Research Article

COMPARISON OF GLEASON GRADUATION BETWEEN BIOPSIES AND SURGICAL PIECE IN PATIENTS WITH PROSTATE CANCER

COMPARAÇÃO DA GRADUAÇÃO DE GLEASON ENTRE BIOPSIAS E A PEÇA CIRÚRGICA EM PACIENTES PORTADORES DE CÂNCER DE PRÓSTATA

COMPARACIÓN DE LA GRADUACIÓN DE GLEASON ENTRE BIOPSIAS Y PIEZA QUIRÚRGICA EN PACIENTES CON CÁNCER DE PRÓSTATA

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How to cite this article:

MUHLBEIER, JPS; MUHLBEIER, MLS; CAMINHA, AR; COLLAÇO, LM Comparison of Gleason grading between biopsies and surgical piece in patients with prostate cancer. **Revista Saúde e Comportamento**, Florianópolis, v.1, n.1, p.11- 22, 2022.

ABSTRACT:

Introduction: Prostate cancer is the most prevalent in men, excluding non-melanoma skin cancer. The Gleason score is most often the main indicator of aggressiveness in prostate cancer, so the results obtained in the biopsy and in the anatomopathological examination of the surgical specimen should be the same. However, for several reasons this often does not happen. The national literature is scarce in discussing the comparison of Gleason grading between biopsies and definitive results of surgical specimens in cases of prostate cancer. **Objectives**: To compare the Gleason score of pre -surgical biopsies and radical prostatectomy specimens, in patients with prostate cancer, to identify possible factors that influence the discrepancy between the results. **Methods**: Retrospective, observational, cross-sectional study where the medical records of patients who underwent prostate biopsy diagnosed with Usual Acinar Adenocarcinoma and who later underwent radical prostatectomy in a private teaching hospital, of a philanthropic nature, located in the city of Curitiba/ Paraná/ Brazil were analyzed. , between January 2014 and December 2018. Gleason scores were obtained from the biopsies and compared to the surgical specimens. The following parameters were also analyzed: 1) blood level of prostate-specific antigen (PSA), 2) Patient's age 3) Prostate size of the surgical

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specimen 4) Presence of a nodule on digital examination of the prostate. The findings were statistically treated by the one test methods way ANOVA, Kruskal - Wallis test and Mann Whitney test with admission of significance for p< 0.05. **Results:** In the 115 patients evaluated, a mean age of 65.5 years was found, ranging from 47 to 83. Comparing the data, it was possible to identify 27 cases in which the Gleason score increased in the surgical specimen (23.47%), 13 cases decreased (11.30%) and 75 cases remained the same (65.21%). The mean prostate size was 38.4cc, ranging from 5.3 to 178. The mean prostate-specific antigen (PSA) was 10.63 ng /ml, ranging from 0.67 to 43.59, with a median of 8. Nodules were detected on digital examination of the prostate in 70 patients. patients (60.89%) In the study of variables according to changes in the Gleason score, age presented p=0.54, PSA p=0.75, prostate size p=0.01 and presence of prostatic nodules p = 0.49. **Conclusion:** In the present study, the concordance of the Gleason score of the pre -surgical prostate biopsy with the prostatectomy was exact in 65.21% of the cases and the factors analyzed that significantly influenced the variation of the score was the size of the prostate.

Keywords: Biopsy; Prostate; Urology; Gleason; Medicine; Men's Health.

RESUMO:

Introdução: O câncer de próstata é o mais prevalente em homens excluindo-se o câncer de pele não melanoma. O score de Gleason é na maioria das vezes o principal indicador de agressividade do câncer de próstata, logo, os resultados obtidos na biopsia e no exame anatomopatológico da peça cirúrgica deveriam ser iguais. Entretanto, por uma série de motivos isso muitas vezes não acontece. A literatura nacional é escassa em discutir a comparação da graduação de Gleason entre biópsias e resultados definitivos das peças cirúrgicas em casos de câncer prostático. **Objetivos**: Comparar o score de Gleason das biopsias pré-cirúrgicas e peças de prostatectomia radical, em pacientes com câncer de próstata, identificar possíveis fatores que influenciem na discrepância entre os resultados. **Métodos**: Estudo observacional transversal retrospectivo onde foram analisados os prontuários de pacientes que realizaram biópsia prostática com diagnóstico de Adenocarcinoma Acinar Usual e que posteriormente foram submetidos a prostatectomia radical em um hospital escola privado, de caráter filantrópico, localizado na cidade de Curitiba/ Paraná/ Brasil, no período de janeiro de 2014 e dezembro de 2018. Foram obtidos os scores de Gleason das biopsias e comparados ao das peças cirúrgicas. Ainda foram analisados os parâmetros: 1) dosagem sanguínea do antígeno prostático específico (PSA),2) Idade do paciente 3) Tamanho prostático da peça cirúrgica 4) Presença de nódulo ao exame digital da próstata. Os achados foram tratados estatisticamente pelos métodos de teste one way ANOVA, teste de Kruskal-Wallis e teste de Mann Whitney com admissão de significância para p< 0,05. **Resultados:** Nos 115 pacientes avaliados foi encontrada média de idade de 65.5 anos variando de 47 a 83. Da comparação dos dados foi possível identificar 27 casos em que o score de Gleason aumentou na peça cirúrgica (23,47%), 13 casos diminuíram (11,30%) e 75 casos permaneceu igual (65,21%). A média do tamanho prostático foi de 38.4cc variando de 5.3 a 178. A média do antígeno prostático específico (PSA) foi de 10.63 ng/ml variando de 0.67 a 43.59 com mediana de 8. Foram detectados nódulos ao exame digital da próstata em 70 pacientes (60,89%) No estudo das variáveis de acordo com as alterações no score de Gleason a idade apresentou p= 0,54, PSA p= 0,75, tamanho da próstata p=0,01 e presença de nódulos prostáticos p= 0,49. **Conclusão**: No presente estudo a concordância do score de Gleason da biópsia de próstata pré-cirúrgica com a prostatectomia foi exata em 65,21% dos casos e dos fatores analisados o que influenciou significativamente na variação do score foi o tamanho da próstata.

Palavras-chave: Biopsia; Próstata; Urologia; Gleason; Medicina; Saúde do Homem.

RESUMEN:

Introducción: El cáncer de próstata es el más prevalente en hombres, excluyendo el cáncer de piel no melanoma. El puntaje de Gleason suele ser el principal indicador de agresividad en el cáncer de próstata, por lo que los resultados obtenidos en la biopsia y en el examen anatomopatológico de la pieza quirúrgica deben ser los mismos. Sin embargo, por una serie de razones esto a menudo no sucede. La literatura nacional es escasa en discutir la comparación del grado de Gleason entre biopsias y resultados definitivos de piezas quirúrgicas en casos de cáncer de próstata. **Objetivos**: Comparar el puntaje de Gleason de biopsias prequirúrgicas y especímenes de prostatectomía radical, en pacientes con cáncer de próstata, para identificar posibles factores que influyan en la discrepancia entre los resultados. **Métodos**: Estudio retrospectivo, observacional, de corte transversal donde se extrajeron las historias clínicas de pacientes a quienes se les realizó biopsia prostática con diagnóstico de Adenocarcinoma Acinar Usual y que posteriormente fueron sometidos a prostatectomía radical en un hospital privado de enseñanza, de carácter filantrópico, ubicado en la ciudad de Curitiba/ Paraná / Brasil, entre enero de 2014 y diciembre de 2018. Se obtuvieron puntajes de Gleason de las biopsias y se compararon con las piezas quirúrgicas. También se analizaron los siguientes parámetros: 1) nivel sanguíneo de antígeno prostático específico (PSA), 2) edad del paciente 3) tamaño prostático de la pieza quirúrgica 4) presencia de un nódulo en el examen digital de la próstata. Los hallazgos se trataron estadísticamente mediante la prueba ANOVA de una vía, la prueba de Kruskal-Wallis y la prueba de Mann Whitney, con significancia tomada en $p<0,05$. **Resultados:** En los 115 pacientes evaluados se encontró una media de edad de 65,5 años, variando de 47 a 83. Comparando los datos fue posible identificar 27 casos en los que el puntaje de Gleason aumentó en la pieza quirúrgica (23,47%), 13 disminuyeron los casos (11,30%) y se mantuvieron 75 casos (65,21%). El tamaño prostático promedio fue de 38,4 cc, con un rango de 5,3 a 178. El antígeno prostático específico (PSA) promedio fue de 10,63 ng/ml, con un rango de 0,67 a 43,59, con una mediana de 8. Se detectaron nódulos en el examen digital de la próstata. en 70 pacientes (60,89%) En el estudio de las variables según cambios en el puntaje de Gleason, la edad presentó $p=0,54$, PSA $p=0,75$, tamaño prostático $p=0,01$ y presencia de nódulos prostáticos $p=0,49$. **Conclusión**: En el presente estudio, la concordancia del puntaje de Gleason de la biopsia de próstata prequirúrgica con la prostatectomía fue exacta en el 65,21% de los casos y los factores analizados que influyeron significativamente en la variación del puntaje fue el tamaño de la próstata.

Descriptores: Biopsia; Próstata; Urología; Gleason; Medicamento; Salud de los hombres.

INTRODUCTION

Cancer was one of the leading causes of death worldwide and between 2014 and 2018 approximately 500,000 new cases were reported in Brazil, placing the country among those with the highest incidence of the disease in the world. Prostate cancer is the most prevalent in men, excluding non-melanoma skin cancer, accounting for 3,764,658 cases worldwide and it is estimated that 1,275,000 new cases will be diagnosed in 2018 [(1)].

For many years the detection of prostate cancer was based solely on the digital examination of the prostate and during this period the disease was diagnosed in very advanced stages without a relevant decrease in the mortality rate. However, with the introduction of Prostate-Specific Antigen (PSA) there was a significant increase in the detection of prostate cancer, especially in early stages, and although the implementation of screening is much discussed, some conducts are indicated.

In a study published[(2)], 12 main global guidelines were analyzed, which identified six points of conduct in common and that should be taken into account in prostate cancer screening, namely: 1) Screening recommendation should be discussed with the patient after explaining all the possible risks and benefits that the procedure may cause; 2) Only the PSA test should be used, together or not as a digital test of the prostate; 3) Screening age in normal risk patients should be 50-55 years at the discretion of the physician and patient; 4) For patients at increased risk, screening begins at age 40 or 45; 5) The interval between exams must be annual or biannual at the discretion of the physician and patient; 6) Screening should be discontinued after age 70 or when the patient has a life expectancy of less than 10 years. It is believed that such recommendations can help to carry out evidence-based screening for one of the biggest men's health problems in the world.

Gleason score of biopsies and radical prostatectomy specimens in patients with prostate cancer and identify possible discrepancies at the two moments. The specific objective is to identify whether the possible factors listed can help to predict possible increases or decreases in the Gleason score.

LITERATURE REVIEW

Although prostate cancer is the most common in solid organs, its biopsy is still performed in a very different way from others [(3)], while most solid organs are biopsied guided

only to the lesion, the prostate still has a somewhat different biopsy. Random. However, new discoveries regarding prostate cancer, such as the concept of active surveillance and better results with robotic surgery, require improved prostate biopsies to be correctly indicated [3].

Gleason score is, in most cases, the main indicator of aggressiveness in prostate cancer[4], therefore, the results obtained in the biopsy and in the anatomopathological examination of the surgical specimen should be the same. However, for a number of reasons this often does not happen and this discrepancy can influence decisions such as allocation to active surveillance.

Gleason score is based on glandular differentiation and tumor growth pattern in relation to the prostatic stroma. There are five histological patterns, pattern 1 – more differentiated and pattern 5 – more undifferentiated. The Rank is given by the sum of the primary standard (more than 50% of the sample) with the secondary standard (second most predominant), and in the case of only one standard, it is considered as primary and secondary. The Gleason score, together with the clinical stage and PSA levels, are preoperative variables, crucial to determine therapeutic approaches [5].

Gleason score discrepancy, such as grading errors, borderline tumors, or sample errors [4], however, more contemporary studies focus on variables that can be used as predictors of these discrepancies.

In a meta-analysis carried out in 2017, there was a variation from 29% to 45% of patients who had an increase in the Gleason score after radical prostatectomy [4] indicating that there are some factors to be observed, among them the most relevant and recurrent were: age, elevated PSA, prostate size and number of positive parts on biopsy.

The undergraduation of the Gleason score causes patients to be classified into lower risk classes than they should actually be, causing an error in the therapeutic definition and reduced oncological success. It is important to understand factors that may cause this phenomenon [6].

Identical scores [7] at both moments were found in exactly 53% of the patients, while in 38% the score was underestimated and in 9% it was overestimated in patients with a mean age of 61 years and a mean preoperative PSA of 8.0 ng /ml, while [5] exact correlation was found in 49.5 % and in 88.7 % there was agreement of more or less one unit and 42% of the cases with underestimation.

The national literature is scarce in discussing the comparison of Gleason grading between biopsies and definitive results of surgical specimens in cases of prostate cancer.

METHODOLOGY

This is a retrospective cross-sectional observational study where the medical records of patients who underwent prostate biopsy diagnosed with Carcinoma containing the Gleason score and who underwent radical prostatectomy in a private philanthropic teaching hospital located in the city of Curitiba were analyzed. Data are from January 2014 to December 2018. Gleason scores from biopsies and surgical specimens were extracted from the medical records. Subsequently, the following were analyzed: 1) blood PSA dosage; 2) Age; 3) Prostatic size of the surgical piece; 4) Presence of a nodule on digital examination of the prostate. The collected data were spread out using the Excel program. Continuous variables expressed as mean ± standard deviation and compared with Student 's t and Mann-Whitney tests or one test way ANOVA, Kruskal - Wallis test. Categorical variables expressed as percentages and compared using the chi - square test or Fisher's exact test, as appropriate. P values less than 0.05 were considered statistically significant. The present study was approved by the Ethics Committee under CAAE number 08209319.0.0000.0103, acceptance number **:** 3,193,223.

RESULTS

Of the 659 patients who underwent biopsy in the urology service between 2014 and 2018, approximately 240 were diagnosed with prostatic carcinoma and among these, we found 115 who had all the data necessary for the research. The age of the patients ranged from 47 to 83 years with a mean of 65.52 years and a standard deviation of 7.51. Among the 115 patients, 70 (60.87%) had nodules on digital examination while in the other 45 (39.13%) nodules were not present. The measurement of the PSA value had a mean of 10.64 ng /ml with a median of 8 ng /ml, ranging from 0.67ng/ml to 43.59 ng /ml and IQR= 5.48 to 11.85. The prostate size had an average of 38.59 cc with a median of 33.20 cc ranging from 5.30 cc to 178 cc with IQR=26.70 to 47.45. The Gleason score values of the biopsies varied according to the table below:

Table 1 - Distribution of the Gleason score of the biopsies

	score	Frequency	percentage
Biopsy main score	two	1	0.86
	3	87	75.65
	4	24	20.8
	5	3	2.6
secondary biopsy score	two	1	0.86
	3	80	69.5
	4	29	25.5

	5	5	4.3
Biopsy total score	5	two	1.73
	6	67	58.26
	7	27	23.47
	8	15	13.04
	9	4	3.47

Source: the authors.

According to the table above, scores of 3 were mostly found, both as primary and secondary, resulting in total scores of 6 in 58.26% of the biopsies.

Table 2 - Gleason score according to ISUP of biopsies

Grade	Frequency	percentage
1	69	60
two	17	14.78
3	10	8.69
4	15	13.04
5	4	3.47
∑	115	100

Source: the authors.

The scores found in the surgical specimens resulting from the radical prostatectomy of these patients can be found in the tables below:

Table 3 - Distribution of Gleason Score of surgical specimens

	score	Frequency	percentage
Surgical piece main score	two	1	0.86
	3	88	76.5
	4	19	16.5
	5	6	5.2
	Free	1	0.86
Surgical piece secondary score	3	66	57.39
	4	36	31.3
	5	12	10.43
	Free	1	0.86
Surgical piece total score	5	1	0.86
	6	51	44.34
	7	42	36.52
	8	11	9.5
	9	9	7.8
	Free	1	0.86

Source: the authors.

Table 4 - Gleason scores according to ISUP in the surgical specimen

Grade	Frequency	percentage
1	52	45.21
two	30	26.08
3	12	10.43
4	11	9.56
5	9	7.82
Free	1	0.86
∑	115	100

Source: the authors.

After analyzing all cases, we identified three results: In 75 patients (65.21%) it remained the same, 27 patients (23.47%) had an increase in the Gleason score in the surgical specimen, 13 patients (11.30%) had a decrease.

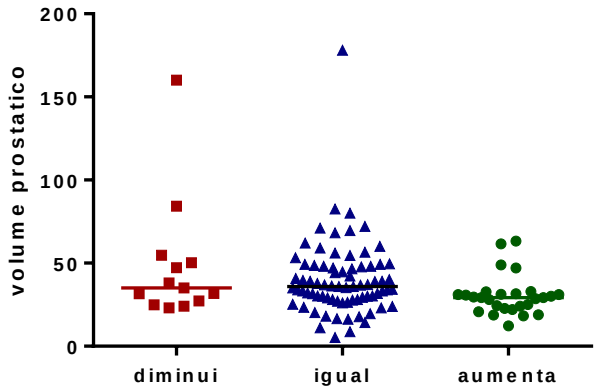
According to the analyzed data, it was possible to prepare table 5 and figure 1, where the sample data separated according to the three possible results and the respective statistical tests are presented.

Table 5 – Study of variables according to changes in the Gleason score

	increase N=27	**Decreases N=13**	**remains the same N=75**	**P**
Age	56-79 Average of 67.46 ±5.51	48.0-83.0 Mean of 65.21±7.73	47.0-77.0 Average of 64.78±7.59	0.54 (#)
PSA	1.37 to 28.0 Median of 8.23 IQR= 5.61-11.64	2.82-24.31 Median of 6.81 IQR=4.68 to 13.68	0.67 to 43.59 Median of 8.0 IQR= 5.51-11.79	0.75 (##)
prostate size	12.20- 63.20 Median of 29.30 IQR=26.05-52.45	23.00- 160.0 Median of 35.0 IQR = 26.05-52.45)	5.30- 178.0 Median of 35.90 IQR=28.0-48.0	**0.0177** (##)

Table 1- (#)_ test= one way ANOVA; (##)- Kruskal - Wallis test; (§) chi square; (§§) - Mann Whitney test
Source: the authors

Figure 1 – Distribution of prostate volume according to the 3 possible outcomes after radical prostatectomy



Source: The authors.

DISCUSSION

Gleason score is a highly effective parameter for making therapeutic decisions in prostate cancer. Correct identification of such a parameter helps in decision making between different options such as active surveillance, radical prostatectomy, radiotherapy or androgen blockade. The sample used for the study was very similar to that found in the world literature. The mean age of 65.52 years (ranging from 47 to 83) is similar to the 63.3 years found in a study with 265 patients and a very similar objective published [8] and also with a Brazilian study it was 63.8 years [9]. The mean PSA value found in our patients was 10.64 ng /ml, while in the study [9] it was 8.76 ng /ml

The main exclusion criterion that was responsible for the greatest decrease in the number of patients was the fact that many did not undergo radical prostatectomy surgery, and some had to have their biopsies repeated for various reasons and, therefore, appeared repeatedly in the initial list.

The grade of 6(3+3) was responsible for 58.26% of the patients' biopsy scores in our study, contrasting with 59% in a study published by the journal Urominas. [9]. In surgical specimens, the prevalent score was 6(3+3) in 44.34%, contrasting with 7(3+4) which was present in 42.9% [9]. These data confirm the need to carry out actions focusing on men's health [10].

The ability to predict the actual score present in the surgical specimen was more than 65% in our study, while in the literature values ranging from 58% [11], 61% [12] are found,

demonstrating that the correct score in the surgical specimen varies greatly, but most often remains between 60 and 70%, therefore, patients who undergo radiotherapy or active surveillance whose final score cannot be accurately evaluated should be carefully observed in order to reduce unsatisfactory oncological results [8].

The use of magnetic resonance had lower rates of sub-staging when compared to traditional methods of transrectal biopsy in about 10%, suggesting that its use in our case could increase the concordance rate in both moments to up to 75%, which would put the procedure performed very close to the upper margin of what is found in the literature on the subject [13].

Among the parameters that were analyzed attempt to find a correlation between differences in graduation, only the prostate volume showed a relevant relationship, with a p=0.0177 being found while the description [14] of a number of predictors of increased Gleason score after radical prostatectomy such as advanced age, increased preoperative PSA and decreased postoperative prostatic weight. On the other hand, lower PSA values and decreased prostate weight were predictors of a postoperative decrease in the total score.

CONCLUSION

Gleason score of the pre -surgical prostate biopsy with the prostatectomy was exact in 65.21% of the cases, putting the service in question. The highest spectrum found in the literature and of the factors analyzed, which significantly influenced the variation of the score, was the size of the prostate.

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Receipt of the originals: 08/23/2022
Accepted for publication: 09/02/22
Publication date: 09/26/2022