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ORIGINAL ARTICLE

Concordance with Histopathology and with Various Parameters in the Grade Groups of Prostate Cancer on Needle Biopsy Versus on Radical Prostatectomy

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Abstract

Introduction: We aimed to define the compatibility between biopsy and surgical pathology results in connection with age, prostate-specific antigen (PSA), prostate volume (PV), and body mass ındex (BMI) in prostate cancer (PCa) patients. PCa is the second most common male cancer in the world. PCa is also the most common urological cancer and is the second most common cancer after lung cancer among all cancers in Türkiye.

Methods: We evaluated 165 PCa patients who were diagnosed with ultrasound-guided transrectal-targeted prostate biopsy and then operated with open radical prostatectomy. We compared the Gleason Scores (GSs) of biopsy specimens and the GSs of the prostatectomy specimens with the relationship of some parameters as age, PSA, PV, and BMI.

Results: Pathology data were at similar compatibility ratio (67%) in both groups < 65 and ≥ 65-year-old Pathology results were consistent in patients with a PSA value <10 ng/mL and ≥10 ng/mL as 66% and 73%, respectively. The histopathological compliance in patients with a PV <80 cc and ≥80 cc was 66% and 93%, respectively. The compatibility of BMI with the pathology results was found at the group with BMI ≥25 kg/cm^2 (64%) and the patients with BMI <25 kg/cm^2 (74%).

Discussion and Conclusion: The harmony between the fine needle biopsies' and the radical prostatectomy specimens' GS varies between 24% and 78% in the literature. When all patients were taken into consideration, a moderate agreement was found between the pathology results of biopsy and the pathology results of surgery (110/165, 67%).

Keywords: Gleason score; pathology; prostate cancer; prostate specific antigen.

Prostate cancer (PCa) is the second most common cancer among men worldwide and the incidence and mortality rates differ among the countries. PCa was reported as most common urological cancer and was the second most common cancer after lung cancer among all cancers in the incidence study conducted by the Turkish Uro-oncology Association[1-3]. At present, one in seven men (16%) will develop PCa during their lifetime, and 1 in 27(3%) will probably die of it[4].

Current diagnostic methods in PCa include the use of a digital rectal examination (DRE), serum PSA, transrectal ultrasound (TRUS)-guided biopsy, multiparametric magnetic resonance imaging (mpMRI), and MRI/Ultrasound Fusion-Guided Prostate Biopsy. PSA and DRE are the most useful

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predictors for positive prostate biopsies differing according to the age, race, and region[5].

The original Gleason grading system, which was based on the architectural pattern of tumor cells in prostatic adenocancer. A high Gleason score (GS) is a sign of cancer aggressiveness. A new PCa grading system stratifies the cancer into prognostic grade groups which are based on various GSs[6,7]. Here in, we compared the GSs of biopsy specimens and the GSs of the prostatectomy specimens with the relationship of some parameters (Age, PSA, prostate volume [PV], and body mass ındex [BMI]).

Materials and Methods

In this study, all the patients who underwent TRUS fine needle prostate biopsy and who later underwent RRP were classified according to age, prostate-specific antigen (PSA) value, PV, and BMI. Considering these parameters, we investigated whether there is a relationship between GSs of fine needle biopsy specimens and GSs of prostatectomy specimens.

One hundred and sixty-five patients who underwent RRP due to PCa between 2006 and 2014 in a tertiary center hospital were included to the study. RRP operations were performed by eight specialist doctors in our urology clinic. Prostate biopsies and operative specimens' pathology database were reviewed retrospectively. This study was also accepted by the administration of Haydarpasa Training Hospital as a specialty thesis.

An abnormal DRE or an elevated age-specific PSA according to reference ranges was accepted as indication for prostate biopsy. PSA screening was performed by Beckman Coutter Kit (Hybretech, San Diego, CA, USA). A written consent paper about the biopsy procedure and explanation of possible complications was taken from patients. PSA values of all patients were measured before DRE and TRUS-guided fine needle prostate biopsy. Age, PSA, and BMI values were noted for all patients who had RRP as definitive treatment. Values of PV found by the water overflow method were recorded during the pathological examination of the surgical specimens.

All men underwent TRUS-guided prostate with Levofloxacin (500 mg BID) prophylaxis. We used an ultrasound machine (Samsung) equipped with 7 Mhz rectal probe and automatic core biopsy device (TruCare MD-TechR) with 18-gauge core tissue biopsy needle. Prostate biopsies were performed in 8-cores before 2009 and then 12-cores protocol. The biopsy specimens were put in a container with 10% formaldehyde.

Histopathological examinations of biopsy and surgical specimens were divided into six groups according to the results of GS and numbered as 0, 1, 2, 3, 4, and 5. Group 0: Gleason 2+3=5, Group 1: Gleason 3+2=5, Group 2: Gleason 3+3=6, Group 3: Gleason 3+4=7, Group 4: Gleason 4+3=7, and Group 5: Gleason was expressed as 4+4=8.We compared GSs obtained from histopathological examinations of biopsy and surgical specimens among the patient groups we created. The patient groups were created by considering age, PSA value at the time of admission, PV detected in pathological examination and BMI of the patients.

Statistical analyses were performed using SPSS version 17.0 software. The compatibility between the pre-operative biopsy results and the histopathological examinations of the surgical specimens was evaluated with the Kappa test. For Kappa coefficient, it was accepted as 0–0.2, very weak, 0.21–0.4 weak, 0.41–0.6 medium, 0.61–0.80 good, and 0.81–1.0 perfect fit. $P<0.05$ was considered significant.

Results

The records of 165 patients who underwent RRP operation with the diagnosis of PCa between 2006 and 2014 were retrospectively reviewed. When GSs of patients' biopsy specimens were examined, GS of seven patients was 5, GS of 114 patients was 6, GS of 42 patients was 7 and GS of two patients was 8. When GS of RRP specimens was examined, GS of six patients was 5, GS of 89 patients was 6, GS of 66 patients was 7, and GS of 4 patients was 8 (Table 1).

We divided the patients into two groups as <65 and ≥65 year-old while evaluating the age parameter. When the pathology results of biopsy and surgical specimens were evaluated in the patient group <65, there was a weak agreement between GSs. (Kappa analysis, $\kappa=0.384$, $p<0.001$).The histopathological compatibility was 100% for GS results, which was defined as Group 5, 69% for Group 2, and 77% for Group 3, and 50% for Group 4, respectively. Results characterized by Groups 0 and 1 were found as 0%. Pathology results were compatible in 56 patients (56/83, 67%).The pathology results of biopsy and surgical specimens in the ≥65-year-old group, the GSs were observed moderately compatible (Kappa analysis, $\kappa=0.416$, $p<0.001$). The compatibility of histopathological results in ≥65-year-old group was found to be 68% for Group 2 and 78% for Group 3. There were no patients aged 65 years or older in Groups 0, 1, 4, and 5. Pathology results were compatible in 54 patients (54/81, 67%) (Fig. 1).

The PCa patients were divided into two groups at the time of admission when evaluating for PSA. One hundred and

Table 1. Distribution of the number of patients in the study by groups considering the biopsy results

Parameters	Gleason classification						Numbers
	0 (2+3=5)	1 (3+2=5)	2 (3+3=6)	3 (3+4=7)	4 (4+3=7)	5 (4+4=8)	Total number
Age							
<65	2	1	61	13	4	2	83
≥65	0	0	57	24	0	0	81
PSA							
<10	1	4	89	23	5	1	123
≥10	0	0	24	8	7	1	40
PV							
<80	3	0	105	30	8	2	148
≥80	0	0	10	4	0	0	14
BMI							
<25	0	0	66	8	8	1	83
≥25	0	4	48	24	0	1	77

PSA: Prostate-specific antigen; BMI: Body mass index; PV: Prostate volume.

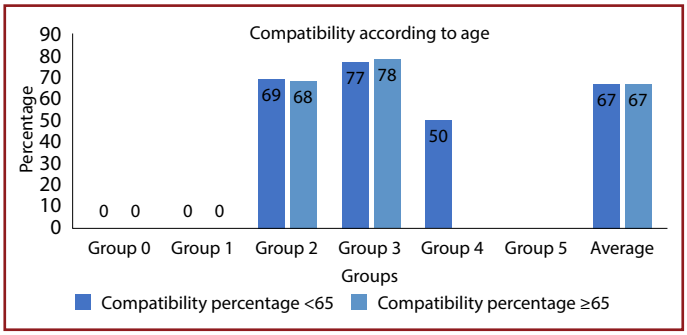

Figure 1. Compliance percentages of biopsy and surgical specimens for <65 and ≥65 years-old according to GS groups.

twenty-three patients were included in the group with a PSA value below 10 ng/mL, and 40 patients were included in the group with a PSA value of 10 ng/mL or above. Two patients were excluded from the study because their PSA data could not be reached. When the pathology results of biopsy and surgical specimens of patients with a PSA value <10 ng/mL were evaluated, there was a weak agreement between GSs (Kappa analysis, κ=0.357, p<0.001). Histopathological compliance was observed to be 100% among the GS pathology results described as Group 5, 67% for Group 2, 78% for Group 3, and 25% for Group 1 and 0% for Group 0, respectively. Pathology results were consistent in a total of 56 patients (81/123, 66%). When the pathology results of biopsy and surgical specimens of patients with a PSA value ≥10 ng/mL were evaluated, there was a moderate agreement between GSs (Kappa analysis, κ=0.540, p<0.001). Histopathological compliance was observed to be 72% among the GS pathology results described as Group 2.75% for Group 3, 67% for Group 4, and 100% for Group 5. There were no patients in Groups 0 and 1. Pathology results were compatible in 29 patients (29/40, 73%) (Fig. 2).

When evaluating the PV, volumes determined by the water overflow method were considered in the pathological examinations of the surgical specimens and the patients were classified into two groups. One hundred and forty-eight patients were found in the group with a PV <80 cc, and 14 patients in the group with a PV of ≥80 cc. Three patients were excluded from the study because their PV data could not be reached. In the group with a PV <80 cc, there was a weak agreement between the pathology results of biopsy and surgical specimens (Kappa analysis, κ=0.381, p<0.001). Histopathological compliance was found to be

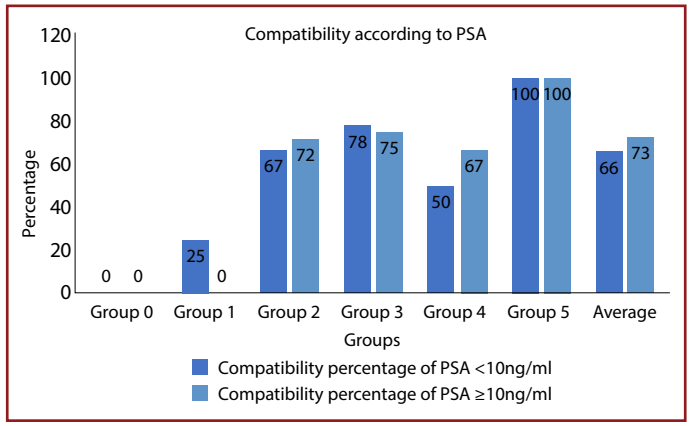

Figure 2. Compliance percentages of the patients with PSA values <10 ng/mL and ≥10 ng/mL according to GS groups.

100% among the pathology results with GS, which was defined as Group 5, 66% for Group 2, 75% for Group 3, and 0% for Group 4. There was no patient in Group 1. Pathology results were found compatible in 97 patients (97/148, 66%). In the group with PV of ≥80 cc, this fit was observed to be perfect (Kappa analysis, κ=0.811, p=0.002). Histopathological compliance was found to be 91% among the pathology results with GS, which was defined as Group 2 and 100% for Group 3. There were no patients in Groups 0, 1, 4, and 5. Pathology results were compatible in 13 patients (13/14, 93%) (Fig. 3).

When evaluating the BMI, patients were divided into two groups. There were 83 patients in the group with BMI <25 kg/m^2 and 77 patients in the group with BMI ≥25 kg/m^2. Five patients were not included in the study because their height and weight could not be reached. It was observed that the histopathological findings obtained in biopsy specimens and the histopathological findings in the surgical specimens were found to be compatible in patients with BMI <25 (Kappa analysis, κ=0.377, p<0.001). It was observed that histopathological compliance was among the pathologies with GS (65%, 70%, and 100%, respectively), which were defined as Groups 2, 3, and 5, and that the result in the pathology described as Group 4 was lower (43%). In total, 53 patients (53/83, 64%) were found to have compatible pathology results. Similarly, in patients with a BMI of 25 kg/m^2 and above, it was observed that the specimens obtained by biopsy and surgery were compatible, and even the compliance was moderately stronger than those with BMI <25 kg/m^2 (Kappa analysis, κ=0.476, p<0.001). This agreement was found to be 100% for the pathology results indicated by Group 1 and Group 5, 71% for Group 2, and 91% for Group 3. Overall, 57 patients (57/77, 74%) had compatible biopsy results. There were no patients in Groups 0 and 4 (Fig. 4).

When 165 patients were examined, it was observed that Group 0 (n=3) and Group 1 (n=4) had very low agreement between the biopsy pathology results and the surgical pathology results (0%, 25%, respectively). There was a moderate agreement between biopsy results and surgical pathology results in Group 4 (n=11), good agreement between group 2 (n=114) and group 3 (n=31) and, there was a perfect match between group 5 (n=2) although the number of patients was low (46%, 68%, 77%, and 100%, respectively). When all patients were taken into consideration, a moderate agreement was found between the pathology results of biopsy and the pathology results of surgery (110/165, 67%) (Kappa analysis, κ=0.401, p<0.001) (Fig. 5).

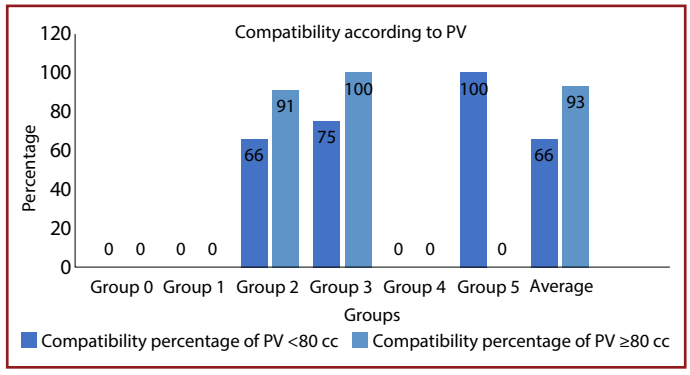

Figure 3. Percentage of compliance of the patients with prostate volume <80 cc and ≥80 cc.

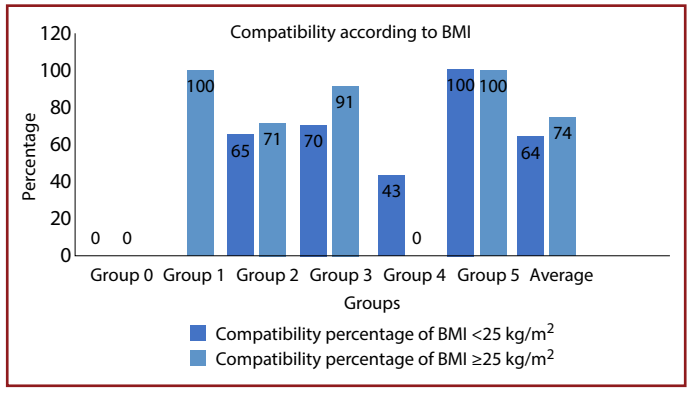

Figure 4. Compliance percentages of patients with BMI <25 kg/m^2 and ≥25 kg/m^2 according to GS groups.

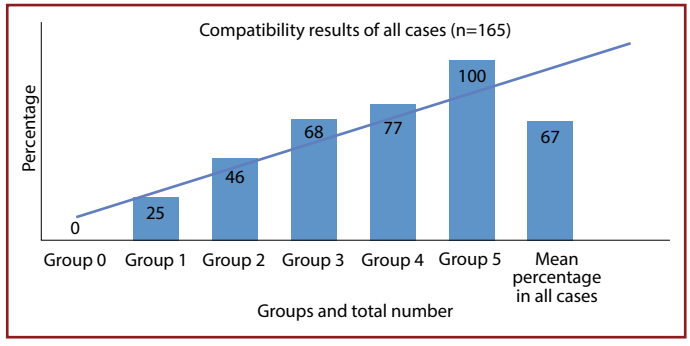

Figure 5. Compliance percentages of patient groups formed according to GS of a total of 165 patients and consistent percentage of GS of biopsy and surgical specimens when all patients are considered.

Discussion

PCa takes the fourth place among cancers worldwide and is the most common solid cancer for men in the developed countries. Radical prostatectomy (RP) is recommended to patients with a life expectancy of at least 10 years and a biopsy diagnosis of PCa, clinically localized or advanced. Therefore, age, comorbidity (hypertension, smoking, diabetes, etc.), and correct clinical staging are important fac-

tors to consider when choosing patients for radical prostatectomy. Pre-operative clinical staging methods used in selecting patients suitable for RP are DRE, TRUS, CT, and mpMRI[8]. However, the results of each of these methods can be misleading, and with these methods, at least one-third of the patients thought to have local disease were found to have penetrated into the capsule. For this reason, it is clear that with this staging done correctly, an increase in disease-free survival and quality of life and can also be cost-effective. It is difficult to guess how PCa will be diagnosed in which patient and how the course of the illness will be. Because of that, several nomograms which have been created by the prognostic factors are frequency referenced sources for predicting the parameters of PCa. The tables of Partin for predicting the RP pathology and the nomograms of Kattan for predicting the recurrences free survival rates are the most frequently used nomograms[9-11].

The GS in the RP specimen has been proven to be a reliable marker of survival. The accuracy of Gleason grade of specimens obtained by fine needle biopsy is also important[12,13]. However, some authors have claimed that there are differences between the GS of the fine needle biopsy samples and the GS after prostatectomy. It has been suggested that these differences arise from the heterogeneity and multicentric of PCa. The harmony between the fine needle biopsy and the radical prostatectomy specimens varies between 24% and 78% in the medical literature[14-17]. When we compared the GSs of 165 patients included in our study, we found that 110 patients' biopsy and surgical pathologies were compatible. Similar to the studies conducted, a moderate agreement was found between the results of biopsy and the results of surgery (110/165, 67%) (Kappa analysis, κ=0.401, $p<0.001$). In another study conducted by Güner et al.[18] was compared the biopsy and final pathology prostatectomy specimen with GS, PSA, age, and BMI. The patients had 22.6% upgrading and 3.6% had downgrading according to GS. Pre-operative PSA with upgrading was significantly higher than those without upgrading results and the age and BMI of the patients with and without upgrading were similar. However, this mismatch was observed to be lower in our study. When incompatible pathologies were evaluated, we found that GSs obtained by biopsy were lower than surgical ones. Since the low GS detected has potentially lower risk of progression, it will affect the preference and results of localized PCa treatment options such as follow-up, cryotherapy, brachytherapy, external radiotherapy, and radical prostatectomy. In other words, the high GSs obtained in the biopsy primarily lead clinicians to active treatment options, which may lead to the application of unnecessary and over-treatments in some patients. On the other hand, low grading is more common in biopsy. This causes patients to be deprived of a curative treatment option such as radical prostatectomy. Considering the recent choices of patients with localized PCa, other active treatments such as external radiotherapy, brachytherapy, and cryotherapy are increasing[19,20]. Since these treatments do not reflect the true GS, such as surgical specimen, as a matter of course the GS in biopsy is the most important criterion at the time of selection. Active surveillance approach is also used for the patients at low-risk group with localized PCa without losing the chance of curative treatment[21]. In this approach, GSs in recurrent prostate biopsies with clinical criteria are taken into consideration. Therefore, taking active surveillance by detecting patients with more aggressive tumors as a lower stage in biopsy means perhaps affecting the outcomes of curative treatments and the prognosis of the disease.

In recent years, the use of mpMRI in the diagnosis and staging of PCa before needle biopsy has achieved wider acceptance, and it has become useful for differentiating the clinically important cancers. Suspicious lesions in mpMRI are graded using the Prostate-Imaging Reporting and Data Scoring System (PIRADS). PIRADS scoring system in mpMRI is predicted statistically significant correlation with inverse histopathological factors in surgical specimen and a higher score may indicate a higher GS[22]. Unfortunately, we did not have the opportunity to use mpMRI in our hospital at the time of study.

PCa occurs mainly in older men; nearly two-thirds were diagnosed in men age 65 or older. The risk of PCa increases in every decade. The average range of age at the time of PCa diagnosis is between 60 until 70 years and about one man in six will be diagnosed with PCa during his lifetime[23,24]. Among the GSs which evaluated with the age parameter, similar compliance percentages were obtained both below 65 and above 65 years of age in our study (Compliance for <65 years; 67% Kappa analysis, κ=0.384, $p<0.001$, fit for ≥65 years; 67% Kappa analysis, κ=0.416, $p<0.001$). Increased PSA values are also thought to increase GSs. However, the effect of age here is to increase the grade by progressing depending on the duration of the disease. We thought that age did not affect the compatibility between biopsy and surgical pathologies.

It is known that serum PSA level still has prognostic value in patients with localized PCa who underwent radical prostatectomy. However, its sensitivity and specificity are not enough to make it an excellent screening test. Because the

elevation of PSA (>2.5 ng/ml) can also be seen in prostatitis and BPH cases. PV and a person's age also contribute to an increase in PSA without PCa. It was found that PSA predicted cancer volume and high Gleason level in the late period[25,26]. In our study, there was a weak-moderate relationship between the biopsy and surgical specimens' GSs according to the serum total PSA levels measured preoperatively. Compliance of patients with a PSA value below 10 ng/mL was 66% (Kappa analysis, κ=0.357, p<0.001), and if patients with a PSA value ≥10 ng/mL were 73% (Kappa analysis, κ=0.540, p<0.001). Although the significance of PSA values in predicting prognosis was known, it was thought that high or low did not affect the consistency between biopsy and surgical GSs.

The large PV may be a disadvantage for the harmony between biopsy and surgery. Because small pieces taken due to the nature of the prostate biopsy could not represent the entire prostate, it was more likely to exhibit a GS different from the final pathology. In large prostates with BPH, an enlarged transition zone may compress the peripheral zone and lead to shorter biopsy cores[27]. However, in the group with a PV of <80 cc, the pathology results of the biopsy and surgical specimens were weak with 66% (Kappa analysis, κ=0.381, p<0.001), and in the group with a PV of 80 cc and above, this agreement was excellent with 93%. (Kappa analysis, κ=0.811, p=0.002). Here in, we think that the number of patients with a PV value of ≥80 cc is less than the number of patients with a small prostate, which prevents us from confirming our opinion. In addition, the experience of the physician who performed the biopsy in the variability of the evaluation and the orientation to the suspicious areas with USG knowledge and the experience of the pathologist who evaluated the specimens were also important.

Epidemiological investigations of the BMI and PCa relationship have reported a mixture of inverse, positive, and undefined results. However, in other respects, obese men may have lower PSA levels and may cause to delayed referral for prostate biopsy and detection of PCa. Because the incidence of non-palpable isoechoic prostate tumors is high, limiting biopsy sites to either ultrasonographically hypoechoic lesions or to palpable abnormal areas tends to miss many PCa[28-30]. Here in, evaluating to BMI was conducted to search to the difficulty of performing prostate biopsy in obese patients. A poor agreement was observed between biopsy and surgical pathologies of patients with BMI <25% in our study (Kappa analysis, κ=0.377, p<0.001). Similarly, moderate compliance was observed with 74% in patients with BMI of 25 kg/cm^2 and above (Kappa analysis, κ=0.476, p<0.001). However, no significant difference was found in the compliance of both pathology results with the BMI parameter.

Conclusion

PCa is the second most common cancer among men in the world. The incompatible pathological results between the biopsy and surgical specimens are potentially affected the preference and results of localized PCa treatment options. In other words, the high GSs obtained in the biopsy primarily lead clinicians to active treatment options such as radical prostatectomy, which may lead to the application of over-treatments in some patients. On the other hand, low grading in biopsy causes the patients to be deprived of a curative treatment option such as radical prostatectomy. The curative treatment of PCa is provided in appropriate patients by radical prostatectomy. However, radical prostatectomy should not be performed on all patients with localized PCa. The accurate clinical staging is important factors to consider when choosing patients for radical prostatectomy[31].

Since the detection of Gleason grade in patients with PCa is an important factor in determining the prognosis of this disease and evaluating treatment options, the accuracy of Gleason grade of specimens obtained by biopsy is important. However, some authors have claimed that there are differences between the GS of the fine needle biopsy samples and the GS after prostatectomy. When the publications are examined, it is seen that the harmony between the biopsy and the radical prostatectomy specimens varies between 24% and 78%[32-34].

In our study, it was found that there was a moderate agreement between the biopsy results and the pathology results obtained by surgery, similar to the previous studies (110/165, 67%) (Kappa analysis, κ=0.401, p<0.001).

As a conclusion, developing and applying new methods to increase percentage of compliance between biopsy and surgical pathology results are essential. The limitations of this study were not having mp-MR imaging during the study; were not having modified pathology methods such as non-invasive fluid biopsies; were not having the advanced modalities such as transrectal prostate elastography, contrast US, and micro-Doppler[35]. As a further study, comparison of the highest and lowest gleasones of biopsies' and surgical specimens' or comparison of the tertiary scores may be studied[36]. It can be thought that advanced diagnostic techniques will decrease the incompatible pathological results between the biopsy and surgi-

cal specimens before the active treatment and prevent the insufficient or over-treatment.

Ethics Committee Approval: Specilization thesis with the approval of cihief physician of Haydarpasa Numune Traing hospital. Year: 2014.

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