

PATHOLOGICAL EXTENSION OF PROSTATE CANCER AS DEFINED BY GLEASON SCORE ON BIOPSY

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ABSTRACT

Introduction: Based on the importance of the Gleason score on the behavior of prostate adenocarcinoma, this study attempts to predict the extension of prostate adenocarcinoma pre-operatively, as defined by the Gleason score on biopsy, in individuals who will undergo radical prostatectomy.

Materials and Methods: We selected 899 individuals who underwent retropubic radical prostatectomy from 1988 to 2004. Clinical and pathological data obtained in the preoperative period were retrospectively analyzed through digital rectal examinations of the prostate, initial serum PSA levels and pathological data provided by biopsy. The Gleason score on biopsy was assessed and divided into 3 groups: 2 to 6, 7, and 8 to 10, and correlated with the possibility of the disease being confined to the prostate.

Results: From the 899 selected patients, 654 (74%) showed Gleason scores of 2 to 6, 165 (18%) had a score of 7 and 80 (9%) had scores of 8 to 10 on biopsy. The likelihood of confined diseases, extraprostatic extensions, invasion of seminal vesicles and lymph nodal involvement were respectively: 74%, 18%, 8% and 0.8% for a Gleason score of 2 to 6, 47%, 30%, 19% and 4% for a Gleason score of 7, and 49%, 29%, 18% and 4% for a Gleason score of 8 to 10.

Conclusion: In patients who will undergo radical prostatectomy due to prostate adenocarcinoma, a Gleason score of 7 on biopsy shows the same behavior as a Gleason score of 8 to 10 in relation to extension of disease.

Key words: prostatic neoplasms; neoplasm staging; biopsy; needle; pathology
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INTRODUCTION

The risk for progression of prostate cancer following radical prostatectomy (RP) is predicted by Gleason score, and pathological and surgical margins (1). The histological grade is regarded as a highly relevant prognostic factor (2,3), and in tumors with high Gleason score, the disease is often associated with aggressive biological behavior and risk of occult disease

(4,5). Attempting to determine the extension of the disease preoperatively is fundamental, since even tumors with a high Gleason score, but in a confined disease, present a disease-free outcome in 60% to 71% of cases (6). It is known that the recurrence of prostate cancer is higher in individuals with Gleason scores of 8 to 10 than with a score of 7, as defined by the surgical specimen. In such cases, the disease is confined in 43.1% and 9.2% for Gleason 7 and 8-10 respectively (7).

Preoperative prediction of the extension of the disease, which is determined by simply discriminating the Gleason score in the histopathology of biopsy fragments, will allow us to anticipate the possibility of extraprostatic disease in patients who will undergo RP.

Since there are no accurate data establishing if the Gleason score on biopsy could predict the location of prostate cancer (confined versus extraprostatic), this study aimed to compare prostate tumors with Gleason scores of 2 to 6, 7 and 8 to 10 as defined by biopsy, and to verify the presence of extraprostatic disease following radical prostatectomy through the pathological parameters of the surgical specimen.

MATERIALS AND METHODS

We retrospectively studied 961 patients undergoing retropubic radical prostatectomy with bilateral selective iliac lymphadenectomy due to prostate adenocarcinoma, in the period from September 1988 to December 2002. The patient age range was from 40 to 83 years, with a mean age of 62.9 ± 7.4 years.

The study included patients whose medical records indicated the total number of fragments removed on biopsy, the number of fragments with cancer, Gleason score, PSA and pathological study of the surgical specimen. Fifty-four patients who received neoadjuvant treatment were excluded, as were another 8 who were diagnosed through endoscopic resection of the prostate or transvesical prostatectomy, thus totaling 899 patients. The mean PSA was 10.1 ± 7.7 ng/mL (ranging from 0.3 to 72 ng/mL). In relation to clinical stage, 432 (48%) patients were classified as T1c, 219 (24%) as T2a, 173 (19.3%) as T2b, 68 (7.6%) as T2c and 7 (0.8%) as T3a. The mean percentage of affected fragments was $41\% \pm 24\%$ (ranging from 5% to 100%). The mean Gleason score on biopsy was 5.8 ± 1.3 .

Pathological Assessment

All surgical specimens, consisting of prostate, seminal vesicles and obturator lymph nodes, were assessed by the same pathologist. Specimens were fixed in 10% formalin for 6 hours in average and un-

derwent a routine of measuring and weighing the gland on a digital balance with 2 decimal places of precision. Thin transversal sections were performed in the surgical margins relative to the bladder neck and the prostate apex. Using the urethra as a reference, the remaining gland had its margins stained with India ink, and was then sequentially sliced each 0.3 millimeters. Eight to 10 sections from each lobe were included for histological study. Seminal vesicles were sectioned at their base, and longitudinal sections were subsequently made for histological examination. Obturator lymph nodes were dissected and sliced for inclusion in the study.

The material underwent the usual processing in preparation for microscopic examination, with dehydration in alcohol, clearing in xylol and embedding in paraffin. Fragments were stained with hematoxylin and eosin and then analyzed under a binocular light microscope. The assessed parameters were:

Histological grade and Gleason score – The Gleason histological classification was used for assessing tumor differentiation, considering exclusively the acinar pattern.

Surgical margins – Positive margins were defined as the presence of a tumor in the surgical transection margins, as defined by the presence of India ink.

Infiltration of periprostatic tissue – Invasion of fat tissue and periprostatic neurovascular plexus was considered as non-confined disease.

Infiltration of seminal vesicles – Involvement of seminal vesicles was considered only when the tumor invaded their parenchyma, and not the adventitial area.

Lymph nodal metastases – Obturator lymph nodes containing tumor are considered as positive metastases.

Statistical analysis was performed with the qui-square test with values of $p < 0.05$ being defined as significant.

RESULTS

Table-1 summarizes the pathological data for the Gleason score on biopsy and the location of prostate adenocarcinoma. Of the 899 selected patients,

Table 1 – Gleason score on biopsy and location of prostate cancer in the surgical specimen.

Gleason Score on Biopsy	Patients	Organ-confined	Extraprostatic	Positive Seminal Vesicle	Positive Lymph Nodes
2 to 6	654 (73%)	484 (74%)	118 (18%)	50 (8%)	2 (< 1 %)
7	165 (18%)	78 (47%)	50 (30%)	31 (19%)	6 (4%)
8 to 10	80 (9%)	39 (49%)	23 (29%)	15 (19%)	3 (3%)
Total	899 (100%)	601 (67%)	191 (21%)	96 (11%)	11 (1%)

2 to 6 vs. 7 or 8 to 10 ($p < 0.05$); 7 vs. 8 to 10 ($p > 0.05$)

we observed that 654 (73%) had a Gleason score of 2 to 6. Another 165 (18%) presented a Gleason score of 7, and 80 (9%) had a Gleason score of 8 to 10, as identified by biopsy. Among the patients with a Gleason score of 7, 78 (47%) had organ-confined location, 50 (30%) presented extraprostatic invasion, 31 (19%) had involvement of seminal vesicle and 6 (4%) showed lymph nodal involvement. Those tumors with a Gleason score of 8 to 10 presented prostate-confined disease in 39 (49%) of patients, 23 of them (29%) had extraprostatic disease and 3 (3%) showed lymph nodes affected by the disease.

There was a significant difference only when comparing Gleason scores of 2 to 6 with a 7 or an 8 to 10, with no significant difference observed between the latter 2 groups.

COMMENTS

Our study showed that in individuals undergoing prostate biopsy, the presence of Gleason pattern 4 or 5 determines a risk of 51 to 53% for extraprostatic disease in the surgical specimen.

Merely dividing the Gleason score into ranges of 2 to 6 and 7 to 10 seems reasonable for predicting the extension of disease, since in univariate analysis the behavior of a Gleason score 7 was statistically identical to the behavior of patients with Gleason scores of 8 to 10. In our opinion, the similarity in findings of extraprostatic disease between 7 and 8 to 10 can be explained by the presence of a pattern of 4 or 5 (8), which is invariably present. Patients with up to 10% of pattern 4 or 5 in the surgical specimen have more than a 70% probability of becoming disease-free, while individuals with more than 50% of pat-

tern 4 or 5 present progressive disease in 82% of cases (9).

The percentage of positive fragments on biopsy correlates to tumor volume. Additionally, the presence of a 4 or 5 pattern in the surgical specimen also determines a worse prognosis concerning outcome (10), however, as we have demonstrated, the chance of identifying confined disease is the same for 7 and for 8 to 10. Moreover, we could observe that patients with a Gleason score lower than 7 present a recurrence of the disease in 13% of cases, and this rate approaches 60% with a Gleason score between 7 and 10 (11). In our sample, we showed that 49% of individuals with a Gleason score between 8 and 10 had confined disease, 19% had neoplastic involvement of the seminal vesicles, and in only 8% of patients with a score lower than or equal to 6 were the seminal vesicles affected by the tumor. There is some controversy as whether a Gleason score of 7 has a different outcome from a score of 8 to 10 in relation to confined disease and recurrence (5). As we know, the Gleason score is composed of the 2 volumetrically prevalent patterns in the specimen, thus a Gleason score of 7 can be 3 + 4 or 4 + 3. Since the percentage of pattern 4 influences whether the disease is confined or not (10), studies comparing Gleason scores of 7, 4 + 3 and 3 + 4 have been published. Chan et al. (12) observed 34.7% of confined disease in patients undergoing radical prostatectomy with a Gleason score of 7 in the surgical specimen. However, the risk of progression was 20% higher with scores of 4 + 3 than in the 3 + 4 group after a 10-year follow-up. However, in order to obtain the results, many of these studies derived from the surgical specimen and not from the biopsy (5), which may not be

equal if we calculate the difference between Gleason scores of 3 + 4 and 4 + 3 from the biopsy fragments. A study conducted by Grober et al. (13) demonstrated that there was no difference between the 2 groups (3 + 4 and 4 + 3) of Gleason score 7 on biopsy in terms of the disease being confined or not, having extraprostatic extension or showing involvement of the seminal vesicles, which agrees with our data. In fact, a score 7 on biopsy should take into account not only the first score pattern, but PSA levels and the number of positive fragments on biopsy as well (14); if we have 4 + 3 with 2 or less fragments affected by tumor in 68.7% of patients, the disease will be confined. On the other hand, if the score is 3 + 4 with more than 2 affected fragments, this number will drop to 41.1%. These data have been confirmed by Peller et al. (15) who, when comparing patients with Gleason scores of 7 and 100% positive fragments on biopsy with a Gleason score of 8 and the same number of positive fragments, were able to show agreement in 97% of cases for predicting confined disease.

When comparing our results with Tefilli et al. (7), we verified that when the Gleason score is between 2 and 6, 74% of the patients have confined disease versus 69% with non-confined disease. On the other hand, with a score of 7, we see 47% versus 43%; that is, quite similar values. However, when comparing patients with a Gleason score between 8 and 10, we found 48.8% of patients with confined disease versus only 9.2% with non-confined disease. This difference can be explained by the fact that the mean PSA in patients with a score of 7 was 12 ng/mL versus 25 ng/mL in patients with a Gleason score between 8 to 10 (7). Epstein et al. (1) found a rate of confined disease of 30% in men with a Gleason score of 7, and, of them, approximately 70% were disease-free after 10 years.

In relation to a Gleason score ≥ 8 , we found 9.5% to 31% of patients with confined disease (7). It is relevant that these patients had localized disease, because 82% of these individuals are not likely to have recurrent disease during a 5-year follow-up, despite the high Gleason score (16). Egan & Bostwick (17) demonstrated that individuals with a Gleason score of 7 had confined disease in 48% of cases versus 53% in men with a Gleason score of 8. In our

study, we found 48.8% of confined disease with a score between 8 and 10. As shown previously, there is a wide variation in results when we attempt to use isolated parameters for predicting confined disease, and this is due to several factors that are involved in prostate adenocarcinoma. Since the construction of the first nomogram for predicting confined disease using PSA, clinical stage and Gleason score, more than one parameter is used in order to reduce the probability of error (3).

CONCLUSION

It is important to consider the presence of Gleason grade 4 or 5 on prostate biopsy for planning the management of prostate cancer. In these cases, the disease is organ-confined in the pathological examination of the surgical specimen in only half the cases.

*Adriana Sanudo
performed the statistical analysis.*

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