

Shear Wave Sonoelastography Findings of Testicles in Chronic Kidney Disease Patients Who Undergo Hemodialysis

Hemodiyalize Giren Son Dönem Böbrek Hastalarında Testis Parankimi Shear-Wave Elastosonografi Bulguları

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ABSTRACT

Objective: Chronic kidney disease (CKD) is known to cause significant deterioration in the function of the testicles and sexual dysfunction in male patients who undergo hemodialysis. The aim of this study was to show the changes in the testicles that occur as a result of hypogonadism secondary to CKD and to analyze the elasticity of the parenchyma by shear wave sonoelastography.

Materials and Methods: In our study we included 28 male patients who undergo dialysis three times per week and 25 healthy volunteers. Firstly, B-mode ultrasonographic evaluation was performed in both testicles for structural analysis and to detect the presence of focal lesions. Afterward, the stiffness of the parenchyma was measured in kilopascals by shear wave sonoelastography.

Results: The CKD group had lower right, left, and mean testicular volumes ($p<0.001$). The CKD group also displayed greater right, left, and mean testicular parenchymal stiffness ($p<0.001$).

Conclusion: CKD patients who undergo hemodialysis demonstrated significant changes in testicular size and stiffness in comparison to healthy volunteers.

Keywords: Elastography, hemodialysis, renal failure, testis, ultrasonography

ÖZ

Amaç: Kronik Böbrek Hastalığı'nın (KBH) testis fonksiyonlarında belirgin ölçüde bozulmaya yol açtığı ve hemodiyalize giren erkek hastalarda cinsel işlev bozukluğunda belirgin bozulmaya neden olduğu bilinmektedir. Çalışmanın amacı KBH'na sekonder olarak gelişen hipogonadizm sonucu testislerde oluşan değişiklikleri ve shear-wave elastosonografi (SWE) ile testis parankiminde oluşan doku elastikiyet kaybını göstermektir.

Gereç ve Yöntem: Çalışmamızda haftada 3 defa hemodiyalize giren 28 erkek hasta ve sağlıklı 25 gönüllü karşılaştırıldı. Önce B-mode ile her iki testis yapısal anormallik ve fokal lezyon varlığı açısından değerlendirildi. Ardından SWE ile testis parankim sertliği kiloPascal olarak ölçüldü.

Bulgular: Kontrol grubuna göre KBH grubunun sağ, sol ve ortalama testis volümü istatistiksel anlamlı olarak daha düşüktü ($p<0,001$). Kontrol grubuna göre KBH grubunun sağ, sol ve ortalama doku sertliği istatistiksel anlamlı olarak daha yüksek bulundu ($p<0,001$).

Sonuç: Hemodiyalize giren KBH'li hastalar sağlıklı gönüllülere kıyasla testis boyut ve yapısında önemli değişiklikler olduğunu göstermektedir.

Anahtar Kelimeler: Elastografi, hemodiyaliz, böbrek yetmezliği, testis, ultrason

Introduction

Chronic kidney disease (CKD) is defined as a decrease in the glomerular filtration rate, which causes electrolyte imbalance and progressive deterioration of metabolic and endocrine functions [1]. The relationship between CKD and hyperparathyroidism, infertility, and sexual dysfunction has not been clearly defined, and this situation affects the general health status of patients as well as their social and economic status [2]. CKD has been shown to cause a significant decrease in testicular function involving steroidogenesis and spermatogenesis, thus leading to Leydig cell dysfunction in male patients undergoing hemodialysis [3]. It has been shown that testosterone levels are lower in patients with CKD, whereas levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), estrogen, and prolactin are higher [4].

Ultrasonography (US) is the method of choice for the evaluation of testis pathologies and is widely used [5]. Although US is highly sensitive for testicular pathologies, it is not sufficient for



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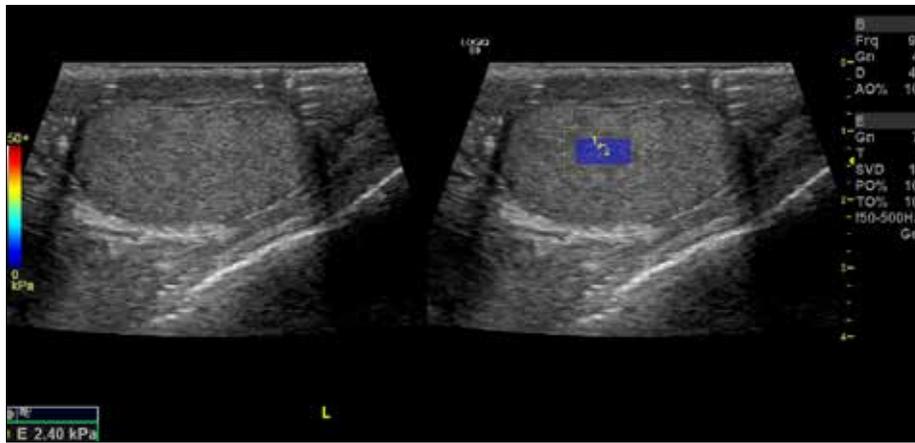


Figure 1. A region of interest (ROI) was placed in the central area of the testis and the tissue elasticity was measured automatically in kilopascals (2.40 kPa) in a 62-year-old male patient.

Table 1. Demographic and clinical characteristics of control and CKD groups			
	Control (n=25)	CKD (n=28)	p-value
Age (years)	44.0±8.6	50.4±15.6	0.071 [†]
Duration of hemodialysis	-	3 years (10 days-20 years)	-
Volumes of testes (mm ³)			
Right	16.2±3.3	9.4±2.7	<0.001 [†]
Left	14.6±3.6	9.5±3.4	<0.001 [†]
Mean	15.4±3.3	9.5±2.9	<0.001 [†]
Elastography (kPa)			
Right	1.7 (0.9-2.7)	2.0 (1.0-4.8)	<0.001 [‡]
Left	1.5 (0.9-3.0)	2.1 (1.0-5.7)	<0.001 [‡]
Mean	1.5 (1.0-2.4)	2.2 (1.1-5.3)	<0.001 [‡]

[†]Student's t-test, [‡]Mann-Whitney U-test.
CKD: chronic kidney disease

Table 2. Degrees of association between duration of hemodialysis and clinical measurements in CKD group		
	Coefficient of correlation	p-value [†]
Volumes of testes		
Right	-0.213	0.276
Left	-0.136	0.489
Mean	-0.158	0.423
Elastography		
Right	-0.088	0.657
Left	-0.142	0.472
Mean	-0.084	0.670

[†]Spearman's correlation test.
CKD: chronic kidney disease

a definitive diagnosis [6]. Sonoelastography (SE) is a new noninvasive diagnostic method that is used to measure the elasticity of biological tissues [7]. It has been shown to be efficient in the evaluation of nodules in the breast, prostate, thyroid, and lymph nodes [8-13]. The use of SE has also started for the discrimination of malignancy in testis lesions [11, 12, 14]. Preliminary research has revealed that the values of elastic-

ity of the testicles are related to their volume and functional capacity [15].

Shear wave sonoelastography (SWSE) sends low-frequency and low-speed acoustic waves perpendicularly to the tissue and measures the elasticity of the tissue quantitatively in kilopascals without applying pressure [16, 17]. The advantage of SE is its ability to make measure-

ments without the need for comparison with other tissues. In this technique, the velocity of shear waves generated by ultrasound pulses that are emitted perpendicularly to the tissue is measured and the elasticity characteristics of the tissue are determined. The quantitative measurement units are kilopascals or centimeters per second [18, 19]. The advantages of this method are the lack of requirement for manual compression and its quantitative measurements [20]. The limited size and shape (restricted to a circle or box) of the region of interest (ROI) are its main limitations [19].

In this study we aimed to demonstrate changes in testicular structure and elasticity due to hypogonadism in patients with CKD using SWSE.

Materials and Methods

After the approval of the ethics committee, 28 male patients (mean age 50, range 28-35) who undergo hemodialysis three times per week and 25 healthy male volunteers (mean age 44, range 20-56) were included in this prospective study. The mean duration of hemodialysis was 3 years (range 10 days-20 years) in the hemodialysis group. Patients with known testicular disease, structural anomalies, or testicular operation were excluded from the study. Informed consent was obtained from all patients included in the study.

A Logiq E9 (GE Healthcare) SE machine was used. Measurements were conducted by a radiologist with 10 years of experience. All measurements were repeated three times and the average value was used. Firstly, both testicles were examined for structural anomalies and the presence of focal lesions by B-mode sonography. Later, the testicular volume was measured. Afterward, an ROI was placed in the central area of the testis and the tissue elasticity was measured automatically in kilopascals (Figure 1).

Statistical analysis

Data analysis was performed using Statistical Package for the Social Sciences for Windows version 11.5 (SPSS Inc.; Chicago, IL, United States). Whether the distributions of continuous variables were normal or not was determined by the Kolmogorov-Smirnov test. Data were shown as the mean±standard deviation or median (minimum-maximum), where applicable. The mean differences between the control and CKD groups were compared by Student's t-test, and the Mann-Whitney U test was applied for comparison of the medians. The degrees of association between continuous variables were determined by Spearman's rank correlation analysis. A p-value of less than 0.05 was considered to be statistically significant.

Table 3. Degrees of association between clinical measurements within control group

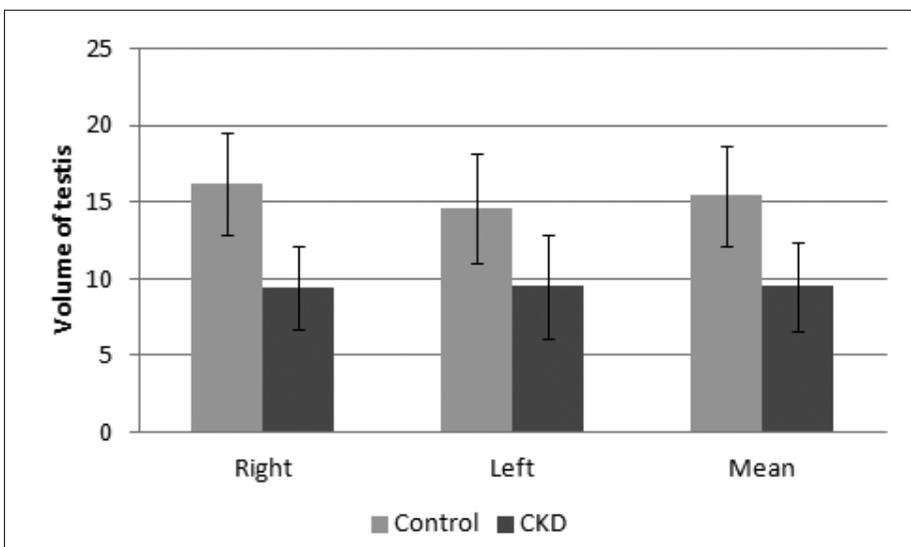
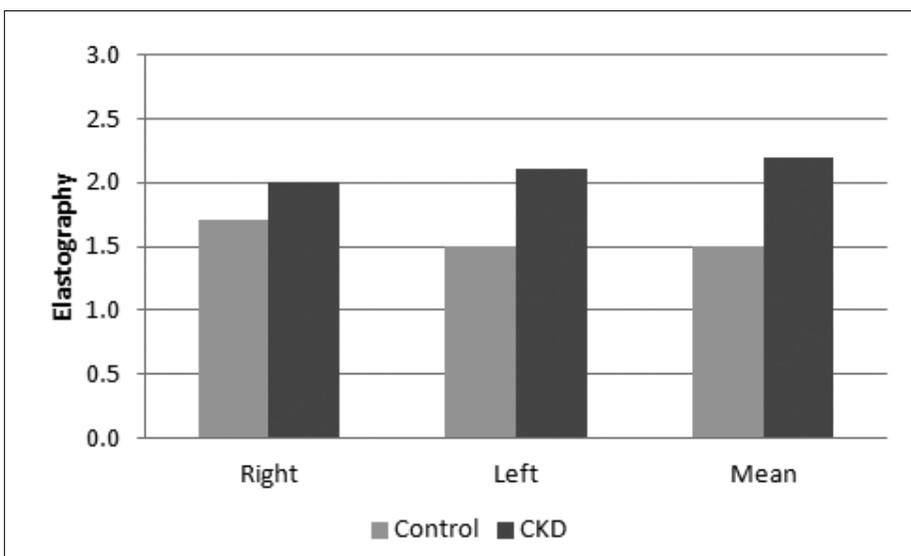
	Coefficient of correlation	p-value [†]
Right testis volume-right elastography	-0.184	0.378
Left testis volume-left elastography	0.003	0.990
Mean testis volume-mean elastography	-0.023	0.915

†Spearman's correlation test.

Table 4. Degrees of association between clinical measurements within CKD group

	Coefficient of correlation	p-value [†]
Right testis volume-right elastography	0.064	0.745
Left testis volume-left elastography	0.095	0.632
Mean testis volume-mean elastography	0.048	0.808

†Spearman's correlation test.

**Figure 2.** Analysis of testis volume in patients with chronic kidney disease (CKD) and the control group.**Figure 3.** Analysis of testis elastographic stiffness in patients with CKD and the control group.

Results

The control and CKD groups had similar mean ages ($p=0.071$). The CKD group had statistically significantly lower right, left, and mean testicular volumes in comparison to the control group ($p<0.001$). The CKD group had statistically significantly stiffer testicular tissue in comparison to the control group ($p<0.001$) (Table 1).

Among the CKD group, testis volume and tissue stiffness did not display a statistically significant correlation with the duration of hemodialysis ($p>0.05$) (Table 2).

Within the control group, no correlation was found between testis volume and tissue stiffness ($p>0.05$) (Table 3).

Among the CKD group, there was no correlation between testis volume and stiffness of the testis ($p>0.05$) (Table 4).

Discussion

It has been shown that CKD and hemodialysis have harmful effects on the hypothalamus-hypophysis-testicle axis [21]. Oxidative stress is also known to cause male infertility via peroxidative injury to the sperm and testes [22, 23]. Hypogonadism is a very common finding in CKD with a reported incidence of 50-75% [24]. Because testosterone is an efficient anabolic hormone, its deficiency causes not only problems related to libido but also several important cardiometabolic side effects. These side effects include deterioration in cognitive functions, decrease in muscle mass, endothelial dysfunction, cardiovascular events, and an increase in the risk of death [25-28]. In a study conducted on 1822 male patients, Haring et al. [28] demonstrated that low levels of total testosterone significantly increased mortality.

US is the primary method used for investigation of the scrotum [29]. Besides its ease of access, it is also tolerable for patients. Grayscale US is usually used for measuring testis volumes and determination of parenchymal echogenicity [30]. Although a slight change in the echogenicity of a testis can represent a decrease in testicular function, it is not easy to detect [15]. Sakamoto et al. [31] demonstrated that there is a strong correlation between testicular function and testis volume. It has been shown that there is a significant decrease in testis volume in patients with CKD [32]. In our research, the testis volume was also significantly lower in patients with CKD (Figure 2).

SE helps to demonstrate pathological changes in the testis parenchyma [30]. SE has been utilized

in many studies of focal testicular lesions [33]. SWSE is a noninvasive method that measures the elasticity of soft tissue quantitatively [34]. With this method, a scissoring wave is produced perpendicularly to the axial displacement caused by a US pulse, which is 1000 times more attenuated in comparison to conventional US [28]. With this method, tissue elasticity can be measured. SE is an advantageous method because there is no need for tissue compression and tissue elasticity can be measured quantitatively in kilopascals [35].

In this study using SWSE, parenchymal stiffness was measured in patients with CKD and the control group. A significant difference was detected in testicular parenchymal stiffness between the CKD and control groups, the CKD group having higher stiffness (Figure 3). This finding shows that there was a significant change in the testis parenchyma as well as in stiffness in patients with CKD. The reason can be attributed to fibrosis, which takes place in patients undergoing hemodialysis. In a study by Shiraishi et al. [32] it was demonstrated that interstitial fibrosis developed in biopsy specimens from hemodialysis patients.

Renal transplantation is the best treatment modality in CKD patients undergoing hemodialysis. In various studies it has been shown that dysfunction of the Leydig cells and decreases in serum FSH, LH, and testosterone levels can be reversed after treatment [3]. However, the extent of reversible fibrosis in the testis is unknown. At this point, SE values for the testis can be utilized. There is still a need for controlled randomized trials.

In a study conducted on 120 male patients by Shiraishi et al. [32] both decreases in testis volume and fibrosis were found to be correlated with the duration of hemodialysis. On the other hand, in our research there was no correlation between the testis volume or parenchymal SE values and the duration of hemodialysis, which could be attributed to the limited number of patients, which was a major limitation of our study.

Finally, the parenchymal fibrosis and decrease in testicular volume that occur in long-term hemodialysis patients can be detected by SE, which can also be used in the evaluation of candidates for renal transplantation, as well as their follow up.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Dişkapi Yıldırım Beyazıt Training and Research Hospital Clinical Research Ethical Committee (15.12.2014/ Decision No: 18/10).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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