



THE IMPACT OF GLEASON SCORE FROM THE BIOPSY AND FROM THE RADICAL PROSTATECTOMY ON THE BIOCHEMICAL PROGRESSION-FREE SURVIVAL

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ABSTRACT

Introduction: Prostate cancer (PCa) in stages T1 and T2 can be treated either with radical prostatectomy (RP) or with radiotherapy. But in the clinical trials, the survival probability after RP is related to the Gleason score (GS) from the operation and the survival probability after radiotherapy - to the GS from the biopsy. Both GSs often do not coincide.

Objective: To study the connection between biopsy/prostatectomy-GS of a homogeneous group of patients, all treated only with RP, and the biochemical progression-free survival (BPFS) of those patients.

Methods: The patients available for analysis were 111. All underwent RP (either open or laparoscopic) in our institution. Information about the GSs and the BPFS was collected and analyzed using IBM SPSS version 23. Parametric and non-parametric statistical methods were used.

Results: Time to biochemical progression is shorter for patients with biopsy- and prostatectomy-GS ≥ 7 compared with biopsy- and prostatectomy-GS < 7 patients.

Discussion: With this study, we show that both GSs have a similar implication on the BPFS, with prostatectomy-GS giving slightly better accuracy than the biopsy-GS in predicting survival.

Conclusion: Both GSs are comparable and can be used when discussing the survival probabilities of the patient and choosing the treatment options.

Keywords: Prostate cancer, Gleason score, Biochemical progression-free survival,

INTRODUCTION

Prostate cancer (PCa) is the most common non-cutaneous malignancy in the USA [1] and in many other western countries. These days, it can be treated with a variety of methods-radical prostatectomy (RP), radiotherapy, hormonal therapy, active surveillance or a combination of them [2, 3]. The golden rule of cancer treatment is maximum effectiveness with minimal side effects. In order to achieve it, tumors are classified according to different systems – thus, patients with similar prognoses are combined into groups, and each group is allocated to the appropriate treatment [2, 3]

The degree of differentiation of the tumor is one of its most important characteristics - in PCa, we use the Gleason score (GS) to classify the patients into groups. The version used now is from 2014 [4]. Patients undergoing RP have their prostate removed and examined completely according to well-established guidelines [5]. In this scenario, we can be sure that the most complete and accurate assessment of the PCa is possible.

But as we mentioned, many patients are treated with other methods, and the assessment of the PCa relies on the GS from the biopsy. Although done according to strict rules [6], it is very often far from perfect. Since pathology is so important in oncology, our study aimed to check if both GSs have a similar impact on the biochemical progression-free survival of patients.

MATERIALS AND METHODS

The patients available for analysis were 111. These were patients hospitalized in the urology clinic of St. Anna's University Hospital in Varna, Bulgaria, during the period January 2013 and May 2020. The prostate cancer was proven with systematic transrectal biopsy of the prostate. The patients underwent radical prostatectomy (either open or laparoscopic). Patients with pre- or postoperative hormonal or radiotherapy were excluded. Information about the BPFS was collected and analyzed using IBM SPSS version 23. Depending on the types of variables and their dis-

tribution, parametric (t-test, ANOVA) and non-parametric (Pearson's chi square test) statistical methods were used. Kaplan-Meier – Log Rank test (Mantel-Cox) and Cox-regression were used for the survival analysis.

RESULTS

The patients with biochemical progression are 52 (46,8%), and the patients without biochemical progression are 59 (53,2%). Table 1 shows the mean values of GS (from the biopsy and from the RP) both in patients with and without biochemical progression.

Table 1. GSs in patients with and without biochemical progression.

	Patients with biochemical progression	Patients without biochemical progression	p
	Mean (SD)	Mean (SD)	
GS from the biopsy	6,54 (2,01)	6,31 (1,14)	0.222
GS from the RP	7,02 (1,87)	5,62 (2,2)	0.003

Between patients with and without biochemical progression, there is no statistically significant difference in biopsy-GS values ($X^2 = 13,362$; $p = ,064$). We found a difference in the GS from the RP. It is significantly higher in the group with biochemical progression ($X^2 = 16,266$; $p = ,039$).

To clarify the problem further, we classified patients into two groups-with $GS \geq 7$ (60 patients or 54,1% of all) and $GS < 7$ (51 patients or 45,9% of all). The lack of difference in the biopsy-GS between the two groups was confirmed ($X^2 = 1,493$; $p = ,222$). Again a statistically significant difference in the prostatectomy-GS between the patients with and without biochemical progression was found ($X^2 = 8,678$; $p = ,003$). The probability of a patient with prostatectomy-GS ≥ 7 to have biochemical progression is 1,9 times higher compared with a patient with prostatectomy-GS < 7 (OR = 1,862, 95%CI = 1,190 – 2,914).

Next, we examined the time to biochemical progression in months (Table 2). For patients with biopsy-GS ≥ 7 , it ranges from 1 to 28 months with an average (mean) time of 6,5 (SD = 2,04) months. For patients with biopsy-GS < 7 it ranges from 1 to 51 months with average(mean) time 15,7 (SD = 3,71) months. A statistically significant difference was found in the time to biochemical progression between patients with biopsy-GS < 7 and patients with biopsy-GS ≥ 7 . It is shorter in the latter group with 9 months ($t = -2,420$; $p = ,023$).

Time to biochemical progression for patients with prostatectomy-GS ≥ 7 ranges from 1 to 28 months with a mean time of 5,93 (SD = 2,23) months. For patients

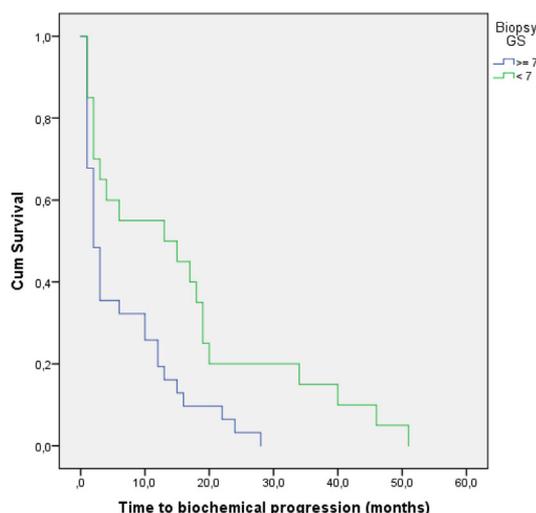
with prostatectomy-GS < 7 it ranges from 1 to 51 months with mean time 19,35 (SD = 5,27) months. A statistically significant difference was found in the time to biochemical progression between patients with prostatectomy-GS < 7 and patients with prostatectomy-GS ≥ 7 . It is shorter in the latter group with 13 months ($t = -3,213$; $p = ,005$).

Table 2. Mean time (months) to biochemical progression

	GS ≥ 7 Mean (SD)	GS < 7 Mean (SD)	p
GS from the biopsy	6,58 (2,04)	15,72 (3,71)	0.023
GS from the RP	5,93 (2,23)	19,35 (5,27)	0.005

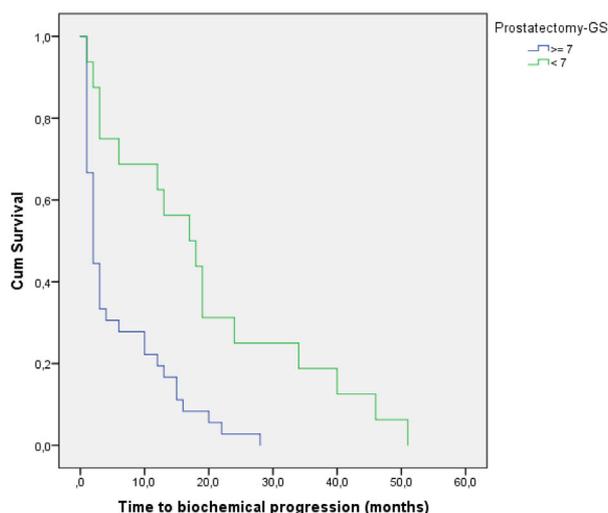
Finally, a survival analysis was done to describe the effect of the studied variables on patients' survival. Patients with biopsy-GS < 7 have longer BPFs compared with patients with biopsy-GS ≥ 7 (Kaplan-Meier – Log Rank test (Mantel-Cox); $X^2 = 7,057$; $p = ,008$)-shown on Figure 1. Actually the former group has two times better survival probability than the latter group (Exp(B) = 2,147; 95%CI = 1,153 – 3,996; $p = ,013$).

Fig. 1. Survival probability for patients with biopsy-GS < 7 and $GS \geq 7$.



Similarly, patients with prostatectomy-GS < 7 have longer BPFs compared with patients with prostatectomy-GS ≥ 7 (Kaplan-Meier – Log Rank test (Mantel-Cox); $X^2 = 12,836$; $p = ,000$)-shown on Figure 2. The former group has three times better survival probability than the latter group (Exp(B) = 3,046; 95%CI = 1,538 – 6,036; $p = ,001$).

Fig. 2. Survival probability for patients with prostatectomy-GS < 7 and GS ≥ 7.



DISCUSSIONS

The overall survival of cancer patients is the most important indicator of the effectiveness of the treatment. Unfortunately for the researchers (and fortunately for the patients) overall survival of many patients with PCa is very long - it is well-established that RP is recommended for patients with life-expectancy of at least 10-15 years. That is why a more convenient (though not so accurate) parameter is used - the biochemical progression-free survival. It is incorporated even in the risk group classification of the European Association of Urology [7]. So in order to check our hypothesis - that both GSs have a similar impact on the survival of the patients - we compared BPFs with the GSs from the biopsy and the RP.

In the initial, more simple analysis, we compared the mean values of GS in the groups with and without biochemical progression. A difference was found only for the prostatectomy-GS but not for the one from the biopsy. Probably it is connected with the fact that the biopsy-GS is not so accurate, which is well-proven in the literature [8, 9, 10, 11, 12]. Next, we made a more sophisticated

analysis comparing the time to biochemical progression in patients with GS ≥ 7 and < 7, further divided into GS from the biopsy and from the RP. Here a statistically significant shorter time to biochemical progression was found for patients with GS ≥ 7 - both for GS from the biopsy and from the PR. The Kaplan-Meier survival analysis also showed that patients with GS < 7 have longer BPFs compared with patients with GS ≥ 7 - again for both GSs.

These results matter in the sense that PCa in stages T1, T2 can be treated either with RP or with radiotherapy - with equal success according to the guidelines of the European Association of Urology [13]. But the problem is that the survival probability after RP is related to the GS from the operation and the survival probability after radiotherapy - to the GS from the biopsy. Both GSs often do not coincide [11, 12, 14, 15]. The results of our study show that both GSs have a similar implication on the BPFs, with prostatectomy-GS giving slightly better results. The advantage of our study is that we use a homogeneous group of patients - all treated only with RP.

Study limitations

Our study has several limitations. (1) The sample includes patients hospitalized in the urology clinic of St. Anna's University Hospital in Varna, Bulgaria between January 2013 and May, 2020 - thus, the sample used was relatively small, and it is not clear how representative the general population is. (2) Our results should be interpreted as pertaining to the time period during which the survey was conducted.

CONCLUSIONS

This study found significantly better survival for patients with GS < 7 compared with patients with GS ≥ 7. This is true for both biopsy- and prostatectomy-GS, although the latter shows a stronger connection with better survival. Still, both GSs can be used when discussing the survival probabilities of the patient and choosing the treatment options.

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