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Transrektal iğne biyopsisinden elde edilen örneklerin 'International Society of Urological Pathology Gleason-scores' değerleri ile karar vermek ne kadar doğru?

Decision-making based on International Society of Urological Pathology Gleason-scores obtained from transrectal needle biopsy of the Prostate: How Accurate Could We Be ?

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Öz

Giriş ve Amaç: Lokalize prostat kanserinin tedavisine ilişkin karar esas olarak transrektal iğne biyopsisinin histopatolojik sonuçlarına bağlıdır. Transrektal iğne biyopsileri ile radikal prostatektomi örneklerinin sonuçları arasındaki uyumun değişken olduğu bildirilmiştir. Bu çalışmada aynı kurumun homojen sonuçlarını incelemeyi amaçladık.

Gereç ve Yöntemler: Radikal prostatektomi (RP) ve transrektal ultrason eşliğinde prostat biyopsisi (TRUS-Bx) işlemlerinin her ikisi de kurumumuzda yapılan 230 hasta çalışmaya dahil edildi. Demografik özellikler, TRUS-Bx öncesi PSA seviyeleri (ng/ml), TRUS-Bx ve RP'den elde edilen örneklerin 'International Society of Urological Pathology (ISUP) Gleason grup dereceleri kaydedildi ve uyum açısından değerlendirildi.

Bulgular:250 hastanın 137'sinde RP örneklerinin ISUP Gleason dereceleri, TRUS-Bx patoloji sonuçları ile uyumluydu (%59,6). İlk biyopside ISUP Gleason derece 2 veya 3 veya 4 veya 5 olduğu bildirilen 125 hastanın 20'sinde (%16) derece düşüşü ve ISUP Gleason derece 1 olduğu bildirilen 147 hastanın 42'sinde (%29) derece yükselişi final patolojilerde izlendi.

Sonuç:RP örneklerinin ISUP Gleason derecelerini öngörmede TRUS-Bx sonuçlarının yetersiz kalabileceği kanısındayız.

Anahtar Kelimeler: Prostat Kanseri, Prostatektomi, Biyopsi

Abstract

Objective: The decision about the treatment of localized prostate cancer (PC) depends mainly on the histopathological results of transrectal needle biopsy. The agreement between the results of transrectal needle biopsies and radical prostatectomy specimens were reported to be varying. In this study, we aimed to investigate one institution's homogenous repertory. A fair agreement could be revealed, and probable strategies to improve the rate of agreement are discussed.

Materials and Methods: 230 eligible patients who underwent radical prostatectomy (RP) and transrectal ultrasound guided prostate biopsy (TRUS-Bx) in our instutition were included in the study. Demographic characteristics, PSA levels (ng/ml) prior to TRUS-Bx, International Society of Urological Pathology (ISUP) Gleason group grades obtained from TRUS-Bx and RP were recorded and evaluated for concordance.

Results:137 of 250 patients RP pathology ISUP Gleason grades were compatible with TRUS-Bx pathology results (%59,6). 20 of 125 (%16) patients who reported to be ISUP Gleason grade 2 or 3 or 4 or 5 in initial biopsy found to be downgraded and 42 of 147 patients (29%), reported to have ISUP Gleason grade 1 upgraded in the final pathology.

Conclusion: In the diagnosis of PC, TRUS-Bx is an insufficient method to show the correct ISUP Gleason grade in radical prostatectomy specimen pathology.

Keywords: Prostate Cancer, Prostatectomy, Biopsi

1. Introduction

PC is the second most frequent cancer diagnosed in men and over one million new cases reported worldwide [1]. Patients with clinically localized low-risk prostate cancer are about one third of newly diagnosed PC cases [2]. Favourable histology in PC is defined as specimens having ISUP Gleason group grade 1. TRUS-Bx is the most appropriate and widely used method for the diagnosis of PC. Biopsy grade of PC is very important in deciding the relevant treatment option such as radical prostatectomy (RP), active surveillance and radiotherapy. When compared to the results obtained from radical prostatectomy specimens, the reported TRUS-Bx results may be found to be irrelevant [3]. In this study, we aimed to investigate one institution's homogenous repertory to reveal the degree of agreement between histological scores.

2. Material and Methods

Patients having a history of both TRUS-Bx and RP in our institution between 2010 and 2018 were screened and included into the study. The patients receiving hormonal treatment that could affect steroidogenesis or medications that could affect Prostate-spesific antigen (PSA) levels were excluded. A total of 230 eligible patients' data were evaluated. All 230 eligible patients were biopsied and operated in our institution and histopathological evaluation of both were performed by the same uropathologist. Demographic characteristics, PSA levels (ng/ml) prior to TRUS-Bx, ISUP Gleason group grades obtained from TRUS-Bx and RP were recorded.

The distribution of the data was checked for normality, and for numeric data (e.g. PSA levels) logarithmic value of the variable was also calculated in order to use in the evaluation of normal distribution. The agreement between the results of TRUS-Bx and RP was evaluated using Cohen's kappa test. For 5 ISUP Gleason grades, the agreement was evaluated (5x5 table), and also another 2x2 table for cumulated ISUP Gleason grades (ISUP Gleason grade-1 vs ISUP Gleason grade-others) was studied. The data were expressed as mean $\pm$ standart deviation or kappa value with confidence intervals (CI). The statistical analyses were performed using SPSS software (v.23).

This study was approved by the Karadeniz Technical University Faculty of Medicine Research Ethics Comittee (Date:03.07.2020, Protocol number: 2020/129).

3. Results

The PSA levels were not found to be normally distributed. Then, logarithmic values of each were calculated and the data were evaluated again, showing normal distribution (Figure-1a and Figure-1b). The agreement between the results of TRUS-Bx and RP in the 5x5 table was found to be 59.6% with a Cohen's kappa value of 0.320 (CI 95% between 0.229 and 0.410 – a fair agreement) as presented in Table-1. For 2x2 table evaluating ISUP Gleason grade-1 vs other ISUP Gleason grades, the agreement was found to be 73.0% with a Cohen's kappa value of 0.448 (CI 95% between 0.333 and 0.562 – a moderate agreement) as presented in Table-2. For ISUP Gleason grade-1 and ISUP Gleason grade-others, descriptive statistical analyses were done for log (PSA) values, showing a mean of 0.91 (CI 95% between 0.87 and 0.95) for ISUP Gleason grade-1, while showing a mean of 1.07 (CI 95% between 1.01 and 1.13) for ISUP Gleason grade-others. The corresponding PSA values of each were calculated as a mean value of 8.13 (with a CI 95% 7.41 to 8.90) for ISUP Gleason grade-1 patients, and a mean value of 11.75 (with a CI 95% 10.23 to 13.49). For a cut-off value of 0.74 for patients reported to be ISUP Gleason grade-2 after TRUS-Bx (corresponding to a PSA value of 5.50 ng/mL) the agreement was calculated as 73.9% with a Cohen's kappa value of 0.463 (CI 95% between 0.350 and 0.575) as presented in Table-3 with an added number of 4 patients agreed to be ISUP Gleason grade-1. There were no statistical differances between the groups according to demographic characteristics.

Figure 1-

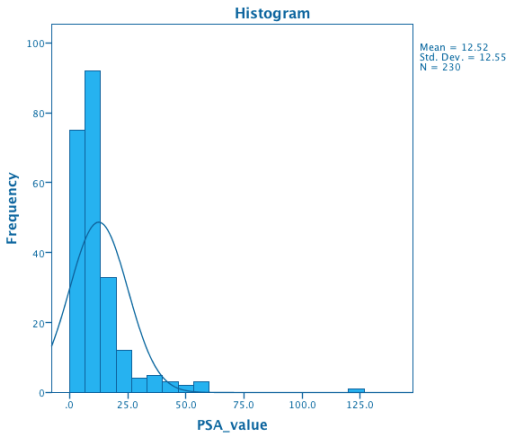

Figure 2

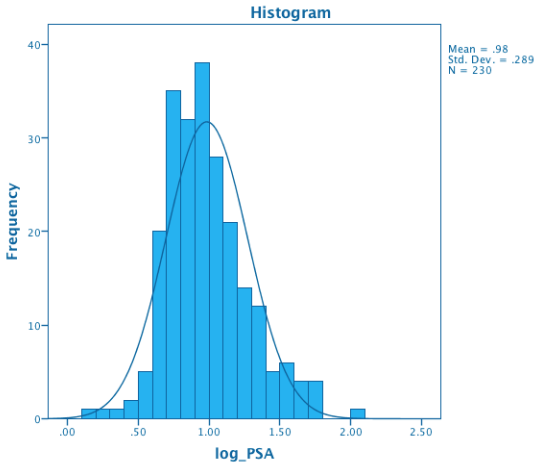

Table-1: The agreement between the results of TRUS-Bx and RP for all ISUP grades

		ISUP grade reported after RP					Total
		1	2	3	4	5	
ISUP grade reported after TRUS-Bx	1	**105**	29	6	6	1	147
	2	13	**20**	5	2	2	42
	3	5	4	**6**	2	5	22
	4	2	3	4	**3**	2	14
	5	0	0	0	2	**3**	5
Total		125	56	21	15	13	230

Agreement 59.6%
Cohen's kappa test : 0.320 (CI 95% between 0.229 and 0.410)

Table-2: The agreement between the results of TRUS-Bx and RP for grouped ISUP grades (ISUP grade-1 vs ISUP grade-others)

		ISUP grade reported after RP		Total
		1	2 or 3 or 4 or 5	
ISUP grade reported after TRUS-Bx	1	**105**	42	147
	2 or 3 or 4 or 5	20	**63**	83
Total		125	105	230

Agreement 73.0%
Cohen's kappa test : 0.448 (CI 95% between 0.333 and 0.562)

Table-3: The agreement between the results of TRUS-Bx and RP for grouped ISUP grades (ISUP grade-1 plus ISUP grade-2 with a PSA value smaller than 5.50 vs others)

		ISUP grade reported after RP		Total
		1	2 or 3 or 4 or 5	
ISUP grade-1 reported after TRUS-Bx or ISUP grade-2 reported after TRUS-Bx but with PSA < 5.50	yes	**109**	44	153
	no	16	**61**	77
Total		125	105	230

Agreement 73.9%
Cohen's kappa test : 0.463 (CI 95% between 0.350 and 0.575)

4. Discussion

PC is one of the significant health problems in men and in cancer-related deaths, taking second place after lung cancer [4]. Definitive diagnosis is made by needle biopsy or surgical specimens of the prostate. TRUS-Bx is the generally used method and it has been a mainstay of urological practice for almost thirty years [5]. Histopathological examination of TRUS-Bx was considered to be crucial, however this method have some limitations such as skipping the diagnosis of cancer and misclassification of cancer grade. Deciding on the treatment alternatives, biopsy grade, PSA value and clinical stage of the cancer are the most important parameters.

When compared to the radical prostatectomy specimens, TRUS-Bx is also associated with upgrading and downgrading of biopsy levels [3]. Upgrading and downgrading can lead to inadequate treatment in some subgroups of patients. Especially, the patients in ISUP grade group-1 are very important because in some subgroups of this group, a treatment alternative such as active surveillance may be recommended to the patients. In this group, if the initial diagnosis in the TRUS-Bx is not sufficient, active surveillance can be recommended to the patients instead of radical prostatectomy. Also in localized prostate cancer, a true Gleason Score (GS) cannot be obtained from non-surgical treatment options such as external radiotherapy, brachytherapy and cryotherapy. Therefore, the GS in needle biopsy, which is one of the parameters used in the treatment decision, becomes more important.

The agreement between ISUP Gleason grades for 5 grade theme was found to be insufficient in our study environment (with a kappa value of 0.320 – a fair agreement). 137 of 230 patients' final pathology ISUP Gleason grades were compatible with initial pathology results. In fact, the discrapencies between biopsy GS's and pathological GS's is not new. There are several studies in the literature showing the compliance problem between TRUS-Bx and RP GS's and it has been reported that concordance ranged from 28% to 68% [6,7]. In our study, the rate of compliance was 59.6% and it was conformable with the literature. The main factors for this

situation are included pathological interpretation, sampling errors, biopsy method, the number of biopsy core sampled and the proportion of cancerous tissue in the biopsy samples. Some of the more common pathology errors in grading limited needle biopsy specimens include overcalling or undercalling Gleason patterns and unable to make the right decision about borderline patterns [8,9,10]. Increasing the number of cores has not been shown to come up with more correct grading and sampling large prostate and anterior tumors involves certain difficulties [11,12]. Ten or twelve core TRUS-Bx is the most commonly used method nevertheless it has low sensitivity for high-grade cancers and one third of the men with low-risk cancers being upgraded at rebiopsies or RP. Clinical studies have shown that magnetic resonance imaging (MRI)-targeted biopsies identify clinical significant cancers more precisely than systemic TRUS-Bx in men however controversy continues over whether MRI-targeted biopsy better predicts final pathology at RP [13,14].

When compared to initial biopsy RP specimens were found to be upgraded in up to 36% with low-grade disease and downgraded in up to 56% with high grade disease [15]. Our results, showing 20 of 125 patients (16%), reported to be ISUP Gleason grade 2 or 3 or 4 or 5, to be found as having ISUP Gleason grade 1 in the RP specimen, may be considered alerting for the mentioned group with favorable histology in the context of probable missing of optimal treatment modalities. The situation necessiates further modalities to decrease the number and ratio of the mentioned group, one of them to be flexible PSA levels. For instance, in our study group, it was found that a selected PSA level of 5.50 ng/mL for ISUP Gleason grade 2 reported group (TRUS-Bx) may add 4 patients to catch the optimal treatment, without a decrease in "agreement" values. On the other hand, 42 of 147 patients (29%), reported to have ISUP Gleason grade 1 upgraded in the final histopathological diagnosis.

5. Limitation

The major limitation of our study was its retrospective nature. Another limitation is the presence of TRUS-Bx only as the method for the inital diagnosis instead of TRUS-Bx combined with targeted biopsies.

6. Conclusion

We concluded that the TRUS-Bx was found to be insufficient in the prediction of final histopathological ISUP Gleason grade diagnosis in patients who underwent RP. Flexible PSA cut-off values for selected group of patients may enhance biopsy agreement, in order to present optimal treatment modalities in PC patients.

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