Table 4. High-grade Gleason patterns (4 or 5) in biopsy Gleason score and prostatectomy specimens

Review	High-Grade GP in Biopsy GS	High-Grade GP in RP Specimens (n)		Sensitivity	Specificity	PPV	NPV
		Positive	Negative				
Local	Positive	797	49	0.581	0.810	0.942	0.140
	Negative	574	206				
Central	Positive	1052	32	0.767	0.876	0.970	0.415
	Negative	319	226				
P value				<.001	.053	.003	<.001

GP, Gleason pattern; NPV, negative predictive value; PPV, positive predictive value; other abbreviations as in Table 2.

COMMENT

In the pretreatment setting for prostate cancer in which clinicians can only use the biopsy information for histologic grade, a more accurate GS correlation between the biopsy and RP specimens must result in more precise evaluation of the disease, regardless of the treatment type planned. However, studies investigating the GS correlation between the biopsy and RP specimens have shown considerable discrepancy—especially of undergrading in biopsy specimens.[4-11] Although the number of patients involved in these studies has varied from 28 to 1455, very few men had high-grade biopsy GSs.[8-10] The present study included the largest number of patients with high-grade biopsy GS (local review 264, central review 168) for investigating the correlation of the GS between the biopsy and RP specimens. Pathology error and sampling error are thought to be the main reasons for the discrepancy.

Steinberg et al[11] previously reported that pathologists at an academic center had a better GS correlation than those at community sites. According to their recent study of 1455 patients, Fine and Epstein[6] reported that the exact GS concordance rate was improved in both community sites (from 34% to 70%) and an academic center (multiple pathologists; from 58% to 76%) compared with the rate in their older study. The effects of education and pathologists' efforts in the United States might have contributed to this improvement.

The present study had some differences from that conducted by Fine and Epstein.[6] First, each Gleason pattern was assigned according to the ISUP consensus, which was published in 2005 after their study period (2002-2003). Second, we used the global GS, considering the entire tumor within the prostate as 1 lesion for both the biopsy and the RP specimens because the GS of each core was not available in most (>95%) of the original pathologic reports. The use of the global GS should be considered a weakness of the present study. In the study by Fine and Epstein,[6] the RP GS was recorded from the dominant tumor or highest grade tumor. However, it was not clearly reported whether the global or highest core GS had been used for the biopsy specimens. Although almost all preoperative nomograms have used the highest core grade of the given case when multiple cores with different GSs are present, and urologists have tended to use the greatest GS to determine their treatment plan, some clinicians might use the global GS. ISUP did not actually specify that the highest core GS should be used for the biopsy GS in each case.[2,16,17] Third, the present study included significantly more patients with greater biopsy and RP specimens than the previous study. In the present study, 67% of the biopsy and 74% of the RP specimens had a GS of ≥7 compared with the previous 26% and 23%, respectively.[6,11] This might have resulted from patient selection bias and ethnic differences in the patients with prostate cancer, because the present cohort of patients underwent RP at academic or community institutions in Japan.[18] In addition to the differences in the distribution of GS, the division of GS 7 into 3 + 4 and 4 + 3 might explain the relatively low exact concordance rate in our study. When GS 3 + 4 and 4 + 3 were combined as 1 entity, the exact concordance rate was high (73.6%) in the present study. However, a GS of 3 + 4 and that of 4 + 3 have different biologic behavior and should not be combined into 1 category.[19]

Reflecting contemporary changes regarding prostate cancer and the Gleason grading system, the ISUP proposed a modified Gleason grading system in 2005.[16] The ISUP consensus has been reported to minimize biopsy undergrading and improve the GS correlation compared with the previous system.[12] In the present study, including patients who underwent RP from 1997 to 2005, biopsy GS 2-4 was originally diagnosed at each institution in 14.6% of all patients compared with 1.6% in another study.[6] ISUP recommended that a GS 2-4 should rarely, if ever, be considered, because of the poor correlation with the RP GS. Most expert uropathologists would not have assigned a GS of 2-4 even before the ISUP consensus.[20] In our study, all locally reviewed biopsy GS 2-4 specimens were upgraded by the central review and 61% actually had a RP GS of ≥7, including 3 patients with a RP specimen GS of 8-10. In addition, no RP specimens in the present study was graded with a GS of 2-4. For the GS categories other than 2-4, we also showed that central review using the ISUP consensus gave a more accurate GS correlation than local review, including biopsy GS 8-10. However, the exact concordance rate was far from perfect (100%) and was less satisfactory even when a central review using the ISUP consensus was done. The actual GS of each patient can be apparent only after RP has been performed. We believe this is an advantage for RP compared with other

treatment modalities that offer patient surveillance and adjuvant treatment according to the biopsy GS only.

High-grade Gleason patterns, either a primary/secondary pattern or a tertiary pattern, in RP specimens have been related to a poor outcome.[13-15] We have demonstrated that the central review biopsy GS using the ISUP consensus is superior to the local review biopsy GS in terms of predicting high-grade Gleason patterns in the RP specimens. It has been reported that the highest core GS has the largest effect on a significant upward shift of the biopsy GS among the reporting rules of the ISUP consensus.[21] Because we used a global biopsy GS for the central review, the difference in the interpretation of each Gleason pattern between the local review and central review might explain our results for high-grade Gleason patterns.

CONCLUSIONS

This is the first study to investigate the significance of dedicated pathologic reassessment using the ISUP consensus for biopsy and RP specimens from academic and community practices. Central pathologic review resulted in a more accurate GS correlation and prediction of high-grade Gleason patterns. We believe that more educational effort is needed for both pathology and urology communities to disseminate the ISUP consensus. We recommend central pathology review by dedicated uropathologists for a study of prostate biopsy and RP specimens from patients at multiple institutions, although the central review will cost more and is time-consuming. We should carefully interpret multicenter study data that have not included a central review. In addition, the exact concordance rate was far from perfect (100%) and was not satisfactory even when a central review using the ISUP consensus was done. Also, the actual GS of each patient can be apparent only when RP has been performed.

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