

Gleason Score Correlation Between Prostate Needle Biopsy and Radical Prostatectomy Materials

Neşe YELDİR¹ , Esin YILDIZ² , Gökçe DÜNDAR³ 

Department of Pathology, ¹Cizre Dr. Selahattin Cizrelioğlu State Hospital, ŞIRNAK, TURKEY, ²Cumhuriyet University Hospital, SİVAS, TURKEY,

³Department of Urology, Cizre Dr. Selahattin Cizrelioğlu State Hospital, ŞIRNAK, TURKEY

ABSTRACT

Objective: Prostate cancer is the second most common cancer in men. Digital rectal examination, transrectal ultrasonography and serum prostate specific antigen represents a diagnostic triad for the detection of prostatic carcinoma. About 50 years ago, Dr. Donald Gleason created a grading system for prostate cancer based on its histologic patterns. Currently, this system maintains its validity with various changes. New updates were made in 2005 and 2014 by the International Society of Urological Pathology. The goal of biopsies is to determine the Gleason score and prognosis in prostatectomy material. The aim of this study was to determine the concordance of the Gleason score, tumor volume and tumor laterality between prostate needle biopsy and prostatectomy materials.

Material and Method: The study was performed with 112 patients who had biopsy and prostatectomy materials. The Gleason grades of the tumors have been evaluated with the new grading system. Tumor volumes were calculated by the number of positive blocks while tumor laterality was evaluated as unilateral or bilateral. Statistical analysis was performed on the obtained data.

Results: Gleason score, tumor volume and tumor laterality discordance between needle biopsy and prostatectomy materials was found to be statistically significant. However, the concordance increased as the Gleason score and tumor volume increased.

Conclusion: Digital examination, serum prostate specific antigen value and needle biopsy together are very sensitive for a prostate adenocarcinoma diagnosis. The Gleason score, localization and volume of the tumors are important for patient follow-up, treatment and prognosis.

Key Words: Prostate, Adenocarcinoma, Needle biopsy, Radical prostatectomy, Gleason score

INTRODUCTION

Prostate cancer is the second most common cancer in men all over the world and is the fifth among causes of cancer-related deaths. Approximately 75% of the diagnosed patients are 65 years of age or older and it is very rare at younger ages including adolescents. Typically, the frequency and mortality rates are increasing with age (1-5).

The triple combination of digital rectal examination, transrectal ultrasonography (TRUS) and serum prostate specific antigen (PSA) are used in screening and early diagnosis. The main role of TRUS in diagnosing prostate cancer is to guide the biopsy. PSA, a proteolytic enzyme, is produced by both normal and tumoral prostatic epithelium. A serum PSA level exceeding 4 ng/ml is abnormal. However, this elevation is not specific to carcinomas but may be due to benign prostatic hyperplasia, prostatitis, infarction and trauma (such as transurethral resection, needle biopsy) (2-4).

Needle biopsy is performed with TRUS guidance in men with a serum PSA and rectal examination abnormality. Patients, who are diagnosed with adenocarcinoma as a result of the biopsy are treated with radical prostatectomy (RP) if clinically appropriate (2,3,5).

Prostate adenocarcinoma is divided into acinar and ductal. Most prostate adenocarcinomas are of the acinar type and usually arise from the peripheral zones of the prostate. Most prostatic adenocarcinomas of peripheral zone origin are multifocal, and therefore most needle biopsies aim to sample posterior peripheral zone tissues from a large number of areas (1-5).

Because the tumor volume in needle biopsy is related to biochemical recurrence and even the radiotherapy response, the core number with tumor and biopsy length are important as well as parameters such as stage and surgical marginal status in RP material (4,5).

In needle biopsy, many techniques have been developed and applied to determine the amount of tumor. Tumor volume may be reported by means of positive cores, ratios of positive cores, millimetric measurement of tumor in all cores, ratio of tumor in each core, and ratio of tumor in the whole specimen (2,6).

Prostate adenocarcinoma has been graded for approximately 50 years by the system recommended by Donald F. Gleason (7). The well-established relationship with the prognosis has made the Gleason grading system an important factor in determining the treatment. Although the Gleason scoring has changed since its first definition to this day, its basic features have not been changed. The last change was made at the International Urological Pathology Community (ISUP) in 2005 and the problems were largely resolved (8). Some postponed issues were also resolved at the November 2014 Chicago meeting. In this meeting, it was also recommended that Gleason scoring be divided into simpler prognostic groups (9). These recommendations were also included in the World Health Organization's (WHO) 2016 'Classification of Urinary System and Male Genital Organ Tumors' book (3).

In needle biopsies, the aim is to assess the Gleason score in the RP material and thus the prognosis (3,7-9). Regarding this goal, we aimed to investigate the adenocarcinoma Gleason score, tumor volume and tumor location laterality concordance between prostate needle biopsy and RP materials in this study.

MATERIALS and METHOD

A total of 112 patients with prostate adenocarcinoma diagnosed with needle biopsy and treated by RP between 2008 and 2016 were included in the study. Archival slides were re-evaluated for Gleason score, tumor extensity and tumor laterality. In addition, concordance between biopsy and RP findings were examined.

When the Gleason score was assessed, the patterns in the 2005 and 2014 updates and new score assessments and the prognostic groups recommended at the 2014 meeting were considered (3,8,9). The most common and worst patterns were detected in the biopsies and the Gleason score was determined by the sum of these scores. In addition, five newly identified prognostic groups were identified for each case (Grade groups 1-5).

Tumor volume in the biopsy material was calculated by the proportion of the tumor length in the tumor-bearing cores to total length of all the cores in mm. In cases where

the tumor extended to reveal benign prostate tissue in the biopsy core, the entire tissue was included in the measurement from one end of the tumor to the other (2,10).

Tumor volume of RP materials was calculated by proportioning the number of tumor-positive paraffin blocks to that of all specimens (11).

With the results obtained, cases were divided into three according to the tumor volumes. These groups were limited (<20%), moderately extensive (20-50%) and extensive (> 50%).

Tumor laterality was assessed as unilateral (right or left) and bilateral (right and left), in both the biopsy and RP materials.

Immunohistochemical studies (p63, HMWCK, AMACR) performed beforehand and during the study on foci with a difficult differential diagnosis (e.g., PIN-adenocarcinoma, adenocarcinoma-ductal carcinoma, PIN-urothelial carcinoma *in situ*) and new sections obtained from the blocks and then stained with H&E were examined.

Immunohistochemical analysis was performed using the Ventana Brand Benchmark XT model automated device.

In the study, the kappa coefficient was used for statistical analysis. Kappa (κ) was measured for grade, volume and laterality between biopsy and RP. The K value ranges between -1 and +1. A value of κ equal to +1 implies perfect concordance between the two methods, while that of -1 implies perfect discordance. If κ assumes the value of 0, then this implies that there was no relationship between the ratings of the two methods, and any concordance or discordance is due to chance alone (12).

RESULTS

The ages of the 112 patients included in the study ranged from 48 to 78 years and the mean age was 64.84. Of these patients, 85 (75.9%) were over 60 years old, 25 (22.3%) were between 50 and 60 years old, and only 2 (1.8%) were under 50 years of age.

All needle biopsies and RP materials of the 112 patients had acinar type prostate adenocarcinoma. Gleason grades of tumoral areas in the biopsies and RP materials of the cases were evaluated and the grade groups were determined.

The distribution of the Gleason grading results of the needle biopsies of the 112 cases was 51 in Grade group 1 (46%), 16 in Grade group 2 (14%), 17 in Grade group 3 (15%), 23 in Grade group 4 (21%), and 5 in Grade group 5 (4%).

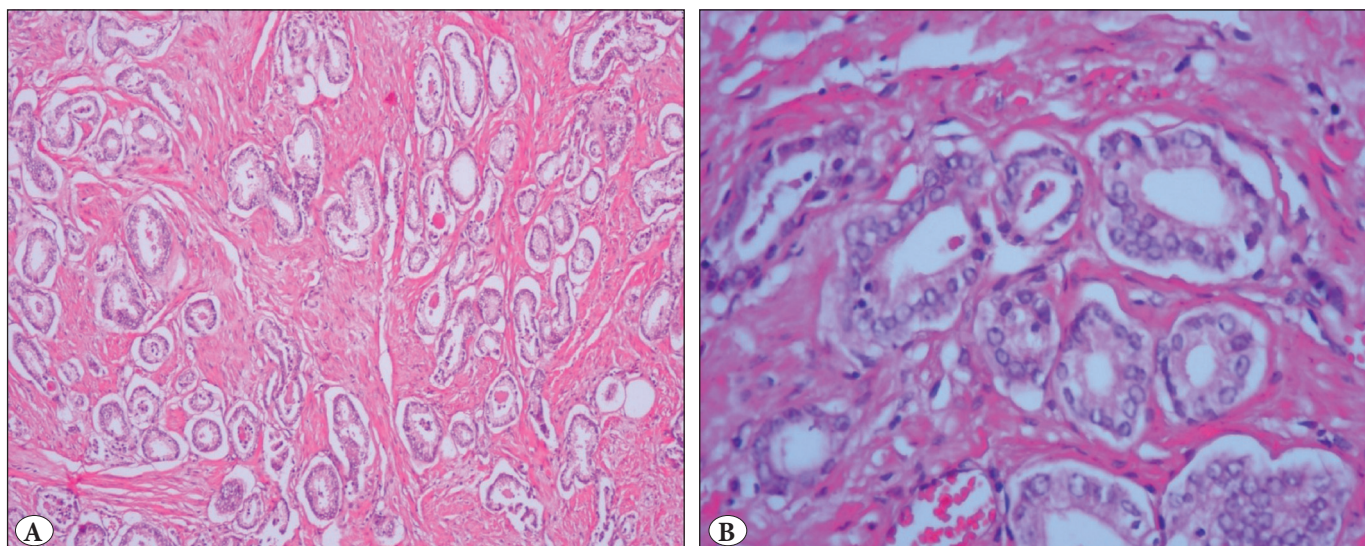


Figure 1: Gleason score 3+3=6 (Grade group 1) adenocarcinoma (H&E; x100, A & x400, B).

When the Gleason grading results of RP materials were examined, 26 were in Grade group 1 (23%) (Figure 1A,B), 28 were in Grade group 2 (25%), 28 were in Grade group 3 (25%) (Figure 2), 23 were in Grade group 4 (21%), and 7 were in Grade group 5 (6%).

Sixty-four (57%) cases had the same Gleason scores in biopsies and RP materials. Gleason grade distribution of the 64 cases were 24 with 1, 8 with 2, 11 with 3, 17 with 4, and 4 with 5. Gleason scores were higher in RP materials compared to biopsies in 39 (35%) cases and lower in nine (8%).

Kappa values for grade were 0.24 (Table I). According to these results, the concordance between the two methods was fair. However, as the Gleason score of the tumor increases, the concordance also increases. The most common discordance type is that the grade of the tumor in needle biopsy is lower than the tumor grade in RP material.

A total of 86 cases were limited (77%), 20 cases were moderately extensive (18%), and 6 cases were extensive (5%) in biopsy materials when 112 cases were evaluated in terms of tumor volume. There were 55 (49%) cases with limited amount of tumor in the RP material, 42 (38%) cases with moderately extensive tumor and 15 (13%) cases with extensive tumor. Ten of the 46 cases with tumor volume below 5% in the biopsy material also had a tumor volume below 5% in RP material and 3 had extensive tumor in RP material. The amount of tumor in the RP material of the remaining 33 cases was thought to be moderately extensive.

Kappa value for tumor volume was 0.21 (Table II). The concordance was fair for tumor volume between biopsy and

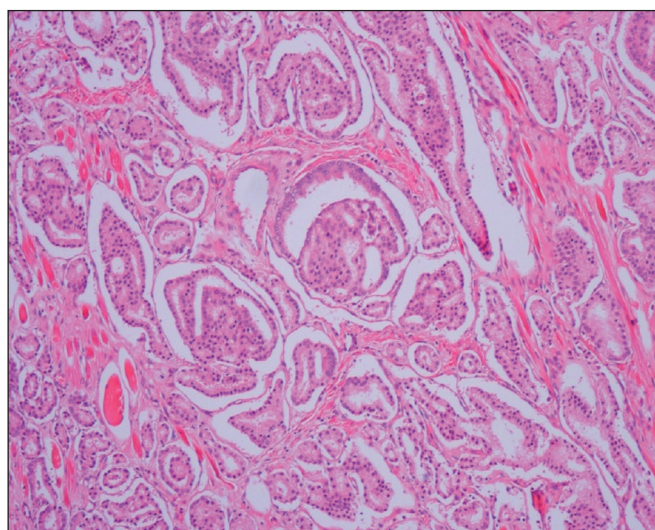


Figure 2: Gleason score 4+3=7 (Grade group 3) adenocarcinoma (H&E; x100).

RP materials of similar tumor grade. The most common incompatibility type was the appearance of a tumor in the lower volume in needle biopsy compared to RP material.

When the laterality of the cases was examined, there were 32 bilateral cases and 80 unilateral cases in biopsy materials. All of the 32 cases with bilateral tumors had undergone RP and there were also bilateral tumors in the RP material. In 80 cases of RP materials with unilateral tumors, there were 18 unilateral and 62 bilateral tumors. The compatibility rate of showing the same laterality of these two methods was 44.6%. Kappa value for tumor laterality was 0.14 (Table III). According to this result, the concordance was slight.

The sensitivity of prostate needle biopsy in identifying adenocarcinoma was 98%, the positive predictive value was 100%, and the negative predictive value was 0 (Table IV).

Immunohistochemical study (p63, HMWCK, AMACR) was performed for 36 needle biopsies and 6 RP cases. Tumoral areas were positively stained with AMACR, negatively with p63 and HMWCK, and PIN areas were positively stained with three antibodies. In two of the cases, immunohistochemistry results for suspected foci outside the tumoral area were positively stained with AMACR, p63 and HMWCK, and thus these foci were also considered to represent tumor (Figure 3A,B).

DISCUSSION

Prostate cancer is the second most common malignancy worldwide. The incidence of a prostate cancer diagnosis differs significantly between the world regions and countries. The highest incidence is in South America, the Caribbean, Brazil, some Western European countries, Australia and New Zealand. The incidence for prostate cancer is 28 per 100,000 in the world, 60 per 100,000 in Europe. The lowest incidence is in Asia, a few Middle Eastern countries and Africa. Both environmental and genetic factors influence this incidence difference (2-4, 13, 14). In Turkey, it is among the most common malignancies

Table I: Biopsy grade and RP grade Cross Tabulation.

		RP Gleason grade					Total (%)	κ
		1	2	3	4	5		
Biopsy Gleason grade	1	24	15	10	2	0	51 (46)	0,24
	2	2	8	6	0	0	16 (14)	
	3	0	3	11	3	0	17 (15)	
	4	0	2	1	17	3	23 (21)	
	5	0	0	0	1	4	5 (4)	
Total (%)		26 (23)	28 (25)	28 (26)	23 (20)	7 (6)	112 (100)	

Table II: Biopsy Tumor Volume and RP Tumor Volume Cross Tabulation.

		RP tumor volume				Total (%)	κ
		Limited	Moderately	Extensive			
Biopsy tumor volume	Limited	51	30	5	86 (77)	0,21	
	Moderately	4	12	4	20 (18)		
	Extensive	0	0	6	6 (5)		
	Total (%)	55 (49)	42 (38)	15 (13%)	112 (100)		

Table III: Biopsy and RP Tumor Lateralities Cross Tabulation.

		RP tumor laterality			Total (%)	κ
		Unilateral	Bilateral			
Biopsy tumor laterality	Unilateral	18	62	80 (71)	0,14	
	Bilateral	0	32	32 (29)		
	Total (%)	18 (16)	94 (84)	112 (100)		

Table IV: Positive and Negative Predictive Values Tabulation for Prostate Needle Biopsy.

		Radical Prostatectomy		Total (%)
		Prostate adenocarcinoma positive	Prostate adenocarcinoma negative	
Prostate Needle Biopsy	Prostate adenocarcinoma positive	110	0	110 (98)
	Prostate adenocarcinoma negative	2	0	2 (2)
	Total (%)	112 (100)	0	112 (100)

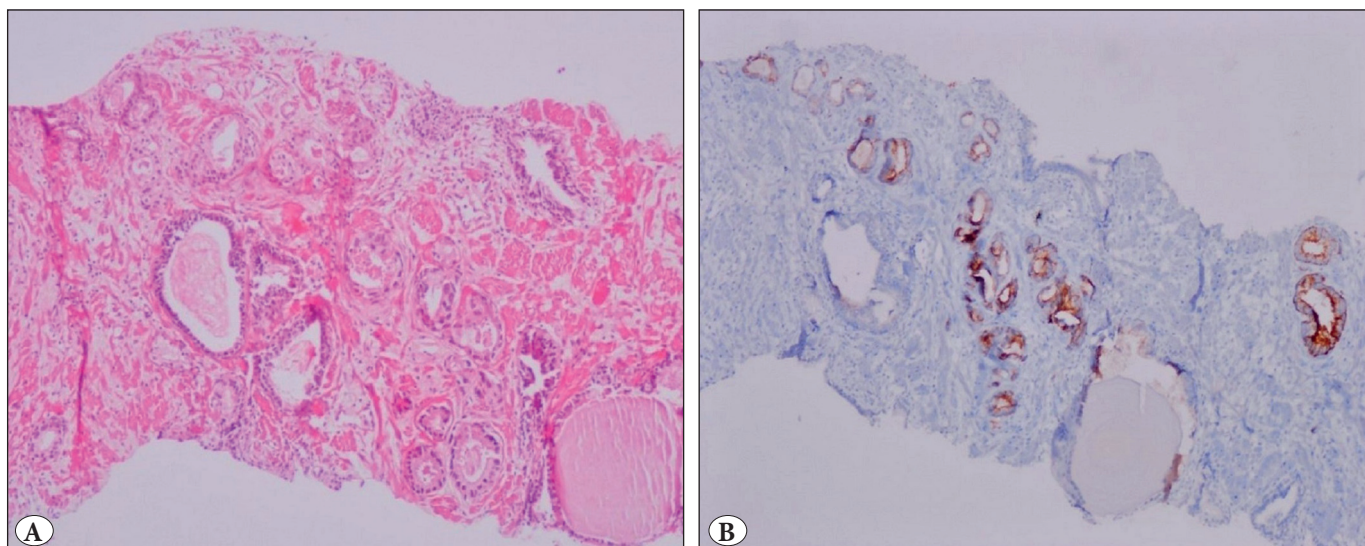


Figure 3: A single microscopic focus of the prostate needle biopsy reveals a tumoral focus less than 1 mm (H&E; x200, **A**) and shows positive staining with AMACR (IHC; x100, **B**).

in men, ranking second after lung cancer, and the incidence is increasing.

Prostate cancer is fifth among cancers causing death in men worldwide. The mortality rate is higher in regions where the black population dominates. The mortality rate is lower in Asia, a few Middle Eastern countries and South Africa (3,4,15,16).

Patient age is strongly associated with the presence of prostate cancer. Most people with cancer are over 60 years old. Only 1% of patients with prostate cancer are under 50 years of age (4). The age distribution of the 112 patients included in the study was 48-78 and the mean age was 64.84. Of these patients, 85 (75.9%) were over 60 years of age, 25 (22.3%) were between 50 and 60 years old, and only 2 (1.8%) were under 50 years of age.

Prostate adenocarcinoma may be suspected clinically with high serum PSA and/or an abnormal digital rectal examination. Digital rectal examination is not sensitive or specific for prostate cancer. Digital rectal examination may not detect 25-50% of prostate cancers detected by PSA. Benign conditions, such as benign prostatic hyperplasia and inflammation, can also be suspected as tumors, giving rise to abnormal palpation (1,4).

TRUS is performed as a primary diagnostic method for patients with suspected clinical prostate cancer with abnormal digital rectal examination and/or serum PSA elevation. TRUS biopsy has significantly increased the prostate cancer diagnosis rate. However, since TRUS is suboptimal in determining tumor volume and extraprostatic

extension, its use for local grading of prostatic cancer is limited (2-5,10).

Open, laparoscopic, or robotic RP is the definitive treatment of localized prostate cancer. RP specimens are needed to characterize the tumor, such as grade, volume, pathologic grade, and surgical margin conditions, which guide treatment management and prognostic assessment (3-5).

In the histopathological evaluation of prostate adenocarcinoma, the system suggested by Donald F. Gleason has been used widely around the world for about 50 years. Donald F. Gleason has developed a classification only based on a structural pattern, and the increased mitosis, which is not a hallmark feature of nuclear properties and prostate adenocarcinoma, has no place in determining patterns. Patterns from 1 to 5 have been identified. According to these patterns, the most common and second most common patterns between 1 and 5 are detected and their sum make up the Gleason score. The most common pattern is called 'primary pattern' and the second most common pattern is called 'secondary pattern' (8,17,18).

In the study, in the light of current advances in the Gleason system, a Gleason score was given to the needle biopsies regardless of how small the tumor was, and immunohistochemical studies were performed when necessary to confirm the diagnosis (3,9).

The Gleason scores of the cases included in the study ranged from 6 to 10. Pattern 3 was seen in 68% of cases and was the most common pattern.

Distribution of cases according to new prognostic groups was as follows: in biopsies, 51 (46%) cases were grade group 1, 16 (14%) cases were grade group 2, 17 (15%) cases were grade group 3 and 23 (21) cases were grade group 4 and 5 (4%) cases were grade group 5. Distribution in RPs was as follows: 26 (23%) cases were grade group 1, 28 (25%) cases were grade group 2, 28 (25%) cases were grade group 3, 23 (21%) cases were grade group 4, and 7 (6%) cases were grade group 5.

No difference was present between biopsies and RP materials of sixty-four (57%) cases in terms of Gleason score. RP materials of thirty nine (35%) RP cases had higher Gleason scores than biopsies, and 9 (8%) patients had lower scores.

In a study conducted by Pourmand et al., 25 (48%) of the 52 patients had the same Gleason scores in biopsies and RP materials, while 19 (36%) had higher scores and 8 (16%) had lower scores in RP materials (19). The results in this study were similar to those of Pourmand et al.

In a study conducted by Khoddami et al., Gleason scores remained the same in 68.2% of cases, while 32.8% showed a score difference of 1 or 2. In RP material obtained after biopsy, grade decreased in 9.1% of cases and grade increased in 22.7%. Sensitivity and positive predictive value of biopsy were 86% and 79% for low grade tumors, 67% and 75% for moderate grade tumors, and 80% and 80% for high grade tumors, respectively (20). In this study of Khoddami et al., the rate of similar scores on biopsy and RP is somewhat higher, and the rate of grade being higher and lower in RP was lower than in this study.

It is important to determine this distinction, since the Gleason score (3+4) and (4+3) cases have prognostic differences in tumors containing areas 3 and 4 pattern (8, 21). We found that 28 (25%) of the patients in this study were grade group 2 (3+4) and 28 (25%) were grade group 3 (4+3).

In needle biopsies, the aim is to determine the Gleason score in the RP material and thus the prognosis with the best possibility and in as many patients as possible. The aim of this study was to determine the compatibility of Gleason score and values of tumor volume and tumor laterality in needle biopsies of prostate adenocarcinomas with the RP materials.

Incompatibility between Gleason scores in needle biopsies and postdiagnostic RP materials is reported at a rate of up to 50% (2). According to results of this study, as the tumor Gleason score increases, the incompatibility between the Gleason scores decreases.

Incompatibility is often caused by sampling errors in needle biopsies or from cases in which it is not possible to determine exactly which pattern is present. Sampling errors include minimal tumor presence in needle biopsies despite extensive tumors in the RP materials and limited tumor tissue observation due to the use of fine needles (2-5).

One study concluded that needle biopsies had a higher error potential in grading well differentiated tumors and Gleason score <7 tumors (22).

Tavangar et al. concluded that the frequency of scoring well differentiated cancers low and poorly differentiated cancers high is very high in biopsies and they draw attention to that the biopsy score of low grade tumors might be lower than the actual score in the RP material in the reporting of prostate specimens and in the management of patients (23).

Although there are many studies evaluating Gleason score compatibility between biopsy and prostatectomy, a small number of these studies have focused on possible causes and effects of incompatibility (2).

The tumor volume in the RP material correlates with the pathological grade and Gleason score. Several methods have been introduced to measure tumor volume. There are controversial studies on the role of tumor volume as an independent predictor in the progression of post-radical prostatectomy disease after the pathological grade and stage have been determined. The International Society of Urological Pathology recommends that tumor volume be measured and indicated objectively in RP materials. The reasoning for the society is to record tumor volume in organ tumors in other systems too (9).

Since the tumor volume in needle biopsy is related to biochemical recurrence, even the radiotherapy response, as well as parameters such as stage and surgical marginal status in RP material, it is also important to determine the number of cores with tumor and the needle biopsy length. (2-5). According to the results of the study, the presence of tumor in the needle biopsy in a few cores and small areas does not accurately reflect the volume of the tumor in the RP material in most cases. The tumor can be seen more extensively in RP material. When an extensive tumor is seen in needle biopsy, frequently an extensive tumor is encountered in RP material too.

Among the cases in the study, Gleason score distribution of 4 cases with an extensive tumor volume over 80% in RP material was 3 with a score of 4+4 = 8 (GG4) and 1 with a score of 3+4 = 7 (GG2). Although the number of cases was small, the grade may be high if tumor volume is high.

Percentage of the volume (length) covered by the biopsy of the tumor is a measure that seems simple, but is difficult, and yet has a significant role in determining the treatment for the patient. Prostate adenocarcinomas are tumors that cannot be described macroscopically and are often multifocal. For this reason, benign areas are left in needle biopsies in most cases. The commonly accepted method used in this study is to give the ratio or length by adding the benign areas to the tumor in the needle biopsy tumor measurements (19,20,24).

Although the prognostic effect of tumor volume in RP materials and the method used to determine tumor volume in RP materials are controversial, it is suggested that the tumor extent should still be noted. A positive block ratio to determine tumor extent is an independent predictor of PSA recurrence, and this simple tumor measurement method is an indicator to determine the amount of tumor volume (11).

We found a positive paraffin block ratio when calculating tumor volume in RP materials as mentioned above. When the tumor volumes of all cases were examined, 84 cases had limited (75%), 20 cases had moderately extensive (18%) and 6 cases had extensive tumors (5%) in biopsy materials. There were 55 (49%) cases with a limited amount of tumor in RP material, 42 (38%) cases with moderately extensive tumor, and 15 (13%) cases with extensive tumor. The concordance was fair for tumor volume between biopsy and RP materials.

Among the cases in the study, Gleason score distribution of 4 cases with tumor volume over 80% in RP materials was 3 with a score of $4+4=8$ (GG4), and 1 with a score of $3+4=7$ (GG2). Although the number of cases was small, the grade may be high if the tumor volume is high.

We diagnosed 31 of the 46 cases with tumor volume below 5% as adenocarcinoma according to the IHC result and the remaining 15 cases were diagnosed without IHC in the biopsy materials included in this study. Of these 46 cases, 22% had a tumor volume below 5% while 6% had extensive tumor volume in the RP materials.

The Gleason score distribution of the 15 patients with tumor volume below 5% in RP materials in the study is as follows: 7 with score of $3+3=6$ (GG1), 4 with score of $3+4=7$ (GG2), 2 with a score of $4+3=7$ (GG3), and 2 with score of $4+4=8$ (GG4). The grade can be high although tumor volume is low.

In one study, prostate TRUS biopsy material revealed clinically significant tumor presence in the majority of cases

with a tumor volume below 0.5 ml and TRUS biopsies were therefore inadequate for the diagnosis and management of tumors with limited tumor volumes. However, it was thought that men with prostate cancer diagnosed with TRUS biopsy should be considered to have a clinically significant tumor in current practice, and that the age, health status and wishes of the patient should also be taken into consideration when determining the treatment approach until a more reliable method for distinguishing the disease in low-volume tumors is established (25).

Another study concluded that TRUS biopsy from 12 cores was a powerful method for predicting locally advanced disease, including the lymph node status in RP (26).

The sensitivity of prostate needle biopsy in identifying adenocarcinoma was 98%, the positive predictive value was 100%, and the negative predictive value was 0.

Studies related to the correlation between tumor laterality in needle biopsies and materials of RP performed afterwards are limited. According to the study, the concordance of tumor laterality between needle biopsies and RP materials was slight and more insignificant than tumor volume and grade.

In the study of Lowenthal et al. conducted with 75 patients, the tumor was reported as unilateral in biopsies and RP materials in 16 cases and unilateral in biopsies and bilateral in RP materials in 59 cases (27).

In the case of prostate adenocarcinoma, studies involving broader analyses are required to reach a definitive conclusion on the prognostic and diagnostic value of laterality. However, since tumor located in both lobes changes the stage from pT2b to pT2c, it is important to determine the laterality of the tumor (23).

In conclusion, digital examination, serum PSA value and needle biopsy together are very sensitive for prostate adenocarcinoma diagnosis. The application of RP to a localized disease diagnosed with adenocarcinoma in needle biopsy is an up-to-date procedure. Needle biopsy is a very reliable method to detect prostate adenocarcinoma and the rate of reflection of Gleason score, tumor volume and laterality in material of RP performed afterward is increased with increasing Gleason score and tumor volume. Gleason score, localization and volume of tumors is important for patient follow-up, treatment and prognosis. The concordance rates will undoubtedly increase with serial sections and immunohistochemical studies on ultrasound-guided needle biopsies of the prostate, which will obtain samples from more cores and in longer sizes.

CONFLICT of INTEREST

The authors declare no conflict of interest.

REFERENCES

- Epstein JI, Lotan TL. The lower urinary tract and male genital system. In: Kumar V, Abul KA, Aster JC, editors. Robbins and Cotran pathologic basis of disease. 9th ed. Philadelphia: Saunders Elsevier; 2015. 859-990.
- Epstein JI. The prostate and seminal vesicles. In: Mills SE, Carter D, Greenson JK, Oberman HA, Reuter V, Stoler MH, editors. Sternberg's diagnostic surgical pathology. 5th ed. Philadelphia: Lippincott Williams Wilkins; 2004. 2083-132.
- Moch H, Humprey PA, Ulbright TM, Reuter VE. Tumours of the prostate. WHO classification tumours of the urinary system and male genital organs. 4th ed. Lyon: IARC Press; 2016. 136-83.
- Rosai J. Male reproductive system. Rosai and Ackerman's surgical pathology. 10th ed. Sydney: Mosby Elsevier; 2011. 1287-398.
- Neşe N. Prostate and seminal vesicle. In: Yörükoğlu K, Tuna B editors. Uropathology. 1st ed. Izmir: Congress Bookshop, Kanyılmaz Printing House; 2016. 319-473.
- Cupp MR, Bostwick DG, Myers RP, Oesterling JE. The volume of prostate cancer in the biopsy specimen can not reliably predict the quantity of cancer in the radical prostatectomy specimen on an individual basis. *J Urol*. 1995;153:1543-8.
- Brimo F, Vollmer RT, Corcos J, Kotar K, Begin LR, Humphrey PA, Bismar TA. Prognostic value of various morphometric measurements of tumour extent in prostate needle core tissue. *Histopathology*. 2008;53:177-83.
- Epstein JI, Allsbrook WC Jr, Amin MB, Egevad LL; ISUP Grading Committee. The 2005 international society of urologic pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma. *Am J Surg Pathol*. 2005;29:1228-42.
- Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR, John K, Humphrey PA; The Grading Committee. The 2014 international society of urological pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma: Definition of grading patterns and proposal for a new grading system. *Am J Surg Pathol*. 2016;40:244-52.
- Gleason DF, Mellinger GT. Prediction of prognosis for prostatic adenocarcinoma by combined histologic grading and clinical staging. *J Urol*. 1974;111:58-64.
- Marks RA, Lin H, Koch MO, Cheng L. Positive-block ratio in radical prostatectomy specimens is an independent predictor of prostate-specific antigen recurrence. *Am J Surg Pathol*. 2007;31:877-81.
- Özdamar K. Biostatistics with SPSS. 4th ed. Eskişehir: Kaan Kitabevi; 2001.
- Prostate Cancer, Nutrition, and Dietary Supplements. PDQ integrative, alternative, and complementary therapies editorial board. PDQ Cancer Information Summaries (Internet). Bethesda (MD): National Cancer Institute (US);2002.2019.
- Genetics of Prostate Cancer. PDQ Cancer Genetics Editorial Board. PDQ Cancer Information Summaries (Internet). Bethesda (MD): National Cancer Institute (US);2002.2018.
- Conti DV, Wang K, Sheng X, Bensen JT, Hazelett DJ, Cook MB. Two novel susceptibility loci for prostate cancer in men of African ancestry. *J Natl Cancer Inst*. 2017;109.
- Cormier L, Kwan L, Reid K, Litwin MS. Knowledge and beliefs among brothers and sons of men with prostate cancer. *Urology*. 2002;59:895-900.
- Yörükoğlu K. Current developments in uropathology. *Turkiye Klinikleri J Med Pathol-Special Topics*. 2016;1:35-40.
- Pierorazio PM, Walsh PC, Partin AW, Epstein JI. Prognostic Gleason grade grouping: Data based on the modified Gleason scoring system. *BJU Int*. 2013;111:753-60.
- Pourmand G, Gooran S, Hossieni SR, Guitynavard F, Safavi M, Sharifi A, Mokhtari E. Correlation of preoperative and radical prostatectomy Gleason score: Examining the predictors of upgrade and downgrade results. *Acta Medica Iran*. 2017;55:249-53.
- Khoddami M, Khademi Y, Aghdam MK, Soltanghorae H. Correlation between Gleason scores in needle biopsy and correspondig radical prostatectomy specimens: A Twelve-year review. *Iran J Pathol*. 2016;11:120-6.
- Gonzalgo ML, Bastian PJ, Mangold LA, Trock BJ, Epstein JI, Walsh PC, Partin AW. Relationship between primary Gleason pattern on needle biopsy and clinicopathologic outcomes among men with Gleason score 7 adenocarcinoma of the prostate. *Urology*. 2006;67:115-9.
- Shen BY, Tsui KH, Chang PL, Chuang CK, Hsieh ML, Huang ST, Wang TM, Lee SH, Huang HC, Huang SC. Correlation between the Gleason scores of needle biopsies and radical prostatectomy specimens. *Chang Gung Med J*. 2003;26: 919-24.
- Tavangar SM, Razi A, Mashayekhi R. Correlation between prostate needle biopsy and radical prostatectomy Gleason grading of 111 cases with prostatic adenocarcinoma. *Urol J*. 2004;1:246-9.
- Epstein JI. Prognostic significance of tumor volume in radical prostatectomy and needle biopsy specimens. *J Urol*. 2011;186:790-7.
- Honig SC, Stilmant MM, Klavans MS, Freedlund MC, Siroky MB. The Role of fine needle aspiration biopsy of the prostate in staging adenocarcinoma. *Cancer*. 1992;69:2978-82.
- Kryvenko ON, Diaz M, Meier FA, Ramineni M, Menon M, Gupta NS. Findings in 12-core transrectal ultrasound-guided prostate needle biopsy that predict more advanced cancer at prostatectomy: Analysis of 388 biopsy-prostatectomy pairs. *Am J Clin Pathol*. 2012;137:739-46.
- Lowenthal BM, Liao X, Wen F, Bagherzadeh N, Mahooti S. Discontinuous unilateral involvement of 12 part core biopsies by adenocarcinoma predicts bilateral involvement of subsequent radical prostatectomy. *Pathol Int*. 2016; 66:438-43.