



The Effect of Differing Gleason Scores at Biopsy on the Odds of Upgrading and the Risk of Death From Prostate Cancer

John G. Phillips,¹ Ayal A. Aizer,¹ Ming-Hui Chen,² Danjie Zhang,² Michelle S. Hirsch,³ Jerome P. Richie,⁴ Clare M. Tempany,⁵ Stephen Williams,⁴ John V. Hegde,⁶ Marian J. Loffredo,⁷ Anthony V. D'Amico⁷

Abstract

We provide evidence that differing Gleason scores (GSs) at biopsy (ComboGS) is associated with an approximately 80% decrease in the odds of upgrading and a 60% decrease in the risk of prostate cancer-specific mortality (PCSM) after definitive treatment. If validated, future randomized noninferiority studies evaluating deescalated treatment approaches in men with ComboGS could be considered.

Introduction/Background: The GS is an established prostate cancer prognostic factor. Whether the presence of differing GSs at biopsy (eg, 4+3 and 3+3), which we term ComboGS, improves the prognosis that would be predicted based on the highest GS (eg, 4+3) because of decreased upgrading is unknown. Therefore, we evaluated the odds of upgrading at time of radical prostatectomy (RP) and the risk of PCSM when ComboGS was present versus absent.

Patients and Methods: Logistic and competing risks regression were performed to assess the effect that ComboGS had on the odds of upgrading at time of RP in the index (n = 134) and validation cohorts (n = 356) and the risk of PCSM after definitive therapy in a long-term cohort (n = 666), adjusting for known predictors of these end points. We calculated and compared the area under the curve using a receiver operating characteristic analysis when ComboGS was included versus excluded from the upgrading models. **Results:** ComboGS was associated with decreased odds of upgrading (index: adjusted odds ratio [AOR], 0.14; 95% confidence interval [CI], 0.04-0.50; *P* = .003; validation: AOR, 0.24; 95% CI, 0.11-0.51; *P* < .001) and added significantly to the predictive value of upgrading for the in-sample index (*P* = .02), validation (*P* = .003), and out-of-sample prediction models (*P* = .002). ComboGS was also associated with a decreased risk of PCSM (adjusted hazard ratio, 0.40; 95% CI, 0.19-0.85; *P* = .02). **Conclusion:** Differing biopsy GSs are associated with a lower odds of upgrading and risk of PCSM. If validated, future randomized noninferiority studies evaluating deescalated treatment approaches in men with ComboGS could be considered.

Clinical Genitourinary Cancer, Vol. 12, No. 5, e181-7 © 2014 Elsevier Inc. All rights reserved.

Keywords: ComboGS, Pathology, Prognostic factors, Prostate cancer-specific mortality, Radical prostatectomy

Introduction

The biopsy Gleason score (GS),¹ defined as the sum of the 2 most predominant Gleason grades (GGs), is a prognostic factor significantly associated with the risk of prostate cancer (PCa)-specific mortality (PCSM) after conservative² or curative management.^{3,4}

Studies have established the association of the commonly used GS levels (ie, 8-10 vs. 7 vs. ≤ 6) with an increased risk of PCSM after adjusting for known prognostic factors.⁵

Approximately one-third of men with clinically localized PCa will be upgraded at the time of radical prostatectomy (RP) because of

John G. Phillips and Ayal A. Aizer contributed equally to this work.

¹Harvard Radiation Oncology Program, Boston, MA

²Department of Statistics, University of Connecticut, Storrs, CT

³Department of Pathology, Brigham and Women's Hospital, Boston, MA

⁴Division of Urology, Department of Surgery, Brigham and Women's Hospital, Boston, MA

⁵Division of MRI, Department of Radiology, Brigham and Women's Hospital, Boston, MA

⁶Harvard Medical School, Boston, MA

⁷Department of Radiation Oncology, Brigham and Women's Hospital and Dana-Farber Cancer Institute, Boston, MA

Submitted: Jan 24, 2014; Revised: Feb 25, 2014; Accepted: Feb 25, 2014; Epub: Mar 3, 2014

Address for correspondence: John G. Phillips, MD, Harvard Radiation Oncology Program, Brigham and Women's Hospital and Dana-Farber Cancer Institute, Department of Radiation Oncology, ASBI/LL2, 75 Francis St, Boston, MA 02115
E-mail contact: jphillips@lroc.harvard.edu

undersampling of occult high-grade PCa at the time of transrectal ultrasound-guided (TRUS) prostate needle biopsy (PNB) and therefore have a worse prognosis than would have been predicted based on the highest biopsy GS.⁶⁻⁹ To improve counseling regarding prognosis, investigators have identified predictors of upgrading based on information available at the time of diagnosis.⁶⁻¹⁶ However, only a single study¹⁷ has observed that the presence of differing GSs (ie, a lower in addition to the highest GS) at biopsy (termed ComboGS in the current study) lowered the odds of upgrading at the time of RP. No study to date, however, has investigated the effect of differing GSs on the risk of PCSM. Therefore, in the current study we evaluated the effect that the presence of ComboGS had on the odds of upgrading and the risk of PCSM.

Patients and Methods

Index and Validation Study Cohorts

The index cohort consisted of 134 consecutive men with localized PCa diagnosed between April 2008 and September 2011 using a 12-core TRUS PNB. Clinically localized PCa was defined as clinical tumor category (T)1c to T2c based on the 2009 American Joint Committee on Cancer PCa staging guidelines.¹⁸ Men underwent an RP at the Brigham and Women's Hospital (BWH) performed by a single surgeon.

The validation cohort consisted of 356 men distinct from the index cohort with localized PCa diagnosed between January 2005 and December 2008 using a median of 12 cores (interquartile range [IQR], 10-12) via a TRUS PNB who underwent RP at the BWH. Of note, 44% of these men had a less than 12-core sample. The index and validation cohorts overlap in time but not in patients treated between April 2008 and December 2008. Therefore, each patient in the index and validation cohort during this overlap time period was mutually exclusive to their respective cohort. All men from the index cohort received surgery by a single urologic oncologist (JPR) whereas men from the validation cohort received surgery by any of the urologic oncologists at the BWH. This study and the prospective acquisition of the data were approved by the Dana Farber Cancer Institute (DFCI) Institutional Review Board (IRB).

The long-term study cohort consisted of 666 consecutive men with localized or locally advanced PCa diagnosed via a TRUS PNB (median of 6 cores; IQR, 5-6 cores). The men were referred to Saint Anne's Hospital (SAH, Fall River, MA), a DFCI/BWH affiliated regional community-based cancer center and treated definitively between October 1989 and July 2000 with either surgery ($n = 44$) if radiation therapy (RT) was declined, 70 Gy of RT ($n = 533$) or 6 months of androgen suppression therapy (AST) and 70 Gy of RT ($n = 89$). All patient data were collected prospectively into a database that was approved by the SAH IRB.

Assignment of GS and Definition of Upgrading

Biopsy and RP GS were assigned by a single genitourinary pathologist in the index cohort whereas any staff genitourinary pathologist at the BWH assigned the biopsy and RP GS in the validation cohort. For the 666 men in the long-term study cohort, biopsy GS was assigned by community pathologists associated with SAH. For men in the index and validation cohorts, GS was assigned per the 2005 International Society of Urological Pathology Consensus Conference (ISUPCC) on Gleason Grading.¹⁹ Because

all men in the long-term cohort were diagnosed before the 2005 ISUPCC, GS in this cohort was assigned using the conventional grading scale of 2 through 10.¹ The presence of tertiary Grade 5 in biopsy or RP specimens was used to obtain the final GS (eg, a GS 4+3 with tertiary grade 5 would be called 4+5). Upgrading was defined as the presence of a greater GS at the time of RP when compared with the biopsy GS (eg, prostatectomy 4+4 vs. biopsy 4+3). However for numerically equal GSs, an increase in the proportion of the predominant GG component conferred a grade change. For example, a GS of 4+3=7 at the time of RP compared with a GS of 3+4=7 at biopsy was considered upgrading.

Definition of ComboGS

ComboGS was defined as present when the biopsy revealed a GS in at least 1 core that was less than the greatest GS observed in the entire biopsy sample (eg, 3+3 and 4+4) or in the case of GS 7 when both 3+4 and 4+3 were present.

Statistical Methods

Comparison of the Distribution of Baseline Characteristics. A comparison of the distribution of clinical characteristics stratified by whether the patient was in the index, validation, or long-term cohort and by the presence or absence of ComboGS was performed using a Mantel-Haenszel²⁰ χ^2 metric for categorical factors and a nonparametric Wilcoxon test for continuous covariates.²¹

Comparison of Upgrading Using Biopsy GS and Presence of ComboGS. A comparison of the odds of upgrading stratified according to biopsy GS and presence or absence of ComboGS was performed for men in the index and validation cohorts using a Mantel-Haenszel²⁰ χ^2 metric.

Logistic Regression and the Odds of Upgrading at the Time of RP. The primary end point of the study was the adjusted odds of upgrading. For the index and validation cohorts, logistic regression multivariable analysis²² was performed to assess the effect that ComboGS had on the odds of upgrading at the time of RP adjusting for the continuous covariates of age, prostate-specific antigen (PSA) level at time of diagnosis, and percent positive biopsies (ppb), and the categorical covariate of clinical T-category (T2 vs. T1c as reference). Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) with 2-sided P values were calculated. Because men with a high ppb and PSA level at diagnosis were more likely to have higher biopsy GS and therefore would have less opportunity for upgrading compared with men with either a high ppb or high PSA level but not both, the possibility of an interaction existed between ppb and PSA level. Therefore, an interaction term between ppb and PSA level was included in the model.

Model Validation

We calculated and compared the area under the curve (AUC) value using a receiver operating characteristic (ROC) analysis²³ when ComboGS was included versus excluded from the logistic regression model for the index and validation cohorts, which is termed an "in-sample" analysis. We assessed model validation by performing a prediction ROC analysis²³ in which we compared the AUCs obtained when ComboGS was included in the model versus

Download English Version:

<https://daneshyari.com/en/article/2752125>

Download Persian Version:

<https://daneshyari.com/article/2752125>

[Daneshyari.com](https://daneshyari.com)