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How does the presence of the pathologist affect the tissue adequacy, and what are the factors affecting the pathologist in proficiency assessment during percutaneous kidney biopsy?

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Research Article

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ABSTRACT

Background: For optimal histomorphological examination, adequacy of kidney biopsy tissue should be obtained. In this study, the effect of a pathologist informing the radiologist about tissue adequacy during the biopsy procedure on obtaining tissue adequacy was examined. Furthermore, we aimed to determine the criteria that the pathologist considered in determining tissue adequacy and the conditions affecting the decision to increase the number of core biopsies, as these have not been previously examined in the literature.

Methods: Tissues containing less than 10 glomeruli were considered inadequate. In some patients, a pathologist accompanied the radiologist during the procedure. Tissue adequacy ratios and biopsy sample numbers were calculated between the two conditions. In the samples taken with the pathologist, the factors affecting the locality decision of the pathologist (cortex/medulla amount, presence of glomerular pathology(global, segmental, crescentic glomeruli) presence of tubular injury, proteinuria; interstitial inflammation and interstitial fibrosis/tubular atrophy ratios, account of normal glomeruli) were examined.

Results: Giving tissue adequacy information during the biopsy procedure had a positive effect on tissue adequacy. The amount of cortex is one of the qualification criteria for the pathologist. The presence of proteinuria and 50% or more inflammation in tissues with sufficient cortex increased the number of biopsy samples.

Conclusion: Determination of tissue adequacy during kidney biopsy is an important and necessary method. The amount of cortex is one of the important parameters in tissue adequacy.

Keywords: Percutaneous renal biopsy, adequacy, nephropathologist

Perkütan böbrek biyopsisi sırasında patoloğun varlığı doku yeterliliğini nasıl etkiler ve yeterlilik değerlendirmesinde patoloğu etkileyen faktörler nelerdir?

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ÖZ

Amaç: Optimal histomorfolojik inceleme için yeterli böbrek biyopsi dokusu alınmalıdır. Bu çalışmada biyopsi işlemi sırasında radyoloğa doku yeterliliği hakkında bilgi veren bir patoloğun yeterli doku elde etme üzerindeki etkisi incelenmiştir. Ayrıca, literatürde daha önce incelenmediği için patoloğun doku yeterliliğini belirlerken dikkate aldığı kriterleri ve kor biyopsi sayısını artırma kararını etkileyen koşulları belirlemeyi amaçladık.

Yöntemler: 10'dan az glomerül içeren dokular yetersiz kabul edildi. Bazı hastalarda işlem sırasında radyoloğa bir patolog eşlik etti. İki koşul arasında doku yeterlilik oranları ve biyopsi örnek sayıları hesaplandı. Patolog eşliğinde alınan örneklerde, patoloğun yeterlilik kararını etkileyen faktörler (korteks/medulla miktarı, glomerüler patoloji(global, segmental, kresentik glomerül), tübüler hasar, proteinüri varlığı, interstisyel inflamasyon ve interstisyel fibrozis/tübüler atrofi oranları, normal glomerül sayısı) incelendi.

Bulgular: Biyopsi işlemi sırasında, dokuların yeterli olup olmadığı bilgisinin verilmesi doku yeterliliğine olumlu etki yaptı. Korteks miktarı patolog için yeterlilik kriterlerindendir. Yeterli kortekse sahip dokularda proteinüri varlığı, %50 ve üzeri inflamasyon varlığı biyopsi örnek sayısını artırmıştır.

Sonuç: Böbrek biyopsi işlemi sırasında doku yeterliliğinin belirlenmesi önemli ve gerekli bir yöntemdir. Doku yeterliliğinde korteks miktarı önemli parametrelerdendir.

Anahtar sözcükler: Perkütan böbrek biyopsisi, yeterlilik, nefropatolog

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Introduction

Histomorphological examination of the kidney biopsy specimen provides an understanding of the pathogenesis of the diseases. In the 1970s, histomorphological findings were accepted as an important determinant of prognosis and treatment [1]. Kidney tissue can be obtained by transjugular, transurethral, and laparoscopic methods, but the most common method preferred today is percutaneous kidney biopsy (PCB) [2]. Proteinuria, hematuria, renal involvement of systemic diseases, and unexplained renal failure are the most common biopsy indications [3]. Studies have reported that kidney biopsy may cause minor and major complications [4]. PCB has a low complication rate and is a safe, gold-standard method[5]. Today, PCB is mostly performed by nephrologists and interventional radiologists [6]. Devices with 14 gauge (G), 16G, and 18G needles are most commonly used [7]. Adequate tissue supply is necessary for the optimal histomorphological examination. There is no clear consensus on the amount and quality of adequate tissue, but taking at least 2 needle biopsies from patients 8-10 is recommended. The aim of this study is to determine the effect of the presence of the pathologist on adequate tissue supply during the biopsy procedure and to examine the factors affecting the pathologist's tissue adequacy assessment and the decision to take more than two biopsy samples.

MATERIALS AND METHODS

The study included 190 patients who underwent nonneoplastic native and transplant kidney biopsies between July 2017 and February 2020. Information on patients was obtained from final approved pathology reports. All biopsies were performed by an experienced radiologist in the interventional radiology unit under standard sterile conditions. General anesthesia or sedation was not applied to any patient. Prilocaine hydrochloride (citanest; zenica medical, paris, france) was used as local anesthetic. Local anesthesia was applied to the skin first and then to the subcutaneous tissues in the planned transition line. After local anesthesia, a small incision was made in the skin, a 17G coaxial needle was passed through the skin-subcutaneous soft tissues, and the kidney was placed at a tangential angle from the lower pole cortex. The inner needle (style) was removed, an automatic biopsy gun with an 18G needle was inserted into the cannula, and biopsy samples were taken. In the case of only the radiologist, 2 biopsy samples were taken, and in the presence of the pathologist, at least 2 and at most 4 biopsy samples were taken according to the tissue adequacy status.

The pathologist used a stereo microscope (Olympus SZ61, Japan) to detect tissue adequacy. The pathologist provided information about tissue adequacy in approximately 10-15 seconds for each biopsy sample. If 2 biopsy samples were considered sufficient, the procedure was terminated. If there was insufficient tissue vision despite 2 biopsy samples, a 3rd or 4th biopsy sample was taken. After the PCB procedure, kidney biopsy samples were delivered to the pathology laboratory within 5-10 minutes. In the final histomorphological examination, the presence of 10 or more glomeruli was considered as adequate tissue. The cases with and without the pathologist accompanying the biopsy procedure were divided into two groups. Tissue adequacy status and biopsy sample numbers were examined between these two groups. In addition, biopsy sample numbers were examined between transplant and native biopsies. In the cases accompanied by the pathologist, the cases with 2 biopsy samples were divided into one group, and the cases with 3+4 biopsy samples were divided into the second group. Between these two groups, the presence of glomerular pathology (global sclerotic glomeruli+ segmental sclerotic glomeruli+cresentic glomeruli), normal glomeruli count, inflammation, interstitial fibrosis/tubular atrophy (IF/TA) ratios, presence of tubular injury and proteinuria were evaluated.

Ethics committee approval of the study was obtained from the ethics committee of Health Sciences University Gaziyaşargil Training and Research Hospital (No: 25.09.2020-586).

Statistical analysis

The population of this retrospective cohort type study consists of 190 patients who underwent non-neoplastic natural or transplant kidney biopsy in the Department of Radiology, Health Sciences University Diyarbakır Gazi Yaşargil Training and Research Hospital between 01.01.2017 and 29.02 2020. Sample selection was not made in the study, and all patients who were treated on the specified dates were included in the study. The dependent variable of the study is glomerular adequacy required for histopathological diagnosis (presence of 10 glomeruli is considered sufficient). Independent variables, number of cores (2 cores and 3+4 cores were categorized into 2 groups by classification together), descriptive information of the patients, presence of glomerular pathology (present/absent); the presence of tubular damage (yes/absent); presence of proteinuria (yes/absent); interstitial inflammation (0-24.25-49, 50 and above) and interstitial fibrosis/tubular atrophy (0-24.25-49, 50 and above). Count data in the study are represented as mean ± standard deviation (SD), 95% confidence intervals (95% CI), percentages, or medians with interquartile ranges (IQR), as appropriate. Distribution normality was analyzed using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Proportional differences were tested using Chi-square/exact tests, as appropriate. Chi-square/exact tests were applied to compare the nominal data. In analyzing independent risk factors predicting an increased number of biopsies, reasonable factors were included in the conditional logistic

regression analysis. P-values of <0.05 was accepted as statistically significant. The data of the patients were analyzed with the statistical program SPSS-22 (SPSS INC., Chicago, IL, USA).

Results

Of the 190 total biopsies in this study, 60% (114/190) were native, and 40% (76/190) were transplanted kidney biopsies. A total of 59.5% of the patients were male, and the mean age was 37±14 years in the native kidney group and 34±14 years in the transplant kidney group.

Table 1 reveals that the biopsy adequacy rate is 98.4% in cases in which adequacy information was provided by the pathologist and 81.5% in cases in which the biopsies were taken only by the radiologist. The rate of adequate biopsy material was found to be higher in cases accompanied by the pathologist than cases without it, and this difference was found to be statistically significant using a Chi-square test (p<0.001).

In all cases in which no pathologist was present during the kidney biopsy procedure, 2 core biopsies were performed. For two patients whose biopsies were accompanied by a pathologist, 1 core biopsy was performed. These patients did not allow the second biopsy sample to be taken due to anxiety they experienced during the procedure. These two available biopsy specimens were reported as inadequate for optimal evaluation. In other cases, the most common number of biopsy cores was 3 (43.2%), followed by 2 (41.6%; Table 2). There is a statistically significant difference between the biopsy procedures performed only by the radiologist and the tissue adequacy ratio in cases accompanied by the pathologist(p<0.001) (Table 2).

Among patients whose biopsies were performed with a pathologist present, while the rate of patients with more than 2 cores taken was 36.8% in patients who underwent transplant biopsy, this rate was 67.1% in patients who underwent native biopsy (Table 3). This difference is statistically significant (Pearson Chi-square test, p=0.002).

In group 2, biopsies from 25 patients (17 patients with 3 core biopsies, 8 patients with 4 core biopsies) either contained less than 0.5 cm of cortex or completely represented the medulla. Two of the cases accompanied by the pathologist consisted of 1 core. In the other 98 patients whose biopsies were accompanied by a pathologist, extracortical factors(presence of glomerular pathology (global sclerotic glomeruli number, segmental sclerotic glomeruli number, crescentic glomerular number, normal glomerular number), rate of inflammation, IF/TA ratio, presence of tubular injury, presence of proteinuria) affecting the pathologist's decision to increase the number of core biopsies were examined (Table 4).

When the number of core biopsies was compared with inflammation and proteinuria, it was seen that there was a statistically significant relationship between 2 core and 3+4 core biopsy (p= 0.035- 0.004). The current situation was compared for glomerular pathology, presence of tubular injury, normal glomeruli count, and IF/TA ratio an,d no significant difference was found(Table 5).

Table 1: Tissue adequacy status in the presence and absence of a pathologist during the biopsy procedure.

			Tissue adequacy		Total	P value
			Inadequate	Adequate		
Pathologist	Absent	Count	12	53	65	< 0.001
		% within patient evaluation	18.5%	81.5%	100.0%	
		% within tissue adequacy	85.7%	30.1%	34.2%	
	Present	Count	2	123	125	
		% within patient evaluation	1.6%	98.4%	100.0%	
		% within tissue adequacy	14.3%	69.9%	65.8%	
Total		Count	14	176	190	
		% within patient evaluation	7.4%	92.6%	100.0%	
		% within tissue adequacy	100.0%	100.0%	100.0%	

Table 2: Patient distribution of biopsy cores in the presence and absence of a pathologist during the biopsy procedure.

			Number of core biopsies				Total	
			1	2	3	4		p-value
Pathologist	Present	Count	2	52	54	17	125	< 0.001
		% within method of taking biopsy	1.6%	41.6%	43.2%	13.6%	100.0%	
		% within the number of core biopsies	100.0 %	44.4%	100.0%	100.0%	65.8%	
	Absent	Count	0	65	0	0	65	
		% within method of taking biopsy	0.0%	100.0%	0.0%	0.0%	100.0%	
		% within the number of core biopsies	0.0%	55.6%	0.0%	0.0%	34.2%	
Total		Count	2	117	54	17	190	
		% within method of taking biopsy	1.1%	61.6%	28.4%	8.9%	100.0%	
		% within the number of core biopsies	100.0 %	100.0%	100.0%	100.0%	100.0%	

Table 3: Comparison of the number of core biopsies in transplant and native biopsies in the presence of pathologist.

			The number of core biopsy		Total	
			2 (group 1)	3+4(group 2)		p-value
Biopsy type	Trans	Count	24	14	38	p= 0.002
		% within biopsy type	63.2%	36.8%	100.0%	
		% within the number of core biopsies	46.2%	19.7%	30.9%	
	Native	Count	28	57	85	
		% within biopsy type	32.9%	67.1%	100.0%	
		% within the number of core biopsies	53.8%	80.3%	69.1%	
Total		Count	52	71	123	
		% within biopsy type	42.3%	57.7%	100.0%	
		% within the number of core biopsies	100.0%	100.0%	100.0%	

Table 4: Comparison of glomerular pathologies with the number of cores

	Mean	Std Deviation	Percentiles 25-75
Global sclerotic glomeruli			
2	4.17	5.16	0- 5.75
3+4	7.63	11.15	1.64-11.15
Segmental sclerotic glomeruli			
2	1.71	3.11	0.0- 3.0
3+4	3.48	5.01	0.74-5.01
Crescentic glomerulus			
2	0.23	1.30	0-0
3+4	0.22	1.47	0.21-1.47
Normal glomeruli			
2	23.77	10.79	16.25-30.00
3+4	27.35	15.72	2.31-15.72

Table 5: Comparison of the variables with the number of core biopsies

	2 Cor	3+4 Cor	Total	p-value
Inflamation				
0-24	36	32	68	0.035
25-49	11	3	14	
≥ 50	5	11	16	
IF/TA				
0-24	43	36	79	0.655
25-49	6	5	11	
≥ 50	3	5	8	
Tubular injury				
Yes	50	45	95	0.632
No	2	1	3	
Proteinuria				
Yes	32	40	72	0.004
No	20	6	26	
Glomerular pathology				
Yes	39	41	80	0.71
No	13	5	18	

IF/TA: Interstitial fibrosis/tubular atrophy.

Discussion

In this study, the pathologist's determination of tissue adequacy during the biopsy process was revealed to positively contribute to obtaining adequate kidney tissue for histomorphological evaluation. The study also identified the influence of several factors on the pathologist's decision to increase the number of core biopsies.

Histological findings of the kidney provide the opportunity to diagnose kidney diseases; reveal pathological processes; and determine the severity and distribution of kidney damage, the amount of chronicity, reversible conditions, and treatment protocol. The importance of renal histomorphology is increasing as new markers emerge that enable us to better understand the pathogenesis of the disease. In the early days, tissue recovery for histomorphological evaluation was performed by surgeons by taking an open biopsy sample; today, the percutaneous procedure is more commonly performed by interventional radiologists, urologists, nephrologists, and even rheumatologists. Many different methods and materials have been used, all of which aimed to provide adequate kidney tissue for histomorphological examination and to minimize the complications that may occur after sampling. If the obtained biopsy sample is not adequate for diagnosis, it will not be possible for nephrologists to determine an appropriate and effective treatment in a timely manner. In addition, taking another biopsy may increase the risk of complications in the patient. Because it is difficult to persuade patients to undergo an invasive kidney biopsy, and some patients may have come from a long distance and have a low socioeconomic level, obtaining a second biopsy from the patient may not be possible. For this reason, it is essential to determine tissue adequacy during the procedure.

In the literature, studies revealing the adequacy rates of kidney biopsies performed in many countries and centers have been published. In some of these studies, the biopsy methods of nephrologists and radiologists who performed biopsy were compared in patients who underwent a native or transplant biopsy [11-14]. In our literature review, we came across a study that mentions the positive contribution of tissue adequacy assessment during biopsy [15]. To our knowledge, our study is the first to examine the factors that affect the pathologist's decision to increase the number of core biopsies (kidney histomorphological findings, the presence of proteinuria), as well as to reveal the positive effect of providing adequacy information during the biopsy procedure.

Tissue adequacy rates differ across literature studies. Regardless of the biopsy procedure used, studies have reported that enough kidney tissue was sampled in 80%–100% of the cases [8,16]. In a recent study [17], this rate was 99%. In another study determining tissue adequacy in transplant biopsies, it was reported that enough tissue was obtained in 2/3 of the cases [18]. Similarly, in another study, the rate of tissue inadequacy was reported to be 25%–30% [19]. In a study in which transplant and native biopsies were evaluated together, it was reported that adequate tissue was obtained in 80.45% of the cases [20]. In a study conducted in 2019, it was reported that the rate of patients with adequate biopsy tissue was 81.2%, the rate of patients sampled at the border for histomorphology was 15.1%, and the rate of patients with inadequate kidney tissue was 3.7% [21]. In another study in which 10 or more glomeruli was considered adequate tissue, the adequacy rate was reported to be 87.2% [22]. We think that these differences may be due to the different criteria for adequacy, the experience of the physician performing the biopsy, the patients' compliance, the differences in techniques and materials used, and the number of cases included in the studies. In addition, we believe that the adequacy criteria for Banff classification in transplant cases may have increased the rate of inadequacy. In our study, when the patients who underwent the transplant and native biopsies accompanied by a pathologist were compared, the percentage of patients who underwent 2 core biopsies was 63.2% among those who underwent a transplant biopsy. At the same time, this rate was 32.9% in patients who had a native biopsy. The difference was statistically significant (p=0.002). We think that this may be due to different renal localizations. In addition, in our study, in which 190 patients were included, the adequate tissue rate was 81.5% in the 65 cases taken only by the radiologist, and the adequate tissue rate was 98.4% in the 125 cases in which the pathologist informed the radiologist during the kidney biopsy procedure. Our study also determined that providing adequate information during the biopsy contributed positively to the supply of adequate tissue for optimal histomorphological evaluation.

While adequate tissue supply is important for optimal histomorphological evaluation in patients with renal biopsy indication, how much of the removed tissue should represent the cortex versus the medulla and how many glomeruli and arteries should be in biopsy samples is not agreed upon. In addition to studies reporting that 1 glomerulus is adequate for the diagnosis of amyloidosis or membranous glomerulonephritis [8,9], there are also studies suggesting that at least 25 glomeruli should be present for the exclusion of focal diseases [9,21,22]. Some researchers think that at least 2 core kidney biopsies should be taken [8-10], as even if the disease can be diagnosed with

1 glomerulus, more kidney tissue is needed to reveal the spread and whether other glomerular pathologies are present and to examine signs of chronicity in the tubulointerstitial compartment and vascular structures. At our center, a minimum of 2 and a maximum of 4 core kidney biopsies are taken. In our study, only 1 core kidney biopsy was taken in two patients. These two patients chose not to have a second core biopsy to be taken of their own accord. Two core biopsies were performed in all cases where the pathologist was absent. Among biopsies performed with a pathologist present, the most common number of core biopsies taken was 3 (43.2%), followed by 2 (41.6%) and 4 (13.6%).

In 25 of the 125 cases in which the pathologist participated in the biopsy procedure and decided to take more than 2 core biopsies, it was determined that there was not adequate cortex in the biopsy samples or that the samples represented only the medulla. Thus, the tissue inadequacy rate for these cases was 20%. The tissue inadequacy rate was 18.5% in cases not accompanied by a pathologist. The fact that these two inadequacy rates are close to each other suggests that the pathologist takes into account the amount of cortex in defining tissue adequacy. In our study, many parameters (glomerular pathology, tubular injury, presence of proteinuria, IF/TA, inflammation percentages, normal glomeruli counts) were compared between the number of core biopsies in 98 cases accompanied by the pathologist. There is a statistically significant difference between 2-core and 3+4 core biopsy cases with inflammation over 50% and the presence of proteinuria. Although global and segmental sclerosis were observed more frequently in cases with 3+4 core biopsies, there was no statistically significant difference between cases with 2 core biopsies. In addition, there is no statistical significance between the number of cores, the presence of tubular injury, the number of normal glomeruli, and the percentage of IF/TA (Table 5).

A limitation of our study is that renal cortex length was not examined.

Providing tissue adequacy information during the biopsy procedure helps ensure that the appropriate amount of tissue is taken. This allows the nephropathologist to write a detailed report containing prognostic information and disease diagnosis for the nephrologist who will treat the patient.

Conclusion

It is necessary to increase the active participation of pathologists in the biopsy procedure and to improve the cooperation of radiologists with nephrologists. Our study revealed that the amount of cortical tissue is important in the pathologist's decision of adequacy during the biopsy procedure. In addition, inflammation over 50% and the presence of proteinuria affect the pathologist's decision to increase the number of cores.

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