

PATHOLOGY

The Impact of ISUP 2005 Consensus on Gleason Grading in Contemporary Practice

P Zareba, J Thompson, A Yilmaz, K Trpkov

Calgary Laboratory Services and University of Calgary, Calgary, AB, Canada

Mod Pathol. 2008; 21(suppl 1): 193A

Background: International Society of Urological Pathology (ISUP) in 2005 attempted to achieve a consensus in the application of Gleason grading system in contemporary practice. We investigated how the ISUP consensus impacted the Gleason grading in a center with a large urological pathology practice.

Design: We compared the Gleason score (GS) distribution and the GS concordance on biopsy and radical prostatectomy (RP) in two patient cohorts (before and after the ISUP consensus) in our institution. Both cohorts had similar demographic, preoperative clinical, and RP characteristics. The first cohort consisted of 908 consecutive patients with matched biopsies and RP, performed from 07/2000 to 06/2004 in our institution, prior to the ISUP consensus. The second cohort consisted of 423 patients with matched biopsies and RPs, performed from 10/2005 to 06/2007, after the ISUP consensus. All biopsies and RPs were reported by one group of pathologists.

Results: The ratio of GS 3+4 vs. 4+3 for GS7 on biopsy and RP was similar in both cohorts. Biopsy GS 7 (3+4 vs. 4+3): 24% vs. 6% (2001-2004) and 35% vs. 8% (2005-2007). RP GS 7 (3+4 vs. 4+3): 39% vs. 9% (2001-2004) and 48% vs. 12% (2005-2007). Biopsy GS compared to RP GS were upgraded in 8% and 5% and downgraded in 29% and 30% in cohorts 2001-2004 and 2005-2007, respectively. The most common change from biopsy to RP in both patient cohorts occurred due to biopsy GS 6 upgrade to RP GS 7 (change in secondary grade from 3 to 4).

Conclusions: We document a trend for upgrading GS on both biopsy and RP in our practice after the ISUP consensus. The significance of this change for patient management and prognosis is uncertain. Although the overall GS concordance on biopsy and RP have not been significantly impacted by the ISUP consensus, the complete agreement for GS7 has improved after the ISUP consensus.

Editorial Comment

The Gleason grading system is the most commonly used grading system for prostate carcinoma in the United States. Due to its unique aspects is gaining worldwide acceptance. The Gleason grading system is solely based on the architectural pattern, cytologic features are not factored in, the overall grade is not based on the highest grade within the tumor, and the prognosis of prostate cancer is intermediate between that of the most predominant pattern of cancer and that of the second most predominant pattern (1-4).

At the International Society of Urological Pathology (ISUP) consensus conference in 2005, the Gleason grading system underwent its first major revision (5). Several important reasons were considered for the need of a revision of the system: 1). In the 1960s, there was no screening for prostate cancer other than by digital rectal examination, as serum PSA had not yet been discovered. In Gleason's 1974 study (1), most (86%) of the men had advanced disease with either local extension out of the prostate on clinical examination or distant metastases. Only 6% of patients had nonpalpable tumor diagnosed by transurethral resection and 8% of patients were diagnosed with a localized nodule on rectal examination; 2). The method of obtaining prostate tissue was also very different from today's practice. Typically, only a couple of thick-gauge needle biopsies were directed into an area of palpable abnormality. The use of 18-gauge thin biopsy needles and the concept of sextant needle biopsies to more extensively sample the prostate were not developed until the 1980s. Consequently, the grading of prostate cancer in thin cores and in multiple cores from different sites of the prostate were not issues in Gleason's era; 3). In the 1960s, radical prostatectomy was relatively uncommon, prostates were not as often removed intact, and glands were not processed in their entirety or as extensively and systematically to the degree currently seen. Further issues relating to radical prostatectomy specimens such as the grading

of multiple nodules within the same prostate or dealing with tertiary patterns were not addressed within the original Gleason system; 4). The Gleason system also predated the use of immunohistochemistry. It is likely that with immunostaining for basal cells many of Gleason's original $1 + 1 = 2$ adenocarcinomas of the prostate would today be regarded as adenosis (atypical adenomatous hyperplasia). Similarly, many of the cases in 1967 diagnosed as cribriform Gleason pattern 3 carcinoma would probably be currently referred to as cribriform high-grade prostatic intraepithelial neoplasia, if labeled with basal cell markers.

Stratifying the Gleason score into prognostic groups 2-4, 5-6, 7, and 8-10, using the modified Gleason grading there is a tendency for a change toward a higher prognostic group in approximately 25% of the biopsies (6). This occurs due to some new pathology criteria used in the revised ISUP grading: a) inclusion of most cribriform patterns in grade (pattern) 4; b) considering ill-defined glands with poorly formed glandular lumina as pattern 4; c) ignoring in high-grade cancer lower grade patterns if they occupy less than 5% of the area of the tumor; d) including high-grade tumor of any quantity within the Gleason score; and, e) for tertiary Gleason patterns, both the primary pattern and the highest grade are recorded.

References

1. Gleason DF, Mellinger GT: Prediction of prognosis for prostatic adenocarcinoma by combined histological grading and clinical staging. *J Urol.* 1974; 111: 58-64.
2. Gleason DF: Histologic grading and clinical staging of prostatic carcinoma. In: Tannenbaum M (ed.), *Urologic pathology: The prostate.* Philadelphia, Lea & Febiger. 1977; pp. 171-98.
3. Gleason DF: Histologic grading of prostate cancer: a perspective. *Hum Pathol.* 1992; 23: 273-9.
4. Gleason DF: Histologic grading of prostatic carcinoma. In: Bostwick DG (ed.), *Pathology of the prostate.* New York, Churchill Livingstone. 1990; pp. 83-93.
5. Epstein JI, Allsbrook WC Jr, Amin MB, Egevad LL; ISUP Grading Committee. The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. *Am J Surg Pathol.* 2005; 29: 1228-42.
6. Guimaraes MS, Billis A, Quintal MM, Magna LA, Ferreira U: The impact of the 2005 International Society of Urological Pathology (ISUP) consensus conference on standard Gleason grading of prostatic carcinoma. *Mod Pathol.* 2006; 19(suppl.1): abstract 139A.

Dr. Athanase Billis

Full-Professor of Pathology

State University of Campinas, Unicamp

Campinas, São Paulo, Brazil

E-mail: athanase@fcm.unicamp.br

A contemporary study correlating prostate needle biopsy and radical prostatectomy Gleason score

Fine SW, Epstein JI

Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, New York 10021, USA

J Urol. 2008; 179: 1335-8; discussion 1338-9

Purpose: We determined whether contemporary practice patterns of Gleason grading for prostate needle biopsy and radical prostatectomy have evolved.

Materials and Methods: We correlated needle biopsy (assigned at Johns Hopkins Hospital and other institutions) and radical prostatectomy Gleason score for 1,455 men who underwent radical prostatectomy at Johns Hopkins Hospital from 2002 to 2003, and compared the results with those of a 1994 study of similar design.

Results: Outside institutions diagnosed Gleason score 2-4 in 1.6% (23 of 1,455) of needle biopsies vs. 22.3% (87 of 390) in 1994. Of needle biopsies labeled Gleason score 2-4, 30.4% revealed radical prostatectomy Gleason score 7-10. In 2002 to 2003 no Johns Hopkins Hospital needle biopsy was assigned Gleason score 2-4. Needle biopsies designated Gleason score 6 or less had 80.0% accuracy with regard to radical prostatectomy Gleason score vs. 63% accuracy in older data. For needle biopsy Gleason score 7 or greater, 35.5% (outside institution) and 24.8% (Johns Hopkins Hospital) of radical prostatectomies displayed Gleason score less than 7. Overall, outside and Johns Hopkins Hospital needle biopsy diagnoses showed 69.7% and 75.9% agreement with radical prostatectomy Gleason score, respectively. Direct comparison of Johns Hopkins Hospital and needle biopsy Gleason scores elsewhere revealed 81.8% agreement, with 87.1% for Gleason score 5-6, 68.1% for Gleason score 7 and 35.1% for Gleason score 8-10. For 59.4% of outside needle biopsies with Gleason score 8-10, Johns Hopkins Hospital Gleason score was 7 or less. Conversely, for 64.9% of Johns Hopkins Hospital needle biopsies with Gleason score 8-10, outside Gleason score was 7 or less. For needle biopsies with Gleason score 5-6, 7 and 8-10, the incidence of nonorgan confined disease at radical prostatectomy was 17.7%, 47.8% and 50.0%, respectively, for Johns Hopkins Hospital vs. 18.2%, 44.6% and 37.5% for outside institutions.

Conclusions: The last decade has seen the near elimination of once prevalent under grading of needle biopsy. All cases still assigned Gleason score 2-4 show Gleason score 5 or greater at radical prostatectomy and nearly a third reveal Gleason score 7-10, reaffirming that Gleason score 2-4 is a needle biopsy diagnosis that should not be made. As evidenced by variable over grading and under grading, as well as poor correlation with pathological stage, difficulties in the assignment of Gleason pattern 4 and overall Gleason score of 8-10 on needle biopsy remain an important issue.

Editorial Comment

This study underlines the issue related to the Gleason score 2-4 in biopsies. In an Editorial published in 2000 (1), Epstein favors that Gleason score 2-4 adenocarcinoma of the prostate on needle biopsy is a diagnosis that should not be made. His arguments are based on the following facts: 1) the vast majority of tumors graded as Gleason score 2-4 on needle biopsy, when reviewed by experts in urologic pathology, are graded as Gleason scores 5-6 or higher; 2) Gleason score has a poor reproducibility in its diagnosis even among urologic pathologists; 3) assigning a Gleason score 2-4 to adenocarcinoma on needle biopsies can adversely impact patient care, because clinicians may assume that low-grade cancers on needle biopsy do not need definitive therapy. Not assigning a Gleason score 2-4 to adenocarcinoma on needle biopsy it does not mean that low-grade prostate does not exist. Gleason score 2-4 adenocarcinomas are typically seen on TURP. Low-grade cancers are rarely seen on needle biopsy because they are predominantly located anteriorly in the prostate within the transition zone and they tend to be small. In a series of 2285 biopsies in consultation, Epstein assigned a Gleason score of 2-4 in only 26/2285 (1.1%) consult biopsies demonstrating cancer.

The 2005 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma recommended that, rather than stating categorically that a Gleason score 4 on needle biopsy should “never” be made, this diagnosis should be made “rarely, if ever”. While recommending that the diagnosis of Gleason score 4 on needle biopsy should be made “rarely, if ever” is similar to “never”, it does allow for the exceedingly rare case where low grade cancer has been sampled on needle biopsy. The consensus conference cautioned that although the potential exists for rendering a diagnosis of Gleason score 4 on needle biopsy, it is a diagnosis that general pathologists should almost never make without consultation to an experienced urologic pathologist.

References

1. Epstein JI: Gleason score 2-4 adenocarcinoma of the prostate on needle biopsy: a diagnosis that should not be made. *Am J Surg Pathol.* 2000; 24: 477-8.

2. Epstein JI, Allsbrook WC Jr, Amin MB, Egevad LL; ISUP Grading Committee: The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. *Am J Surg Pathol.* 2005; 29: 1228-42.

Dr. Athanase Billis
Full-Professor of Pathology
State University of Campinas, Unicamp
Campinas, São Paulo, Brazil
E-mail: athanase@fcm.unicamp.br