Original Article

Factors effective on survival after radical prostatectomy: To what extent is pre-operative biopsy Gleason scoring is confident in predicting the prognosis?

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Abstract

In the present study, the effect of different grades on independent survival from the biochemical relapse was investigated through comparison of the histological grades of the biopsy and prostatectomy materials in patients undergoing radical prostatectomy (RP). A total of 152 patients undergoing RP following biopsy were retrospectively investigated in an attempt to reveal the effect of discordance between needle biopsy Gleason score and RP Gleason score on prostate specific antigen relapse-free survival. Accordingly, while 58.3% (14/24) survival was seen in the patients in Group 1 (high-graded) with Gleason score 7, 93.7% (15/16) survival has been seen in the patients in Group 2 (low-graded) and Group 3 (same Gleason scores) with Gleason score 7. The difference in-between has been statically found significant ($P < 0.001$). Similarly, while a 10% (1/10) survival is seen in the patients in Group 1 with Gleason score 8 and above, 75% (3/4) survival has been observed in the patients in Group 2 and 3 with Gleason score 8 and above. Also in this comparison, the difference in-between has been statically found significant ($P = 0.041$). Eventually, different grading, particularly determination of Gleason score higher than the RP specimen biopsy also bring about bad pathologic parameters and shortened survival periods.

Key Words: Gleason score, prostate carcinoma, radical prostatectomy, upgrading

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INTRODUCTION

Prostate cancer (PCa), the most common cancer diagnosed in men, ranks second among all cancer-related deaths.[1] Autopsy studies suggest the likelihood that a male at around the age of 50 may suffer from PCa is 30% to 50%, while the likelihood approaches 80% at around 80 years of age.[2]

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Digital rectal examination (DRE) and tumor markers (prostate specific antigen [PSA]) are among the most common modalities appearing in the diagnosis of PCa. Transrectal ultrasonography (TRUS), thanks to its ease of application and low cost and guiding role in the implementation of biopsy procedure in cases suspected to possess PCa, proved to the most commonly used radiological method. Today, the diagnosis of PCa is the most frequently established through prostate needle biopsy (TRUS-Bx) performed under the guidance of TRUS in patients suspected to suffer from PCa on the basis of laboratory and physical examination findings. Despite absence of a consensus on the number of biopsy specimens that should be taken and their localizations, general inclination shows up as taking a total of 12 core biopsy specimens, three from the midline and the lateral regions, where the sensitivity and specificity turned out to be optimum.[3]

Although there appears to be a sizable number of scoring system utilized in the histological grading of PCa, it is the Gleason Scoring System which is currently the most widely accepted scoring system.[4] Defined by Gleason and Mellinger in 1967, this system proved to be a crucial parameter for both the behavior and clinical prognosis of the cancer and therefore is utilized in such nomograms as Partin and Kattan. Rather than cellular changes, Gleason scoring system is based much more on the structural architecture of the tumoral glands on a grading scale of 1-5. Grade 1 is defined as well-differentiated, whereas grade 5 is defined as poorly differentiated. The biopsy Gleason score is a sum of the primary grade (namely, the majority of tumor) and a secondary grade (allocated to the minority of the tumor). Accordingly, the Gleason score can range from 2 (1 + 1 = 2) to 10 (5 + 5). The ultimate sum is then used to refer the following grading groups: Well-differentiation,[2-4] moderate-differentiation,[5,6] moderate-to-poor differentiation[7] and poor-differentiation.[8-10]

This grading is also applied on the prostatectomy specimen in order to provide a clearer prediction regarding the clinical prognosis in patients undergoing a radical prostatectomy (RP) after biopsy. Biopsy Gleason grades demonstrate a high-degree correlation with RP Gleason grades.[5,6] However, there are some studies suggesting more rapid disease progression in patients in whom biopsy and RP scores turned out to be discordant.[7]

In the present study, the effect of different grades on independent survival from the biochemical relapse was investigated through comparison of the histological grades of the biopsy and prostatectomy materials in patients undergoing RP who had been diagnosed to suffer from PCa by TRUS-guided needle biopsy.

MATERIALS AND METHODS

A total of 152 patients undergoing RP following biopsy were retrospectively investigated in an attempt to reveal the effect of discordance between needle biopsy Gleason score and RP Gleason score on PSA relapse-free survival (PSA-RFS).

The study populated was composed of a total of 152 consecutive patients undergoing RP dictated by prostate needle biopsy procedure which had been implemented on account of findings compatible with cancer on the basis of high PSA level and/or DRE between January 2008 and December 2012. The demographic data and serum PSA levels were recorded in all patients before the biopsy procedure; moreover, the pathological data obtained from biopsy and prostatectomy specimens were compared in the light of clinical findings.

Philips 260 Corvus Ultrasound Device with biplanar multi-sector 3.5-5 MHz transrectal ultrasound probe was used during TRUS-Bx. In contrast, the biopsy specimens were obtained using Pajunk DeltaCut biopsy gun 18 gauges, Tru-Cut automatic biopsy needle so as to be 12 or 16 cores.

Retropubic RP procedure was implemented in patients who had been diagnosed with PCa on the basis of biopsy and deemed to be candidate for RP.

The patients were subdivided into two groups as those upgraded from a lower biopsy Gleason score to a higher grade prostatectomy Gleason score (upgrading group) and those downgraded from a higher biopsy score to a lower prostatectomy score (downgrading group), comparing them in terms of biochemical RFS.

In the statistical analysis of the study, firstly, the groups based distributions of variables have been tested by Kolmogorov-Smirnov and Shapiro Wilk tests and in failure of ensuring the assumption of a normal distribution, non-parametric testing methods have been selected. In this context, in order to compare the variables obtained through measuring in both independent groups, Mann-Whitney U-test has been applied and as for in the evaluation of the difference between more than two independent groups, Kruskal Wallis test has been implemented and in case where the difference was found to be significant, the groups creating such differences have been determined with the multiple comparison tests. Chi-square and/or Fisher's exact test has been applied in the examination of the relationship and inter-groups differences in terms of categorical variables. For the purpose of determination of the risk factors thought to have affected the time elapsed until the recurrence, firstly the single variable Cox regression analyses have been carried out and the variables which had significance level of 0.25 and lower have been included to the multi variable logistic regression model. The odds related to the variables left in the model as a result of analysis 95% confidence intervals and *P* values have been summarized in the relevant tables. Moreover the outcomes of other demographic and group comparisons pertaining to the study are presented in the qualitative variables ratio and in median (minimum-maximum) in the quantitative variables. In realization of statistical analyses of the study, SPSS 15.0 program has been employed and $P < 0.05$ was adopted as the limit of statistical significance.

RESULTS

Mean age of the patients was 64.3 (49-75) years; mean PSA value was 9.2 (1.7-35) ng/ml; mean free/total (F/T) PSA ratio was %14.4 (5-48); mean prostate volume was 38.9 (15-95) cc; and mean follow-up duration was calculated to be 32.4 (7-90) months [Table 1].

It was revealed upon evaluation of the pathological data regarding the patients included in the study that mean rate of prostate biopsy core positivity was %41.1 (5-100) and mean biopsy Gleason score was found to be 6.3 (6-9). Evaluation of the RP specimens, on the other hand, revealed a surgical border positivity to be 30.9%; presence of high-grade prostatic intraepithelial neoplasia (HGPIN) to be 40.1%; perineural (PN) invasion rate to be 54.6%; seminal vesical (SV) invasion rate to be 17.1%; and mean Gleason score to be 6.5 (6-9). Furthermore, mean Gleason score calculated in the prostatectomy specimens was found to be statistically greater compared with the mean biopsy Gleason score ($P = 0.026$) [Table 2].

When looked at the independent survival of patients with biochemical recurrence according to the degree of RP Gleason; the survival rates independent from PSA have been respectively achieved to be 96.5% in the patients whose Gleason degree was 3 + 3 = 6, 67.6% in the patients whose Gleason degree was 3 + 4 = 7, 35.2% in the patients whose Gleason degree 4 + 3 = 7 and 21.4% in the patients whose Gleason degree was above 7. The difference between groups was statistically significant ($P < 0.001$) [Table 3].

During prostatectomy, the patients have been separated into three groups according to the biopsy pathology to be the ones with high-degree (Group 1, upgrading), the ones with low degree (Group 2, downgrading) and the ones who did not have any changes in their Gleason scores (Group 3) and the clinicopathological data have been looked into in this direction as well. The first group has consisted of 51 (33.5%), second Group 20 (13.2%) and third Group 81 (53.3%) patients. The groups have been compared from the perspective of age, mean PSA values, mean F/T PSA rate, mean prostate dimension and mean prostate biopsy core percentage, positive surgical margins, presence of HGPIN, PN invasion, seminal vesicle invasion and the mean follow-up and PSA recurrence rates.

According to these comparisons, while positive surgical margins was found to be significantly low ($P = 0.025$) in Group 2 patients, difference in terms of other parameters has not been identified [Table 4].

For the purpose of investigating the study groups and other clinicopathological data their impacts to PSA - free survival have been analyzed individually and by a multivariable analysis. The parameters sought during single variable analysis such

Table 1: Demographic characteristics of the patients

Number of patients	152
Mean age (year)	64.3 (49-75)
Mean PSA (ng/ml)	9.2 (1.7-35)
Mean F/T PSA ratio (%)	14.4 (5-48)
Mean prostate volume (cc)	38.9 (15-95)
Mean follow-up duration (months)	32.4 (7-90)

PSA: Prostate specific antigen, F/T: Free/total

Table 2: Pre-and post-operative data of the patients

Biopsy specimen	
Rate of core positivity (%)	41.1 (5-100)
Mean Gleason score***	6.3 (6-9)
Gleason 3+3=6	103 (67.7%)
Gleason 3+4=7	27 (17.7%)
Gleason 4+3=7	14 (9.2%)
Gleason 4+4=8	6 (3.9%)
Gleason 4+5=9	2 (1.3%)
Radical prostatectomy specimen	
Surgical border positivity	47 (30.9%)
Presence of HGPIN	61 (40.1%)
PN	83 (54.6%)
SV invasion	26 (17.1%)
Mean Gleason score***	6.5 (6-9)
Gleason 3+3=6	87 (57.2%)
Gleason 3+4=7	34 (22.3%)
Gleason 4+3=7	17 (11.1%)
Gleason 4+4=8	6 (3.9%)
Gleason 4+5=9	5 (3.2%)
Gleason 5+4=9	3 (1.9%)

***P=0.026. HGPIN: High grade prostatic intraepithelial neoplasia, PN: Perineural, SV: Seminal vesical

Table 3: Gleason degrees-based survival rates independent from PSA

	Number of patients	PSA reoccurrence	PFS (%)	*P*
Gleason 3+3=6	87	3	96.5	<0.001
Gleason 3+4=7	34	11	67.6	
Gleason 4+3=7	17	11	35.2	
Gleason≥8	14	11	21.4	
Total	152	36	76.31	

PSA: Prostate specific antigen, PFS: Progression free survival

Table 4: Clinicopathologic characteristics of the study groups

	Group 1	Group 2	Group 3	*P* value
Number of patients (%)	51 (33.5%)	20 (13.2%)	81 (53.3%)	
Mean age (year, ±SD)	65.27 (±5.0)	62 (±4.7)	64.42 (±6.3)	0.101
Mean PSA (ng/ml, ±SD)	9.65 (±6.8)	9.59 (±5.2)	8.95 (±6.6)	0.830
Mean F/T PSA rate (±SD%)	14.16 (±8.8)	13.6 (±5.2)	14.91 (±6.5)	0.712
Mean prostate dimension (cc, ±SD)	36.45 (±11.4)	39.9 (±12.9)	40.25 (±16.1)	0.320
Biopsy positive core rate (±SD%)	42.8 (±28.8)	39.4 (±27.5)	40.2 (±26.3)	0.836
Positive surgical margins (%)	23 (48.9)	4 (8.5)	20 (42.6)	0.025**
HGPIN presence (%)	20 (32.8)	7 (11.5)	34 (55.7)	0.839
PN (%)	33 (39.8)	9 (10.8)	41 (49.4)	0.186
SV invasion (%)	14 (53.8)	3 (11.5)	9 (34.6)	0.051
Mean follow-up time (m, ±SD)	35.98 (±15.9)	30 (±18.7)	30.84 (±16.8)	0.185
PSA reoccurrence rate (%)	31/36 (86.1)	1/36 (2.7)	4/36 (11.1)	0.280

Group 1: Patients upgraded according to the biopsy in prostatectomy (upgrading), Group 2: Patients downgraded according to the biopsy in prostatectomy (downgrading), Group 3: Patients with equal biopsy and prostatectomy Gleason scores. PSA: Prostate specific antigen, SD: Standard deviation, F/T: Free/total, HGPIN: High grade prostatic intraepithelial neoplasia, PN: Perineural, SV: Seminal vesical

as age, PSA, F/T PSA rate, prostate dimension, prostate biopsy core percentage, positive surgical margins, presence of HGPIN, presence of PN invasion have been found to be high-grading (upgrading, Group 1) in the RP and low-grading (downgrading, Group 2) in the RP.

According to the results of single variable analysis, the age, positive surgical margins, presence of PN invasion and high-grading (Group 1) in the prostatectomy has been found to be a significantly and statistically effective on PSA - free survival [Table 5].

According to the results of single variable analysis, the age, Positive biopsy core percentage, positive surgical margins, PN invasion, SV invasion, high-grading in the prostatectomy and low-grading in the prostatectomy have been included to the multi variable analysis. Accordingly, in consequence of the multi variable analysis, it has been found that the high-grading (Group 1) in the prostatectomy and surgical margin positivity was significantly and statistically effective on PSA - free survival. According to this outcome, the presence of positive surgical margins in the RP specimen increases reoccurrence of PSA in 3.492 times and emerging of a higher grading (upgrading) versus the prostatectomy specimen biopsy increases reoccurrence of PSA in 11.876 times [Table 6].

In order to investigate whether or not the low survival time determined in the patients who were high-graded in the prostatectomy depended on the rise in mean Gleason degree, the patients who were high-graded (Group 1) and low-graded group (Group 2) and those ones in the control group who had the same Gleason scores (Group 3) have also been compared in terms of survival.

Accordingly, while 58.3% (14/24) survival was seen in the patients in Group 1 with Gleason score 7, 93.7% (15/16) survival has been seen in the patients in Group 2 and 3 with Gleason score 7. The difference in-between has been statically found significant ($P < 0.001$). Similarly, while a 10% (1/10) survival is seen in the patients in Group 1 with Gleason score 8 and above, 75% (3/4) survival has been observed in the patients in Group 2 and 3 with Gleason score 8 and above. Also in this comparison, the difference in-between has been statically found significant ($P = 0.041$) [Table 7].

PSA reoccurrence has developed within the follow-up period in 36 of 15w2 patients admitted to the study and PSA - free survival rate has been calculated to be 76.31%. Survival/time curve of the patients in the study has been shown in (Kaplan-Meier) Graph 1.

Table 5: Parameters effecting the PSA-free survival in the single variable analysis

Parameter	OR	95%	*P* value
Age	1.089	1.002-1.183	0.045
PSA	1.026	0.985-1.069	0.259
F/T PSA rate	1.007	0.961-1.055	0.774
Prostate dimension	0.982	0.958-1.007	0.256
Positive biopsy core percentage	2.350	0.692-7.979	0.171
Positive surgical margins	3.199	1.922-5.984	0.003
Presence of HGPIN	0.805	0.412-1.573	0.526
Presence of PN invasion	1.837	0.918-3.677	0.033
SV invasion	0.517	0.249-1.073	0.077
High-grading (Group 1)	4.166	1.136-7.084	0.009
Low-grading (Group 2)	0.870	0.519-1.355	0.239

PSA: Prostate specific antigen, F/T: Free/total, HGPIN: High grade prostatic intraepithelial neoplasia, PN: Perineural, SV: Seminal vesical, OR: Odds ratio, CI: Confidence interval

Table 6: Parameters effecting the PSA-free survival in the multi variable analysis

Parameter	OR	95%	*P* value
Age	1.058	0.988-1.132	0.105
Positive biopsy core percentage	0.850	0.419-1.726	0.654
Positive surgical margins	3.492	1.721-7.084	0.001
PN invasion	0.542	0.222-1.325	0.179
SV invasion	1.624	0.717-3.680	0.245
High-grading (Group 1)	11.876	4.166-33.851	0.001
Low-grading (Group 2)	1.211	0.133-11.032	0.847

OR: Odds ratio, PSA: Prostate specific antigen, PN: Perineural, SV: Seminal vesical, CI: Confidence interval

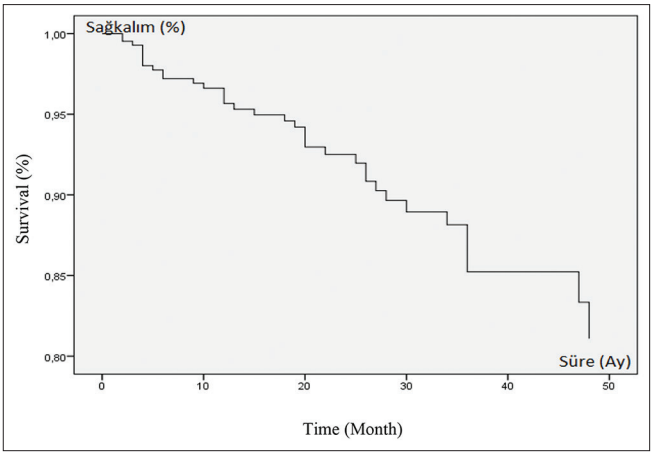
Table 7: Group-based survival difference in the patients with same Gleason score

	Group 1 survival (%)	Group 2 and Group 3 survival (%)	*P* value
Gleason score=7	14/35 (40)	15/16 (93.7)	<0.001
Gleason score≥8	1/10 (10)	3/4 (75)	0.041

DISCUSSION

In PCa diagnosis, while a rise takes place in PCa incidence diagnosis upon advent of PSA into clinical use, the studies for studies for the early - phase detection of PCa has increased with description of prostate anatomy and anatomic RP by Walsh as well. Today, the most important method used in diagnosis of PCa is the prostate biopsy performed through transrectal ultrasound guidance.

In predicting survival in patients with PCa after RP, many clinical and pathological parameters are utilized. Among these, the most important preoperative PSA level, histological grade, surgical margin status and clinical stage of cancer can be enumerated. In the study by Roehl *et al*. have carried out on 3.478 patients, while a 10-year survival with the RP has been determined to be 91% in the patients whose POSA level was below 2.6 ng/ml, it has been determined to be 47% in the patients with PSA level is above 10 ng/ml.[8] Assuming 10 ng/ml to be the threshold value in our study, PSA levels



Graph 1: Time - dependent cumulative "biochemical recurrence - free survival" probabilities of patients in the study group

have been evaluated in two groups. No difference has been statically determined between PSA - free survival rates of both groups $P = 0.259$). Therefore, reaching a different result in the literature might be attributed to the smallness of the group and the lack of follow-up as long as other studies in the literature. In addition, the fact that specific sub-groups were not created for PSA values below 10 ng/ml in our study might have affected the result as well.

The common result in the studies carried concerning the positive surgical margins being another parameters effect ting the survival is in direction that the positive surgical margins has severely reduced PSA - ğ free survival. As demonstrated in 1.000 - *p*atient studies by Hull *et al.*, while 5 and 10-year survival rates are respectively 84.6% and 80.4% in the patients with negative surgical margins, these rates drop down to 41.6% and 36.4%[9] in the patients with positive surgical margins. Also in our study, while PSA reoccurrence has developed in 13 of 105 *p*atients (12.4%) with negative surgical margins, PSA reoccurrence has been found in 23 (48.9%) of 47 *p*atients with positive surgical margins and the difference in-between has been found to be statistically significant ($P = 0.001$) and has been seen to be in compliance with the literature. Moreover, in the multi variable analysis, it has been shown that the positive surgical margins have increased PSA reoccurrence risk by 3.492 times.

The information related to the impact of bio-chemical reoccurrence - free survival of PN invasion is not clear in the literature. PSA level in the majority of studies, the relationship among PSA level, positive surgical situation and Gleason score and PN invasion have been discussed however, a study which has directly researched effect of PN invasion to PSA - free survival is rare.

In the retrospective examination studies of 124 *p*atients conducted by Ishizaki *et al.*, a significant relationship ($P = 0.001$) has been found between positive core percentage and Gleason score in PN invasion in consequence of a multi variable analysis.[10] Nevertheless, the study performed by Tanaka *et al.* and published in year 2011 is sound survival study and in this study covering 468 patients, in addition to PSA level, prostatectomy Gleason score and positive biopsy core percentage, it has been shown that the PN invasion is the predictive factor[11] in predicting PSA-free survival. In our study, although presence of PN invasion from the standpoint of analysis of a single PSA relapse is significant ($P = 0.033$), this relationship has failed to be demonstrated in the multi variable analysis ($P = 0.176$).

In addition, in this study, the pathologic parameters like presence of HGPIN, seminal vesicle invasion and positive biopsy core percentage have also been examined from the perspective of PSA relapse. While PSA relapse was seen in 16 (26.2%) of 61 patients bearing HGPIN, PSA relapse has been seen in 20 (21.9%) of 91 patients not bearing HGPIN ($P = 0.526$). Similarly, while PSA relapse is seen in 10 (38.4%) of 26 patients having seminal al vesicle invasion, reoccurrence has been seen in 26 (20.6%) of 126 patients whose seminal vesicles were intact ($P = 0.051$). When the patients were compared according to their positive biopsy core percentages (in below and above of 50%); PSA reoccurrence has been determined in 14 (23%) of 61 patients whose positive core rate was 50 and above, as for 22 (24.2%) of 91 patients whose positive core rate was below 50% in biopsy, relapse has been determined ($P = 0.171$). It is known that these parameters are being associated with the PSA relapse. For example; in the study of Pierorazio *et al.*, published in year 2010 and based on retrospective review of 9381 patients; positive biopsy core rate being more than 50% and vesicle invasion have been shown as independent predictive factors predicting PSA relapse.[12] In our study, even though the relationship between the seminal vesicle invasion and PSA relapse was close to the value we accept to be the statistical significance limit ($P = 0.051$), none of the parameters has been deemed in the adequate prediction value in terms of PSA relapse.

Histological grade of PCa is one of the most important parameters used in prediction of survival independent from biochemical reoccurrence survival. The studies comparing Gleason grade of the prostatectomy specimen and the survival bears a torch to the literature. In the studies Pierorazio *et al.*, have published in early 2013 in which they retrospectively evaluated 7869 patients in terms of survival in dependent from biochemical relapse; they have examined the patients in five different groups; ones with Gleason grades respectively 6 and lower, $3 + 4 = 7$, $4 + 3 = 7$, $4 + 4 = 8$ and 9-10. According to the study groups, 5-year PSA - free survival rates are have been determined respectively 96.6%, 88.1%,

69.7%, 63.7% and 34.5% and they have found the difference in-between ($P < 0.001$) to be statistically significant.[13] When the patients in our study were evaluated by being divided into groups according to their total Gleason scores, PSA - free survival rates have been found to be respectively; 96.5% in ones with Gleason scores 6, 67.6% in 3 + 4 = 7, 35.2% in 4 + 3 = 7 and 21.4% in ones with Gleason score 8 and above ($P < 0.001$). When looked from this aspect, it is seen that the survival rates have come out in line with the literature however, when 32.4-month follow-up is taken into consideration, it is seen that it remained lower than what was expected. In this result; the fact that all patients who had a RP had been included to the study and remarkable part of the patients have been operated recently, it seems that these facts have been effective for the follow-up time to become shortened.

The PCa - related point reached at today is that Gleason grading system cannot be disregarded. In many clinics, it has been likely to be effective also in treatment decision as much as in drawing up post-treatment monitoring and planning. Gleason score determined in biopsy specimen and Gleason score determined in RP specimen are not always same and the conditions and estimations identified prior to operation are likely to change following operation. When looked at the studies conducted in relation to this topic, the most outstanding feature in common is the existence of grading difference between the specimen of biopsy and prostatectomy at a degree which cannot be underestimated. For example; in multi-centered 1,113 - illnesses study by Freedland *et al*., published in 2007, they have discovered 27% high-grading and 11% low-grading; and shown that high-grading has created a significant risk in terms of bio-chemic al progression. Another result of the same study is that high PSA in multi-variant analysis and high positive core rate in biopsy and obesity in biopsy were found to be significant. A > gain in this study; the researchers have also showed that high-grading could be prevented by increasing biopsy core number and thus unpredictable bio-chemical reoccurrences avoided.[14] Another study published by Kim *et al*., in year 2013 has revealed high-grading in 194 (43%) of 451 patients and therefore have stated that presence of a preoperative prostate volume was predictive.[15] Again, In their 907-Illnesses study, Park *et al*., has identified 25.6% high-grading in 66 patients who have received PCa diagnosis with Gleason score 3 + 4 = 7 in the biopsy and have found that preoperative PSA level to be predictive for this.[16]

In general, the studies in the literature indicate that high-grading has led to bad pathologic results yet, does not talk about its direct impact on PSA relapse. In the 144 - illness series Köksal *et al*., have published in 2000, high-grading has been determined in 25% of 110 patients with Gleason score 6 and lower in biopsy and it has been seen that cancer was limited by prostate at a rate of 11% in these patients.[17] Nevertheless, in their publication of Yoo *et al*., pertaining to year 2001, 1,582 patients have been examined and it has been seen that the parameters like clinic and pathologic phase, tumor volume and positive surgical margin were determined at higher rates in the patients who were low or high-graded jupon prostatectomy. Namely, according to this study, both high-grading and low-grading have indicated bad prognosis. In the same study, it has been pointed out that grading difference (low or high) between RP and biopsy was significant in prediction of survival independent from biochemical reoccurrence however, it was also stated that it could not be shown to be an independent predictive factor.[7]

Furthermore, in our study, the patients have been evaluated in three different groups; ones high-graded according to biopsy in prostatectomy (Group 1, up grading), ones low-graded (Group 2, downgrading) and ones with same biopsy and prostatectomy grades (Group 3, control). According to our results, upgrading has been found at the rate of 33.5% (51/152) and downgrading at the rate of 13.2% (20/1562) and they were deemed to be at literature standards. In general, mean biopsy Gleason scores (6.3) is significantly lower than mean prostatectomy Gleason scores (6.5) ($P = 0.026$).

Negative surgical margin is determined to be the unique clinicopathologic factor predicting downgrading ($P = 0.025$). From this aspect, although seminal vesicle invasion is also very close to significance limit, prediction value has not been deemed adequate ($P = 0.051$). When looked at inter-groups survival rates, it is seen that it is 39.2% (20/51) in Group 1, 95% (19/20) in Group 2 and 95% (77/81) in Group 3. Difference between the survival rates has been found to be significant in terms of statistics ($P = 0.009$). When a multi-variant analysis is made with these outcomes, it has been determined that positive surgical margin ($P = 001$) and upgrading in RP specimen ($P = 0.001$) have been identified to be the independent predictive factors from the aspect PSA relapse. While positive surgical margin increased PSA relapse risk in 3.492 times, upgrading has increased it in 11.876 times.

In addition, in order to enable whether or not the survival periods being shorter in this study for the patients upgraded according to biopsy in prostatectomy specimen depended on increased Gleason score is perceivable, also the PSA - free survivals of the patients having the same Gleason score yet being in different groups have been also investigated. According

to this, in the patients in the upgrading group (Group 1) with Gleason score 7 and above 8, PSA - free lower survival has been traced at a significant rate according to the patients in other groups having the same Gleason scores.

CONCLUSION

When making prostate diagnosis by biopsy, Gleason scores different from those of prostatectomy that cannot be ignored are being come across. This difference is mostly accompanied by annoying clinical results during follow-ups.

The reason why the Gleason score determined in the RP specimen is different from that one determined in the biopsy is not made clear yet. Moreover, the reliability of the parameters which can predicate this different grading is disputable level due existence studies showing opposite results. It is known that transitional zone cancers have much lower Gleason grades; therefore, improper biopsy technique may lead to taking specimen from the transitional zone instead of rather than peripheral zone thus may prepare grounds for making downgrading.

Again, the crushing artifacts which might develop at the time when the particle is being taken or placed into transport bottle, coincidence of part taken from the edge of prostatic acini and therefore, lumen could not be seen thus grading failed to be correctly made might be the causes leading to different grading.

Eventually, no matter whatever the reason, different grading, particularly determination of Gleason score higher than the RP specimen biopsy also bring about bad pathologic parameters and shortened survival periods.

In deciding to treat patients diagnosed with PCa by biopsy, it should be remembered that the biopsy outcome is misleading from the aspect of Gleason grade at a rate of 50% in literature. In this case, the patients in position of conforming the criteria and whose active surgical candidacy is disputable might be having been deprived from the chance of being guided to other treatment alternatives, such as RT.

In the light of information today, the reason and predictive of this grading difference are not clearly known and therefore, it is impossible to avoid them. In order to enable it to be clearly comprehended and at least for it to be likely to be minimized so as to make a minimal effect on survival, larger series of patients with longer follow-up periods of comparative studies are needed.

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