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THE USE OF COLOR DOPPLER ULTRASONOGRAPHY IN NEPHROLOGY

PRIMENA KOLOR DOPLER ULTRASONOGRAFIJE U NEFROLOGIJI

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Key words
nephrology, color Doppler ultrasonography, resistance index.

Apstrakt

Kolor Dopler ultrasonografija neinvazivno ispituje promene u vaskualrnoj perfuziji. Na Univerzitetskoj Klinici za nefrologiju u Skoplju od 1996. godine uvedena je Doppler ultrasonografija sa HDI 3000, ATL aparatom. U periodu od tri godine obavljeno je ukupno 2581 KDUS ispitivanja, u 2005. g.-883, u 2006. g.-908, u 2007. g.-790 bolesnika. Indeks rezistencije (IR) je meren postojećim programom aparata. U najvećem broju su ispitivani transplantirani bolesnici. U 98 slučajeva je ispitivana reakcija hroničnog odbacivanja, u 58 akutno odbacivanje i u 38 slučajeva postojala je sumnja na stenozu/trombozu renalne arterije. U bolesnika sa dijabetičnom nefropatijom, određivali smo da li se IR može upotrebiti kao indikator; u 108 slučajeva našli smo povećan IR>0.68. U signifikantnom postotku ispitivanih bolesnika, 12.85%, nezavisno od indikacija za Doppler US, nađena je nefroarterioloskleroza, RI>0.64. Stenoza renalne arterije je bila suspektna u 52 slučaja (razlika od 0.04 imeđu IR desne i leve renalne arterije). Akutna bubrežna slabost procenjivana je u 53 slučaja. U odnosu na neoplazme, patološka, markantno povećana vaskularizacija, detektirana je u 34 slučaja suspektnih za bubrežni karcinom, u 46 slučajeva suspektna za testikularne tumore, 19 slučajeva suspektna za neoplazmu prostate i u 32 slučaja supektna za tumore drugih lokalizacija. U kombinaciji sa istorijom bolesti, kliničkim i laboratorijskim ispitivanjima, KDUS doprinosi u postavljanju dijagnoze, poboljšava brigu za bolesnike i efikasnost lečenja.

INTRODUCTION

Ultrasonography has become a routine modality in the evaluation of renal medical pathologies. Available since the 1980s, color Doppler ultrasonography (CDUS), Doppler effect named after Chr. Doppler, 1803-1853, has allowed evaluation of changes of renal perfusion noninvasively by interrogating intrarenal arteries or showing general renal perfusion in color (1). Real time US and Doppler techniques provide morphologic and functional information on altered blood flow and urinary flow in patients with renal diseases (2, 3). Resistance index (RI) value, as a useful parameter for quantifying the alterations in renal blood flow that may occur with renal disease, have been most frequently used in clinical practice. Normal ranges for RI values varied among authors who used different sonography machines and examined subjects of different ages with different diseases. It is reported to vary from 0.58 to 0.68 in normal (control) kidneys or normally functioning allograft (4). The largest series to date reported a mean RI of 0.60±0.01 for subjects without preexisting renal disease (5). Platt suggested 0.70 as a reasonable upper limit for normal RI values after examine patients with various renal diseases (6). These days a value of 0.68 is accepted as upper limit of normal in adult population, border values are from 0.65 to 0.68. Intrarenal RI measurements are not free of error and variability (7). Conditions other than renal disease might affect the RI as very high or very low heart rates, the age of the patient, dehydratation, and hypotension. There is no difference between the mean RI of the right and left kidneys, mean RI difference, 0.02.

Today, color Doppler ultrasound is a routinely used technique in the daily work of nephrologists. The aim of the study was to show our experience in Doppler examination during three years (2005, 2006 and 2007).

MATERIAL I METHODS

Color Doppler ultrasound includes measurement of the shift in frequency of received ultrasonic signals. Depending on flow direction, the signals are displayed in different colors, usually in red and blue. The frequency increases when ultrasound is reflected as particles moving toward the transducer. Reflection from particles moving away from the transducer displays a lower frequency. All CDUS instruments allow the accomplishment of spectral analysis of sig-

nals coming from any point of the image field and velocity is measured at any point in time during the pulse cycle. The resistance parameter, RI is determined as follows: RI = (PSV – EDV)/PSV where PSV is peak systolic flow velocity, EDV is end-diastolic flow velocity. Since 1982 year ultrasonography is a routine method at the University Clinic of nephrology, Skopje and in 1996 Doppler examination was introduced (8). A total of 2581 CDUS examinations were performed during three years on Macedonian Caucasian patients, aged 15-88 years. US examination was performed with HDI 3000, ATL machine, with multifrequency 3.5 MHz trasducer (frequency 2.0–5.0 MHz) (Advanced Technology laboratories, Bothell, Washington, USA). Doppler US examination was performed with subjects in a supine position after they rested for 15 minutes. For the Doppler study, the wall filter is set to the minimum (50 Hz) and the sample volume is set at 2-5 mm. The method for measuring RI has been published (9). Resistive indexes (RIs) of the renal parenchyma were measured in each kidney using existing software capabilities of the scanner. After a proper velocity waveform was obtained, the mean RI was calculated by using six measurements taken for each patient. Intrarenal RI values were obtained from intraparenchimal (arcuate or interlober) arteries of both kidneys. Three different measurements were obtained for each kidney in different portions (upper, middle and lower pole). Mean RI value for each kidney was calculated from all measurements. A mean RI value was obtained for each patient by averaging the two kidneys' mean RI values. All Doppler examinations were performed by the same examiner (blinded to renal status of the patients). Additionally, seventy of explored patients with diabetic nephropathy (DN) were divided based on their intrarenal RI values: group 1 (n=33) had values of <0.68 and group 2 (n=37) had values ≥ 0.68. Clinical parameters and renal function were evaluated at baseline and after 12 and 24 months: systolic and diastolic blood pressure (BP), mean BP, body mass index (BMI), serum glucose, serum creatinine, blood urea nitrogen, total protein, albumin, serum cholesterol, high density lipoprotein, triglycerides, electrolytes, 24-hour urine samples were obtained for creatinine clearance rate (CCr) and proteinuria. The diagnosis of type 2 DM was based on a previous history of diabetes or criteria according to the WHO. Blood samples were collected after an overnight fast and standard laboratory methods were used. CCr was calculated from 24-hour urine samples and serum creatinine levels, with Cockroft-Gault formula, as follows: [(140-age) xBW x88.4]/72xsCr, for man and [(140-age) xBWx75.14] /72xsCr, for woman.

RESULTS

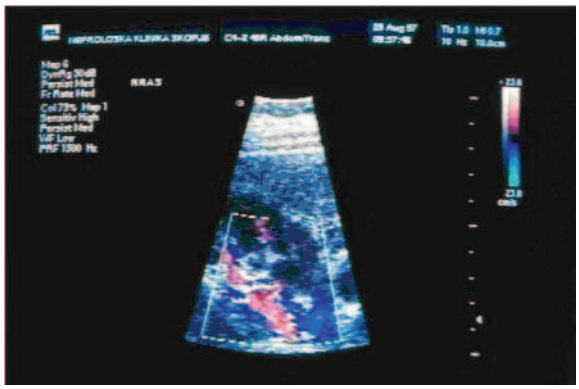
A total of 883 CDUS examinations were performend during year 2005, 908 during 2006; and 790 examinations during 2007. The most examinations, 194 (7.52%), were performed on transplant patients; depend of the necessarity patients were checked several times. Indications for CDUS were: in 98 cases chronic allograft rejection, in 58 cases accute rejection; and in 38 cases there was a suspition of stenosis/thrombosis of renal artery (in 9 cases the same was confirmed with other methods). Renal artery stenosis, a difference of 0.04 between RI right and left renal artery, as a cause of the secondary arterial hypertension was suspect in 52 cases (2.02%). In seven patients the diagnosis was confirmed with percutaneous angioplasty and they were treated by placing a stent at the same time, Picture 1. Accute renal failure was indication for CDUS in 53 patients (2.05%), Picture 2. In 12.85% of all examined cases (exept the transplanted kidneys) we found nephroarteriolosclerosis, RI >0.64. Regarding neoplasms, pathological, remarkable increased vascularisation, we found in 131 cases, 5.08%. In 34 patients there was a suspicion for renal cancer, in 19 cases for prostate neoplasm, in 46 cases a testicular tumour was suspected and in the rest of the 32 cases tumours of other localisations were suspected. In 108/150 examinations of patients with DN we found RI >0.68. A total of seventy Macedonian Caucasian patients with Diabetes mellitus and DN (aged 38-72 years); 68 patients ended the prospective two years follow-up study (one patients died because of cancer, one due to a heart attack). We wondered whether the intrarenal RI can be used as an indicator of progression in patients with DN. Patients were divided in two groups based on their intrarenal RI values, RI <0.68 and RI ≥ 0.68. All patients with RI ≥ 0.68 had statistically significant higher serum creatinine and lower CCr compare with patients with RI <0.68 during the follow up. Regarding glycemia and proteinuria there were no significant differences between the groups at any time point. A significant difference was found between the groups in the systolic and mean BP, but not in the diastolic BP. A significant difference for RI values was also observed between the groups during the whole follow-up period (Table 1).

DISCUSSION

Resistance index can be measured in each blood vessel but nowdays its current use in the diagnosis of renal diseases, especially renovascular disease, ischemic and diabetic nephropathy, and in the transplant kidneys. We should understand the pathophysiology of renal disease and how it affects the Doppler arterial waveform if we want to use RI value as a parameter for measuring changes in renal status (4). It is universally accepted that the terms ' resistive index' and ' renal vascular resistance' can be used interchangeably, although the relationship between these factors and other variables has not been determined. Conditions that affect vascular distensibility, such as artery interstitial fibrosis and vascular stiffening, might substantially affect the RI. The significance of the CDUS in the evaluation of the renal vascular resistance in patients with essential hypertension (EH) is still not clearly determined but it seems that has a great benefit in diagnosis of ischemic nephropathy. Galesic et al. found that the RI values correlated with the duration of HTA as well as with the patients' age. Increased RI would be a sign of hypertensive nephrosclerosis and renal failure (10). Patients with EH and RI ≥ 0.63 have two times increased risk of developing renal dysfunction (11). Patients with EH have an increased renal vascular resistance in comparison to normotensive people and show decreased renal perfusion. The increased RI in mild EH could be related to a functional vasoconstriction, while in moderate and long-standing HTA the increased RI could be the result of hypertensive nehprosclerosis (12, 13). Studies in patients with diabetic nephropathy suggested that the postglomerular vessels were the major contributor to increased resistance, although glomerulosclerosis and not interstitial fibrosis is the histological hallmark of this disease. In the early nonproteinuric

stage with hyperfiltration and enlarged kidneys, RI is still normal and increases when microalbuminuria appears and the kidneys are reduced (14, 15). Decreased renal function in DN is more in relation with renal arteries disease than with glomerular disease (16). We found the excellent correlation between RI and renal functional parameters. We were able to confirm relationship between CCr and age and RI and age in DN patients as it was done previously. Initialy higher RI may reflect accelerated impairment of the renal function. Beside good glycemic control, control of the weight and the decreased blood pressure there is no effect of protection if initial RI is >0.68. When RI increases to the value of 0.68, the risk of further impairment of renal function continues to escalate. Our results are in agreement with other authors who also found a higher correlation between serum creatinine, creatinine clearance and RI and suggest that RI is independent risk factor for the progression of diabetic nephropathy and chronic renal failure (17, 18, 19).

Doppler US is an integral part of the care of patients with renal allograft. CDUS has a critical role in the diagnosis of vascular lesions and an acute rejection. Transplant renal artery stenosis (TRAS) is the most common vascular complication. Marked downstream turbulence had to be present in the artery distally of a region with local flow increase in order to make a diagnosis of TRAS (sensitivity for RI, 58% to 100% with the majority greater than 90%; specificity, 87% to 100%). Arterial occlusion is best diagnosed as a lack of arterial flow within the kidney beyond the site of occlusion (20, 21). Complete renal vein thrombosis (RVT) is rare complication but early recognition is mandatory because it may leads to graft loss. Acute rejections produce increases of intraparenchimal pressure and renal artery flow resistance. Chudek et al. published that ischemic injury, which occurred prior to organ harvesting, played a dominant role determing intrarenal resistance in the early posttransplant period (22). Series of measurements of RI are required for diagnosis of chronic rejection. Early diagnosis of the renal artery stenosis (RAS) as a cause of secondary hypertension, ischemic nephropathy and renal failure is very important. Although renal RI is not a perfect test for renovascular disease, it can provide useful diagnostic information. Doppler US is useful as first screening test for patients suspected for RAS (13, 23). Schwerk et all. found that the difference in RI of at least 5% between kidneys is indicative of RAS on the side where a lower RI is (24). Doppler US criteria for RAS ≥50% is peac systolic velocity (PSV) ≥200 cm/sec or renal/aorta velocity ratio (RAR) =70% (25). In recent years few studies have reported the value of CDUS in predicting clinical response to intervention and revascularization in RAS (26, 27). Today there are many indications for use Doppler US in all fields of medicine, especially in the nephrology practice. The quality of life and long-term survival of patients on hemodialysis is dependant on the adequacy of dialysis via an appropriately placed vascular access. Patients with poor functioning AVF had significantly less arterial internal diameter with higher arterial RI, less venous internal diameter with less venous blood flow velocity and volume (28). Also, Doppler US is important for early and precise differentiation of obstructive from non-obstructive uropathy and permits prompt and appropriate therapy, which is essential to minimize the devastating effects of obstruction on urinary tract structure and function (2, 3). Furthermore, Doppler US successfully is used in early detection and diagnosis of urinary



Picture 1. Renal artery stenosis.

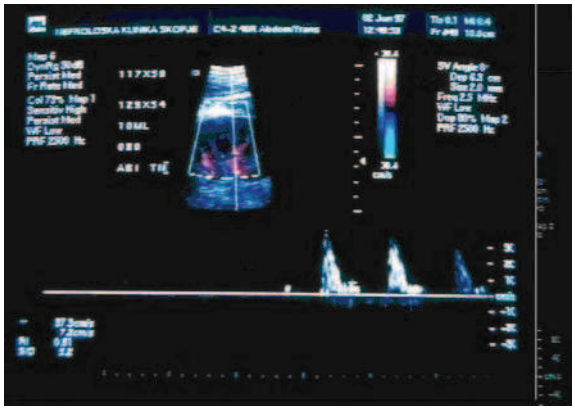
Table 1: Clinical data of patients with diabetic nephropathy

	At baseline			After 12 months			After 24 months		
	I	II	P<	I	II	P<	I	II	P<
n	33	37							
Age (years)	53±9	63±6	0.01						
Duration of diabetes (years)	4.4±4.0	9.2±6.5	0.01						
Duration of hypertension (years)	3.4±5.9	5.4±8.3	NS						
sCr (mmol/l)	78.7±15.0	103.0±42.0	0.01	84.2±17.1	124.3±25.0	0.01	85.4±11.7	136.2±84.2	0.03
CcR (ml/min)	105.8±20.3	75.4±17	0.01	102.8±25	64.6±26.7	0.01	103.8±26.7	136.2±84.2	0.01
Proteinuria (g/24h)	1.1±0.9	1.9±1.9	0.05	1.2±0.8	2.0±1.7	0.03	1.3±0.7	1.8±1.2	NS
SBP (mmHg)	143.8±25.3	156.6±26.3	0.05	126.5±12.0	138.9±16.5	0.01	125.6±14.1	135.2±12.5	0.03
DBP (mmHg)	87.6±15.6	89.2±150	NS	80.0±7.2	80.9±6.3	NS	77.2±6.3	79.7±5.5	NS
Mean BP (mmHg)	66.7±13.6	74.7±14.3	0.03	57.7±7.1	67.3±12.3	0.01	58.0±8.7	64.1±9.3	0.03
Glycemia (mmol/l)RI	8.1±3.5 0.6194± 0.003943	8.8±3.4 0.7154± 0.003860	NS 0.01	6.9±1.7 0.6322± 0.004022	7.0±1.9 0.7320± .003871	NS 0.01	6.2±1.7 0.6613± 0.004463	6.5±2.2 0.7600± 0.004472	NS 0.01

Group I, RI≥0.68; Group II, RI ≥0.68; Cr, creatinine; CCr, creatinine clearance rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; RI, resistive index; NS, not significant.

tract tumors and tumors of other localization. This includes diagnosis on the basis of the morphology on a grayscale sonographic exam and noninvasive evaluation of organ and tumor vasculature. Doppler US contributes to tumor detection and provides diagnostic information for its characterization, staging, treatment planning, and follow-up (29).

We can conclude that Doppler US measurement of resistive index is an important integral part of ultrasound examination in nephrology. RI is changing in different diseases, both inside and outside the kidneys, and is simple and useful marker of renovascular resistance. It is expected that the existing controversy regarding the role of RI will be eliminated in the coming studies. Doppler US is easy, fast and non-invasive method that should be correctly performed to provide useful clinical informations. Use of ultrasound contrast media, which increases the reflection capacity of blood, improves the quantification of tissue perfusion and is believed that in near future Doppler US will replace methods such as scintigraphy and angiography without impairing diagnostic reliability.



Picture 2. Accute renal failure due to tubular necrosis.

Abstract

Color Doppler ultrasonography (CDUS) and resistive index (RI) is widely used for the assessment of alterations of vascular perfusion noninvasively showing general perfusion in color. Since 1996, at our Clinic ultrasound examination by a Doppler apparatus is performed with HDI 3000, ATL machine. A total of 2581 CDUS examinations were retrospectively evaluated during three years; in 2005-883, in 2006-908, in 2007-790 patients. Transplanted patients were the most examinated. Chronic rejection reaction was evaluated in 98 cases, in 58 cases acute rejection and in 38 cases we postulated renal artery stenosis or thrombosis. In patients with Dabetes type 2 and diabetic nephropathy we ask ed whether the RI can be used as a indicator of progression; in 108/150 cases we found an increased RI>0.68. In a significant percentage of examined patients, 12.85%, independently of the indications for Doppler US, nephroarteriolosclerosis with RI>0.64 was found. There were 52 cases with suspected renal artery stenosis, 0.04 differences between RI on right and left renal artery. Acute renal failure was suspected in 53 cases. Pathological, marked increased vascularization typical for neoplasms, was noticed in 34 cases suspected for renal carcinoma, in 46 cases suspected for testicular tumors, 19 cases suspected for prostatae neoplasm and in 32 cases suspected for tumor in other localizations. Color Doppler US with RI as a noninvasive, easily available, diagnostic procedure brings significant informations in providing the diagnosis.

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