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Correlation Between Gleason Scores on Prostatic Biopsies and Prostatectomy Specimens in 40 Patients Undergoing More Than 12 Core Biopsies

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ABSTRACT

Summary: The Gleason score obtained on prostatic biopsies is a key parameter in the management of localized prostate cancer.

Objectives: We conducted this study to evaluate the correlation between Gleason scores (GS) obtained on prostate biopsies and radical prostatectomy to establish the accuracy of biopsy grading in the prediction of final grades.

Materials and Methods: Forty patients with localized prostate cancer diagnosed between 2000 and 2010, and treated with radical prostatectomy, were included in this study. All patients underwent transrectal needle biopsies (TRNB) with at least 12 cores. Gleason scores on biopsies and radical prostatectomy specimens were determined and the concordance between the 2 scores was then evaluated. Histological grading using the conventional Gleason grading system (3 groups) and the modified Gleason grading system (5 groups) was also performed. The correlation between grades obtained on biopsies and radical prostatectomy specimens was also evaluated.

Results: The mean age of patients was 61.1 years, with a mean PSA value of 10 ng/ml. In 32.5% of cases, the biopsy's Gleason score correlated with the one obtained on radical prostatectomy. Using the conventional Gleason grading system, the correlation highly improved, with 62.5% of patients remaining in the same group after radical prostatectomy. However, using modified Gleason grading, the correlation was slightly improved and estimated at 37%.

Conclusion: In this study we have noticed that the accuracy of Gleason scores determined by transrectal needle biopsy in patients with prostate cancer seems unreliable. The classification of patients into 3 distinct groups (well, moderately, and poorly differentiated tumors) increases the concordance between the biopsy GS and the definitive GS, but the modified Gleason grading system seems to be more precise and better reflects the Gleason score.

INTRODUCTION

Prostate cancer is an increasingly frequent pathology, and it is considered the second most frequent urinary cancer in Tunisian men [1]. After the clinical or biochemical suspicion of prostate cancer, the diagnosis can be histologically confirmed on transrectal needle biopsy. Moreover, the degree of tumor differentiation is determined by establishing the Gleason score (GS). This score is obtained by combining the primary and secondary patterns for a number score from 2 to 10 [2,3]. It is one of the most powerful predictors of biological behavior, and it is one of the most influential factors used to determine treatment for prostate cancer and a choice of external radiotherapy, brachytherapy, cryotherapy, or radical

KEYWORDS: Prostate carcinoma, prostate biopsy, radical prostatectomy, pathology, Gleason score

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prostatectomy [5]. However, in some cases, the GS established on transrectal needle biopsy could be different from the one for radical prostatectomy, which has a very important impact on prognosis and therapeutic options [3-6].

In this retrospective study, we evaluate the correlation between Gleason scores obtained on prostate biopsies and radical prostatectomy to establish the accuracy of biopsy grading in the prediction of final grades.

MATERIALS AND METHODS

We retrospectively analyzed the medical records of 40 patients who had undergone radical prostatectomy for prostate cancer, from January 2000 to February 2010.

Exclusion criteria included patients who underwent prostate biopsies who showed a high or low PIN grade, patients using 5-alpha-reductase inhibitors, and patients with a positive biopsy for prostate cancer that were not candidates for/refused radical prostatectomy. Inclusion criteria included patients who underwent transrectal needle biopsy with at least 12 cores and were candidates for radical prostatectomy.

The diagnosis was made on transrectal needle biopsy (TRNB), which was performed on patients with elevated serum PSA and/or abnormal digital rectal examination findings. Patients underwent at least 12 core biopsies (from the apex, the middle, and the base of the prostate, with 4 cores for each site). Additional target biopsies were performed when needed (prostatic nodes; hypoechogenic lesions). The same senior pathologist examined all the biopsies. Various preoperative biopsy findings were recorded, including the primary and secondary Gleason pattern grade from each positive biopsy site. The Gleason score was then established by combining the highest Gleason score among all biopsy sites and the Gleason score from the site with the highest tumor volume on the needle biopsy. The tumor was then classified using the conventional Gleason grading system with 3 categories: Well-differentiated tumors (score: 2 to 4), moderately differentiated tumors (score: 5 to 7), and poorly differentiated tumors (score: 8 to 10) [2]. The modified Gleason grading system included 5 categories: Well-differentiated cancer (score: 2 to 6), moderately differentiated (score: 3 + 4 = 7), Moderately/poorly differentiated (score: 4 + 3 = 7), poorly differentiated (score: 8), and undifferentiated (score: 9 to 10) [7]. The 2002 TNM staging system of the American Joint Committee on Cancer (AJCC) was used for clinical staging.

All these patients underwent an open, retropubic radical prostatectomy. For each patient, we evaluated these parameters: Serum PSA level, clinical stages, biopsy data, and postoperative criteria (pathological TNM stage 2002, Gleason score). The highest GS established on the TRNB and radical prostatectomy specimens were compared. A "downgrade" was defined as the Gleason score for the prostatectomy specimen greater than that of the biopsy specimen, whereas an "upgrade" was defined as the opposite.

Table 1. Gleason score biopsy and after radical prostatectomy.

Biopsy/ Prostatectomy	4	5	6	7	8	9	Total
4	0	0	1	0	0	0	1
5	0	0	0	0	1	0	1
6	0	1	11	9	4	1	26
7	0	0	1	1	0	1	3
8	0	0	1	3	1	1	6
9	0	0	2	0	1	0	3
Total	0	1	16	13	7	3	40

Statistical analysis was performed using the Student *t* test for continuous variables, Pearson's chi-square test, and Fisher's exact test for categorical variables. The software used for statistical analysis was SPSS version 12.0 (SPSS Inc., Chicago, IL, USA). A *P* value of less than 0.05 was considered statistically significant.

RESULTS

There were 40 patients with a mean age of 61.1 ± 4.4 years (52 to 69) and a mean serum PSA level of 10 ± 6.3 ng/ml (1.9 to 26.3). For the TRNB, the mean GS established was 6.52 (4 to 9). Among the 40 patients, 1 (2.5%) had a GS of 4 (2 + 2), 1 (2.5%) had a GS of 5 (2 + 3), 26 (65%) had a GS of 6 (3 + 3), 1 (2.5%) had a GS of 7 (3 + 4), 2 (5%) had a GS of 7 (4 + 3), 6 (15%) had a GS of 8 (4 + 4), 1 (2.5%) had a GS of 9 (5 + 4), and 2 (5%) had a GS of 9 (4 + 5) (Table I).

For the radical prostatectomy specimens, the mean GS was 6.87 (5 to 9). One case (2.5%) had a GS estimated at 5 (2 + 3), 16 cases (40%) had a GS estimated at 6 (3 + 3), 13 cases (32.5%) had a GS estimated at 7 (9 patients exhibited a pattern of 3 + 4, and 4 patients exhibited a pattern of 4 + 3), 7 cases (17.5%) had a GS estimated at 8 (2 cases showed a pattern of 3 + 5 and 5 cases a pattern of 4 + 4), and 3 cases (7.5%) had a GS estimated at 9 (2 cases exhibited a pattern of 4 + 5 and 1 case had a pattern of 5 + 4) (Table I).

For the group of 26 patients with TRNB GS estimated at 6, 11 cases (42.3%) had identical Gleason scores on the needle biopsy and prostatectomy specimens, whereas 14 cases (53.8%) were under-graded (9 cases with radical prostatectomy GS of 7, 4

Table 2. Concordance results of the Gleason score biopsy/radical prostatectomy.

	Concordance	No Concordance	Total
Biopsy GS 4-5	0	2	2
Biopsy GS 6	11	15	26
Biopsy GS 7	1	2	3
Biopsy GS 8	1	5	6
Biopsy GS 9	0	3	3
Total	13	27	40

Table 3. Concordance results of the Gleason score biopsy/radical prostatectomy.

GS Biopsy/ Prostatectomy	Well	Moderate	Poor	Total
Well	0	1	0	1
Moderate	1	22	7	30
Poor	0	6	3	9
Total	1	29	10	40

Table 4. Concordance results for tumor differentiation: biopsy/radical prostatectomy (conventional Gleason grading system).

GS Biopsy/ Prostatectomy	Concordance	No Concordance	Total
Well	0	1	1
Moderate	22	8	30
Poor	3	6	9
Total	25	15	40

cases with a GS of 8, and 1 case with a GS of 9), and 1 case (3.8%) was over-graded (GS on radical prostatectomy estimated at 5) (Table 2). For the group of 7 patients with TRNB GS estimated at 7, concordance with radical prostatectomy specimen GS was observed in only 1 case. There was an under-grade in 1 case (GS estimated at 9 after radical prostatectomy) and an over-grade in 1 case (GS 6 after radical prostatectomy). For the group of 6 patients with TRNB GS estimated at 8, there was concordance with radical prostatectomy specimen GS in only 1 case, an over-grade in 4 cases (1 case with GS estimated at 7 and 3 cases with GS estimated at 6 after radical prostatectomy), and an under-grade in 1 case (GS estimated at 9 after radical prostatectomy). For the 3 patients with TRNB GS estimated at 9, there was an over-grade in all cases (2 case with GS estimated at 6 and 1 case with GS estimated at 8 after radical prostatectomy) (Table 2).

Overall, the preoperative biopsy predicted the prostatectomy Gleason score accurately in 13 cases (32.5%), with the highest accuracy rates obtained for Gleason scores of 6. The Gleason scores were discordant in 27 cases (67.5%), with an under-grade in 45% of cases and an over-grade in 22.5% of cases. The difference between the 2 GS in these cases was not significant (P = 10.6).

Using the conventional Gleason grading system to classify the results obtained on TRNB, this series accounted for 1 well-differentiated tumor, 30 moderately differentiated tumors, and 9 poorly differentiated tumors (Table 3). Comparing the results of TRNB using this classification to the results of radical prostatectomy specimens showed that the concordance highly improved, estimated at 62.5% (N = 25). There was an under-grade in 20% (N = 8) and an over-grade in 17.5% (N = 7) (Table 4). The difference between the 2 GS in different groups was also not significant (P = 1.0).

The majority of tumors were classified as moderately differentiated (score: 5 to 7) on TRNB (75%) as well as on radical prostatectomy specimens (72.5%). The highest accuracy rate was noted in this group (73.3%). Using the modified Gleason grading system for classification, the series of biopsies accounted for 28 well-differentiated, 3 moderately differentiated, 6 poorly differentiated, and 3 undifferentiated tumors (Table 5). The concordance according to the 5 groups was 35% (N = 14), under-staging in 20% (N = 8), and over-staging in 45% (N = 18) (Table 6). The difference between the 2 GS in the 5 groups was not significant (P = 0.40). The majority of patients using this new classification also had well-differentiated tumors (score: 2 to 6) on biopsy (70%) and prostatectomy specimens (45%). The highest accuracy rate was also noted in this group (46.4%) (Table 6).

DISCUSSION

In clinical practice, treatment decisions for prostate cancer depend on many factors, including prostatic biopsy GS, preoperative PSA, and clinical stages [8]. The Gleason score is a system based on tumor architecture. It is determined by adding the scores of the 2 most represented volumetric quotas. The course of action is based on the hypothetical correlation between Gleason score of the biopsy and that of the prostatectomy specimen. Gleason score represents the

Table 5. Tumor differentiation: Biopsy/radical prostatectomy (modified Gleason grading system).

GS Biopsy/ Prostatectomy	Well Differentiated Cancer	Moderately Differentiated (Score: 3 + 4)	Moderately-Poorly Differentiated (Score: 4 + 3)	Poorly Differentiated (Score: 8)	Undifferentiated (Score: 9-10)	Total
Well differentiated cancer (score: 2-6)	13	6	3	5	1	28
Moderately differentiated (score: 3 + 4)	2	0	1	0	0	3
Moderately-poorly differentiated (score: 4 + 3)	0	0	0	0	0	0
Poorly differeniated (score: 8)	1	3	0	1	1	6
Undifferentiated (score: 9-10)	2	0	0	1	0	3
Total	18	9	4	7	2	40

histological assessment of the different cellular differentiation degrees in prostate cancer. The most frequent tumor patterns are regarded as primary grade while those that are next in frequency are regarded as secondary grade. The sum of both patterns enables classification on the basis of differentiation and a good prognosis of patterns (a good prognosis and good cellular differentiation yields a GS of 2 to 5, a medium prognosis and moderate cellular differentiation a GS of 6 to 7, and a bad prognosis and bad cellular differentiation a GS of 8 to 10) [2,9]. Recent studies have focused on the discordance in GS between TRNB and radical prostatectomy specimens. Global discordance varies from 31 to 72% [3,5,6,9-18] (Table 5). Under-staging ranges from 26 to 46% [3,5,6,9-13,16,19,20]. Our results accord with those reported in medical literature.

Several factors could explain this discordance and must be taken into consideration when the treatment decision is based on Gleason score:

- The prostatic biopsies are heterogeneous and do not fully reflect the real tumor architecture.
- The reproducibility of the GS is low during iterative analysis by the same or by other pathologists [2,21].
- Other factors, including PSA level, prostate volume, size of the tumor mass, and preoperative clinical stage, are known to be associated with discordance of the GS between TRNB and radical prostatectomy [22,23].

The clinical implication of this discordance is very important.

Table 6. Concordance results and tumor differentiation: Biopsy/radical prostatectomy (modified Gleason grading system).

GS Biopsy/ Prostatectomy	Concordance	No Concordance	Total
Well differentiated (score: 2-6)	13	15	28
Moderately differentiated (score: 3 + 4)	0	3	3
Moderately-poorly differentiated (score: 4 +)	0	0	0
Poorly differentiated (score: 8)	1	5	6
Undifferentiated (score: 9-10)	0	3	3
Total	14	26	40

Indeed, an under-grade on biopsy should not have any impact on treatment decisions, especially if the patient does not change groups. However, in some cases, the therapeutic attitude may

be different between 2 very close GS. For example, a patient with a GS of 8 will not be a candidate for prostatectomy while those with a GS of 7 may benefit from surgery. Therefore, many studies focused on different factors causing this discordance between TRNB GS and RP GS and the ways to overcome these obstacles.

Because of the heterogeneity of prostatic biopsies, some series studied the impact of increasing the number of biopsy cores to decrease the discrepancy of the 2 GS. Kahl et al. found that an extended biopsy scheme with cores numbering more than 12 can help to acquire more accurate GS than a biopsy scheme with cores numbering less than 12 [24]. Moon [25] suggests that at least 13 cores should be taken during TRNB and more aggressive biopsies should be performed at the apex and of hypoechogenic lesions for more precise GS, preoperatively. San Francisco et al. [26] compared 2 groups of patients with a different number of biopsy cores who underwent radical prostatectomy: A group of 340 patients (biopsies with 9 cylinders or less) and a group of 126 patients (biopsies with 10 cylinders or more). They found a concordance with 67 and 76% of cases, respectively. Thus, they concluded that increasing the number of biopsy cylinders better defines the final GS after radical prostatectomy. Divrik et al. [27] also showed that an extended biopsy scheme beyond its superior diagnostic capability also improves the concordance of Gleason scores of needle biopsies and radical prostatectomy specimens. However, Thickman found that there is no interest in increasing the number of carrots to improve the prediction of the GS [15].

Arrabal-Polo et al. [28], comparing 2 groups of patients who underwent radical prostatectomy after sextant prostate biopsy in 98 patients (64% correlation) and 12 cylinder in 30 patients (60% correlation), also didn't find a significant difference in GS correlation.

For the other factors causing the GS discordance, Nayyar et al. reported that upgrading the GS was not associated with a high PSA level [29], whereas Dong et al. reported that a PSA level greater than 5.0 ng/ml is associated with upgrading the GS [30]. Freedland et al. and Tilki et al. also reported that a high PSA level is associated with upgrading the GS [31,32]. In our study, however, we did not determine the PSA level to be a predictive parameter of upgrading.

Another reported factor involved in GS discordance is the prostate volume. Moussa et al. reported that smaller prostate volume is associated with upgrading the GS [33]. Furthermore, Turley et al. reported that patients with a prostate volume $\leq$ 20 cm^3 had more than 5 times the risk of upgrading compared with patients with a prostate volume $\geq$ 60 cm^3 [34]. In Moon's study [25], patients with a prostate volume $\leq$ 36.5 cm^3 had a higher risk of upgrading after radical prostatectomy. Different results have been found by different studies, and until now the accuracy of GS established on TRNB is still problematic, especially since therapeutic attitude is often based on this GS. The largest discrepancies in GS were found for well-differentiated tumors [14,21,35,36], as in our study. It is worth mentioning that patients with a GS of 7 (78%) show the highest percentage of concordance, patients with a GS of 6 or less show the highest percentage of under-staging, and cases with a GS of 8 to 10 (35%) show the highest percentage of over-staging [6]. Garnett found a concordance of 30% and noted that the prediction of the GS is more accurate when the scores are high [37]. Prost et al. [18] reported the same conclusions; the correlation was 54, 73, and 100%, respectively, for groups of tumors well, moderately, and poorly differentiated. The same conclusions were reported by Köksal and Rodríguez Faba [9,38].

In our study, the concordance between TRNB GS and RP GS was 32.5% for a GS of 6 and 7, and the correlation was around 70%, a similar value to that seen in Algaba's and Bostwick's studies [10,16, 35]. In contrast to the other studies [13,18, 37], in our series, the over-grading was more frequent for a higher GS, estimated at 66.6% for a GS of 8 and 100% for a GS of 9.

The classification of patients into 3 distinct groups (well, moderately, and poorly differentiated tumors) allows better concordance between the TRNB results and RP results. Using this conventional Gleason grading system, the correlation in our series was highly improved with 62.5% of patients remaining in the same group after radical prostatectomy. Similar results were found by Cookson et al. [17] who reported a high correlation of 80% between biopsy and final specimen using this classification. This correlation was of 72.6% in the Prost [18] series. Table 7 resumes the correlation of Gleason scores between prostatic biopsy and radical prostatectomy specimens in the literature. In our series we also studied the correlation between the TRNB results and RP results using the modified Gleason grading system with 5 groups of tumor differentiation. We found that the correlation did not significantly improve (in only 35% of cases) with this new classification.

There are many limitations in our study. First, this is a single institute, retrospective study dealing with a relatively small population. Second, this study did not identify the relation between "no concordance" and clinical and biochemical factors such as the PSA level, the free PSA, and prostate volume. Third, because the biopsy strategy was not consistent and because of the number of urologists, we are not sure that the biopsy specimens were taken at exactly the same location in every patient.

And finally, the biopsies and the radical prostatectomy specimens were examined by only 1 pathologist, which allows a uniform interpretation of the results but depends also on the pathologist's experience. Our result implies that more than half of the patients diagnosed with a GS of 6 by TRNB had more

Table 7. Literature review: Correlation of Gleason scores between prostatic biopsy and radical prostatectomy specimens.

Author	Number of Patients	Concordance (%)	Under-staging (%)	Over-staging (%)
Spires [14]	67	58	4.5	-
Bostwick [16]	316	35	-	-
Thickman [15]	124	28	-	-
Cookson [17]	226	31	54	15
Prost [18]	84	37	-	-
Salomon [13]	180	38.8	43.8	17
Kvale [5]	1116	53	38	9
Noguchi [12]	222	36	46	18
Rajinikanth [6]	1363	69	26	5
Altay [11]	61	45.9	42.26	11.84
Montesino [3]	173	52.6	32.4	15
Rodriguez Faba [9]	129	55.8	37.2	7
Algaba Arrea [10]	215	49.7	38.6	11.6
Our series	40	32.5	-	-

aggressive cancer than they seemed to have. Therefore, even if patients are diagnosed with moderate-risk prostate cancer after TRNB, physicians should always consider parameters that can be predictive of over-grading. This awareness affects treatment policy, particularly the watchful waiting criteria.

CONCLUSIONS

In this study, we have noticed that the accuracy of Gleason scores determined by transrectal needle biopsy in patients with prostate cancer seems to be very low. The greatest correlation percentage is found in tumors showing a moderated degree of cellular differentiation (GS of 5 to 7), whereas the over-grading was more frequent for a higher GS.

The classification of patients into 3 distinct groups (tumors well, moderately, and poorly differentiated) increases the correlation between the biopsy GS and final score. The modified Gleason grading system didn't reflect the definitive GS. In practice, physicians must be aware of the limits of the GS established on biopsy and clinical and biochemical parameters must be used with the biopsy GS to provide better information concerning prognosis, and the most adapted therapeutic option for the patient and his prostatic carcinoma.

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