Gazi Tıp Dergisi / Gazi Medical Journal

ARAŞTIRMA - RESEARCH ARTICLE

2007: Cilt 18: Sayı 2: 81-85

DIAGNOSTIC VALUE OF INTRAVENOUS CONTRAST ENHANCED POWER DOPPLER ULTRASOUND IN CHILDREN WITH ACUTE PYELONEPHRITIS

Gonca ERBAŞ[1], Hakan ÖZDEMİR[1], Cem YÜCEL[1], Evrim ABAMOR[2], L. Özlem KAPUCU[2], Ozan ÖZKAYA[3], Oğuz SÖYLEMEZOĞLU[3]

Purpose: Acute pyelonephritis (APN) is a major cause of morbidity in children with urinary tract infection and can result in irreversible renal scarring. Renal scarring can be prevented by early diagnosis and aggressive treatment. DMSA renal cortical scintigraphy is regarded as the gold standard method for the diagnosis of APN. The purpose of our prospective study was to determine the effectiveness of contrast-enhanced PDUS in the diagnosis of APN.

Materials and Methods: Twenty-three patients (20 female, 3 male; 5 months to 9 years) were evaluated with B-mode ultrasound, PDUS, contrast-enhanced PDUS and Tc-99m-DMSA scintigraphy. Scintigraphy was considered the gold standard method. The sonographic findings were correlated with scintigraphic data.

Results: The sensitivity rates of B-mode ultrasound, PDUS and contrast-enhanced PDUS were (respectively) 30%, 78% and 86%; specificity rates were 84.09%, 59.09% and 79.54%; accuracy rates were 64.49%, 65.94% and 81.88%; positive predictive values were 51.72%, 52.00% and 70.49%; and the negative predictive values were 67.88%, 82.53% and 90.90%.

Conclusion: The sensitivity of B-mode US in the diagnosis of APN is very low and the diagnostic value of this modality is doubtful. The sensitivity of PDUS is high enough but the specificity of this technique is lower than expected. Contrast-enhanced PDUS achieved high sensitivity and specificity rates. We think that this imaging modality can be part of the diagnostic and follow-up protocol for APN and even may replace scintigraphic techniques.

Key Words: Akut pyelonefrit, kontrastlı power Doppler US.

AKUT PYELONEFRİTLİ ÇOCUKLARDA İNTRAVENÖZ KONTRASTLI POWER DOPPLER SONOGRAFİNİN TANIYA KATKISI

Amaç: Akut pyelonefrit (APN), çocukluk çağının üriner enfeksiyonları içinde kalıcı renal skarlara yolaçabilen önemli bir morbidite nedenidir. Renal skar gelişimi erken tanı ve uygun tedavi ile önlenebilir. DMSA renal kortikal sintigrafi günümüzde APN teşhisinde altın standart yöntem olarak kabul edilmektedir. Bu prospektif çalışmanın amacı kontrastlı power Doppler US'nin APN teşhisindeki etkinliğini ortaya koymaktır.

Materyal ve Metot: APN ön tanılı 23 hasta (20 kız, 3 erkek; 5 ay-9 yaş) B-mode ultrason, PDUS, kontrastlı PDUS ve Tc-99m-DMSA sintigrafi ile incelenmiştir. Sintigrafi altın standart yöntem olarak Kabul edilmiştir. Sonografik bulgular sintigrafik bulgularla kıyaslanmıştır.

Bulgular: B-mod ultrason, PDUS ve kontrastlı PDUS'nin duyarlılık değerleri (sırasıyla) % 30, % 78, % 86; özgüllük değerleri % 84.09, % 59.09, % 79.54; doğruluk değerleri % 64.49, % 65.94, % 81.88; pozitif kestirim değerleri % 51.72, % 52.00, % 70.49 ve negative kestirim değerleri % 67.88, % 82.53 and % 90.90 olarak bulunmuştur.

Sonuç: APN tanısında B-mod sonografinin duyarlılığı çok düşük olup, tanısal değeri tartışmalıdır. PDUS'nin duyarlılığı yüksek ancak özgüllüğü sınırlıdır. Kontrastlı PDUS tetkiki ile yüksek duyarlılık ve özgüllük değerlerine ulaşılmış olup, bu yöntemin APN'nin tanı ve takip protokolünde yer alabileceği, hatta bu konudaki bilgi birikimi ve tecrübe arttıkça sintigrafinin yerini alabileceği düşünülmektedir.

Anahtar Kelimeler: Akut pyelonefrit, kontrastlı power Doppler US.

Presented as a scientific poster at EANM Congress, Paris, Eur J Nuc Med 27: p698, May 2000

[1] Gazi University School of Medicine Radiology Department
[2] Gazi University School of Medicine Nuclear Medicine Department
[3] Gazi University School of Medicine Pediatric Nephrology Department

INTRODUCTION:

Acute pyelonephritis (APN) is an important cause of fever in the pediatric age group. Some 3% of girls and 1% of boys have an APN attack at least once during the entire childhood period (1). The clinical presentation of APN is usually nonspecific, especially in newborns and infants. APN may cause irreversible renal scars, and give rise to hypertension, proteinuria and chronic renal insufficiency as late sequelae. Pyelonephritis-associated late sequelae can be prevented or diminished if diagnosed early and treated appropriately. Thus diagnostic imaging is very important. Renal cortical scintigraphy is generally regarded as the gold standard method for diagnosing APN and related sequelae. Computed tomography (CT) and magnetic resonance imaging (MRI) are alternative diagnostic tools; both have high resolution imaging capacity, high sensitivity and specificity rates close to those of scintigraphy but also both have some restrictions related to their techniques. Patients are exposed to the risk of ionizing radiation and potential side effects of iodinated contrast materials when they undergo CT. MRI is a safer modality without any ionizing radiation risk but is much more susceptible to motion artifacts; general anesthesia is almost always needed to overcome this problem. Gray scale ultrasound (US) has been widely performed for evaluating congenital urinary abnormalities, collecting system dilatation or urinary system stones in routine practice but has a low sensitivity for depicting changes due to pyelonephritis. With the increasing use of power Doppler US (PDUS), many studies for depicting APN were carried out but the results are inconclusive. Renal cortical scintigraphy remains the gold standard imaging modality for APN and related sequelae. Radiological practice gained a new perspective with US contrast agents. Use of these agents when PDUS is performed allows visualization of low caliber vessels that could not be seen before with Doppler US. Imaging the tissue perfusion is possible with this technique. In this study, our purpose was to evaluate the diagnostic value of contrast-enhanced PDUS in children with suspected pyelonephritis.

MATERIALS AND METHODS:

Twenty-three children (3 boys, 20 girls), 5 months to 9 years old (mean 18.9 months), were included in this prospective study between July 1999 and February 2000. All patients were admitted to hospital and hospitalized with the suspicion of acute pyelonephritis (APN) according to initial physical examination and laboratory findings. Tc-99m DMSA renal cortical scintigraphy, gray scale US, PDUS and contrast-enhanced PDUS were performed in all patients. Inclusion criteria (for suspected APN) were axillary temperature >38 °C, erythrocyte sedimentation rate >20 mm/h, CRP >24 mg/L, positive urine culture (more than 105 colony), elevated WBC count (>10,000/mm3) and WBC in urine sediment microscopy.

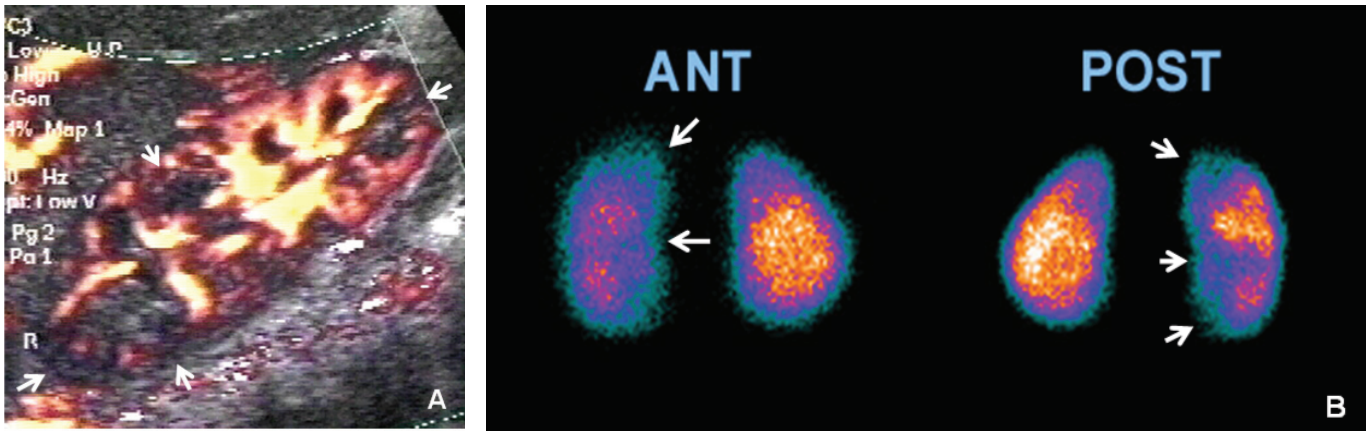

Figure 1: A- Contrast-enhanced PDUS. Hypoperfusion foci in three zones of the right kidney (arrows).

US examinations were done by two radiologists with the same US device (ATL HDI 5000 system, ATL Bothell, WA, USA) using C 8-5 microconvex and C 7-4 convex transducers. The observers were blinded to the scintigraphic findings and the patient's clinical data before the examination. The final diagnosis was made by the consensus of both observers. IV anesthesia/sedation was used for uncooperative children (n=19) with 1 mg/kg ketamine HCl (Ketalar 50 mg/ml/10 ml flacon-Eczacıbaşı) or 0.07-0.1 mg/kg midazolam (Dormicum 5 mg/5 ml ampoule Roche). The patients were examined in the prone position to avoid or minimize motion artifacts due to respiratory movements. During the examination, the same PDUS imaging parameters were adjusted before and after contrast administration. The kidneys were examined first with gray scale US, and collecting system dilatation, renal scars, edema and isolated hypo- and hyperechoic foci were noted. After that, PDUS was performed in both transverse and longitudinal planes for evaluating perfusion. Low perfusion areas were recorded. The kidneys were divided into three zones for determining the hypoperfusion areas: upper pole, middle zone and lower pole. IV contrast material (Levovist 2.5 g, Schering, Berlin, Germany) was administered via a peripheral venous catheter. The selected concentration of contrast material was 200 mg/ml for children younger than 6 years and 300 mg/ml for children older than 6 years. Half of the appropriately prepared solution was administered just before the examination of the right kidney and the remaining contrast material was administered before the other side was imaged. Both kidneys were evaluated within 10 min of contrast administration (maximum half-life of contrast material). Areas of hypoperfusion were recorded with respect to their location. The results were compared with renal cortical scintigraphy findings.

The patients underwent Tc-99m DMSA (Technetium-99m 2,3-dimercaptosuccinic acid) static renal scintigraphy synchronously with US examination (within 24 hours). The scintigraphic evaluation was performed 4 hours after the administration of 1 MBq/kg Tc-99m DMSA (min. 15 MBq, max. 70 MBq). Scintigraphic imaging was performed with a gamma camera (GE STARCAM 4000i), using a low energy general purpose collimator. Planar static images were generated in 4 different positions: anterior abdominal, posterior abdominal, and left and right oblique abdominal positions. Images were evaluated by two observers blinded to the patient data and US findings, and the final diagnosis was made by consensus. Tc-99m DMSA uptake of the kidney was estimated at 5 levels:

Grade (G) 0: normal activity,

G1: mildly decreased activity,

G2: markedly decreased activity,

G3: no activity,

G4: scar-related cortical defect.

During this study, 46 kidneys of 23 patients and totally 138 renal zones were evaluated with US and scintigraphy.

Scintigraphy was regarded as the gold standard imaging modality. Sonographic findings were compared with scintigraphic findings. US findings were classified as true positive, true negative, false positive and false negative compared to scintigraphic findings. Classification was carried out for renal zones, for kidneys and for patients separately. Using these data, sensitivity, specificity, accuracy, positive and negative predictive values were calculated for zones, kidneys and patients.

RESULTS

All of the patients included in this study were admitted to hospital with nonspecific symptoms related to acute pyelonephritis (APN), such as fever, nausea, vomiting, diarrhea, restlessness, and dysuria. Eighteen of the 23 (78%) patients were admitted during their first APN attack. The remaining five (22%) patients had a past history of at least one urinary

Table 1: Lesions depicted with DMSA scintigraphy.

LESION GRADE	RIGHT KIDNEY	LEFT KIDNEY	TOTAL
G1	10	9	19
G2	3	15	18
G3	5	8	13
TOTAL	18	32	50

Table 2: Comparison of three US techniques for depicting lesions in renal zones.

		B MODE US	PDUS	CE-PDUS*
SENSITIVITY (%)	RIGHT	27.77	77.77	**83.33**
	LEFT	31.25	78.12	**87.50**
	TOTAL	**30.00**	**78.00**	86.00
SPECIFICITY (%)	RIGHT	82.35	62.74	**80.39**
	LEFT	86.48	54.05	**78.37**
	TOTAL	**84.09**	**59.09**	79.54
ACCURACY (%)	RIGHT	68.11	66.66	**81.15**
	LEFT	60.86	65.21	**82.60**
	TOTAL	**64.49**	**65.94**	81.88
POSITIVE PREDICTIVE VALUE (%)	RIGHT	35.71	42.42	**60.00**
	LEFT	66.66	59.52	**77.77**
	TOTAL	**51.72**	**52.00**	70.49
NEGATIVE PREDICTIVE VALUE (%)	RIGHT	76.36	88.88	**93.18**
	LEFT	59.25	74.07	**87.87**
	TOTAL	67.88	82.53	90.90

* CE-PDUS: contrast-enhanced PDUS

infection attack. US and scintigraphic examinations were performed within 1-5 days (mean 2 days) of hospitalization. WBC counts were significantly high (>10,000/mm3) in 19 (82%) patients. Increased ESR was found in 75% of patients, CRP values were high in 72%, and urine culture was positive in 83%. In the positive urine culture group, the colony count was less than 100,000 in 3 patients. The colony counts were 50,000 in 2 of them and 20,000 in one. Although the significant threshold count was considered 50,000 colonies in certain studies in the literature (2), we regard a 100,000 colony count as the significant threshold for positive urine culture and so urine culture was significant in 16/23 (69%) of our patients. The documented microorganisms were E. coli in 14 patients, Clebsiella in one and Enterococci in one (in 3 patients with a 50,000 colony count or less, the microorganism was E. coli). Pyuria was found in urine microscopy in all patients (>5 leukocytes in x40 magnification).

When renal zones were considered, abnormal findings were observed with B mode US in 29 of 138 renal zones (21%). Fourteen lesions were found in the right kidney and 15 in the left. When the kidneys were considered, 16 of the 46 kidneys (34.78%, 8 right, 8 left) were abnormal with B mode US. The following findings were depicted: diffuse edema in 5 kidneys, hypoechoic areas in 9 kidneys, hyperechoic focus compressed collecting system, scar-related hyperechoic focus in one kidney, double collecting system in one kidney and focal caliectasis in one kidney. B mode US depicted lesions related to APN in 13 of the 23 patients (56.52%).

Power Doppler US (PDUS) depicted APN-related foci of hypoperfusion in 75 of 138 zones (54.34%). Thirty-three of them were in the right kidneys and the remaining 42 were in the left. APN-related lesions were found in 39 of the 46 kidneys (84.78%) and 22 of the 23 (95.6%) patients.

Contrast-enhanced PDUS depicted hypoperfused foci in 61 of the 138 renal zones (44.2%, 25 in the right kidney, 36 in the left), 34 of the 46 kidneys (73.9%) and 20 of the 23 patients (86.95%) (Figure 1).

B- Tc 99m DMSA scintigraphy in anterior and posterior projections. G3 lesions in upper, middle and lower zones of the right kidney (arrows). The left kidney is normal.

One patient suffered mild pain and erythema at the injection site. No other major or minor undesired side effects related to the contrast agent itself or the injection were found in the remaining 22 patients.

DMSA scintigraphy depicted lesions in 50 of the 138 zones (36.23%). Eighteen of them were in the right kidneys and 32 were in left. Nineteen of these lesions were Grade 1 (G1), 18 were G2, and 13 were G3. APN-related lesions were found in 27 of the 46 kidneys (58.69%) and 17 of the 23 patients (73.91%) (Table 1).

B mode, power Doppler and contrast-enhanced power Doppler US findings were compared with scintigraphic findings.

B mode US depicted 3 of the 19 G1 lesions (15.78%), 6 of the 18 G2 lesions (33.3%) and 6 of the 13 G3 lesions (46.15%), in total 15 of the 50 lesions (30%).

PDUS depicted 14 of the 19 G1 lesions (73.68%), 15 of the 18 G2 lesions (83.3%) and 10 of the 13 G3 lesions (76.92%), in total 39 of the 50 lesions (78%).

Contrast-enhanced PDUS depicted 15 of the 19 G1 lesions (78.94%), 16 of the 18 G2 lesions (88.8%) and 12 of the 13 G3 lesions (92.3%), in total 43 of the 50 lesions (86%).

The sensitivity, specificity, accuracy, negative predictive and positive predictive values were calculated for the three US technique es (Table 2).

DISCUSSION

APN is an important cause of late renal sequelae such as renal scarring, hypertension and chronic renal insufficiency. The younger the patient is, the higher the probability of renal scarring is. Late APN-related sequelae can be prevented by an accurate diagnosis in the early stages and appropriate antibiotic therapy. Clinical and laboratory findings are generally not sensitive and specific enough, especially in infants and young children. Many imaging modalities have been used for diagnosing APN, such as US, CT, MRI, scintigraphy and IV pyelography. DMSA renal cortical scintigraphy is regarded as the gold standard imaging modality by many authors (3). APN-related lesions appear as areas with well-defined margins of decreased activity or loss of activity without any volume loss or contour irregularity upon scintigraphic examination. Renal scar appears as sharp-edged cortical volume loss. Renal dysfunction can be depicted in the early stages of the disease but this modality cannot show anatomical detail. The photopenic areas seen with DMSA scintigraphy may reveal ischemic areas due to APN but may also appear in such events as abscesses or cysts. These kinds of lesion may give rise to misinterpretation and false positive results.

Contrast-enhanced CT is another modality of choice. The ionizing radiation dose that the patient is exposed to during a CT examination restricts the use of CT in diagnosing APN, especially in children. In addition, CT examinations may result in contrast-related allergic and renal side effects. Sedation is usually needed for the pediatric age group. CT must be used only in selected patients. MRI is a modality of choice for evaluating APN-related lesions but it is relatively expensive, the examination takes a considerable time, it is susceptible to respiratory and other motion artifacts, and sedation or even general anesthesia has to be performed, especially in the pediatric age group, for adequate quality images, and so MRI is only used in selected patients in routine practice.

B mode US is widely used for evaluating congenital abnormalities, stones, dilatation of the collecting system, and perirenal areas in routine practice, but has low sensitivity in depicting APN-related changes. In the literature, 20%-69% sensitivity rates have been reported (4).

Color Doppler US is a useful method for evaluating vessels, and allows the collection of data about flow velocity and direction. Because color Doppler signals originate from the frequency shift created by moving blood cells and the frequency shift is related to flow velocity, the evaluation of low caliber, slow flowing vessels such as those in the renal cortex is usually not possible with color Doppler US. The sensitivity of color Doppler US in diagnosing APN is reported as 63% in the literature (5). Since the introduction of power Doppler US, many studies have been carried out to compare PDUS with CT and DMSA scintigraphy. The results are controversial (6, 7). Hypoperfusion or no detectible perfusion areas on PDUS represent APN-related ischemic foci. This US technique is susceptible to motion artifacts. Patient cooperation with is very important to prevent motion artifacts. This is almost always impossible in young children and infants and so subjects are usually sedated during the examination. Tissue thickness-related signal loss is a major disadvantage of PDUS and causes reduced sensitivity in adults and obese patients and in areas where the kidneys obscured by other organs. These kinds of signal loss may sometimes be misinterpreted as hypoperfusion. This can be prevented by examining the patient in the prone position. IV contrast agents bring a new perspective to PDUS. With these agents, low caliber and low velocity vessels are visible and interpretable with PDUS. This technique is a reliable and sensitive imaging tool with no ionizing radiation risk. The contrast material we used in this study is well tolerated by our patient group. No systemic or local adverse reaction was found except for in one patient, in which local erythema occurred shortly after the contrast injection.

When compared to scintigraphy, the distribution of false positive lesions depicted with contrast-enhanced PDUS was as follows: upper pole 11, middle zone 2, and lower pole 6. The evaluation of upper poles can be relatively difficult due to the superposition of ribs and solid organs. When the subject holds his or her breath the diaphragm is depressed, and the upper poles of the kidneys move inferiorly and can be evaluated without superposition of the ribs. However, it is almost impossible to get subjects in the pediatric age group to hold their breath, especially when they are very young. The mean age of our study population was 18.9 months. In addition, examinations were usually performed with IV sedation. With PDUS, the false positive lesions depicted were as follows: upper pole 15, middle zone 7, and lower pole 14. The probable cause of this difference was that there was no time restriction for PDUS but the examination had to be completed in 10 minutes (the half-life of the contrast material) when contrast-enhanced PDUS was performed. Furthermore, the results of experimental animal studies documented that the sensitivity of renal cortical scintigraphy in depicting APN is 87%-89% (8, 9). Moreover, it is known that collecting system dilatation may be misinterpreted as APN lesions. False positive lesions depicted with power Doppler US techniques may represent real lesions that could not depicted with scintigraphy, but our results were not pathologically proven and we regard scintigraphy as the gold standard imaging modality.

When we considered lesions in renal zones, the sensitivity values achieved with PDUS and contrast enhanced PDUS were 78% and 86%, respectively (for all grade lesions). The specificity was raised from 59.09% to 79.54% with contrast administration. The sensitivity of PDUS and contrast-enhanced PDUS for depicting G1 lesions was 73.68% and 78.94%, for G2 lesions was 83.33% and 88.88%, and for G3 lesions was 76.92% and 92.30%, respectively. In a previous study, in which we compared PDUS and renal cortical scintigraphy for APN-related lesions, we found sensitivity values of PDUS of 37.1% for G1-G2 lesions and 77.14% for G3-G4 lesions (10). IV sedation was not given to patients in that study. The primary reason for the increase in sensitivity values for G1 and G2 lesions with PDUS in this study is probably IV sedation. In addition, the increased experience with PDUS applications

in APN patients may result in better sensitivity and specificity values.

In conclusion, Tc 99m DMSA renal cortical scintigraphy is a well-established imaging modality that is widely regarded as the gold standard imaging modality. Interobserver agreement values are up to 90% (8, 9). PDUS is an easily applicable, cheap and noninvasive imaging tool but false positive results decrease the specificity values. Using IV contrast media when performing PDUS increases the specificity of the technique. We found specificity values of contrast-enhanced PDUS in depicting APN related lesions of 79.54%.

The results of our study showed that sensitivity values of >85% in renal zone-based evaluations, and up to 100% in kidney and patient-based evaluations can achieved with contrast-enhanced power Doppler ultrasound in depicting APN-related lesions.

Correspondence Address
Gonca ERBAŞ MD
Gazi University School of Medicine Radiology Department 06510,
Beşevler, Ankara-TURKEY
e-mail: goncaerbas@gazi.edu.tr
Phone: 312 2025151 Fax: 312 212 19 40

REFERENCES

1. Wimberg J, Anderson HJ, Bergstrom T. Epidemiology of symptomatic UTI in childhood. Acta Paediat Scand 1974; 63 (supp 252): 1-20.
2. Hoberman A, Waldt ER, Reynolds EA. Is urine culture necessary to rule out urinary tract infection in young febrile children? Pediatr Infect Dis J 1996; 15: 304.
3. el Hajjar M, Launay S, Hossein-Foucher C, Foulard M, Robert Y. Power Doppler sonography and acute pyelonephritis in children: comparison with Tc-DMSA scintigraphy Arch Pediatr. 2002; 9: 21-5.
4. Lavocat MP, Granjon D, Allard D. Imaging of pyelonephritis. Pediatr Radiol 1997; 27: 162.
5. Eggli KD, Eggli D. Color Doppler Sonography in pyelonephritis. Pediatr Radiol 1992; 22: 422.
6. Winters WD. Power Doppler Sonographic evaluation of acute pyelonephritis in children. J Ultrasound Med 1996; 15: 91-96.
7. Dacher JN, Pfister C, Monroc M. Power Doppler Sonographic pattern of APN in children: Comparison with CT. AJR 1996; 166: 1451-55.
8. Piepsz A, Clarke SEM, MacKenzie R, Gordon I. A study on the interobserver variability in reporting on 99m Tc-DMSA scintigraphy. Eur J Nucl Med 1993; 20: 867.
9. Majd M, Rushton HG. 99mTc-DMSA renal cortical scintigraphy to detect experimental acute pyelonephritis in piglets: comparison of planar pinhole and SPECT imaging. J Nuc Med 1996; 37: 1731-34.
10. Özdemir H, Kapucu Ö, Yücel C. Akut pyelonefritli çocukların tanı ve izleminde Tc99m-DMSA sintigrafi ve power Doppler ultrasonografinin karşılaştırılması. 4. Tıbbi Görüntüleme ve Girişimsel Radyoloji Kongresi RAD99 Ekim 1999 Belek-Antalya P306.