committee on Cancer (AJCC) for pathologic stage [14]. A tertiary Gleason pattern of 5 in radical prostatectomy specimen was defined as the presence of Gleason pattern 5 occupying less than 5% of the tumor volume [13].

Pre-operative clinicopathological features were compared with the RP findings. The captured parameters were pre-operative PSA; GS in individual cores; highest BGS; number of cores; number of positive cores; number of cores containing high GS; the maximal volume (%) of high-GS cancer per core (MVPC); final GS at RP including the presence of tertiary pattern in RP, and pT and pN stages.

2.2. Statistical analysis

All analyses were performed using the Statistica 10 software (Statsoft Inc, Tulsa, OK). Pre-operative PSA and biopsy characteristics were compared between cases with different final GS or pT stage on RPs using appropriate comparative tests (ie, Fisher exact test for categorical variables, Mann-Whitney *U* test for ordinal variables, and analysis of variance for continuous variables). A multivariate analysis was performed using the logistic regression model to evaluate the association between final GS and potential pre-operative predictive factors, including pre-operative PSA level, biopsy GS, number of cores with high-GS cancer, and MVPC. $P < .05$ was considered as statistically significant.