DTI SHOWS THE EARLY EFFECTS OF URETERORENOSCOPY AND URETERAL STENT PLACEMENT ON THE OBSTRUCTED KIDNEYS

Original Article

DTI OBSTRÜKTE BÖBREKTE ÜRETERORENOSKOPİ VE ÜRETERAL STENT YERLEŞTİRİLMESİNİN ERKEN ETKİLERİNİ GÖSTERİR

Esin Yencilek

Haydarpasa Numune Education and Training Hospital, Department of Radiology, Istanbul, Turkey

Özgür Kılıçkesmez

Istanbul Education Hospital, Department of Radiology, Istanbul, Turkey

Zeynep Fırat

Yeditepe University Medical School, Department of Radiology, Istanbul, Turkey

Bengi Gürses

Yeditepe University Medical School, Department of Radiology, Istanbul, Turkey

Neslihan Tasdelen

Yeditepe University Medical School, Department of Radiology, Istanbul, Turkey

Hakan Koyuncu

Yeditepe University Medical School, Department of Urology, Istanbul, Turkey

Bilal Eryıldırım

Kartal Lutfi Kırdar Training and Research Hospital, Department of Urology, Istanbul, Turkey

Corresponding Author

Esin YENCİLEK
Haydarpasa Numune Education and Research Hospital, Department of Radiology, Tibbiye Cad. No: 40 Uskudar, Istanbul, Turkey
Tel: 02165423232
Fax: 02163360565
Email: e.yenclek@yahoo.com

ABSTRACT

Introduction: To evaluate the early effects of ureterorenoscopy (URS) and ureteral stent placement (USP) on obstructed kidneys by using Diffusion tensor imaging (DTI) at 3 Tesla magnetic resonance imaging.

Methods: Ten controls and 32 patients with ureteropelvic junction and ureteral stones with partial and complete obstructions treated with URS and USP were included. 19 had partial and 13 complete obstruction. Fourteen were treated with URS and the rest of them with USP. DTI was performed using a 3 Tesla magnet and single shot echo–planar sequence before and 24 hours after the treatment. Regions of interests (ROI) were placed on the corticomedullary junction for the measurement of fractional anisotropy (FA) and apparent diffusion coefficient (ADC). The FA and ADC of the treated kidneys were compared with their pretreatment values.

Results: Initial ADC and FA levels of the obstructed kidneys were lower than non-obstructed kidneys in patient and the control groups. After treatment, ADC and FA values increased. The statistical evaluation showed significant difference regarding ADC and FA among the obstructed versus non-obstructed URS patients and control group (p=0.01 and p=0.04, respectively).

Conclusion: ADC and FA parameters may help to demonstrate ultrastructural recovery in the obstructed kidneys after treatment.

Key words: Diffusion tensor imaging; MRI; Ureterorenoscopy; Ureteral stent; Hydronephrosis

ÖZET

Amaç: Bu çalışmada 3 Tesla Manyetik Rezonans'ta Diffüzyon Tensör Görüntüleme kullanarak obstrükte böbrekte üreterorenoskopi (URS) ve üreteral stent yerleştirilmesinin (USP) erken dönem etkilerini araştırdık.

Materyal ve Metod: 10 sağlıklı ile parsiyel ya da tam obstrüksiyonu olan üreteropelvik bileşke ve üreteral taşı olan 32 hasta çalışmaya alındı. 32 hastanın 19'unda parsiyel 13'ünde komplet obstrüksiyon vardı. Çalışmadaki tüm hastalar urs ve usp ile tedavi edildiler. Obstrüksiyon, 14 hastada URS ile geri kalan 18 hastada ise USP ile tedavi edildi. DTI inceleme 3 Tesla MR'da uyglandı ve "single shot echo–planar sekans" tedaviden önce ve tedaviden 24 saat sonra uygulandı. "Regions of interests" (ROI) fraksiyonel anizotropi (FA) ve "apparent diffusion coefficient" (ADC) ölçümü için kortikomedüller bileşkeye konuldu. Tedavi edilen FA ve ADC değerleri aynı böbreğin böbreğin tedavi öncesi değerleriyle karşılaştırıldı.

Sonuçlar: Obstrükte böbreğin başlangıç ADC değerleri non-obstrükte böbreğin ve kontrol grubundaki böbreklerin ADC değerlerinden düşüktü. Obstrükte böbrekteki ADC düşüklüğü istatistiksel olarak anlamlı idi (p=0.01). Tedavi sonrası obstrükte böbrekte ADC değeri yükseldi ve non-obstrükte ve kontrol gruplarındaki ADC ile karşılaştırılabilir seviyeye geldi. Tedavi sonrası gruplar arasındaki fark istatistiksel anlamsızdı. FA değerleri de ADC'ye benzer şekilde tedavi öncesi ve sonrası farklı idi.

Yorum: DTI'nin bir parametresi olan FA ölçümü obstrükte böbrekteki tedavi sonrası ortaya çıkan ultrastrüktürel iyileşmenin gösterilmesinde faydalı olabilir.

Anahtar kelimeler: Diffüyon Tensör İmaj, MRI; ureterorenoskopi, üreteral stent, hidronefroz

INTRODUCTION

Urinary stone disease is common urologic problem. Unless the obstruction corrected, the functional impairment persists and irreversible renal damage may occure. Therefore, early diagnosis and treatment is important. Before gross pathologic changes, lymphatic dilation, interstitial edema, tubular and glomerular preservation can be seen as microscopic findings [1].

There are different therapeutic approaches for ureteral stones depending on stone size, location and anatomical variations of the urogenital tract [2]. After the diagnosis of such stones, the placement of an internal ureteral stent or nephrostomy tube has been the classic established procedure performed when conservative medical management does not resolve symptoms and for preventing damage to a blocked kidney, until a procedure to remove the stone can be performed [3, 4]. Obviously, when stones are associated with sepsis, the obstruction should be relieved first and the infection dealt before treating the stone. These maneuvers are usually followed by ureterorenoscopy (URS) or shock wave lithotripsy (SWL) for prompt relief of obstruction and colic pain [5].

Until recently evaluation of renal functional status has been studied with intravenous pyelography, scintigraphy, Doppler ultrasound and diffusion-weighted magnetic resonance imaging (DW-MRI) [6, 7]. The need to use noninvasive techniques for accurate morphological and functional study for the assessment and therapeutic planning in kidney diseases increased the research in the diagnostic magnetic resonance imaging (MRI). DW-MRI is a technique that provides information about molecular diffusion, which is also known as Brownian motion. This technique is capable of quantitative assessment of molecular motion in relation to the microstructural organization of the tissue being studied [6]. The apparent diffusion coefficient (ADC) is the main parameter derived from diffusion sequences which reflects the combined effects of capillary perfusion and diffusion of water in the extracellular space. However, DW-MRI measures diffusion of water molecules

only in one direction. In organized tissue structures, such as kidneys containing tubules, collecting ducts and vessels, diffusion has anisotropic features. Diffusion anisotropy can be evaluated with diffusion tensor imaging (DTI), which is capable of detecting anisotropy by analysis of diffusion along at least 6 directions [8].

There are papers evaluating the efficacy of DW-MRI in early hydronephrosis in the literature [7, 9-11]. To the best of our knowledge this is the first study aiming to find out the value of DTI to determine the effects of obstruction on the renal parenchyma and the degree of recovery after treatment non-invasively.

MATERIALS AND METHODS

Study population

A total of 32 patients with ureteropelvic junction and ureteral stones with partial and complete obstructions treated with URS and USP along with 20 kidneys of 10 healthy controls were included in this prospective study. Of the 32 patients 19 had partial and 13 complete obstruction. 14 of the patients were treated with URS and the rest of them with ureteral stent placement (USP) initially. All the patients were evaluated before and after the treatment. Of the study population 21 were male and 11 were female) with a mean age of 34 (range: 24-41 years). The control group was consisted of 6 males and 4 females with a mean age of 31 (range: 21-38 years). DTI was performed before and 24 hours after the treatment. The exclusion criteria were previous renal surgery, diabetes, hypertension or any systemic disease which may involve the kidneys. The study was approved by the local ethics comittee. Informed consent was obtained from each subject prior to the MRI examination. The average duration of the procedure was 14.5 minutes. All the MRI examinations were performed in the fasting state to minimize artifacts.

MRI

MRI examinations were performed using a 3 Tesla scanner (Intera Achieva, Philips, The Netherlands) equipped with high-performance gradients of a maximum strength of 80 mT/m and a slew rate of 200 mT/m/ms with a six-channel phased array SENSE Torso coil. In all the subjects, T2-weighted turbo spin echo (TSE) (slice thickness: 3mm, TR: 2729 ms; TE: 68 ms; matrix: 300×432, acquisition time: 3.44 minutes) and DTI using single shot echo planar imaging (ss-EPI) (slice thickness: 3mm, TR: 10000 ms; TE: 60 ms; matrix: 100×132; voxel size: 1.67×1.65×3.00 mm, acquisition time: 6.12 minutes, b: 700 s/mm2 (with sixteen diffusion directions information) sequences were obtained in the coronal plane with breath-holding. Field of view (FOV), slice thickness and slice gap values were identical for both sequences for anatomical correlation during analysis of DTI data. Parallel imaging method was used with a SENSE factor of 2.

DTI data analysis

Initially, DTI images were evaluated by one of the authors to decide whether the image quality was satisfactory for analysis. In 2 subjects, there were intense motion artifacts, and they were excluded from the study. For the remaining 32 subjects, and 10 healthy controls all the acquired datasets were transferred to the manufacturer supplied software Extended MR Workspace 2.6.3.3 (Philips Medical Systems, Netherland) for analysis. fractional anisotropy (FA) maps, ADC maps and color maps were acquired. The T2-weighted images were reviewed initially for anatomical guidance to discriminate the the midcoronal and adjacent slices.

Three separate free hand regions of interest (ROIs) were placed on the corticomedullary junction of whole kidney as large as possible on the midcoronal and adjacent 2 paracoronal slices to increase the signal to noise ratio by two experienced abdominal

radiologists in aggreement. Statistical analysis was performed with One Way ANNOVA for multiple groups and student's t test for 2 groups comparision. any p values smaller than 0.05 were regarded as statistically significant. Tractography was performed with streamlines fiber tracking algorithm. Anisotropy and angular thresholds were set in the range of 0.12–0.20 and 20-25°, minimum FA 0.15, minumum fiber length 10 mm respectively. The orientation of the kidney fibers in cortex and medulla were evaluated using tractography technique. Red color represented right-left; blue color craniocaudal and green color antero-posterior orientation of diffusion. Changes in intensity of the color showed different strengths of anisotropy.

RESULTS

A total of 32 patients and 10 healthy controls were included in the DTI analysis. For all of the 32 subjects, the DTI image quality was satisfactory for further evaluation. DTI was initially performed within the first 24-48 hours after the diagnosis of obstructive stone disease established with unenhanced computed tomography (CT). Post-treatment DTI was performed 24 hours after the procedure (Figure 1 a-d, Figure 2 a, b). Measurements included corticomedullary junction.

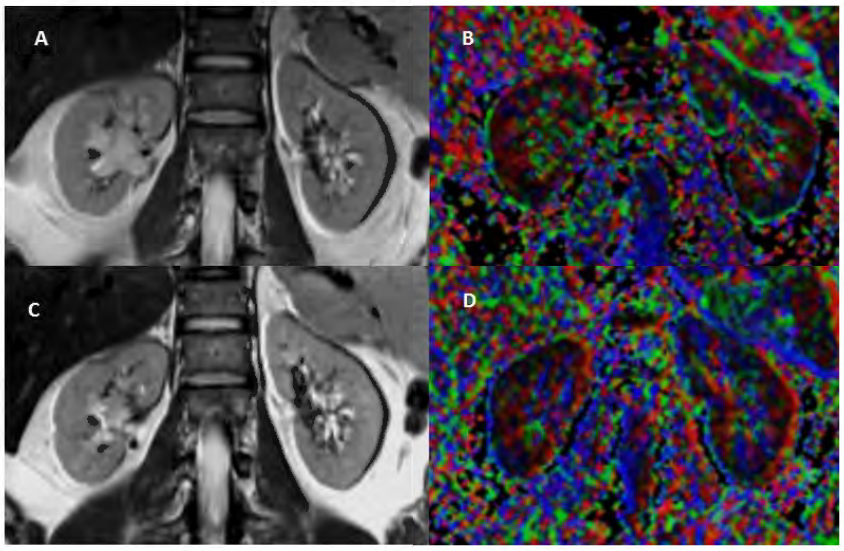

Figure 1: Coronal (a) Pretreatment HASTE sequence of the kidneys shows hydronephrosis on the right side (b) DTI (color coded FA map) of the kidneys do not reveal a visible difference, however measurement of the kidney parenchyma disclosed a slight increased FA value of the right kidney (c) HASTE following URS treatment revealed regressed hydronephrosis (d) DTI, (color coded FA map) of the kidneys, do not reveal a visible difference. Measurement of the kidney parenchyma disclosed normalizing FA value of the right kidney.

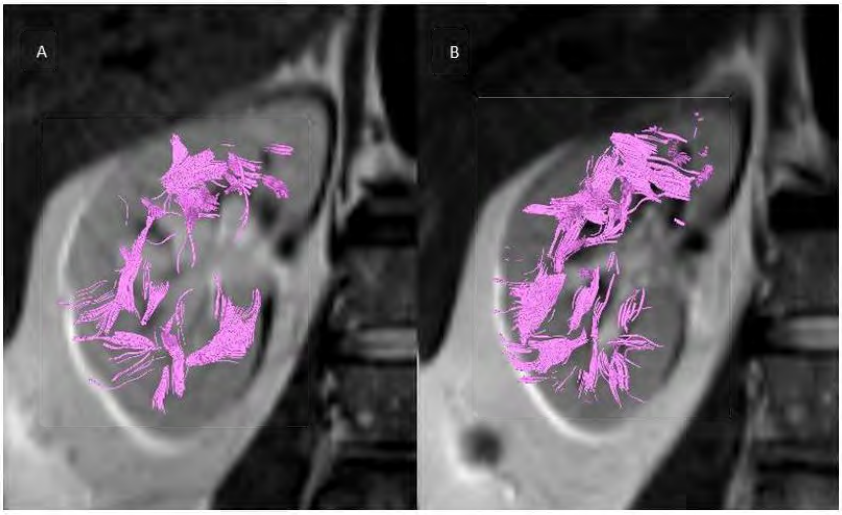

Figure 2: Coronal (a) Pre and post treatment diffusion tensor tractography images of the same patient with figure-1. Pretreatment image on the right side shows the radial organized diffusion pattern of the renal medulla (b) Posttreatment tractography of the kidney revealed increased amount of radial structures of the medulla.

In the quantitative analysis the mean ADC value (2.14±0.43 mm2/s) and FA (0,29 ± 0,14) of the control group was not statistically different from the non-obstructed kidneys of the patient group.

The pre and post treatment ADC and FA values are given in detail in Tables 1 and 2.

Renal Stent Group	**Pre t. ADC**	**Post t. ADC**	***p* value**
Obstructed kidney	1,87 ± 0,36	2,03 ± 0,40	0,08
Normal kidney	2,12 ± 0,32	2,35 ± 0,35	0,1
URS Group			
Obstructed kidney	1,99 ± 0,40	2,15 ± 0,39	0,01
Normal kidney	2,20 ± 0,43	2,28 ± 0,33	0,2

Table 1. ADC values (DWI) of the stent and URS groups prior and following treatment.

- *URS: Ureterorenoscopy*
- *t: Treatment*
- *DWI: Diffusion Weighted Imaging*
- *ADC: Apparent Diffusion Coefficients of the medulla*

Renal Stent Group	**Pre t. FA**	**Post t. FA**	***p* value**
Obstructed kidney	0,28 ± 0,11	0,28 ± 0,12	0,3
Normal kidney	0,28 ± 0,12	0,27 ± 0,12	0,8
URS Group			
Obstructed kidney	0,28 ± 0,12	0,25 ± 0,11	0,04
Normal kidney	0,27 ± 0,12	0,28 ± 0,13	0,7

Table 2. FA values (DTI) of the stent and URS groups prior and following treatment.

- *URS: Ureterorenoscopy*
- *t: Treatment*
- *DTI: Diffusion tensor imaging*
- *FA: Fractional anisotropy*

After the treatment the ADC values increased both in the obstructed and non-obstructed kidneys of the patient group. The statistical evaluation showed significant difference among the patient versus control and non-obstructed group of URS patients (p = 0.01). Similarly decreased FA values measured in the URS group showed statistical significance (p = 0.04).

DISCUSSION

Diffusion-weighted imaging of the kidney has proven to be feasible in a clinical setting and to provide information about various focal and diffuse renal diseases. Several previous reports have shown that the ADC of the kidney changes in diffuse parenchymal disease and helps to identify renal lesions [8]. Diffusion is a three-dimensional (3D) process. For this reason, molecular mobility in organized tissue does not necessarily occur the same in all directions. The predominant function of the kidneys is to transport water, and structures like vessels, tubules, and collecting ducts are oriented in a radial fashion, resulting in anisotropic diffusion properties [12]. DW-MRI, performed only in one direction, has the possibility to result in loss of important data in terms of anisotropy, for certain tissues. Basic anatomical components of kidney with radial orientation in the medulla can be best evaluated with DTI, which differently from DW-MRI is capable of detecting anisotropy by analysis of diffusion along at least 6 directions [13].

The diagnosis of obstruction limited to the detection of a dilated collecting system on imaging studies can be misleading because a nondilated collecting system does not exclude the presence of an obstruction. This is particularly the case for the intrarenal collecting system, which can only slightly expand in case of ureteral obstruction. Alternatively, a dilated upper urinary tract may be present in unobstructed kidneys. In difficult clinical situations such as these, DW-MRI as a noninvasive method without administration of contrast material and without ionizing radiation may prove to be of help in decision making and the avoidance of unnecessary procedures [10].

The present study was performed to investigate the value of DTI in determining the effects of treatment related recovery of the kidney parenchyma. We were able to acquire both ADC and FA which are the quantitative parameters of DW-MRI and DTI respectively. Our results showed elevation of the ADC levels both in the obstructed and non-obstructed kidneys of the patient group, whereas this increase was more pronounced in the obstructed kidneys and statistically significant in the URS subgroup. The

increasing ADC values of the non-obstructed kidneys is associated with hydration status. With the increased amount of hydration the ADC tends to increase and FA decreases to some extent (14). Our patients were hydrated for medical treatment of the obstructive renal diasease beginning from the initial diagnosis and this resulted to increase in the ADC level.

In a study by Bozgeyik et al. obstructed kidneys had lower ADC values compared to normal kidneys but these alterations were statistically insignificant [11]. Their findings may be related to the short duration and mild obstruction of the ureter. In our study ADC values of the obstructed kidneys were statistically different from both the control group and the non-obstructed kidney group ($P < 0.05$). Furtheremore in the URS group post-treatment ADC and FA values recovered to normal levels and this was statistically significant. Unilateral ureteral occlusion was performed in a porcine model by Muller et al. [15]. ADC values were decreased in obstructed kidneys and slightly increased in contralateral kidneys. A similar study was performed by Pedersen et al. in pig kidneys. The ADC values of the medulla and cortex was significantly reduced 24 h after occlusion in acute ureter occlusion [16]. In contrast, ADC values of both cortex and medulla was increased at chronic unilateral partial obstruction. ADCvalues of normal kidneys for cortex and medulla were found as $(2.07\pm0.27)\times10^{-3}$ and $(2.10\pm0.24)\times10^{-3}$.

Obstruction leads to biochemical, immunologic, hemodynamic, and functional changes of the kidney. Gross pathologic changes observed in the early phase (first 42 hours) are dilation of the pelvis and ureter and blunting of the papillary tips the microscopic pathologic findings observed in this phase are lymphatic dilation, interstitial edema, tubular and glomerular preservation. Impedance to the flow of urine, urinary tract dilatation, reduction in flow rate, raised intrarenal pressures are generally considered to have an essential influence on the pathogenesis of renal damage in obstruction [17].

The first step in the treatment for acute renal colic caused by obstructing ureteral stones is medical relief of symptoms. When a drug therapy does not resolve the symptoms, the placement of a ureteral catheter or a nephrostomy tube has routinely represented the next step. These easy maneuvers can offer a prompt relief from pain for the patient and they are usually followed by URS or SWL, which currently represents the mainstay of treatment for symptomatic ureteral Stones [18, 19].

There are some limitations of our study and the most important one is inevitable variations in hydration status of patients, although all of the patients were imagined with hydration in the second imaging. Another important limitation can be regarded as the use of a breath-holding protocol instead of respiratory trigger method, because breath-holding may cause some difficulties in patients with lack of cooperation about breath holding, and finally the third limitation is the low number of the patient group.

In conclusion our study showed that renal ADC and FA values which are quantitative parameters acquired non-invasively with MRI recover to normal levels after URS treatment. This normalization is also seen in the stent group however this was not statistically significant.

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