ÖZ

Amaç: Renal ektopi ve füzyon anomalili hastalarda (1) Hilson perfüzyon indeksi ile böbreklerin perfüzyon fonksiyonunu belirlemek ve (2) dinamik böbrek sintigrافisi ile böbrek fonksiyonlarını değerlendirmek.

Gereç ve Yöntem

Bulgar
29 hastada (%3) renal ektopi ve füzyon anomalisi olduğu belirlendi. Pelvik ektøpik böbreklerin ortalamada uzunluğu orotopik böbreklerden anlamlı derecede kısaydı (sirasiyla 91,0 mm ± 18,9 ve 111,0 mm ± 10,3, p = 0,001). Hilson perfüzyon indeksinin ortalama değeri, orotopik böbreklere kıyasla ektøpik böbrekle anlamlı olarak daha yüksekti (sirasiyla 86,4 ± 67,1’e karşılık 36,8 ± 18,0, p = 0,001). Çapraz renal ektopi, pelvis ektropi ve at nali böbrekler arasında perfüzyon/ekstraksiyon fonksiyonları ile ekskresyon fonksiyonları arasında istatistiksel olarak anlamlı fark yoktu (sirasiyla p = 0,079 ve p = 0,879). Pelvis ektropik böbreklerde ekstraksiyon fonksiyonları, orotopik böbreklere kıyasla anlamlı derecede bozulmuştu (p = 0,001). Pelvis ektropik böbreklerin ekskresyon fonksiyonları ile orotopik böbreklerin ekskresyon fonksiyonları arasında anlamlı fark yoktu (p = 0,116).

Sonuç
Hilson perfüzyon indeksi, renal ektopi ve füzyon anomalisi olan böbreklerin perfüzyon fonksiyonlarının sintigrافik değerlendirilmesinde yararlı olabilir.

Anahtar Kelimeler: Tc-99m DTPA, sintigrافi, fonksiyon

Abstract
Objective
(1) To assess the perfusion functions of the kidneys by Hilson’s perfusion index and (2) to evaluate the renal functions of the patients with renal ectopia and fusion anomalies by dynamic renal scintigraphy.
Materials and Methods
A total of 959 patients referred for Tc-99m DTPA dynamic renal scintigraphy were investigated retrospectively. We evaluated the functions and diuretic response of the kidneys on the time-activity curves (TACs) and performed quantitative analysis. Hilson’s index was used for the evaluation of perfusion of the kidneys.

Results
Renal ectopia and fusion anomalies were reported in 29 (3%) patients. The mean length of the kidneys with pelvic ectopic kidneys were significantly shorter than the orthotopic kidneys (91.0 mm ± 18.9 and 111.0 mm ± 10.3, respectively, p = 0.001). The mean value of Hilson’s perfusion index was significantly higher in the kidneys with ectopia compared to the orthotopic kidneys (86.4 ± 67.1 vs. 36.8 ± 18.0, respectively, p = 0.001). There was no significant difference when we compared the perfusion/extraction functions and the excretion functions of the kidneys among crossed-fused renal ectopic (CFRE), pelvic ectopic, and horseshoe kidneys (p = 0.079 and p = 0.879, respectively). Extraction functions were significantly impaired in the pelvic ectopic kidneys compared to the orthotopic kidneys (p = 0.001). There was no significant difference between excretion functions of pelvic kidneys and orthotopic kidneys (p = 0.116).

Conclusion
Hilson’s perfusion index may be useful in scintigraphic assessment of perfusion functions of the kidneys with renal ectopia and fusion anomalies.

Keywords: Tc-99m DTPA, scintigraphy, function

Introduction
The kidneys are retroperitoneal organs that are usually located each on either side of the vertebral column, and anterior to the psoas muscles. Normal embryologic development of kidneys starts in the pelvis and each kidney ascends and rotates through 90 degrees as it reaches the renal fossa (1). Although most cases are idiopathic, teratogenic drugs, genetic diseases, and chromosomal abnormalities may be related to pelvic ectopia (2). When one or both of the kidneys do not ascend to the retroperitoneal renal fossa as in normal fetal development, renal ectopia occurs (3). If the kidney does not ascend from the correct side of the pelvis, it is known as simple ectopia, which is the most common type. On the other hand, the kidneys may ascend or “overshoot” to a higher location than normal, resulting in thoracic kidney, which is the less common form of ectopic kidneys (less than 0.01%) (4, 5). Other known ectopia types are iliac, abdominal, and cross ectopic kidneys. The incidence of the ectopic kidney is approximately 1 in 900 births, nevertheless, only about 1 in 10 of these can be diagnosed clinically (6, 7).

Henot was the first to describe the fused ectopic kidney, in 1830 (8). The horseshoe kidney is the most common type of fused kidneys, which is more frequent in males and has an incidence of 0.25%. The first horseshoe kidney was documented by Da Carpi, in 1522 (9). Etiology of horseshoe kidneys include abnormal migration of nephrogenic cells across the primitive streak, maternal factors such as teratogenic drug exposure during pregnancy (thalidomide), alcohol consumption, and poor glycemic control, or structural factors (flexion/rotation of the caudal spine and narrowed fork of umbilical arteries during migration) (10, 11).

Cross-ectopic kidney or crossed fused renal ectopia (CFRE) is first defined by Pannorlus, in 1964, and it is the second most common type of the fused kidney (12). The incidence of CFRE is reported as 0.05-0.1% of the healthy population (13).

The technetium-99m diethylene triamine penta acetic acid (Tc-99m DTPA) dynamic scintigraphy provide quantifiable renal function, and anatomic evaluation of the kidneys (14). Although in the literature, Hilson’s perfusion index had not been used in kidneys other than renal transplants, to our knowledge, we considered the index may be useful for the evaluation of ectopic kidneys (15). The pelvic kidneys were situated at the pelvis, therefore we considered to use Hilson’s perfusion index for the patients with pelvic ectopia. In our study, we assessed perfusion of the kidneys by Hilson’s perfusion index and evaluated kidney functions of patients with renal ectopia and fusion anomalies by dynamic renal scintigraphy.

Materials and Methods
A retrospective analysis of the hospital registry was carried out to collect the medical data of the patients. A total of 959 consecutive patients (478 F, 481 M, 43.08 years ± 15.63 (range of age: 12-86)), who were referred for a Tc-99m DTPA dynamic renal scintigraphy between July 2013 and January 2018, were retrospectively evaluated. Renal ectopia and fusion
anomalies (12 F, 17 M, 35.62 years ± 14.18 (range of age: 12-66)) were detected in 29 patients. Inclusion criteria of the study were: (i) diagnosis of renal ectopia or fusions anomalies, and (ii) existing serum urea and creatinine levels. Exclusion criteria were as follows: (i) scintigraphic images not-achievable, (ii) solitary kidney, (iii) low-quality acquisition due to technical or patient-related problems (low-quality bolus injection, dehydrated patient, patient motion, patients with nephrostomy or urinary diversion, premature termination of the study etc.), and (iv) serum biochemical markers not available. The study has the approval of the Local ethics committee (No: 11.06.2018-51/12).

We evaluated the functions and diuretic response of the kidneys on the time-activity curves (TACs) and quantitative analysis along with a visual evaluation of the dynamic scintigraphy images.

In our daily routine protocol, all patients are administered an average dose of 185 ± 37 MBq (5 ± 1 mCi) Tc-99m DTPA which was adjusted according to the weight and/or age of the patients. Intravenous bolus injection of Tc-99m DTPA was administered to the patients in the supine position with the start of the acquisition in the dual-head gamma camera (Siemens ecam-signature; Siemens, Hoffman Estates, Illinois, USA) equipped with low energy high-resolution parallel hole collimator. Dynamic images were acquired over 40 minutes, in the anterior projection of the abdomen and pelvis with a 64x64 matrix, with 1.0 zoom. The energy window was maintained at 20%, with the photopeak centered at 140 keV. The dynamic study consisted of two phases. At the blood-flow phase of the dynamic acquisition, the images were obtained at a rate of 1 s per frame during the first 60 s and in the subsequent functional phase, images were obtained at a rate of 60 s per frame during the next 40 min. Delayed postvoid static images after 40 and 80 min of the initiation of the study were then acquired in the same projection with the dynamic study over 60 s, in a 128x128 matrix in all patients. Furosemide was administered at the 20 min after the initiation of the study (F + 20 protocol). None of the patients had a bladder catheterization. The dose of furosemide was 0.5 mg/kg or a maximum dose of 40 mg for adult patients and 1.0 mg/kg or a maximum dose of 20 mg for child patients. We measured the length of the kidneys from the extreme superior and inferior tips and width of the kidneys from the extreme lateral and medial sides of the kidneys. Consequently, we performed a qualitative visual analysis by evaluating blood flow, renal extraction, and excretion of the radiopharmaceutical. Hilson’s perfusion indices of kidneys were calculated as the ratio of the area under the curve of the region of interests (ROIs) obtained from abdominal aorta to peak divided by the area under the curve that were obtained predominantly from cortex of the kidney to peak, multiplied by 100. We considered renal blood flow as normal if Hilson’s perfusion index was below 150 (15). The extraction function was evaluated as normal if the peaks of the renogram curve were observed within the first 2-5 min of functional phase (16). Dilated non-obstructed kidneys could have a normal function but not give a renogram peak within 5 min, thus evaluated with serum urea and creatinine levels. The excretion function was classified in 3 groups; normal excretion, delayed excretion responding to the diuretic, and excretion failure with poor response to the diuretic, according to the semiquantitative evaluation of TACs and images. The ROI was manually drawn on the frame of the kidney at 20th and 40th mins of the study and kidney counts were obtained from each fused kidney, each component (right and left kidneys) of horseshoe kidneys. If the ratio of kidney counts at 40th min to that at 20th min was above 50% it was accepted as normal excretion, if this ratio is 20-50% then delayed excretion failure responding to diuretics, if the ratio is <20% then excretion failure with poor response to diuretics. All Tc-99m DTPA scintigraphies were re-evaluated by two nuclear medicine specialists blinded to the results of all clinical and radiological findings.

In thirteen of these 29 patients Tc-99m DMSA renal cortical scintigraphy images were available. Our injection, image acquisition, and evaluation protocol for routine Tc-99m DMSA renal cortical scintigraphy is as follows: One million counts of anterior, posterior, bilateral lateral, and oblique views with a 256x256 matrix size, 1.23 zoom, were obtained 2-4 h after the intravenous administration of 148-259 MBq (4-7 mCi) of Tc-99m DMSA. The relative split renal cortical functions of the kidneys were calculated with the geometric mean of the counts subtracted from the background from anterior and posterior projections of both kidneys. Planar images of Tc-99m DMSA were evaluated visually and semi-quantitatively. Split renal functions were calculated, as well.

Statistical Analysis
We used the results of Fisher’s exact test or Pearson chi-square test to compare the extraction and excretion functions of the kidneys between the renal ectopia and renal fusion anomalies, gender or the side of the anomaly if more than 20% of the table cells had expected frequencies less than five. Kruskal Wallis test and Mann Whitney U test were performed for the comparison of differential renal functions calculated in Tc-99m DTPA dynamic renal scintigraphy and split
renal functions measured from Tc-99m DMSA cortical renal scintigraphy. Statistical analysis was carried out using the Statistical Package for Social Sciences-SPSS 17 (ABD, Chicago, Illinois, USA).

**Results**

Renal ectopia or fusion anomalies were reported in 29 (3%) of 959 patients. The pelvic ectopic kidney was the most frequent anomaly (n = 16, 55.2%), thirteen of whom had a left-sided ectopia. Horseshoe kidney was the second most common type that was reported in nine patients (31.0%) and CFRE was observed in four patients (5.4%) including a left-to-right sigmoid type in one patient, two-disc kidneys and a left-to-right L-shaped kidney.

The anomaly types of the kidneys were not statistically different between genders (p = 0.884). Demographic features of the patients were outlined in Table 1.

The mean length of the pelvic ectopic kidneys was significantly shorter than the orthotopic kidneys (91.0 mm ± 18.9 and 111.0 mm ± 10.3, respectively, p = 0.001). However, the mean width of the pelvic ectopic kidneys was not different from the normal kidneys (48.9 mm ± 13.5 and 51.5 ± 6.7, respectively, p = 0.497). Similarly, the mean length and mean width of kidneys were not significantly different between CFRE and the orthotopic kidneys (length: 96.6 mm ± 8.2 and 97.5 mm ± 10.9, width: 50.0 mm ± 13.8 and 55.1 mm ± 9.0, respectively).

There was no statistically significant difference between the mean length of the right and left components (101.9 mm ± 16.6 and 101.6 mm ± 17.4, respectively), and between the mean width of the right and left components of the horseshoe kidneys (50.7 mm ± 9.9 and 49.1 mm ± 13.3, respectively).

The mean value of the Hilson's perfusion index was significantly higher in ectopic kidneys when compared to orthotopic kidneys (86.4 ± 67.1 vs. 36.8 ± 18.0, respectively, p = 0.001). Evaluation of 58 kidneys (including both components of horseshoe kidneys) revealed an impaired extraction function in 12 (16.2%) kidneys. Five kidneys (6.8%) showed a delayed excretion function responded to diuretic and three kidneys (4.1%) exhibited a delayed excretion function with poor diuretic response (Table 2). The functions of the kidneys in one patient with sigmoid kidney and two patients with disc kidney were normal, whereas the perfusion and extraction functions of the L-shaped kidney were impaired. There was no significant difference when the perfusion/extraction functions and the excretion functions of the kidneys were compared among CFRE, pelvic ectopic, and horseshoe kidneys (p = 0.079 and p = 0.879, respectively). The excretion functions were impaired in 8 of the 16 pelvic ectopic kidneys (50%), whereas extraction functions of the orthotopic kidneys were normal in all patients with pelvic ectopia (p = 0.001). There was no significant difference between excretion functions of pelvic kidneys and orthotopic kidneys (p = 0.116). Moreover, the extraction and excretion functions of the kidneys were not significantly different between left-sided and right-sided anomalies (p = 0.880 and p = 0.169, respectively).

The mean split renal function of pelvic ectopic kidneys was 34.6% ± 13.5. The split renal functions of the kidney of 13 patients, whose Tc-99m DMSA scintigraphy images were available, were calculated in patients with CRFE (2 patients), pelvic kidneys (7 patients), and horseshoe kidneys (4 patients, 8 components) (42.0% ± 1.4, 40.9% ± 10.8, and 50.0% ± 11.6, respectively).

**Discussion**

In this study, the ectopic kidneys showed higher Hilson's perfusion index values compared to orthotopic kidneys and the extraction functions of the pelvic kidneys were impaired, however, excretion functions of the pelvic kidneys were not different when compared with the orthotopic kidneys.

Renal ectopia and fusion anomalies are uncommon and sometimes overlooked. Notwithstanding, complications such as urinary obstruction, obstructive uropathy, vesicoureteral reflux, infections, nephrolithiasis, and vascular involvement may occur and may lead to serious health problems that can progress to end-stage renal disease if left untreated (17). However, limited published data exist regarding the scintigraphic evaluation of patients with renal ectopia and fusion anomalies.

In patients with CFRE, the ectopic kidneys were fused from their upper pole to the lower pole of the orthotopic kidney. In cases of the cross renal ectopia, generally, cross ectopic kidney is fused to the other kidney. Frequently, upper pole of the cross ectopic kidney is fused to the lower pole of the contralateral kidney (7). The fusion of the kidneys was considered to be caused by a converging course taken by the ureteric buds, that force the metanephric blastemas to merge or a mechanical relation between metanephroi and the umbilical arteries during the development of the kidneys. Nephrogenic cells from the posterior
Table 1
Demographic features of the patients

<table>
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<th>No</th>
<th>Age</th>
<th>Gender</th>
<th>Anomaly Type</th>
<th>Urine (N: 17-43 mg/dL)</th>
<th>Creatinine (N: 0.84-1.25 mg/dL)</th>
<th>Side of the kidney</th>
<th>Diameters (mm)</th>
<th>Perfusion Index</th>
<th>Extraction Function</th>
<th>Excretion Function</th>
<th>DMoSA (%)</th>
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</table>
nephrogenic area of the epiblast form the isthmus of the horseshoe kidneys after the fifth week of gestation, before renal ascent (18). In lump kidneys or disc kidneys, larger portions of kidneys are fused. The defective ureteral bud causes the kidney to migrate to the opposite side and the metanephric blastema is induced on that side, eventually forms a crossed renal ectopia. An ectopic kidney is a result of a failure in the normal ascent and medial rotation of the ureteric bud and metanephrogenic blastema once they contact each other (19).

In our study, the mean length of the pelvic ectopic kidneys measured from the DTPA images was shorter than the orthotopic kidneys, on the other hand, the mean length and mean width of kidneys with CFRE were not significantly different from those of the orthotopic kidneys. The ectopic kidneys are usually smaller than the orthotopic kidneys because they may have fetal lobulations and their axis may be medial or vertical (20). The development of kidney and vascularization pattern may arrest when the ascending ceases (21) as a result the ectopic kidney may have smaller size and may have reduced number of nephrons.

Hilson’s perfusion index has been used to differentiate normal grafts and those with impaired function in patients with the renal transplant (15). The pelvic kidney may have arterial variations which may originate from the aortic bifurcation, the common iliac, or the external iliac artery (22) or may have an accessory or anomalous renal artery (23). The anomalous arterial blood supply may be the reason for the decreased perfusion function and high Hilson’s perfusion index values of the ectopic kidneys.

In this study, the extraction functions of the pelvic kidneys was impaired compared with the orthotopic kidneys, however, excretion functions of the pelvic and orthotopic kidneys were not different. Extraction and excretion functions of the ectopic kidneys are usually decreased. In a study, decreased renal functions were reported in Tc-99m DMSA scintigraphy in 74 of 82 patients with simple renal ectopy (24). In another study, the evidence of outflow obstruction was reported in 38% of patients with ectopic kidneys (25). However, these findings require confirmation by large, randomized, prospective studies.

The split renal functions were not compared because of the small number of patients who had Tc-99m DMSA scintigraphy images and the results could not be attributable to the population. Khan et al. reported that the differential functions of the kidneys were similar at various locations of the ectopic kidneys (25). Although Tc-99m DMSA is the gold standard method for the calculation of the split renal functions, Tc-99m DMSA studies were available in only a small number of patients.

The anatomic evaluation along with functional assessment has a critical importance in patients with renal ectopia and fusion anomalies. Although other imaging modalities (such as ultrasonography, computed tomography, and intravenous pyelography (IVP)) display anatomical detail, scintigraphy can provide non-invasive information regarding the dynamic renal functions (26). Dynamic renal scintigraphy helps to assess the renal perfusion, extraction and excretion functions and static images are valuable in the evaluation of the vesicoureteral reflux. Since the intravenous contrast agents are not used, scintigraphy neither causes nephrotoxicity nor induces an allergic reaction. Moreover, dynamic renal scintigraphy is ad-

<table>
<thead>
<tr>
<th>Anomaly Type</th>
<th>Normal Extraction</th>
<th>Impaired Extraction</th>
<th>Normal Excretion</th>
<th>Delayed Excretion (Response to Diuretic)</th>
<th>Excretion Failure (Poor Response to Diuretic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelvic ectopic kidney</td>
<td>8</td>
<td>8</td>
<td>12</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Normal kidney in pelvic ectopia</td>
<td>16</td>
<td>-</td>
<td>15</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Horseshoe kidney</td>
<td>14</td>
<td>4</td>
<td>11</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>CFRE</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Normal kidney in patients with CFRE</td>
<td>4</td>
<td>-</td>
<td>3</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>13</td>
<td>45</td>
<td>9</td>
<td>4</td>
</tr>
</tbody>
</table>

CFRE: Crossed Fused Renal Ectopia
vantageous over IVP in visualizing both renal parenchyma and the collecting system in patients with renal disorder. Although they can be normal in anatomic imaging modalities, the kidneys may not be functioning properly. Therefore, anatomic evaluation alone may lead the clinician to overlook the diagnosis and preclude successful treatment of the patient.

Our study is conducted retrospectively in patients who were referred to our department that the outcomes of the study might be affected and could not be translated to the general population. Since renal ectopia and fusion anomalies are rare, our study sample size was small. A prospective study with a larger number of patients performed in patients with ectopic kidneys might better evaluate the functions of the kidneys with scintigraphy. The depth of kidneys could be taken into consideration if all the patients had undergone a Tc-99m DMSA scintigraphy.

Conclusion

In conclusion, the results from this study suggest that Hilson’s perfusion index may be valuable for the evaluation of perfusion functions of the renal ectopia and fusion anomalies.

Conflict of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

References