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CONCORDANCE BETWEEN GLEASON SCORES OF THE TRANSRECTAL PROSTATE BIOPSY AND THE SURGICAL SPECIMEN IN A REFERENCE HOSPITAL

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ABSTRACT

The main parameter for prognosis and treatment of prostate cancer is the Gleason score (GS), obtained by transrectal prostate biopsy, which will predict the degree of cell differentiation of the tumor. Often, GS before and after the surgery disagree, implicating in wrong choices of treatment, being more or less aggressive than the necessary, affecting the prognosis and life quality of the patient. **Purpose:** Compare GS of the transrectal prostate biopsyand surgical specimen after radicalprostatectomy. **Materials and Methods:** Cross-sectional observational study, with retrospective analysis of medical records. Kappa test was used to assess the concordance of GS of biopsy and surgical specimen, considering a good K value above 0.5. **Results:** From the 86 selected medical records, GS at the time of biopsy was evaluated and compared with GS on the surgical specimen, resulting in 52.74% of concordance. In relation to the discordant results, there was 41.66% of sub gradation and 8.33% of super gradation. **Conclusions:** these resultsare in accordance with the global range of GS concordance, but falling below the ideal.Future studies evaluating other variables, the improvement of the biopsy technique and requests for slide review, may contribute to an increase in the degree of GS concordance.

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INTRODUCTION

In Brazil, prostate cancer (PC) is the second most incident cancer among men. It is considered a cancer of the third age, since three quarters of the cases occur from the age of 65 (Inca, 2020). The diagnosis of PC usually occurs after screening, given that the disease usually has an asymptomatic course (Collin *et al*., 2009). According to the Brazilian Society of Urology (SBU), screening for PC is indicated through prostatic specific antigen (PSA) measurement and digital rectal examination, for all men over 50 years of age, and individuals with a higher risk of developing the disease should start screening at age 45 (Steffen *et al*., 2018). Transrectal prostate biopsy (TBx) is indicatedin cases where the patient's life expectancy exceeds ten years and when there is a suspicious digital rectal exam for malignancy, or when the serum PSA values are altered in the individualized analysis.

Through biopsy, the injury risk score is obtained, defined by the Gleason Score (GS), a classification system for prostate adenocarcinomas, which, according to the changes in the architectural patterns of neoplastic cells, could be classified as Gleason 1, 2, 3, 4 or 5; where a primary grade is assigned to the predominant pattern in the sample, and a secondary grade is assigned to the second most frequent pattern. The two patterns are added together, making up the GS (Gleason and Mellinger, 1974). Currently, only Gleason 3, 4 and 5 patterns are considered malignant neoplasms (Epstein *et al*., 2005). In 2014, after revision, the International Society of Urological Pathology (ISUP), agreed on undergraduate groups (Epstein *et al*., 2016). According to Bekelman *et al*. (2018), patients can be classified according to GS and PSA in:

- clinically localized and very low or low risk, when GS is less than or equal to 6, and serum PSA is less than 10.0 ng/mL;

- clinically localized and intermediate risk, when the tumor is more extensive, involving more than half of a lobe [T2b] or with bilateral disease [T2c], but with no detectable extraprostatic extension;
- clinically located at high risk, with extraprostatic extension or PSA greater than or equal to 20.0 ng/mL or GS 8 to 10.

The GS of TBx has an important prognostic role, since it allows predicting the pathological stage. The precise graduation of prostatic adenocarcinoma is a fundamental component in the planning of the different therapeutic options, taking into account that it has a correlation with capsular penetration rates, margin positivity, invasion of seminal vesicles and lymph node involvement. Because of that, the congruence between the GS of the TBxand the GS of the surgical specimen is very important(Arellano, Castillo and Metrebián, 2004). The main objective of this study was to evaluate the concordance rate between GS before (TBx) and after radical prostatectomy (RP)(in the surgical specimen), in a public Hospital in southern Brazil.

MATERIALS AND METHODS

Cross-sectional observational study, with retrospective data collected from medical records, and results of pathological analysis exams of patients seen at the uro-oncology service of a public hospital. Inclusion criteria were male patients, diagnosed with prostatic adenocarcinoma, who underwent RP between the years 2012 and 2018.Exclusion criteria were patients who underwent some type of neoadjuvant therapy, or patients who did not undergo RP.The study was approved by the local Ethics and Research Committee. It was defined that there was agreement when the primary and secondary GS of the TBxwas exactly equal to the GS of the surgical specimen.In addition, the percentage of concordance, sub gradation (GS of the TBxwas lower than the GS of the surgical specimen) and super gradation (GS of the TBxwas higher than the GS of the surgical specimen) were calculated. Continuous variables (age, PSA) were assessed using the mean and standard deviation. The categorical variables (race, surgical diagnosis, GS and staging), were analyzed as absolute values and percentages. For the accuracy of the estimates, a 95% confidence interval was considered, and the p value was statistically significant when $p < 0.05$. The statistical analysis was performed with the aid of the IBM SPSS Statistics program. The Kappa test was used to assess the concordance of ordinary strategic variables (GS of the TBx and GS of the surgical specimen), considering a good K value above 0.5 (Landis and Koch, 1977).

RESULTS

In total, 86 medical records were evaluated,and 84 presented the GS results before and after surgery and were used to assess the concordance rate.

The mean age (n= 83)of patients was 63.39 years, with a standard deviation of 6.60 years, with the earliest diagnosis at 47 years and the latest at 77 years. The total pre-surgical PSA (n= 55)values ranged from 2.6 to 34 ng/dL, with an average of 12.52 ng/dL and standard deviation of 8.04ng/dL. In addition, 74 patients (90.24%) were white. The distribution frequencies of the GS degrees are shown in Table 1.The GS concordancebetween the TBx and the surgery specimens in this study was 52.74%.The Kappa statistic concordance test generated a coefficient of 0.5274, with $p < 0.001$, being classified asof moderate concordance according to the interpretation proposed by Landis & Koch(9). In relation to the discordant results, there was sub gradation in 35 patients (41.66%), and super gradation in 7 patients (8.33%), as shown in Table 2.

The 5 degree of GS obtained the highest concordance (100%). On the other hand, 3 degree of GS presented the lowest concordance (22.22%), also presenting the highest percentage of subgradation (55.56%). The4 degree of GS was the one with the highest amount of supergradation (45.46%) (Table 2). The most recurrent tumor size among patients was pT2c according to the TNM classification, indicating a tumor confined to the prostate with involvement of the two prostatic lobes. The frequencies of the other T stages can be seen in Table 3.

Table 1 – Frequencies of GS from TBx and surgical specimens

Gleason score (pattern)	TBx (%)	Surgicalspecimens (%)
1 (3+3)	39 (46,42)	21 (25)
2 (3+4)	19 (22,61)	24 (28,57)
3 (4+3)	9 (10,71)	14 (16,66)
4 (3+5, 4+4, 5+3)	11 (13,09)	16 (19,04)
5 (4+5, 5+4, 5+5)	6 (7,14)	9 (10,71)
Total	84 (100)	84 (100)

Legend: Gleason score (pattern) – the composite GS is derived by adding together the numerical values for the two most prevalent differentiation patterns (a primary grade and a secondary grade). TBx, transrectal prostate biopsy.

Table 2 - Comparative study of GS concordance, sub gradation and super gradation.

GS	Concordance (%)	Sub gradation (%)	Supergradation (%)	Total (%)
1	20 (51,28)	19 (48,72)	0 (0)	39 (46,43)
2	10 (52,63)	9 (47,37)	0 (0)	19 (22,62)
3	2 (22,22)	5 (55,56)	2 (22,22)	9 (10,71)
4	4 (36,36)	2 (18,18)	5 (45,46)	11 (13,10)
5	6 (100)	0 (0)	0 (0)	6 (7,14)
Total	42 (52,74)	35 (41,67)	7 (8,33)	84 (100)

Legend: Comparative study of concordance, sub gradation and super gradation between the prostatic needle biopsies and surgical specimens.

Table 3 - Frequency of T staging in the surgery specimens

T Staging	n (%)
pT1c	2 (3,33)
pT2a	8 (13,33)
pT2c	19 (31,66)
pT3a	17 (28,33)
pT3b	14 (23,33)
Total	60 (100)

Legend: pT1c – tumor identified by needle biopsy found in one or both sides, but not palpable; pT2a – tumor involves one-half of one side or less; pT2c – tumor involves both sides; pT3a – extraprostatic extension (unilateral or bilateral); pT3b – tumor invades seminal vesicle(s).

DISCUSSION

In the context of PC, the GS is important for the surgical decision, technique choice, radiotherapy, chemotherapy, and prognosis. Because of that, the concordance between GS in the TBx and surgical specimen is crucial,once it is not expected to observe after the surgery, that the approach realized was more or less aggressive than the necessary. This study obtained

aconcordance rate of 52.74% among GS onTBx and surgical specimens. In the discordant samples, there was 41.66% of sub gradation, and 8.33% of super gradation. Similar to our results, some studies have obtained a GS concordance rate between 47.1 to 49.5%, with a sub gradation and a super gradationrates of 40.6 to 42% and 8.6 to 12,3%, respectively (Arellano, Castillo and Metrebián, 2004; Guimarães *et al*., 2008). However, De Souza Moreira *et al*.(2012)demonstrated a GSconcordance rate of 72.86%. In recent years, a greater number of nuclei have been used in biopsies, previously 6 to 8 nuclei were used, today 10 to 16, in an attempt to improve agreementof GS(De Souza Moreira *et al*., 2012).The concordance rate of GS of the present study (52.74 %) is within the range evidenced by the literature for biopsies in which a greater quantity of prostatic nuclei were used, which promoted an increase in GS agreement ratefrom 35%- 76% (in those studies before 2005, which used less prostatic nuclei in biopsies) to 50%-76% (Lima, Soares and Rhoden, 2013). However, the concordance rate observed in our study is lower than those observed in the study ofFine and Epstein(2008) (76%). What can explain this difference is the fact that this latter study was conducted in a greater center, with more specialized pathologists.In this same view,some studies demonstrate that the pathologist's experience over time is directly proportional to the accuracy in appraising the biopsies (Arellano, Castillo and Metrebián, 2004; Epstein and Potter, 2001).

Siddiqui *et al*. (2013) demonstrates in their study that magnetic resonance fusion biopsy found a 32% increase in GS concordance when compared to 12-core ultrasound biopsy, highlighting its role in detecting high-risk tumors, clinically significant, which may not be detected by 12-core biopsy. These data demonstrate thatthe GS concordance rate between biopsies and surgical specimens is constantly improving worldwide. In this study, grade5 GS obtained 100% of concordance. This finding could be explained by the architectural pattern of Gleason grade 5, which involves lesions with minimal glandular differentiation and diffuse stromal infiltration by tumor cells, which could be more easily visualized by the pathologists on the anatomopathological slides (Gleason and Mellinger, 1974). In GS grades 1 and 2, there were 51.28% and 52.63% of agreement, respectively, and 48.71% and 47.36%, of sub grading, respectively. The literature shows that GS less than 7 on biopsy, associated with PSA greater than or equal to 10 ng/mL, increases cases of sub gradation (10). In this study, grade 3 GS was the one with the lowest rate of agreement (22.22%), also presenting the highest rate of sub gradation (55.56%). In this particular degree, such discordance causesthe stage of cancer to pass from intermediate to high risk.In addition, thereis the fact that there is a variable period of time between performingthe biopsy and performing the tumor removal surgery, which can also contribute to GS sub gradation (Draisma *et al*., 2006).However, this period of timevariation has not been evaluated in this study.

Among the clinicopathological parameters, the average age of patients, 63.39 years, is slightly above the literature. De Souza Moreira *et al*. (2012) obtained61.5 years. This fact can be justified by the level of the population education and the regional culture in postponing the demand for health services, especially among the male population (Inca, 2020). The mean PSA was 12.52 ng/mL, a value slightly higher than that found in the literature, 7.1 and8.0 ng/mL (Kvale *et al*., 2009; Moreira Leite *et al*., 2009). This data highlights the fact that most cases of PC in this study are at intermediate risk of progression, given that only PSA values less than 10 ng/mL are classified as low risk. The most recurrent tumor size in this study was pT2c according to the TNM classification (31.66%).In the others studies 45.5%to 73.9% of patientswere in pT2 stage (Kvale *et al*., 2009; Moreira Leite *et al*., 2009). However, in absolute numbers, most patients in the present study were in pT3 stage, which means that the tumor extends through the prostatic capsule and, therefore, presents a high risk of progression. This corroborates the factregarding the regional culture in postponing the demand for medical services, and due to a failure in PC screening programs in the basic health system. In conclusion, in the present study, the GS concordance rate between TBx and the surgical specimenswas 52.75%,similar to that found in several other national and international studies, despite being below the ideal levels. This implicates in wrong choices of treatment,being more or less aggressive than the necessary, affecting the prognosis and the quality of life of the patient. Future studies evaluating other variables, the improvement of the biopsy technique and the requirement for review of pathological slides by a second pathologist, may contribute to an increase in the degree of GS agreement rate.

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