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New Prostate Cancer Grading System Predicts Long-term Survival Following Surgery for Gleason Score 8–10 Prostate Cancer

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Abstract

Background: The newly proposed five-tiered prostate cancer grading system (PCGS) divides Gleason score (GS) 8–10 disease into GS 8 and GS 9–10 on the basis of biochemical recurrence (BCR) following radical prostatectomy (RP) as an outcome. However, BCR does not necessarily portend worse survival outcomes.
Objective: To assess the significance of distinguishing GS 8 versus 9–10 disease in terms of long-term survival outcomes for both the preoperative setting using biopsy (Bx) GS and the postoperative setting with RP GS.
Design, setting, and participants: Of 23 918 men who underwent RP between 1984 and 2014, there were 721 men with biopsy GS 8–10, and 1047 men with RP GS 8–10.
Outcome measures and statistical analysis: Clinicopathologic characteristics were compared between men with GS 8 and those with GS 9–10. We compared all-cause mortality (ACM) and prostate cancer–specific mortality (PCSM) risk between the groups using Cox regression and competing-risks analyses, adjusting for other perioperative variables and death from other causes as the competing event.
Results and limitations: Compared to men with GS 8, men with GS 9–10 had later RP year and higher pathologic stage. Among men with Bx GS 8–10, 115 died (82 due to PC) with median follow-up of 3 yr (interquartile range [IQR] 1–7) for both overall and cancer-specific survival. Of men with RP GS 8–10, 221 died (151 due to PC) with median follow-up of 4 yr (IQR 2–8) and 4 yr (IQR 2–9) for overall and cancer-specific survival, respectively. PC-specific survival rates were significantly lower for men with GS 9–10 compared to men with GS 8 for both Bx (hazard ratio [HR] 2.13, 95% confidence interval [CI] 1.37–3.30; $p < 0.01$) and RP GS (HR 2.38, 95% CI 1.74–3.28; $p < 0.01$). This association persisted in multivariable models after adjusting for perioperative variables.
Conclusions: Men with GS 9–10 had higher ACM and PCSM rates compared to those with GS 8. GS 8 and GS 9–10 PC should be considered separately in both the preoperative and postoperative setting as suggested by the new PCGS.
Patient summary: The prostate cancer grading system can predict mortality risk after radical prostatectomy (RP) for men with Gleason score 8–10 disease based on both biopsy and RP Gleason scores. There are significant differences in all-cause mortality and prostate cancer–specific mortality following surgery between men with Gleason score 8 and those with Gleason score 9–10 disease.

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1. Introduction

In 1974, Gleason and Mellinger proposed the prostate cancer (PC) grading system as the sum of the two most common grade patterns [1]. Since then, there have been two major updates owing to the evolving diagnosis and treatment of PC [2,3]. For example, Gleason score (GS) 2–5 distinctions are no longer used. In addition, certain patterns such as poorly formed glands and cribriform glomeruloid cancers are now considered Gleason pattern 4 [2–4]. Compared to other clinicopathologic factors and molecular markers, GS remains the single most powerful predictor of PC outcomes [4].

Although various GS groupings have been used in clinical practice [5–12], most researchers have combined GS 8 and GS 9–10 into a single high-grade entity [9,13–15]. In the new five-tiered prostate cancer grading system (PCGS) proposed by Epstein and colleagues [16], the high-grade entity (GS $\geq$8) is divided into GS 8 and GS 9–10 because men with GS 9–10 had a much higher likelihood of biochemical recurrence (BCR) following radical prostatectomy (RP) than those with GS 8. Recently, this new PCGS was validated using multi-institutional and multimodal therapy data with BCR as an endpoint [17,18]. However, BCR does not necessarily portend worse survival outcomes [19,20]. In this study, we assessed long-term survival outcomes (prostate cancer–specific mortality [PCSM] and all-cause mortality [ACM]) following RP for GS 8 versus GS 9–10 disease using data for a large cohort of RP patients at a single institution. Specifically, we investigated the prognostic value of the new grading system in two clinical settings: preoperative (biopsy) GS and postoperative (RP) GS.

2. Patients and methods

Following institutional review board approval at Johns Hopkins, we reviewed data for 23 918 men who underwent RP at our institution between 1984 and 2014. After excluding patients with biopsy (Bx) GS $<$ 8 and RP GS $<$ 8, incomplete clinicopathologic or follow-up data, or a history of neoadjuvant treatment, there were 721 men with Bx GS 8–10 and 1047 men with RP GS 8–10 (Fig. 1). Most men were treated only with RP until BCR.

Clinical and pathologic stages were assigned in accordance with the American Joint Committee on Cancer staging system [21]. One of the authors of the current article led a consensus on updating the Gleason grading system in 2004 [2]. Men with GS $<$ 8 were appropriately reclassified since 2004, while men with GS 8–10 were properly classified since 1984. Therefore, we decided to perform long-term survival analyses solely evaluating men with GS 8–10, and to focus on the distinction of GS 8 disease from the former "high-risk" clump of GS 8–10.

Baseline characteristics and pathologic outcomes were compared between men with GS 8 and GS 9–10 using χ^2 tests for categorical data and Student's *t*-test or the nonparametric alternative Wilcoxon sum rank test for continuous data.

Information on survival status and cause of death was obtained from patient follow-up, the Social Security Administration Death Index, and the Centers for Disease Control National Death Index. PCSM was designated when the underlying cause of death was PC or the patient had castration-resistant PC at the time of death.

PCSM was calculated for men with GS 8 versus GS 9–10, and PCSM estimates were compared between the groups using a competing-risks model. A cumulative incidence function was also generated for each

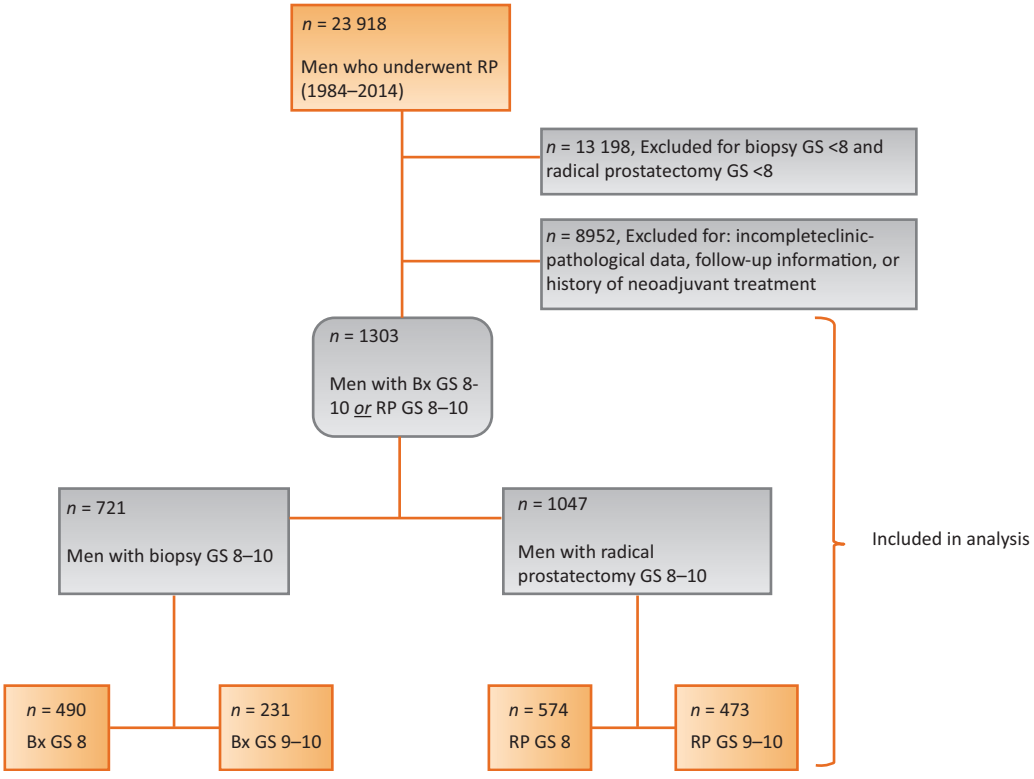

Fig. 1 – Flowchart for study inclusion. RP = radical prostatectomy; GS = Gleason score; Bx = biopsy.

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