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Correlation between Prostate Needle Biopsy and Radical Prostatectomy Gleason Gradings of 111 Cases with Prostatic Adenocarcinoma

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ABSTRACT

Purpose: There are conflicting reports in the literature about correlation of biopsy and prostatectomy Gleason scores in prostate carcinoma. The goal of this study was to determine the correlation of grading in these two types of pathologic materials.

Materials and methods: The coupled Hematoxylin and Eosin slides of 111 patients with prostate carcinoma were collected. Gleason scores were determined. Patients who had undergone any therapy except surgery were excluded from the study. Correlation between grades was calculated by determination of correlation coefficient. Accuracy of biopsy grading in prediction of final grade was also determined by measuring the sensitivity, specificity, and positive and negative predictive values.

Results: In 50 cases (45%), grade was underestimated in the biopsy. After dividing the cases into Gleason scores of 2 to 4, 5 to 6, 7, and 8 to 10, the most of undergraded cases (84.2%) were in the first group (Gleason score 2 to 4) and this rate reached 5% in the fourth group (Gleason score 8 to 10). The correlation coefficient measured was 0.535 in grade to grade comparing and 0.514 in group to group comparison of the specimens. In low-grade tumors, grading in biopsy, in spite of high sensitivity (90.9%), had low positive predictive value (26.3%).

Conclusion: There is a moderate direct linear relationship between scores in biopsy and prostatectomy specimens. But there is a high probability of underestimation of real Gleason score of the radical prostatectomy specimen in low-grade tumors. Pathologists and urologists must consider the phenomenon of undergrading in reporting prostate specimens and managing patients.

KEY WORDS: Gleason grading, needle biopsy, adenocarcinoma of prostate

Introduction

The grading system for prostatic adenocarcinoma, developed by Gleason, has a strong prognostic value. The primary and secondary patterns are combined to give a Gleason score or sum. When only a minute focus of tumor is present in the specimen, the score is determined by doubling the number of Gleason pattern.[1] It has been claimed that Gleason score in biopsy specimen correlates with prostatectomy Gleason score and in combination with pretreatment

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serum prostate-specific antigen (PSA) and digital rectal examination results, it can predict tumor stage and lymph node metastasis.[2] There are studies in the literature that have specifically correlated needle biopsy and prostatectomy Gleason scores.[3-6] In many of these studies it has been noted that when in biopsy specimen, one encounters a low-grade tumor, in a notable percent of cases the Gleason score will be higher in prostatectomy specimen. Thus, Gleason grading of a seemingly low-grade tumor in biopsy specimens may have unwanted effects on management of such patients. The aim of this study was to investigate the correlation between Gleason score of biopsy and prostatectomy specimens.

Materials and Methods

Between 2000 and 2003, consecutive paired biopsy and prostatectomy specimens from 111 cases of prostatic adenocarcinoma, which were diagnosed by prostatic needle biopsy and had undergone radical prostatectomy in follow-up, were selected. Patients who had undergone neoadjuvant therapy as radiotherapy or androgen-deprivation therapy were excluded from the study. All biopsy specimens had been taken by 18-gauge needle, mostly under the guide of ultrasonography, but the number of cores was varying between 4 and 10, because of different clinical experience of the urologists. The primary and secondary Gleason patterns and final Gleason scores of paired biopsy and prostatectomy (minimum of three slides per patient) were determined separately, blindly and without matching of paired samples. The analysis of agreement between biopsy and prostatectomy Gleason scores was based on individual scores and after assignment to one of the four groups defined as Gleason scores of 2 to 4, 5 to 6, 7 and 8 to 10. Correlation between Gleason scores of biopsy and prostatectomy specimens was analyzed by calculating the coefficient of agreement (Kappa) and Pearson's correlation coefficient using SPSS 11.5 software. Accuracy of biopsy was also evaluated by determination of sensitivity, specificity, and positive and negative predictive values.

Results

Median age of the patients was 62 ± 10.6 (range 39 to 89) years. The most prevalent score was 6 (20.7%) in biopsy specimens and 7 (23.4%) in prostatectomy specimens (tables 1, 2). There

TABLE 1. *Correlation of biopsy and prostatectomy Gleason scores*

	Grade	2	3	4	5	6	7	8	9	10	Total
Biopsy	2	1	0	2	2	1	2	1	0	0	9
	3	0	2	2	3	1	2	2	0	0	12
	4	0	0	3	2	3	4	3	2	0	17
	5	0	0	0	6	3	0	4	0	0	13
	6	0	1	0	0	15	4	1	2	0	23
	7	0	0	0	1	2	11	3	0	0	17
	8	0	0	0	0	0	2	9	1	0	12
	9	0	0	0	0	0	1	1	6	0	8
	10	0	0	0	0	0	0	0	0	0	0
	total	1	3	7	14	25	26	24	11	0	111

Pearson's R = 0.535, Kappa = 0.392 (P <0.0001)

TABLE 2. *Correlation of biopsy and prostatectomy Gleason scores by group assignment*

		Prostatectomy				
	Grade	1	2	3	4	total
Biopsy	1	10	12	8	8	38
	2	1	24	4	5	36
	3	0	3	11	3	17
	4	0	0	3	17	20
	total	11	39	26	35	111

Pearson's R = 0.514, Kappa = 0.419 (P <0.0001)

was no score 10 tumor in any of biopsy or surgical specimens. Most of the tumors in biopsy specimens were in the first grading group (low-grade, Gleason score 2 to 4) and most of the tumors in prostatectomy specimens were in the second group (medium-grade, Gleason score 5 to 6). The correlation between the Gleason scores of biopsy and prostatectomy is shown in Table 1. The Gleason scores were similar in 47.7%, and differed by 1 point in 18% of cases. Overall, 45% were undergraded and 7.2% overgraded. Considering a maximal difference of one number as a desirable correlation, in 65.7% of the cases correlation was seen between biopsy and prostatectomy specimens. The most undergrading cases (84.2%) was observed in first group (Gleason score 2 to 4) and the most overgrading cases was seen in the last group (Gleason score 8 to 10). Kappa analysis yielded a value of 0.392 and Pearson's R was measured as 0.535 (table 1), corresponding to a moderate agreement beyond chance and relative direct correlation between the biopsy and prostatectomy specimens. After grouping, the same analysis was done for the Gleason score group assignments (table 2). In this instance 55.8% of cases remained within the same group, 37.8% were undergraded and 6.3% were overgraded. Kappa and Pearson's R yielded values of 0.419 and 0.514 respectively. The accuracy based on these group assignments is given in table 3. The sensitivity and positive predictive value for a biopsy Gleason score of 2 to 4 (low-grade carcinoma in biopsy specimen) was 90.9% and 26.3%, respectively, while for Gleason score

TABLE 3. *Accuracy of biopsy Gleason score in predicting final surgical Gleason group*

Score Groups	Sensitivity		Positive Predictive Value	
	Number/Total	%	Number/Total	%
2 to 4	10/11	90.9	10/38	26.3
5 to 6	24/39	61.6	24/36	66.7
7	11/26	42.3	11/17	64.7
8 to 10	17/35	48.6	17/20	85.0

of 8 to 10 (high-grade carcinoma in biopsy) was 48.6% and 85%, respectively. There is clear evidence that more well-differentiated cancers have a higher frequency of being underscored and the poorly differentiated cancers being overscored in biopsy specimens. The correlation between the biopsy Gleason score and surgical Gleason score is shown in figure 1. The relationship between these, in the sense that well-differentiated cancers are consistently undergraded and poorly differentiated cancers are consistently overgraded, is well fit by a linear regression (r^2 = 0.29, P = 0.0001).

Discussion

Gleason grading system is important in determination of prognosis and management of prostatic adenocarcinoma.[7] Gleason score in association with pretreatment serum PSA level and result of digital rectal examination predicts tumor stage and existence of lymph node metastasis.[8] Consequently, it is necessary to determine the accuracy of needle biopsy scoring and correlation of this score with the one assigned to radical prostatectomy specimens. There are some studies in the literature comparing Gleason scores of biopsy and prostatectomy, in most of which it has been indicated that in some cases, especially when one encounters a low-grade tumor in biopsy, the assigned score underestimates the final score in the prostatectomy specimen and contrarily needle biopsy scoring overestimates prostatectomy scores to some extent in high-grade tumors.[3-6,8-13] Pearson's correlation coefficient and Kappa coefficient of agreement were calculated as 0.535 and 0.392, respectively, implying a moderate direct relationship between biopsy and prostatectomy Gleason scores (tables 1,2). The relationship between the biopsy Gleason score, in the sense that well-differentiated cancers are consistently undergraded and poorly-differentiated cancers overgraded is well shown in figure 1. In low-grade tumors (Gleason grade 2 to 4) 84.2% of cases were undergraded. In comparison, only 5% undergrading was found in high-grade tumors. On the other hand, needle biopsy Gleason scores of 20% of high-grade tumors were overestimated, while no overgrading was observed in low-grade tumors. As an index of accuracy, the positive predictive value of Gleason scoring in biopsy was only 26.3% in low-grade tumors and reached to 85% in high-grade tumors, implying insufficient accuracy in low-grade tumors (table 3).

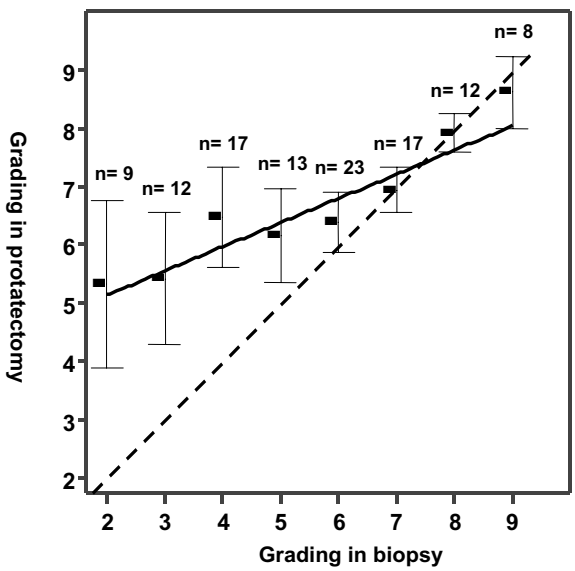

FIG. 1. Relationship between the biopsy Gleason score and surgical Gleason score. Error bars represent the 95% confidence interval about the mean. The number of cases in different groups is indicated above error bars. Regression is indicated by the solid line (r^2 = 0.29, P = 0.0001). The dashed line represents perfect correlation.

Different factors have been suggested as the reasons of this significant undergrading of low-grade tumors in biopsy specimens. Its consistency in different studies implies that it is more a systematic bias toward undergrading, rather than an error in pathologic interpretation. Gleason has proposed that the undergrading may be due to several sources including reluctance of pathologists to characterize a small amount of high-grade tumor in an otherwise low-grade background.[4] Other factors may contribute to the discrepancies between Gleason score of biopsies and surgical specimens as the amount of cancerous tissue present within biopsy material and sampling effects.[4] To determine whether the amount of cancerous tissue in the biopsy specimen is responsible for the Gleason score difference between the prostatectomy and biopsy, a correlation analysis has been performed by King,[4] Bostwick,[9] and Steinberg;[3] none of them have found any significant correlation. Since prostate cancer is often multifocal, with a

heterogeneous population of tumor cells, a certain degree of sampling error is inevitable. This may result in sampling an area that consists of more high-grade or low-grade tumor samples than the actual tumor.

It has been suggested that to overcome sampling error one must either perform a directed biopsy (if there is an ultrasound-visible lesion) or increase the number of biopsies obtained. Some studies suggest that sampling error might be significantly reduced by obtaining more biopsies.[12,14] Some authors propose a modification to the Gleason system to include "tertiary" or the third most prevalent pattern in the scoring,[15] but King[4] argues that this modification may even increase the error of sampling. Also a routine consensus approach to pathologic evaluation of prostate adenocarcinoma seems useful.

Conclusion

According to our findings, there is a moderate direct linear relationship between scores in biopsy and prostatectomy specimens. But there is a high probability of underestimation of real Gleason score of the radical prostatectomy specimen in low-grade tumors. Pathologists and urologists must consider the phenomenon of undergrading in reporting prostate specimens and managing patients.

It must be emphasized that radical therapies for localized prostate adenocarcinoma are sometimes determined or excluded from consideration on the basis of the biopsy Gleason score. Now the differences between the histological grade in biopsies and surgical specimens are being understood. Therefore, staging of organ confined prostate cancer, when based on biopsy grading, should include the likelihood of histological overestimation in the surgical specimen.

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