Evaluation of Kidneys with Renal Doppler Ultrasonography and Ultrasound Elastography in Patients with Type 2 Diabetes Mellitus

Tip 2 Diabetes Mellituslu Hastalarda Böbreklerin Renal Doppler Ultrasonografi ve Ultrason Elastografi ile Değerlendirilmesi

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Abstract

Background: In this study, we aimed to detect diabetic nephropathy at an early stage by comparing the findings of Shear-Wave Elastography and Color Doppler Ultrasonography of both kidney parenchyma of patients with Type 2 Diabetes Mellitus and healthy volunteers.

Materials and Methods: This study included 100 patients diagnosed with Type 2 Diabetes Mellitus and without additional chronic diease (Hypertension etc.) (49 females over 18 years old, 51 males over 18 years old) and 100 healthy volunteers (45 females over 18 years old, 55 males over 18 years old). Shear wave elastography examination and renal artery Resistive Index values were obtained from both kidney parenchyma. All SWE examinations and measurements with Color Doppler were performed using Philips Epiq 7. Measurements were made with a 1-5 MHz convex ultrasonography probe. During the elastography method, shear waves were created by successive pressures applied to the skin tissue with the ultrasound probe. As a result of these processes, values in kPa (kilopascal) were obtained. Resistive Index values were obtained in the examination performed with Color Doppler Ultrasonography.

Results: In the patient group, the elastography values were measured as 7.02±2.15 kPa (kilopascal) in the right kidney parenchyma and 6.90±2.09 kPa in the left. In the control group, the elasticity values were measured as 4.14±0.98 kPa in the right kidney parenchyma and 4.11±0.85 kPa in the left. Both kidney parenchyma elasto values were found to be higher in the patient group compared to the control group (p<0.05). There was no statistically significant difference between the right and left kidney parenchyma elasto values in both groups (p>0.05). The RI (Resistive Index) mean values were determined as 0.59±0.05 in the right kidney and 0.59±0.04 in the left kidney in the patient group and 0.52±0.05 in the right kidney and 0.52±0.05 in the left kidney in the control group. Resistive index values of both kidneys were found to be higher in the patient group compared to the control group (p<0.05). There was no statistically significant difference between the right and left kidney resistive index values in both groups (p>0.05).

Conclusions: The elastography values and the RI values were significantly higher in the patients with Type 2 DM than in the control group. However, there are many studies in the literature on shear-wave elastography results of renal pathologies. We hope that our study will lead to more comprehensive and controlled studies on this subject.

Key Words: Shear wave elastography, kidney, Doppler, Type II Diabetes Mellitus

Öz

Amaç: Bu çalışmada Tip 2 Diabetes Mellitus olan hastalarla sağlıklı gönüllülerin her iki böbrek parankiminin Shear-Wave Elastografi ve Renkli Doppler Ultrasonografi bulguları ile karşılaştırarak diyabetik nefropatiyi erken dönemde saptamayı amaçladık.

Materyal ve Metod: Bu çalışmaya 100 Tip 2 Diabetes Mellitus tanısı alan ve ek kronik hastalığı olmayan (Hipertansiyon vb.) hasta (18 yaş üstü 49 kadın, 18 yaş üstü 51 erkek) ve 100 sağlıklı gönüllü (18 yaş üstü 45 kadın, 18 yaş üstü 55 erkek) dahil edildi. Her iki böbrek parankiminden shear wave elastografi incelemesi ve renal arter Resistive Index değerleri alındı. Bütün SWE ile yapılan incelemeler ve Renkli Doppler ile yapılan ölçümler Philips Epiq 7 cihazı kullanılarak gerçekleştirildi.1-5 MHz konveks ultrasonografi probuyla ölçümler yapıldı. Elastografi yöntemi sırasında kayma dalgaları (shear-wave), ultrason probu ile ardarda cilt dokusuna uygulanan basılar ile oluşturuldu.Bu işlemler sonucunda kPa (kilopaskal) cinsinden değerler elde edildi. Renkli Doppler Ultrasonografi ile yapılan incelemede ise Rezistif İndeks değerleri elde edildi.

Bulgular: Hasta grubunda elastografi değerleri sağ böbrek parankiminde 7,02±2,15 kPa (kilopaskal), solda 6,90±2,09 kPa olarak ölçüldü. Kontrol grubunda elastisite değerleri sağ böbrek parankiminde 4,14±0,98 kPa, solda 4,11±0,85 kPa olarak ölçüldü. Her iki böbrek parankim elasto değerleri hasta grubunda kontrol grubuna kıyasla daha yüksek olduğu saptandı (p<0.05). Her iki grupta da sağ ve sol böbrek parankim elasto değerleri arasında istatiksel olarak anlamlı fark izlenmedi (p>0.05).RI (Rezistif İndeks) ortalama değerleri hasta grubunda sağ böbrekte 0,59±0,05 ve sol böbrekte 0,59±0,04, kontrol grubunda sağ böbrekte 0,52±0,05 ve sol böbrekte 0,52±0,05 olarak belirlendi. Her iki böbrek rezistif indeks değerleri hasta grubunda kontrol grubuna kıyasla daha yüksek olduğu saptandı (p<0.05). Her iki grupta da sağ ve sol böbrek rezistif indeks değerleri arasında istatiksel olarak anlamlı fark izlenmedi (p>0.05).

Sonuç: Tip 2 DM'li hastalarda elastografi değerleri ve RI değerleri kontrol grubuna göre anlamlı olarak yüksekti. Fakat literatürde renal patolojilerin shear-wave elastografi sonuçları ile ilgili birçok çalışma mevcuttur. Yaptığımız çalışmanın bu konu üzerinde daha kapsamlı ve kontrollü çalışmalara yol göstereceğini umut ediyoruz.

Anahtar Kelimeler: Shear wave elastografi, böbrek, Doppler, Tip II Diabetes Mellitus

Introduction

Despite all the preventative measures taken, diabetes mellitus (DM) continues to increase worldwide as a healthcare problem with severe effects on individual health.The most recently published study according to their information, the International Diabetes Federation and WHO will be reached in the 2030s it seems to have already reached its predicted prevalence (1, 2). With diabetes mellitus if glucose intolerance and impaired fasting glucose are also taken into account, almost 25-30 % of the population are affected (2).Acute complications caused by DM include diabetic ketoacidosis, lactic acidosis, hyperglycemic hyperosmolar state and hypoglycemia. Further complications are the negative effects of diabetes in the non-vascular and vascular systems, and thereby in all organ systems, which are proportional to the degree and duration of hyperglycemia in the disease process. By creating organ dysfunction, these changes cause morbidity in diabetic patients and increase mortality rates (3). As a major microvascular complication of diabetes, diabetic nephropathy (DN) is a significant cause of increased morbidity and mortality (4). In the majority of developed countries, DN is a serious public health problem, which is the leading cause of end-stage renal failure and is seen together with increased cardiovascular disease. (5).

Ultrasound elastography is a method that was developed to visualise the degree of soft tissue stiffness. Shear-wave elastography (SWE) is more reliable, objective and repeatable than older methods, like compressive elastography (6). Another property of shear-wave elastography is that it can differentiate local lesions and tissues according to the degree of tissue stiffness (7).

Doppler ultrasound is an ultrasonography technique which determines the direction and rate of blood flow and provides information about vascular structures. Renal Doppler US is an extremely valuable method in identifying renal vascular pathologies. In some cases, even if there is felt to be a need for methods such as CT, MRI, and angiography, renal Doppler US is an extremely reliable first-stage diagnostic method as it is non-invasive, does not require a contrast agent and works on the principle of sound waves (8).

The aim of the current study was to use SWE to obtain quantitative data of kPa units of the degree of stiffness of the parenchyma in both kidneys of patients with Type 2 DM and of the vascular resistance of both kidneys with the RI formula using the colour Doppler US technique, and to compare these data with those of a healthy population to determine early stage renal fibrosis.

Materials and Methods

This prospective study included 100 patients (49 females over 18 years old, 51 males over 18 years old) diagnosed with Type 2 diabetes mellitus and without additional chronic disease (Hypertension,etc.) who were referred to the Radiology Department between January 2019 and June 2019, and as the control group, it consisted of 100 volunteers (45

females over 18 years old, 55 males over 18 years old). Control group consisted of 100 healthy volunteers with similar demographic characteristics without a known disease. Approval for the study was granted by the Local Ethics Committee (decision no:21/12/2018-E.50134). Written informed consent was obtained from all the participants.

No drugs or contrast agents were administered for visualisation during the procedure to both groups. Neither patients nor healthy volunteers were exposed to radiation with the use of this method. The examinations were made with the patient supine and in the lateral decubitus position, and while holding the breath. During the procedure, first B-mode imaging was applied to visualise the kidneys, then the transfer was made to elastography mode synchronised with the B-mode imaging technique. Following the elastography procedure, the Resistive Index values were measured with spectral Doppler ultrasonography examination.

Measurements were taken of the bilateral middle renal cortical parenchyma of the patients diagnosed with Type 2 DM and the healthy control group from SWE examination with B-mode US visualisation. The Resistive Index (RI) values were examined with the spectral Doppler US technique in both groups. All the SWE examinations and measurements taken with colour Doppler were performed on a ultrasound device (Philips Epic 7, Philips Medical System, The Netherlands). The measurements were taken using a 5 MHz convex ultrasonography probe (Figure 1-2).

Figure 1. ROI placed in the middle pole of the right kidney in a patient with Type 2 Diabetes Mellitus and parenchyma measurement of elasticity.

The real-time SWE and colour Doppler US examinations were performed by a single radiologist with 5 years of experience. In each examined case, three measurement was made of the bilateral kidneys of a region of interest (ROI) 15 x 10mm in size in the mid-section of the cortex parenchyma. A standard rectangular ROI was used. As a result of these procedures, values were obtained as kilopascal (kPa) units.

Data obtained in the study were analysed statistically using SPSS vn. 20.0 software. Conformity of the data to normal dist-

ribution was assessed using the Shapiro-Wilk test. The Student's t-test was applied to parameters with normal distribution. The Mann Whitney-U test was applied to parameters with non-normally distributed.Continuous variables were stated as mean ± standard deviation values. The Pearson Chi-square test was applied to categorical data. A value of $p<0.05$ was accepted as statistically significant.

Figure 2. Parenchymal flexibility in a healthy adult can be determined by ROI placed at the mid pole of the right kidney measurement.

Results

Evaluation was made of a total of 200 subjects, as 100 patients and 100 control subjects. The patient group comprised 51% males and 49% females with a mean age of 49.11 (min.40, max. 63) years. The control group comprised 55% males and 45% females with a mean age of 48.38 (min. 38, max. 65) years. As the age and gender values of the two groups were homogenous (Table 1). It was thought that effects on the measured values arising from age or gender-related confounding factors could be eliminated and this can be considered a strength of the study

In the patient group, the mean elastography values were measured as 7.02±2.15 kPa in the right kidney parenchyma and 6.90±2.09 kPa in the left. In the control group, the elasticity mean values were measured as 4.14±0.98 kPa in the right kidney parenchyma and 4.11±0.85 kPa in the left (Table 2). The elastography values of the parenchyma in both kidneys were determined to be statistically significantly higher in the patient group than in the control group ($p<0.05$). In both groups, no statistically significant difference was determined between the elastography values of the right and left kidney parenchyma ($p>0.05$).

The RI mean values were determined as 0.59±0.05 in the right kidney and 0.59±0.04 in the left kidney in the patient group and 0.52±0.05 in the right kidney and 0.52±0.05 in the left kidney in the control group (Table 2). In the results of the current study, the RI values of the patients with Type 2 DM were found to be statistically significantly higher than those of the healthy control group ($p<0.05$). At the same time, in both groups, no significant difference was determined between the RI values of both kidneys ($p>0.05$).

Table 1. Distribution of groups by gender

	Patient (n=100)	Control (n=100)	Total
Gender (%)			
Male	51(48.1%)	55 (51.9%)	106 (53.0%)
Female	49 (52.1%)	45 (47.9%)	94 (47.0%)

Table 2. The descriptive and comperative statistics of the parameters belonging patient and control groups

	Patient (n=100 Mean ± SD	Control (n=100) Mean ± SD	P
Age, years	49.11 ± 6.76	48.38 ± 6.83	-
Right Kidney Elastography (kPa)	7.02 ± 2.15	4.14 ± 0.98	<0.05
Left Kidney Elastography (kPa)	6.90 ± 2.09	4.11 ± 0.85	<0.05
Right Kidney Resistive Indeks	0.59 ± 0.05	0.52 ± 0.05	<0.05
Left Kidney Resistive Indeks	0.59 ± 0.04	0.52 ± 0.05	<0.05

M (Mean), SD (Standart deviation)

Discussion

In our study, elastography values and RI values were significantly higher in patients with Type 2 DM compared to the control group. Thus, it can be said that it is possible to determine kidney fibrosis and to predict the possibility of developing diabetic nephropathy without the need for biopsy with non-invasive SWE and color Doppler US methods. However, more comprehensive and controlled studies are needed on this subject.

DN is a significant health problem as an increasing number of patients develop end-stage renal failure. DN is defined as continuous urine albumin stick positivity or >300 mg albumin excretion in a diabetic patient with no other kidney disease (9). The prevalence of DN in all diabetics has been reported as 4-8%. The incidence of DN seen 20 years after diagnosis in Type 2 DM patients is 25%. Up to 20% of these patients have progressive renal failure within 10 years and progress to end-stage renal failure (10). In chronic renal disease and progression, fibrosis developing in the interstitium and glomerules plays an important role. Renal fibrosis is thought to be one of the main reasons in the pathophysiology and progresson of chronic renal disease (11). Put simply, renal fibrosis can be defined as chronic damage in the kidney becoming a failed

wound healing process (12). Researchers have investigated this topic of the link between renal fibrosis and chronic renal disease. Although it is possible to identify renal fibrosis in the early period with biopsy, the risks engendered by the invasive nature of this procedure make it difficult to use as a diagnostic method. Therefore, the search for non-invasive methods which could show renal fibrosis has become the subject of new studies (13).

Of the non-invasive methods for the determination of renal fibrosis, evaluation of tissue stiffness with US is a method which can be used. The elasticity of tissues with US can be examined with Shear wave elastography (4). Previous studies have determined that together with fibrosis development in the process of chronic renal disease, vascular resistance also increases (14). It is possible to determine renal vascular resistance with the renal artery spectral Doppler US method. Vascular resistance is calculated with the RI formula $[(Vmax-Vmin)/Vmax]$ (5).

No study could be found in literature in which the bilateral kidneys of Type 2 DM patients were evaluated with SWE and the RI vale with the colour Doppler US technique. However, there are several studies that have elastographically evaluated kidneys affected by various diseases, including DM, and normal kidneys.

In a study by Koç et al (15) of 52 patients with Type 2 DM, and 53 patients with no DM, the renal elasticity values measured with shear-wave ultrasonography were determined to be higher in Type 2 DM patients than in those without Type 2. Kamal et al (16) compared renal elasticity values with the shear-wave ultrasonography technique in patients with grade 3-4 chronic kidney disease associated with diabetic kidney disease and in 23 healthy volunteers. Renal elasticity values were measured as 23.72±14.33 kPa in patients with chronic renal disease associated with diabetic kidney disease and as 9.02±2.42 in the healthy control group, and the difference was determined to be statistically significant. In a study by Samir et al (17), 25 patients with chronic renal disease were compared with a control group of 20 healthy subjects. Elasticity values evaluated with shear-wave elastography were determined to be increased in the patients with chronic renal disease.

In the current study, no statistically significant difference was determined between the elastography measurements according to age and gender (p>0.05). In a study by Grass et al of a healthy paediatric age group and young adults, there was no significant relationship between the elastography values and gender, similar to the current study.(18).

Fiorini et al measured the intrarenal RI values in patients with Type 1 and Type 2 DM with diabetic nephropathy, and the RI values of the Type 2 DM patients were determined to be significantly higher than those of the Type 1 DM patients (19). In a study by Tatsuo et al, renal RI values were found to be higher than those of a healthy control group (20). In another study by Toledo et al, the elevated RI values of patients with chronic kidney disease were found to be associated

with increased mortality (21). Yuko et al evaluated the relationship between RI values and the etiology of chronic kidney disease. The study with a control group included a total of 245 subjects, and patients were grouped according to the etiology of chronic kidney disease. Higher RI values were determined in the group with diabetic nephropathy compared to the other groups. This result was thought to be due to increased systemic atherosclerosis in diabetic patients (22). Similar to many previous studies, the RI values in the current study patient group were determined to be significantly higher than those of the control group. These results were initially thought to be related to the predominance of renal fibrosis but they could also be associated with atherosclerosis in diabetic patients. RI values examined with colour Doppler ultrasonography can be considered a parameter of importance in the follow-up of chronic kidney disease, and especially in patients with diabetic nephropathy.

The limitations of our study, the diagnosis of diabetic nephropathy were made only clinically and laboratory. Patients were not performed renal biopsy.

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