DOPPLER ULTRASONOGRAPHY: A TOOL FOR NEPHROLOGISTS
– SINGLE CENTRE EXPERIENCE

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Abstract: Colour Doppler duplex ultrasonography (CDUS) has allowed non-invasive assessment of alterations of vascular perfusion showing general perfusion in colour.

Since 1996, ultrasound examination by a duplex Doppler apparatus has been performed with an HDI 3000, ATL machine. We have retrospectively evaluated all patients (pts) with colour Doppler duplex examination for the last three years. Resistive indexes (RIs) are measured in each kidney using the existing software capabilities of the scanner.

A total of 2581 CDUS examinations were performed over the past three years; in 2005 – 883 pts, in 2006 – 908 pts and in 2007 – 790 pts. Most of these examinations were on transplant pts. In 98 cases we examined chronic rejection reactions, in 58 cases acute rejection and in 38 cases we postulated renal artery stenosis or thrombosis. We used CDUS to determine whether the RI can be used as a predictor in pts with Diabetic Nephropathy; in 108 cases we found an increased RI > 0.68. There is a positive correlation between the RI and the severity of arteriolosclerosis in the majority of pts, 331, where we found nephroarteriolosclerosis (RI > 0.64). In 52 cases renal artery stenosis was suspected (0.04 differences between RI on right and left renal artery). Acute renal failure was suspected in 53 cases. According to neoplasms, pathological, marked increased vascularization was noticed in 34 cases suspected for renal carcinoma, in 46 cases suspected of testicular tumours, 19 cases suspected of prostate neoplasm and in 32 cases suspected of tumours in other localizations.

In combination with patient history, clinical and laboratory examination CDUS provides very useful information in accomplishing the diagnosis.

Key words: kidney, colour Doppler duplex ultrasonography, resistive index.
Introduction

Ultrasound imaging (US) is a commonly used technique in the diagnosis of renal diseases. In previous years US was limited to assessing renal anatomy and pathologic changes in the collecting system. During the past decades (available since the 1980s), colour Doppler duplex ultrasonography (CDUS), (Doppler effect named after Chr. Doppler, 1803–13) has allowed noninvasive assessment of alterations of renal perfusion by interrogating intrarenal arteries or showing general renal perfusion in colour [1]. Thus, real time US and Doppler techniques provide not only morphologic, but also functional information on altered blood and urinary flows in patients with renal diseases [2, 3]. CDUS includes measurement of the shift in frequency of received ultrasonic signals. Depending on flow direction, the signals are displayed in different colours, 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. Varying degrees of frequency shifts are represented by more or less intensive colours. In Doppler US these shifts in frequency – that depend on velocity and flow direction – are superimposed in colour on the conventional B-scan image. All CDUS instruments allow the accomplishment of spectral analysis of signals coming from any point of the image field. This allows velocity measurements at any point in time during the pulse cycle. Among resistance parameters measured by duplex Doppler US, resistance index (RI) value, as a useful parameter for quantifying the alterations in renal blood flow that may occur with renal disease, has been most frequently used in clinical practice. The resistance parameter, RI is determined as follows:

\[ RI = \frac{PSV - EDV}{PSV} \]

PSV = peak systolic flow velocity, EDV = end-diastolic flow velocity.

Most studies have stressed the need for a precise technique [4]. The highest frequency probe that gives measurable waveforms should be used, supplemented by CDUS for vessel localization. Arcuate arteries (at the cortico-medullary junction) or interlobar arteries (on the edge of medulary pyramide) are then insonated using a 2-to 4-mm Doppler gate. Flow velocities are determined from signals that are stable for at least five pulse beats, and measurements represent the average of five complete waveforms for each kidney.

The intra-operator coefficients of variance are small, less than 4–5%. However, it is difficult to establish a normal range for RI because of limitations in the gold standard proof of normal renal status. Normal ranges for RI values varied among reports by other 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
allografts [4]. Several studies have shown that a normal mean renal RI is approximately 0.60. 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 examining patients with various renal diseases [6]. These days a value of 0.70 is accepted by most investigators as the upper limit of normal in the adult population. However, intrarenal RI measurements are not free of error and variability [7]. Conditions other than renal disease might affect the RI, such as very high or very low heart rates [8]. Another factor of variability is the age of the patient [9]. The RI value could exceed 0.70 without renal disease in children; a mean RI greater than 0.70 can be seen through at least the first 4 years of life [10]. In elderly patients the normal RI can also exceed 0.70 [11]. It is unclear whether this is a normal phenomenon, due to age-related changes in vascular compliance, or the result of small vessel changes in the kidney due to ageing. Moreover, dehydration, hypotension and a low heart rate appear to cause an elevated RI without a true change in renal vascular impedance [12]. There is no difference between the mean RI of the right and left kidneys, a mean RI difference, 0.02.

In recent years there has been suspicion regarding the role of renal Doppler sonography. We should understand the pathophysiology of renal disease and how it affects the Doppler arterial waveform if we want to use the RI value as a parameter for measuring changes in renal status [4]. Several studies have provided a theoretic basis for understanding the abnormal arterial spectra that may be seen with renal disease. These articles may explain why Doppler sonography may not be helpful in certain situations. It was almost universally accepted that the terms ‘resistive index’ and ‘renal vascular resistance’ could be used interchangeably, although the relationship between these factors and other variables has not been determined. A series of in vitro and in vivo experiments were performed to assess the impact of changes in vascular resistance and compliance on the RI [13]. Compliance is the rate of change of volume of a vessel as a function of pressure. A pulsating artery whose diameter expands in systole and contracts in diastole is the visual manifestation of the effect of compliance. The RI was dependent on vascular compliance and resistance, becoming less dependent on resistance as compliance decreased, and being completely independent of vascular resistance when compliance was zero. Tublin et al. found that the RI increased only with marked increases in renal vascular resistance and the RI was affected by changes in driving pulse pressures. A linear relationship was shown between the pulse pressure index (systolic pressure – diastolic pressure/systolic pressure) and the RI [14]. Conditions that affect vascular distensibility, such as renal artery interstitial fibrosis and vascular stiffening, might substantially affect the RI.

Chronic renal disease is characterized by a progressive loss of renal function resulting in end-stage renal failure. Progressive chronic renal disease
probably reflects a nonspecific renal scarring process characterized by interstitial fibrosis, loss of capillaries and glomeruli, resulting in a reduction in the number and area of renal vessels. Renal scarring leads to a reduction in the intrarenal vessel area, which in turn may be responsible for an increased intrarenal vascular resistance [15]. How much the three different renal vascular beds, preglomerular vessels, glomerular capillaries, and postglomerular vessels contribute to the raised RI is unclear. Assessment of intrarenal vascular resistance may therefore be helpful in determining the degree of intrarenal damage and may be useful in predicting the subsequent function of the diseased kidney. An increased RI value $> 80$ is a strong predictor of renal functional decline in patients with renal artery stenosis (RAS), despite correction of the stenosis [16].

Studies in patients with diabetic nephropathy (DN) suggested that the postglomerular vessels are the major contributor to increased resistance, although glomerulosclerosis and not interstitial fibrosis is the histological hallmark of this disease. Patients with essential hypertension (HTA) have a higher renal vascular resistance, even without overt nephropathy, and uniformly show decreased renal perfusion [17]. In a hypertensive patient’s glomerular filtration the rate is generally maintained, also suggesting a more pronounced vasoconstriction or scarring distal to the glomerulus [17]. Nevertheless, the pathognomonic histological sign of hypertensive nephropathy is preglomerular arteriolar hyalinosis. Aside from this condition, the alteration in renal vascular resistance is probably functional and reversible in early renal insufficiency and structural and irreversible in advanced renal disease.

These days renal Doppler sonography has been established as a routine modality and as a diagnostic tool of the daily nephrological work-up. In this article we discuss proposed applications and controversies of intrarenal Doppler sonography in nephrology and we present some of our experience. Since 1996, US examination by a duplex Doppler apparatus has been performed with HDI 3000, ATL machine. We retrospectively evaluated all patients with colour Doppler duplex examination for the last three years. A total of 2581 CDUS examinations were performed during the past three years; 883 pts in 2005, 908 in 2006, and 790 in 2007. Resistive indexes were measured in each kidney using the existing software (automated algorithm) capabilities of the scanner.

**Doppler ultrasound in renal parenchimal diseases**

Sonography is often used as the initial imaging procedure in the examination of patients with renal parenchymal diseases and renal failure. The clinical value of CDUS in diagnosis of renal parenchymal diseases, especially glomerular diseases, remains controversial. The RI has been used to evaluate renal parenchymal disease. Studies have shown that an RI of or equal to 0.70 is sugge-
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stive of tubulointerstitial (TI) disease or a vasculitis. Patients with a purely glomerular disease often had an RI that was < 0.70. In the initial work performed by Platt et al. CDUS was used to assist in differentiating obstructive from nonobstructive pyelocaliectasis. They examined 50 patients with nonobstructive renal disease (renal medical disease) and found abnormal intrarenal arterial Doppler signals in just over half [18]. It appeared clear that certain renal diseases produced states of increased renal vascular resistance (resulting in RI elevation); whereas other renal diseases produced no significant Doppler changes. Also, in another study, Platt et al. in their prospective study found renal Doppler analysis with RI measurements to be promising in differentiating major types of renal medical disease [6]. Their findings suggest that factors affecting relative renal echogenicity are not identical to the processes that alter the Doppler signal. Renal Doppler imaging did discriminate between major forms of renal disease. In renal parenchimal diseases, there is a loss of diastolic flow indicating an increase in vascular resistance or an increase in parenchimal pressure within the kidney resulting in an increased RI obtained from intrarenal Doppler spectra [9]. There is a significant positive correlation between the RI and the severity of arteriolar sclerosis, glomerular sclerosis, oedema, and focal fibrosis [19].

The potential of Doppler sonography to serve as a useful adjunct for the assessment of renal disease was advanced in a series of articles published recently. Boddi et al. studied renal RI in patients with chronic TI nephritis. They found that RI measurement allows the early identification of both normotensive and hypertensive patients with chronic TI nephritis, when renal function is still preserved. Renal RI values were linearly related to uraemia and to filtration ratio values [20]. Other authors investigated whether RI at biopsy could be related directly to vascular or TI changes in the kidney, to the clinical and histopathologic parameters and to renal outcome in patients followed up for more than 2 years. They show a direct relationship between RI and arteriosclerosis in damaged kidneys. RI at renal biopsy may be useful as one of the prognostic markers for renal outcome; patients with progression of renal impairment had a significantly increased RI at biopsy compared with patients without progression [21]. Sigiura et al. compared histologic changes in biopsy specimens with RI in 60 patients with primary and secondary glomerular diseases. TI injury scores were significantly higher in patients with RI exceeding 0.65 than in patients with a lower value [22]. Recently it was found that the mean RI in patients with glomerular diseases of 0.68 was statistically significantly higher than in controls. The mean RI was highest in patients with membranoproliferative glomerulonephritis, and the value was statistically significantly higher than in other forms of glomerulonephritis. Also, the RI significantly correlated with serum creatinine and creatinine clearance [23].

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Several studies have suggested that CDUS might aid in the management of established renal disease. Changes in the Doppler waveform were observed with the renal microangiopathy associated with the haemolytic-uraemic syndrome (HUS) in children. Doppler US could predict renal recovery from HUS before clinical improvement [24, 25]. Similarly, the RI was thought to correlate well with renal involvement in patients with progressive systemic sclerosis [26]. Some researches reported that Doppler US was useful in predicting the outcome of 34 patients with various degrees of lupus nephritis. In a prospective study an elevated RI value was a predictor of poor renal outcome, even in patients with normal baseline renal function [27]. Doppler US and RI are also suggested as a useful tool in differentiating the more common causes of acute renal failure such as acute tubular necrosis and pre-renal failure. Patients with acute tubular necrosis (excluding hepatorenal syndrome) often had an RI of $> 0.75$ whereas those with pre-renal failure (excluding patients with severe prolonged pre-renal failure which can lead to acute tubular necrosis) had a value of $< 0.75$. However, there are limitations to the clinical application of these values [28, 29]. In a series published more recently Heine et al. showed that in patients with chronic kidney disease, intrarenal RI linearly increased with a progressive impairment of renal function and independently reflected both local renal damage and systemic vascular disease [30].

**Doppler ultrasound in diabetic nephropathy**

Diabetes mellitus (DM), a chronic and evolutionary illness, complicates itself naturally as a result of vascular attacks. All arteries, from the thickest to the smallest, are reached by the disease, the appearance of the vascular complications being variable during the time [31]. Diabetic nephropathy is the most frequent clinical manifestation of microangiopathy. So far, there have been few reports describing the application of CDUS in patients with DM [32]. CDUS and RI are useful for demonstrating haemodynamic abnormalities present in DN [33]. Sonographic and Doppler features are variable at the different stages of the disease. In the early stage of DN, asymptomatic DN, in which renal function is normal, the intrarenal RI is also normal [34, 35]. These results do not agree with the results of a French study in which RI values of DM patients both with and without renal insufficiency were shown to be significantly elevated [36]. In advanced stages, the RI is increased [9, 37, 38]. As renal function becomes impaired, the serum creatinine concentration (SCC) increases and the creatinine clearance (CCR) decreases; at the same time, intrarenal RI values also increase to abnormal levels [37]. Only a few studies compared intrarenal RI values with SCC and CCR in DN [39]. Platt et al. showed a high level of correlation bet-
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Activation of the renin-angiotensin system (RAS) is reported to contribute to intrarenal haemodynamic abnormality in diabetic patients. ACE inhibitors have been shown to delay the progression of DN, slowing the decrease in GFR by decreasing the intraglomerular capillary pressure. Recently, Taniwaki et al. evaluated the effect of RAS blockade by captopril on intrarenal haemodynamic changes by examining changes in RI in normotensive patients with type 2 DM. Their results showed that in diabetic patients, both with normo- and microalbuminuria, RI values after the test were significantly lower than baseline values, which is not the case with healthy subjects. With multiple regression analysis HbA1c and baseline plasma rennin activity significantly and independently affected the magnitude of the decrease in RI values after captopril administration in diabetic patients [40]. Advanced arteriosclerosis occurs with increasing age. In addition, diabetes is a strong risk factor for arteriosclerosis, and a long duration of diabetes is a significant risk factor for advanced arteriosclerosis. Taken together, one can speculate that significant contributions of patient age and duration of diabetes to increased RI values may be due to advanced arteriosclerosis. Furthermore, renal diseases in DM patients are known to be a risk factor for widespread vascular injury. Recently, Ohta et al. evaluated the relationship between RI and pulse wave velocity (PWV, a measure of arterial stiffness), which reflects atherosclerosis, and determined whether renal RI differs depending on the underlying renal disease in 245 patients. They found that the RI of the main renal arteries was significantly higher in patients with DN than in others. The intrarenal vascular resistance appears to increase to a greater extent in DN. Their results indicate that the increased RI of the renal arteries is associated with the severity of systemic atherosclerosis [41].

At the Nephrology Clinic, Clinical Centre, Skopje, there was a follow-up study on 70 patients with DN. In 108/150 examinations of patients with DN we found an increased RI > 0.68. After initial presentation 70 patients were seen after 3, 6, 9, 12, 15 and 18 months. We used CDUS analysis to determine whether the intrarenal RI can be used as a predictor in these patients. Patients were divided based on their intrarenal RI values. Group 1 (n = 45) had values of ≥ 70. Group 2 (n = 25) had values < 70. The difference in age between patients in group 1 (mean, 53 years ± 8) and patients in group 2 (mean, 55 years ± 11) was not statistically significant. There was no significant difference in the duration of diabetes between the groups, 14.3 ± 8.2 years in group 1, 11.2 ± 7.3 years in group 2. There were no significant differences in the serum glucose, glycosylated haemoglobin HbA1c, blood urea nitrogen, albumin and electrolytes. All our patients at baseline had higher SCC and lower CCR. In patients with RI ≥ 70, SCC was 165 ± 52 μmol/l with CCR of 50.9 ± 8.8 ml/min. In patients with RI < 70, SCR was 150 ± 20 μmol/l with CCR of 54.9 ± 6.7 ml/min. At the
end of the follow-up, after 18 months, SCC and CCR expressed statistically significant differences between the two groups of patients. Twenty patients from group 1 had a decline in renal function after 18 months. In comparison, among patients with intrarenal RI values < 70 only 6 had a decline in renal function. Regarding proteinuria, there were statistically significant increases and differences between the groups after 9 and 18 months. Mean blood pressure was significantly higher in the patients with RI ≥ 70 at baseline (107 ± 12 mmHg vs. 97 ± 11 mmHg) and after 18 months (115 ± 7 mmHg vs. 103 ± 10 mmHg). The statistical significance of differences for RI values was observed between the groups during the follow-up period. In multiple regression analysis, RI values in DN patients were significantly affected by Delta CCR, proteinuria and mean blood pressure. The relationship between the RI values and Delta CCR in DN patients showed a negative correlation coefficient of $r = -0.388$ ($P < 0.01$). There was no relationship between CCR and age and RI and age in DN patients. With linear regression analysis a significant, negative correlation existed between the RI values and CCR in DN patients, $r = -0.630$ ($P < 0.01$).

**Doppler ultrasound in assessment of renal transplant**

In renal transplantation US including colour Doppler have become an integral part of the care of patients with renal allograft. US is indicated in all patients with allograft dysfunction or urinary tract abnormalities. The transplanted kidney is a solitary kidney and may compensate by hypertrophy and display increased renal blood flow leading to higher velocities, even when the diameter of the transplant renal artery has remained normal. CDUS has a critical role in the diagnosis of vascular lesions [43, 44]. Good images of the transplant kidney are possible because of the location, which is close to the body surface in the iliac fossa. Assessment of perfusion of the graft is the main examination in patients with postoperative anuria. Complete and partial infarction of the transplant may also be reliably detected at a later stage. Partial infarction of the transplant secondary to occlusion of the pole arteries or segmental arteries displays a local deficit of perfusion [45]. In the immediate postoperative period US is useful in diagnosing such surgical causes of delayed graft function as thrombosis of the renal artery or vein, urinary obstruction caused by ureteral kinks, and urine leak. Changes in the sonographic appearance of the renal parenchyma can be very suggestive of acute rejection (AR). Sonography also is essential for guiding a percutaneous biopsy. Measurement of RI is of use in differentiating common causes of acute renal failure. In general, studies show excellent sensitivity and specificity in diagnosing a range of vascular disorders in renal allografts. CDUS also can be used to aid in the detection of flow and complications. It is important to recognize the venous system, which, when dilated, can mimic hydronephrosis. The distinction is made readily by CDUS [43].
Most of our examinations, 194 (7.52%) were on transplanted patients. There were 68 transplanted patients, 32 men and 36 women, mean age 33 years. If it was necessary, for example in every case of sudden oliguria or deterioration of allograft function, patients were controlled and screened several times. Chronic allograft rejection was found in 98 examinations, acute rejection in 58, and in 38 examinations transplant renal artery stenosis (TRAS) or thrombosis was suspected. If there was no obstruction or TRAS, an ultrasound guided allograft biopsy was performed.

**Vascular disorders**

Vascular complications after renal transplantation account for less than 10% of all complications but they are an important cause of graft dysfunction. TRAS is the most common vascular complication, usually occurring within the first three years after transplantation. The incidence of TRAS is 1–12%. Considering the risk of transplant loss while promising therapeutic possibilities exist, a screening diagnostic method would be useful. Stenosis at the anastomosis is believed to be a result of surgical technique. Colour Doppler may suggest TRAS when turbulent flow is seen. Reported sensitives for RI range from 58% to 100% with the majority greater than 90%. Specificities of 87% to 100% have been reported. Marked renal artery occlusion is rarer; the sensitivity and specificity of Doppler US are nearly 100%. Arterial occlusion is best diagnosed as a lack of arterial flow within the kidney beyond the site of the occlusion. If the main renal artery is occluded, no venous flow will be detected. If there is segmental arterial occlusion, venous flow will be absent only in the affected segment [43]. Goel et al. showed in 51 transplant patients that high-probability DUS and corresponding clinical findings are likely to identify a significant stenosis that is responsive to treatment [46]. Both high and low velocities are seen within a stenosis. With increasing impairment of flow velocity vectors are pointing in different directions. This phenomenon is referred to as ‘spectral broadening’. Poststenotic spectra are modified by turbulences. Marked downstream turbulence has to be present in the artery distally of a region with local flow increase in order to make a diagnosis of TRAS [47]. An increase in flow velocity produces less intense colours in Doppler US. Other signs of stenosis, poststenotic turbulences and marginal flow reversals, produce a mosaic-like pattern of red and blue. The Doppler spectrum also provides some information about the characteristics of the stenosis. Some authors consider flow velocities of 100 cm/s as diagnostic of stenosis, whereas others suspect stenosis only at velocities exceeding 190 cm/s. Hollenbeck accepts that an increase in flow velocity of more than 150% (compared to normal areas of the transplant artery) suggests the presence of stenosis. Based on a local increase in flow velocity exceeding 150% and simultaneous evidence of poststenotic turbulences on the
colour image, he recognized transplant artery stenosis with a sensitivity of 92% and a specificity of 96% [45].

Complete renal vein thrombosis (RVT) is rare and uncommon. RVT occurs early after the operation when there are surgical problems with the anastomoses. Recognition of complete renal vein thrombosis is mandatory because it may lead to graft loss. CDUS is superior to all other imaging modalities for the diagnosis of complete transplant RVT. CDUS finding is a lack of venous flow signals within the parenchyma tissue and in the main renal vein. The diagnosis is confirmed when this finding is associated with a negative reversed diastolic flow within the renal artery [45].

Arteriovenous fistulas (AVF) and intrarenal pseudoaneurysms (PA) are the result of trauma, most often they are complications of transplant biopsy. Most are small, spontaneously resolve and have no clinical significance. An AVF occurs in up to 17.5% of all transplanted kidneys. With CDUS AVF is diagnosed as an area of disorganized flow, blue-red in appearance. In the PA there is the typical pattern of high flow during systole and outflow during diastole. Extrarenal AVF and PA are the result of surgical technique. Doppler interrogation of the collection will show the characteristic to-and-from flow and may show the neck of the pseudoaneurysm [43].

**Transplant rejection**

Acute rejections produce a rise in intraparenchimal pressure and in renal artery flow resistance. This leads to a decrease of end-diastolic and mean flow velocity and thus to an increase of RI values. CDUS might serve as a non-invasive screening method. The RI has proved useful in the recognition of rejection and an elevated RI was initially considered a finding specific for rejection. But there are numerous intra- and extrarenal causes that also lead to higher RI. Some researchers have since documented the lack of specificity of an elevated RI [4]. It is unclear whether high RI reflects local renal damage or systemic vessel disease. Heine *et al.* found that intrarenal RI is associated with traditional cardiovascular risk factors as well as with subclinical atherosclerotic vessel damage and thus should not be considered specific markers of renal damage [48]. In a series published by Chudek *et al.*, ischemic injury, which occurred mainly prior to organ harvesting, played a dominant role in determining intrarenal resistance in the early posttransplant period. Differences between the groups (patients with immediate, slow, and delayed graft function; RI 0.72, 0.78, and 0.83, respectively) were highly significant [49]. RI should be measured repeatedly in individual graft recipients. In acute postischaemic renal failure the RI tends to decrease over time. If, during the course of postischaemic acute renal failure, RI decrease first and increase subsequently an acute rejection reaction is likely. Baxter found that results were clearly improved when
serial measurements were performed [44]. The period between the examinations varied between 2 and 4 days at the most with a sensitivity of 90% and a specificity of 76%. Unfortunately measurements of RIs are not suitable for the diagnosis of chronic rejection. Recently, encouraging results were obtained by Kahraman et al. who tested whether early CDUS findings were predictive of 1-month and 1-year allograft functions in 45 noncomplicated renal transplant recipients. They found a significant decline in allograft function among cases with RI > 0.70; patients with impaired allograft function have higher RI values [50].

**Doppler ultrasound in renal artery stenosis**

Renal artery stenosis is a common cause of secondary hypertension (HTA) and may cause renal insufficiency. It is important to identify such patients; renovascular disease is present in about 10–40% of patients with ESRD. It is mandatory to evaluate the functional significance of a stenosis before intervention. Angiography is the gold standard for the morphologic visualization of RAS. However, angiography is costly, invasive, and associated with inherent morbidity. Therefore, is cannot be used as a screening method. Non-invasive imaging techniques to diagnose renovascular hypertension include duplex/colour Doppler, magnetic resonance angiogram, computed tomography angiogram, and angiotensin-converting enzyme (ACE) inhibition renography. Over the past years there have been several CDUS studies which have attempted to evaluate the renal arteries. [51]. Radermacher suggests although renal RI is not a perfect test for renovascular disease, it can provide useful diagnostic information [52]. Kawarada et al. found, in 60 patients, that the measurements of peak systolic velocity in the renal artery and a ration of PSV in the renal artery to the aorta examined as duplex US parameters is not only noninvasive but also highly precise in detecting patients with haemodynamically significant RAS [53]. Some authors have recommended examination of the main renal arteries, peak systolic velocity and renal artery to aortic ratio. Others have examined the downstream haemodynamic effects from renal artery stenosis by evaluating the intrarenal vasculature, early systolic peak, acceleration, and acceleration time. A number of parameters have been reported for the identification of a haemodynamically significant RAS. The most widely accepted criteria are: 1) a ratio of the peak systolic velocity in the renal artery to the peak systolic velocity in the adjacent aorta of > 3.5 or 2) a peak systolic velocity of > 180 cm/s. Reported sensitivities range from 84% to 98% and specificities from 90% to 98% for the detection of angiographically significant main RAS when compared to Doppler US [54].

Few studies have reported the value of CDUS in predicting clinical response of RVH to intervention. An enthusiastic application of renal duplex US, is justified [55]. In recent years the use of renal RI to predict the response to

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intervention has become more wide-spread. CDUS to evaluate renal RI or captopril scintigraphy is the best method by which to classify patients as responders or non-responders to intervention. In patients with a renal RI \( \geq 80\% \), improvement of renal function or blood pressure is highly unlikely, despite successful correction of RAS. [56]. Voiculescu et al. studied 50 patients with unilateral stenosis and hypertension. They found significant differences only for RI and plasma renin activity measurements between responders and non-responders. The highest sensitivities and specificities predicting which patients will not improve were found for RIs \( > 0.55 \). They conclude that an RI of a poststenotic kidney above 0.55 can predict a poor outcome concerning arterial blood pressure response after restoration of renal blood flow for unilateral RAS [57]. In 52 cases of our examinations, 2.0%, RAS was postulated as a cause of secondary HTA. A difference of 0.04 in RI between the right and left renal artery was considered as significant. Unfortunately, not all patients proceeded with further diagnostic procedures; only in three cases was RAS confirmed with angiography.

Doppler ultrasound in essential hypertension

Hypertension is one of the most common medical disorders identified. High blood pressure affects 20–25% of the population in western and developing countries. Nevertheless, because HTA may cause renal insufficiency it is important to identify such patients in the large hypertensive population. Renal vascular resistance is regulated by an intricate balance of several vasodilating and constricting systems such as sympathetic neural tone, thromboxane, endothelin, prostacyclin, and nitric oxide. Any disturbance in this balance leads to renal vasoconstriction and causes HTA. The significance of the CDUS in the evaluation of renal vascular resistance in patients with essential HTA is still not clearly determined. There are only a few published studies in this field [58, 59]. Galesic et al. found that the RI values correlated with the duration of HTA as well as with the patients’ age [60].

The evaluation of blood flow and abnormalities of renal and intrarenal arteries with Doppler has potential value as a diagnostic tool in essential HTA, because this disease is characterized by an increased vascular resistance in comparison to normotensive people [58]. In essential HTA the kidney is affected by hypertensive arteriolar alterations, and renal blood flow may be reduced as a result of arteriolar constriction in the early stage. The early phase of established essential HTA in young patients is haemodynamically characterized by an increase in cardiac output, while total peripheral arterial resistance remains normal. On the other hand, in normotensive persons, an increase in cardiac output would lead to fall of total peripheral resistance. When the patient with essential
HTA reaches middle age, cardiac output and other indices of sympathetic activity revert to normal. Total peripheral arterial resistance becomes distinctly elevated and represents the haemodynamic hallmark of essential HTA. The elderly patient with essential HTA is therefore characterized by high total peripheral resistance as a result of atherosclerosis of intrarenal arteries and a low cardiac output [61].

The increased RI in mild HTA could be related to a functional vasoconstriction, while in moderate and long-standing HTA the increased RI could be the result of hypertensive nephrosclerosis. Galesic et al. have observed that RI of intrarenal arteries correlated well with ocular and cardiac involvement [62]. Pontremoli et al. concluded that increased RI should be regarded as a marker of early renal and systemic vascular damage, helping to identify HTA patients at higher risk [63]. The underlying mechanism for the increase in RI in essential HTA is not well understood. The increased RI could partly be caused by functional vascular changes that are vasoconstriction mediated by the sympathetic nervous system or by circulating norepinephrine and angiotensin II, endothelin, prostacyclin, and nitric oxide. Therefore, the increase of RI could be reversible to some extent. Increased RI in hypertensives is at least partly dependent on renal functional vascular changes. An important rationale for antihypertensive treatment is to preserve the renal function. One explanation for the preservation of the renal function in hypertensives treated with ACE inhibitors is the ability of ACE inhibitors to decrease the renal vascular resistance. Palatresi et al. [64] in agreement with Jensen et al. [65] found a significant correlation between RI and renal plasma flow and/or renal vascular resistance. These findings clearly indicate that this index is useful for non-invasively assessing the renal function [62]. Nonetheless, the association between increased renal RI and atherosclerotic vascular damage has led us to believe that it may signal the presence of intrarenal atherosclerosis. Previous studies have shown that the RI is a reliable marker for moderate and severe renal arteriosclerosis. Because renal haemodynamic changes can occur before the onset of early systems, evaluation of renal RI might be useful for the assessment of early renal arterio-atherosclerosis caused by hypertension [66]. In our patients, there was a positive correlation between RI and the severity of HTA. In the majority of patients, 331/512, we found nephroarteriolarosclerosis (RI > 0.64).

**Doppler ultrasound in obstructive uropathy**

When a dilated collecting system is observed with US, it is important to differentiate obstructive from non-obstructive dilatation. Early and precise diagnosis of obstructive uropathy permits prompt and appropriate therapy, which is essential to minimize the devastating effects of obstruction on the urinary tract structure and function. Urinary obstruction (UO) in the early stages can be dif-
Difficult to diagnose. Plain abdominal radiography, standard renal US and intravenous urography are the usual imaging modalities for evaluating acute renal colic. In recent years, the introduction of CDUS has improved the clinical application of US in patients with UO by using the RI. The RI reflects changes in the renal vascular resistance that occurs with UO. In the setting of obstructive dilatation, renal vascular resistance increases due to the presence of a potent renal vasoconstriction, thromboxane A2. An elevation of the pressure in the intrarenal collecting system occurs with acute urinary obstruction. This causes reduction in renal blood flow as a result of increased renovascular resistance. This increase in intrarenal vascular resistance is responsible for a diminished diastolic blood-flow velocity in the intrarenal arteries and the RI increases. Obstruction alters the venous flow to a greater extent than the arterial flow, and a comparison between the venous flow in obstructed and unobstructed kidneys may improve diagnostic accuracy [2, 67]. This is consistent with the results of Pepe et al. They conclude that CDUS improves the diagnostic accuracy of US in distinguishing between obstructive and non-obstructive dilatation with high sensitivity and specificity. They recommended CDUS especially for the follow-up of patients after ESWL, pregnant women and children [68]. Some authors found that CDUS has a very good sensitivity in detecting the renal obstruction before the dilatation of the collecting system is installed [69]. Haroun et al. performed a study of 46 healthy individuals and of 42 patients presenting with acute renal colic. Their study showed that RI was related to excretion delay in cases of complete obstruction, for which RI was higher in non-excreting than delayed-excreting kidneys; this was not found, however, in cases of partial obstruction [70]. However, there some divergent results have been reported. Gurel et al. published that RI is not sensitive in differentiating obstructive and nonobstructive urinary calculi in patients with acute renal colic. [71]. The high false-negative rate may, in some cases, be due to low-grade, extremely early obstruction. In these settings and with severe long-standing obstruction, arterial distensibility would be marginally affected because interstitial pressure is relatively normal. The increased reliability of CDUS when a furosemide challenge is used might also suggest the impact of acutely elevated interstitial pressures on renal blood flow and the RI.

Other applications of Doppler ultrasound

Oncologic indications for US are many. They include the detection of tumours as well as their diagnosis on the basis of their morphology on a grayscale sonographic exam. The incorporation of Doppler technology permits the noninvasive evaluation of organ and tumour vasculature. Conventional Doppler may show blood flow in hypervascular tumours. Imaging contributes to the cli-
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Clinical management of patients with renal tumours in providing diagnostic information for tumour detection, characterization, staging, treatment planning, and follow-up [72]. In our examinations, pathological, markedly increased vascularization was noticed in 34 cases suspected of renal carcinoma, in 46 cases of suspected testicular tumours, 19 cases of suspected prostate neoplasm and 32 cases of suspected tumours in other localizations.

The long-term survival and quality of life of patients on haemodialysis is dependent on the adequacy of dialysis via an appropriately placed vascular access. The optimal vascular access is the autologous arteriovenous fistula. CDUS is a useful non-invasive method to evaluate arterial vessels prior to AVF construction. The study by Lomonte et al. documented the changes in brachial blood flow rate consequent to radiocephalic wrist AVF maturation by means of CDUS of the brachial artery. This measure may be helpful in monitoring which AVFs will probably fail [73]. Patients with poor functioning AVF had significantly less arterial internal diameter, higher arterial RI, less venous internal diameter, and less venous blood flow velocity and volume [74]. The most common reason for fistula failure is thrombosis caused by stenosis. CDUS has proven to be effective in the assessment of anatomical vascular features. They evaluated completely asymptomatic, mature AVF with CDUS in 139 patients and found a high level of abnormalities present in well-functioning mature AVFs [75]. Also, CDUS has the ability to reveal causes of ischemic steal syndrome in patients with antebraclial accesses and hand ischemia [76].

Summary

The results of Doppler US have been very positive, with substantial improvement in patient care and physician efficiency. These benefits, plus the fact that renal Doppler US is straightforward and does not require expensive equipment, indicate that US should become an integral procedure in the practice of nephrology. Doppler US is economically feasible, and nephrologists should be able to recover the costs. With colour Doppler US organ perfusion is reliably recorded, and this procedure may in the future replace isotope nephrography. In many situations the use of Doppler US avoids scintigraphy and angiography without impairing diagnostic reliability.

The quantification of tissue perfusion will be improved by the application of ultrasound contrast media. These products bind micro-air-vesicles e.g. to galactose particles, and thus increase the reflection capacity of blood. The results obtained with contrast echographic method suggest that it can be useful.
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Резиме

ДОПЛИЕР УЛТРАСОНОГРАФИЈА: ДИЈАГНОСТИЧКО СРЕДСТВО ЗА НЕФРОЛОЗИТЕ – ИСКУСТВО НА ЕДЕН ЦЕНТАР

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Колор доплер дуплекс ултрасонографијата (КДУС), прикажувајки боја, овозможува неинзавизивна проценка на промените во васкуларната перфузија.

Од 1996 год, ултрасонографското испитување со дуплекс доплер опрема се изведува со HDI 3000, ATL апарат. Ретроспективно ги евалуираше сите пациенти (пц) кои се испитувани со колор доплер дуплекс ултрасонографија во последните три години. Индексот на резистенција (ИР) е мерен на секој бубрег користејќи ја постоечката програма на скенерот.


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нефропатија; во 108 случаи најдена зголемен ИР > 0,68. Постои позитивна корелација помеѓу ИР и тежината на артериолосклерозата, во повеќето случаи на здрав (331), најдена е нефроларелосклероза (ИР > 0,64). Во 52 случаи беше сусpektna стеноза на реналната артерија (разлика од 0,04 помеѓу ИР на десната и левата ренална артерија). Акутна бубренка болест беше сусpektna во 53 случаи. Во однос на неоплазмите, патолошка, мар-кантно зголемена васкуларизација беше нотирана во 34 случаи сусpektnи за карцином на бубрег, во 46 случаи сусpektnи за тестичулиарни тумори, во 19 случаи сусpektnи за неоплазма на простата и во 32 случаи сусpektnи за тумор на друга локализација.

КДУС во комбинациjа со исторijата на болеста, клиниките и лабораториските испитувања придонесува за корисна информациjа во поставuвање на дијагнозата.

Ключни зборови: бубрег, колор дуплекс доплер ултрасонографгиjа, индекс на резистенциjа.

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