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The Evaluation of Renal Hemodynamics with Doppler Ultrasonography

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1. Introduction

Gray-scale renal ultrasonography (US) is still performed as a matter of course during the initial evaluation of both native and transplant renal dysfunction. The results, however, often fail to impact on the differential diagnosis or management of renal diseases. Despite major technological advances, gray-scale renal US has remained largely unchanged since the 1970s. It provides only basic anatomical data, such as renal length, cortical thickness, and collecting system dilatation grades. While these may assist in the analysis of disease chronicity, ultrasonographic findings are often normal in spite of the presence of severe renal dysfunction. Clinicians and radiologists are agreed that even the increased renal echogenicity accompanied by renal failure (medical renal disease) requires greater specificity and sensitivity to make it clinically relevant. Collecting system dilatation detection is reliable, though it is not always possible to distinguish between obstructive and non-obstructive pelvicaliectasis on the basis of gray-scale US alone. This purely anatomic approach to renal US, combined with other improved and more economical modalities, has led to nephrologists, internists, and urologists becoming more involved in the field of radiology (Tublin et al., 2003).

Doppler ultrasonographic examination of vascular structures is a fundamental diagnostic technique and one that can also be used to examine organs. Doppler ultrasonographic examination of the kidney, a particularly highly perfused organ, increases the effectiveness of the technique. Color, power and spectral Doppler also supply additional hemodynamics data in addition to the morphological analysis. Renal and extrarenal pathologies as well as other factors also alter renal hemodynamics. Hemodynamic change can be distinguished by variation in intrarenal arterial waveforms. Color Doppler accelerates and facilitates imaging, while duplex Doppler US provides quantitative hemodynamic data. Diseases impacting on organ blood flow may be further characterized by duplex Doppler US. Quantitative Doppler ultrasonographic data include blood flow velocities and volumes. Semi-quantitative data include the indices calculated from blood flow velocities obtained from the spectral Doppler spectrum in renal vessels during the cardiac cycle. These establish resistance to blood flow in the vascular lumen and are a significant source of information about organ perfusion. Three major indices are used in clinical practice: the Systole - Diastole (S/D) ratio, the Pulsatility Index (PI) and the Resistive Index (RI) (also known as the Pourcelot index, resistivity index or resistance index).

$$S / D = \text{Peak Systolic Velocity} / \text{End Diastolic Velocity}$$

$$PI = (\text{Peak Systolic Velocity} - \text{End Diastolic Velocity}) / \text{Mean Velocity}$$

$$RI = (\text{Peak Systolic Velocity} - \text{End Diastolic Velocity}) / \text{Peak Systolic Velocity}$$

Under normal homeostatic conditions the renal circulation offers low impedance to blood flow throughout the cardiac cycle with continuous antegrade flow during diastole. However, during conditions associated with increased renal vascular resistance, the decrease in renal diastolic blood flow is more pronounced than the decrease in the systolic component. During extreme elevations of renal vascular resistance diastolic flow may be nondetectable or may even show retrograde propagation. Therefore, Doppler ability to characterize altered waveforms in response to elevations of renal vascular resistance may be used to calculate the RI and PI. They were initially introduced for the purpose of determining peripheral vascular diseases. They are also used for the analysis of pathological blood flow patterns and may possibly be used to discriminate among various pathophysiological conditions of the kidney. Resistive index is more widely used than the S/D ratio and PI. Doppler waveform studies are noninvasive, painless, readily available, and relatively easy to perform and learn. Moreover, Doppler ultrasound obviates the need for ionizing radiation and intravenous contrast material administration in situations in which they may be undesirable, such as pregnancy, allergy and renal insufficiency (Rawashdeh et al., 2001).

2. The renal doppler US technique

2.1 Human medicine

The patient has to fast for 8 h prior to the Doppler ultrasonographic examination of the native kidney. The transducer must be positioned so as to visualize the lateral or posterolateral aspect of the kidney. In this position, Doppler examination can be performed with the lowest appropriate angle (0-60°), establishing an appropriate approach toward vascular structures in the periphery of the hilus and permitting visualization of the kidney without obstruction by gases present in the segments of the intestine and causing artifact. Doppler analysis is then performed.

In intrarenal Doppler ultrasonographic examination, the majority of studies of the potential that have used Doppler US for renal disease evaluation emphasize the importance of applying the most careful technique. It is important to use the highest frequency probe gives that measurable waveforms, with the additional use of color or power Doppler US as appropriate for vessel localization. The arcuate arteries (at the corticomedullary junction) or inter pyelocaliectasic lobar arteries (adjacent to the medullary pyramids) are subsequently insonated with a 2-4 mm Doppler gate. The spectral samples/specimens from the arteries must be analyzed once they have been obtained from three different sites (the cranial, middle and caudal poles). Waveforms should be optimized for measurement by the use of the lowest pulse repetition frequency without aliasing (to maximize waveform size), the highest gain without obscuring background noise, and the lowest degree of wall filter. Three to five reproducible waveforms from each kidney are obtained. Subsequently, the renal Doppler values from these are averaged to establish mean RI and PI values for each kidney.

Once intrarenal Doppler evaluation of the kidney on the investigated side has been completed, the main renal artery and/or veins are analyzed directly. Because of their dimensions, colored Doppler imaging yields no significant contribution to the analysis of these structures, in contrast to intrarenal examination, and gray-scale US is generally employed. However, color Doppler examination is necessary in renal vein thrombosis. The patient is placed in the decubitus or semi-decubitus position, with the kidney to be examined on top, thus permitting transversal visualization of the kidney and including an image of the abdominal aorta. The lateral tip of the transducer is angled slightly toward the caudal aspect, permitting appropriate imaging of the course of the main arterial artery or vein.

It is easier to investigate graft (transplanted) kidneys in the caudal abdomen, located close to the abdominal wall and retroperitoneally, with gray-scale and Doppler US than native kidneys. The hilus must be positioned posteromedially as the transplant kidney is visualized. Gray-scale and intrarenal Doppler evaluations are then performed. Renal artery and vein examination are performed with Doppler mode in the final stage of transplant kidney examination (Platt, 1992; Rawashdeh et al., 2001; Ruggerenti et al., 2001; Tublin et al., 2003; Zubarev, 2001).

2.2 Veterinary medicine

The main renal artery and vein in dogs and cats can be imaged from the hilus of the kidneys as far as their point of origin from the aorta and to the caudal vena cava, respectively. Renal artery diameters are calculated in systole on the basis of gray-scale echo mode. Doppler measurements are performed at the same point (Fig. 1A). In intrarenal Doppler, interlobar branches can be imaged in the proximity of the central echocomplex, since these radiate from the pelvis in the direction of the corticomedullary junction. After branching into arcuate arteries, interlobar arteries flow in the corticomedullary junction. Color Doppler ultrasound can be used to observe the interlobular arteries originating from the arcuate arteries in the cortex. The veins run parallel to the arteries. They are usually wider than the adjacent arteries. The renal arteries exhibit a typical parabolic flow velocity profile (*i.e.*, systolic peaks with broad velocity distribution and no spectral window). The systolic peak is always broad, and it is sometimes possible to observe an *early systolic peak*. Low resistance flow can be determined from a high, continuous diastolic flow, gradually declining during diastole. Following the systolic peak, there is a slight fall in velocity, and then another increase (diastolic peak velocity), gradually decreasing in the rest of the diastole (Fig. 1B). Renal vein flow may exhibit minor changes because of changes in the right atrial and intra-abdominal pressure. An increased forward flow wave follows each heartbeat. If the contractions are in sufficiently close proximity, the next wave (on the Doppler tracing) is superimposed on the previous one, resulting in faster flow. In the event of a more protracted pause between ventricular contractions, the velocity slowly declines in the renal veins superimposed on the previous one, again resulting in faster flow. If the pause between two ventricular contractions is longer, velocity in the renal veins gradually declines; 3.5-7.5 MHz linear or convex transducers can be used. Equipment settings are standardized, and should include a minimum wall filter setting of 50 Hz and a Doppler sample volume between 1 and 3 mm (Szatmari et al., 2001).

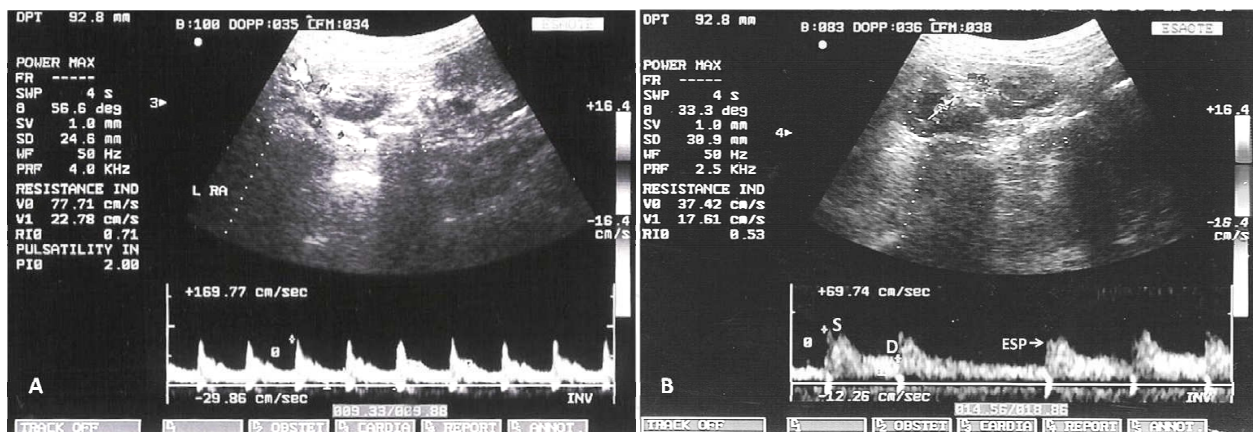


Fig. 1. Duplex Doppler ultrasound images of the left renal artery (A) and the left kidney (B), exhibiting peak systolic blood flow velocity (S), end-diastolic blood flow velocity (D) and early systolic peak (ESP) in a healthy dog.

3. Renal resistive index

3.1 Theory

Recent *in vitro* experiments at the University of Michigan have demonstrated the importance of vascular compliance in RI analysis (Tublin et al., 2003, as cited in Bude & Rubin, 1999). Compliance may be defined as the rate of volume change of a vessel as a function of pressure. A pulsating artery expanding in systole and contracting in diastole is a visual manifestation of the effect of compliance. The aim of the *in vitro* experiments was to assess the impact on RI of changes in vascular resistance and compliance. RI was dependent on vascular compliance and resistance. As compliance increased, it became increasingly less dependent on resistance. With zero compliance it was totally independent of vascular resistance. The same team performed another *in vitro* study in which RI decreased with increases in the cross-sectional area of the distal arterial bed. This was again independent from compliance and vascular resistance. Similar *ex vivo* results were produced in a series of experiments from Albany Medical College (Tublin et al., 2003, as cited in Tublin et al., 1999). A pulsatile perfusion system was used to perfuse rabbit kidneys *ex vivo*. Renal vascular resistance, systole, diastole, pulse pressure, and pulse rate were controlled and monitored, while RI was measured simultaneously. A linear relationship was determined between the RI and changes in renal vascular resistance of a pharmacological nature. However, elevation in RI could be related to non-physiological factors that cause in renal vascular resistance. Changes in the RI observed with intense vasoconstriction were only very slightly greater than RI measurement variability. However, RI was significantly affected by alterations in driving pulse pressures. The experiments revealed a linear relationship between RI and the pulse pressure index. The Albany group then performed a series of follow-up *ex vivo* experiments intended to indirectly explore the effect on RI of changes in vascular distensibility (Tublin et al., 2003, as cited in Murphy & Tublin, 2000). They subjected isolated rabbit kidneys to pulsatile perfusion while the renal pelvis was pressurized via the ureter. The team's hypothesis was that subsequent increases in renal interstitial pressure would reduce arterial distensibility and that this would be most apparent during diastole. Arterial distensibility was indirectly assessed on the basis of changes in vascular conductance (flow

/ pressure). They determined that graded increases in renal pelvic pressures led to heightened renal vascular resistance, and that lowered mean conductance led to a higher conductance index (systolic conductance – diastolic conductance / systolic conductance) and increased RI. Their findings emphasize the importance of the interaction among vascular distensibility, resistance, and pulsatile flow in RI analysis. Claudon et al. (1999) replicated many of these findings in a study assessing changes in pig renal blood flow during acute urinary obstruction using contrast-enhanced harmonic sonography. The results of these trials confirm that disease phenomena impacting on vascular distensibility, such as renal artery interstitial fibrosis and vascular stiffening, may also substantially affect the RI.

The unsatisfactory nature of the results obtained using the RI to evaluate ureteral obstruction may perhaps be ascribed to this body of experimental research. The high false-negative rate attendant upon the technique may be due, in some cases, to low-grade, extremely early obstruction or forniceal rupture. At the settings involved and with severe long-standing obstruction, arterial distensibility will only be very slightly affected, since interstitial pressures are relatively normal. The increased reliability of Doppler US in the event of a furosemide challenge being used might also suggest the impact on renal blood flow and the RI of acutely elevated interstitial pressures.

The complex interaction between renal vascular resistance and compliance may also partly account for Doppler US's inability to consistently differentiate types of intrinsic renal disease. It is possible that early reports of elevated RIs with vascular–interstitial disease (but without glomerulopathies) are primarily due to the lower levels of tissue and vascular compliance associated with renal diseases of these kinds (and not only associated with increased renal vascular resistance). Subsequent rather pessimistic reports may also be ascribed to differing patient populations and mixed renal diseases; one isolated RI on its own may not help in the differential diagnosis of intrinsic renal disease because of mixed histology and varying effects on vascular compliance and resistance (Alterini et al., 1996; Pontremoki et al., 1999; Shimizu et al., 2001).

3.2 Resistive index of normal kidneys

3.2.1 Human

3.2.1.1 Adults

A number of studies have cited a value of approximately 0.60 for a normal mean intrarenal RI. The largest series so far (58 patients) reported a mean (\pm SD) RI of 0.60 ± 0.01 for subjects without pre-existing renal disease (Keogan et al., 1996). Three previous studies cited similar normal mean RI values of 0.64 ± 0.05 (21 patients) (Norris et al. 1984), 0.58 ± 0.05 (109 kidneys) (Platt et al., 1989a), and 0.62 ± 0.04 (28 patients) (Kim et al., 1992). The renal vascular bed in a normal kidney exhibits low blood flow impedance, as reflected by continuous forward flow in diastole in normal adult kidneys (Shokeir et al., 1997a). Most sonographers now regard the upper threshold of the normal intrarenal RI in adults to be 0.70 (Platt et al., 1991a; Platt, 1992).

3.2.1.2 Children and the elderly

Recent studies have shown that mean intrarenal RI is age-dependent, particularly in infants (Kuzmic et al., 2000; Murat et al., 2005; Sigirci et al., 2006; Vade et al., 1993; Wong et al.,

1989). In children, the mean RI frequently exceeds 0.70 during the first year of life. A mean RI of over 0.70 can be observed during the first four years of life at least (Andriani et al., 2001; Bude et al., 1992). In humans, active plasma renin levels are sharply elevated at birth and decrease gradually with age (Fiselier et al., 1984). By 4–8 years, active renin levels exceed those in adults only very slightly. Other renal functional parameters also differ at birth from the corresponding levels in adults. Renal blood flow rate, glomerular filtration rate and tubular excretory capacity for sodium *para*-aminohippuric acid are lower at birth but generally assume adult levels by the age of two. They usually do not mature concurrently. Maturation of renal blood flow rate is, to some extent at least, due to a decrease in renal vascular resistance (Murat et al., 2005). Sigirci et al. (2006) suggested that intrarenal RI was higher for children up to 54 months old than for adults. Therefore, the adult mean intrarenal RI criterion of 0.70 should be applicable to children 54 months old and older. The age dependency of the intrarenal RI is directly related to that of plasma renin and aldosterone levels in healthy children whom Doppler parameters and blood analysis are evaluated synchronously.

The intrarenal RI values in patients aged over 60 tend to be higher than those in younger adults (Rawashdeh et al., 2001; Terry et al., 1992). This may be ascribed to true renal dysfunction in senescent kidneys and that is not solely due to misleading variations or an age-dependent variability in the RI (Platt et al., 1994a). This suggestion is based on the fact that elevated values in patients over 60 are correlated with compromised creatinine clearance. Another study demonstrated that average RI levels increases by 0.002 on an annual basis (Keogan et al., 1996). This is possibly due to a progressive decrease per decade of some 10%, the result of functional and anatomical changes in the renal vasculature with increasing age (Rawashdeh et al., 2001).

3.2.2 Animals

In a study involving 20 healthy young pigs, Rawashdeh et al. (2000) demonstrated a normal RI range of 0.48 to 0.85 (0.63 ± 0.09). Pope et al. (1996) reported a 95% confidence interval (CI) from 0.43 to 0.63 (0.53 ± 0.05) in another porcine study. Baseline values in studies on rabbits vary between 0.51 ± 0.04 and 0.54 ± 0.11 (Chu et al., 2011; Kaya et al., 2010; Kaya et al., 2011). An intrarenal RI range of 0.52 - 0.73 have been reported for healthy dogs (Nyland et al., 1993), and of 0.44 - 0.71 for healthy cats (Rivers et al., 1996). Another study reported an intrarenal RI was 0.61 ± 0.06 in 22 normal kidneys in dogs (Morrow et al., 1996). In 11 mongrel dogs, the RI range was 0.54 to 0.75 (0.64 ± 0.05) (Dodd et al., 1991a). However, Ulrich et al. (1995) reported a 95% CI of 0.46 - 0.62 (0.54 ± 0.04) in six mongrel dogs. In a study of healthy Persian cats, main renal artery RI values for the right kidney were 0.52 ± 0.07 and 0.55 ± 0.07 for the left kidney, with an intrarenal RI value obtained from the interlobar arteries of 0.51 ± 0.07 (Carvalho & Chammas, 2011). Another study reported intrarenal RI values for normal cats as 0.59 ± 0.05 for the right kidney and 0.56 ± 0.06 for the left kidney, with no statistically significant differences observed between them (Nyland et al., 1993). In another study, intrarenal RI values for mixed-breed cats were 0.61 ± 0.04 , and 0.60 ± 0.07 for Turkish angora cats (Gonul et al., 2011). There is no considerable difference among breeds, but species. Such findings may simply reflect the varied nature of the species and breed studies' inherent physiological qualities (Rawashdeh et al., 2001). Renal dimensions and intrarenal RI have been correlated to the body weight of cats (Park et al., 2008). Studies comping with the age-intrarenal RI relationship and renin-angiotension-

aldosterone system are limited. Mechanism by renin-angiotension-aldosterone system plays a role has not been clearly established in dogs and its effect in clinic application is not yet completely understood. In a study by Chang et al. (2010), the intrarenal RI in dogs younger than 4 months was higher than in older dogs. Therefore, the use of 0.73 as the upper limit for intrarenal RI in normal dogs is not appropriate for dogs younger than 4 months. They also stated that plasma renin activity was an important factor in the age dependency of the RI in dogs <4 months of age (Chang et al., 2010).

An elevation in the mean intrarenal RI (>0.70) has been determined for the clinical diagnosis of canine acute renal failure and congenital dysplasia. Considering RI greater than 0.70 abnormal, the sensitivity and specificity of the RI in differentiating between normal and abnormal kidneys were shown to be 38 and 96%, respectively (Morrow et al., 1996). When vascular resistance rises, diastolic blood flow is reduced to a greater degree than systolic blood flow (Rifkin et al., 1987). The relatively greater decrease in end diastolic velocity compared to peak systolic velocity then causes an elevation in RI and PI. The upper threshold for RI and PI need to be established in order to identify an abnormally increased vascular resistance. There are slight differences in the upper threshold (calculated as means + 2 standard deviations) for RI between various studies. Some suggest an upper value of 0.70 for cats and dogs (Morrow et al., 1996; Rivers et al., 1996). This is the same value as that proposed as a limit for normal mean intrarenal RI in humans. Other studies have suggested an upper value of 0.73 for dogs and 0.71 for cats (Nyland et al., 1993; Rivers et al., 1997a).

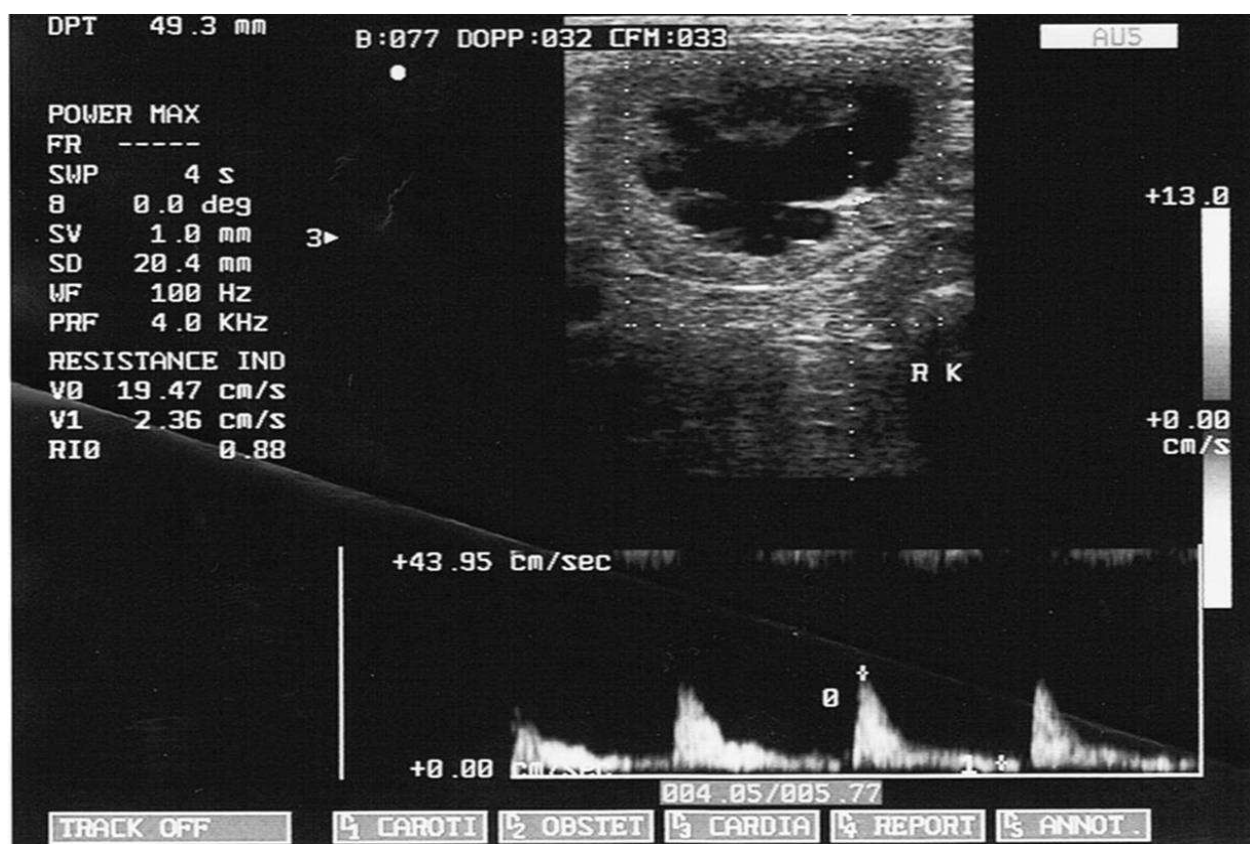


Fig. 2. Duplex Doppler ultrasound image of hydronephrotic kidney developed after the right ureter ligation in an ovariohysterectomized cat. Increased intrarenal RI (0.88) in intrarenal arterial flow pattern is shown.

Novellas et al. (2007) suggested a similar upper threshold for the RI of 0.72 for dogs and 0.70 for cats (Fig. 2.). The same study suggests an upper level for intrarenal PI of 1.52 in dogs and 1.29 in cats. However, an earlier study suggested a mean intrarenal PI value of 0.80 ± 0.13 (Morrow et al., 1996) and emphasized that the upper threshold value should be 1.06 (Novellas et al., 2007). However, no sensitivity and specificity were reported in these studies.

4. Factors affecting renal resistive index

4.1 Pulse and blood pressure

Tublin et al. (1999) reported a significant direct linear relationship between intrarenal RI and pulse pressure. This suggests that RI increases in line with the widening of the pressure difference between systole and diastole. In the event of an elevated RI being observed in a patient with presumed normal kidneys, the data should be correlated with the patient's heart rate and blood pressure. Heart rate and blood pressure at physiological extremes can alter the intrarenal RI without renal pathology being present. It is therefore important to establish these two variables in order to interpret the intrarenal RI accurately. Significant hypotension and a low heart rate can produce an elevation of RI without a true change in renal vascular impedance (Mostbeck et al., 1990). Hypotension reduces diastolic volume in the spectrum. This, in turn, leads to a significant elevation in RI value. Bradycardia and hypertension also lead to elevated intrarenal RI. If blood pressure and heart flow are stable, an increase in heart level causes intrarenal RI to fall. Tachycardia also leads to a fall in intrarenal RI (Shokeir et al., 1997a).

4.2 Dehydration

The intrarenal RI values ≥ 0.70 have been reported in 54% of non-obstructed kidneys in fasting children. The intrarenal RI resumes its normal value after hydration, indicating the importance of oral hydration at least for the proper interpretation of Doppler studies (Shokeir et al., 1996, 1997a).

4.3 Anesthesia

Doppler US is used in human medicine to determine blood flow without sedation. However, sedation may be required prior to imaging in veterinary medicine for purposes of restraint because poor patient cooperation, high respiratory and heart rates and voluntary movement may interfere with the outcome, particularly in cases involving detailed investigation, such as abdominal vascular US. Anesthetic agents may change systemic and renal hemodynamics and subsequently impact on vascular resistance. Extensive data on the cardiovascular effects of drugs can be obtained through Doppler flow technology using high-resolution vessel images together with hemodynamic monitoring. A combination of atropine, diazepam, acepromazine, and ketamine has been shown to reduce the intrarenal RI in healthy dogs (Rivers et al., 1997b). Sedation with a combination of atropine, acepromazine, and ketamine did not alter the intrarenal RI in cats (Rivers et al., 1996). Yet, anesthesia with isoflurane did increase both the intrarenal RI and PI in cats (Mitchell et al., 1998). In one study coping with the effects of short-term anesthetics on renal hemodynamics it was shown that while propofol had a minimal effect, a xylazine-ketamine combination and thiopental caused a significant drop in intrarenal RI (Kaya et al., 2011).

4.4 Extrarenal factors

The effect of vascular compliance on RI may account for the positive nature of studies investigating the usefulness of Doppler US in assessing end-organ damage in patients with hypertension and arteriosclerosis. Several recent studies showed that an elevated RI was correlated with left ventricular hypertrophy and carotid intimal thickening (Alterini et al., 1996; Pontremoki et al., 1999; Shimizu et al., 2001). Studies have also identified compression as an extraneous factor capable of elevating intrarenal RI. Compression may result from the effects of hematoma or another lesion occupying space and exerting pressure in the area surrounding the kidney. Subcapsular or perinephric fluid collection has also been associated with increased intrarenal RI in humans. Manual compression transmitted through the ultrasound transducer may lead to false iatrogenic increases in intrarenal RI, as well (Pozniak et al., 1988).

4.5 Renal medical diseases

Nephrologists and radiologists have long been frustrated by the lack of specificity inherent in gray-scale examination in evaluating intrinsic renal disease. Although renal size, cortical thickness, and echogenicity may be helpful in assessing disease chronicity, these are typically of no assistance in the differential diagnosis or management of renal disease. Doppler US possibly being able to serve as a useful adjunct for the gray-scale assessment of renal disease was proposed in a series of papers by the University of Michigan team. In Platt et al. (1990)'s preliminary research, 41 patients' renal biopsy results were correlated with RI analysis. In this study, normal RI values were determined in patients with isolated glomerular disease (mean, 0.58), whereas subjects with vascular or interstitial disease had significantly elevated RI values (means, 0.87 and 0.75, respectively).

Patriquin et al. (1989) reported an elevated RI during the anuric-oliguric phase of acute renal failure in 17 children. Intrarenal RI has also been thought to exhibit strong correlation with renal involvement in progressive systemic sclerosis (Aikimbaev et al., 2001). Hepatorenal failure is a well-known complication associated with established liver disease. It is characterized by early renal hemodynamic changes (vasoconstriction) prior to clinically recognized kidney disease. It should be possible to detect this renal vasoconstriction (increased renal vascular resistance) noninvasively by the use of Doppler US. It is also possible to identify nonazotemic patients with liver disease, a subgroup at significantly greater risk for subsequent kidney dysfunction and the hepatorenal syndrome using renal duplex Doppler US (Platt et al., 1994b). Doppler US's ability to identify latent hepatorenal syndrome before liver transplantation was again demonstrated by the University of Michigan group (Platt et al., 1992). Doppler US was useful outcome predictor in patients with lupus nephritis: an elevated RI value was shown to predict poor renal outcome in a prospective series involving 34 patients with various degrees of nephritis, including in subjects with normal baseline renal functions (Platt et al., 1997). Doppler US has also been proposed as a useful tool for the analysis of non-obstructive acute renal failure; an RI greater than 0.07 was determined as a reliable discriminator between acute tubular necrosis and prerenal failure (Platt et al., 1991b). Diabetes also affects intrarenal RI values; intrarenal RI is particularly elevated in established diabetic nephropathy. The intrarenal RI may actually fall to levels significantly below normal during the early stages of preclinical diabetic nephropathy, which is probably associated with the state of decreased renal vascular

resistance accompanying preglomerular vasodilatation in the early stages of diabetic kidney involvement (Derchi et al., 1994; Platt et al., 1994a). The intrarenal RI has also found adherents as a useful marker of diabetic nephropathy (Frauchiger et al., 2000; Soldo et al., 1997). In contrast, other studies have suggested that Doppler US provides little more than serum creatinine levels and creatinine clearance rates in patients with early diabetic nephropathy and normal renal functions (Marzano et al., 1998; Okten et al., 1999; Sari et al., 1999). The intrarenal RI is significantly greater in pregnant patients with pyelonephritis than in pregnant women without pyelonephritis (Keogan et al., 1996b). Biopsy correlated studies have verified these findings and assessed the role of the intrarenal RI for differentiating among various renal medical diseases with encouraging results (Platt et al., 1990; Platt et al., 1991b). Therefore, it may be difficult to diagnose unilateral obstruction in patients with a known renal medical condition. However, renal medical disease is usually a bilateral symmetrical affliction (Rawashdeh et al., 2001).

Earlier studies reported elevated renal vascular impedance with chronic hypertension (Norris et al., 1989) and acute renal failure (Wong et al., 1989). The intrarenal PI and RI would appear to be closely related to renal hemodynamic parameters and creatinine clearance in patients with chronic renal failure and hypertension (Petersen et al., 1995). Platt et al. (1989b) found elevated intrarenal RI in half of 50 patients with renal medical diseases. An elevated intrarenal RI could therefore be due to renal disease or obstruction, in the context of known medical renal disease and pyelocaliectasis, thus limiting the value of an abnormal intrarenal RI in this particular situation.

In a dog with acute tubular necrosis intrarenal RI values were observed to be greater than 0.73, normalizing after effective treatment (Daley et al., 1994). One retrospective study investigated intrarenal RI levels in 67 dogs with spontaneous non-obstructive renal disease. Histopathological or cytological findings were present in 12 of these, four of which had tubulointerstitial disease with or without glomerular disease, and three had glomerular disease alone. Three of the four dogs with tubulointerstitial disease had intrarenal values greater than 0.73, while lower values were observed in the three animals with glomerular disease alone. The authors suggested that increased intrarenal RI was compatible with tubulointerstitial, as opposed to glomerular disease (Marrow et al., 1996). In our clinical observations, intrarenal RI may increase in dogs with pyelonephritis (Fig. 3.). The correlation between serum creatinine concentration and intrarenal RI in humans is positive, but weak. Proteinuria has not been associated with increased intrarenal RI in humans (Platt et al., 1990, Platt 1992). Similarly, no statistically significant correlation between individual dog and cat intrarenal RI and serum creatinine concentration was determined. Neither was any statistically significant correlation identified between individual dog intrarenal RI and urine protein-to-creatinine ratio in that study. Intrarenal RI values broadly overlapped compared with urine output in cats with non-obstructive renal disease. The sensitivity was reported to be 57% in dogs with increased intrarenal RI in determining non-obstructive renal disease (tubulointerstitial or glomerular disease) (Rivers et al., 1997a). Another study reported a sensitivity of 38% for increased intrarenal RI (>0.70) in the detection of non-obstructive renal disease in 67 dogs. Sensitivity of 90% has been reported for increased intrarenal RI in the determination of non-obstructive renal disease in azotemic cats. Increased intrarenal RI has a 40% level of detection of renal obstruction in cats with pelvicooureteral dilation during gray-scale US (Morrow et al., 1996). Increased intrarenal RI

in dogs and cats with higher relative renal cortex echogenicity may be the result of renal disease, as opposed to normal variation; further studies involving clinicopathological analysis of such subjects are now required. Increased intrarenal RI values observed in azotemic dogs with spontaneous non-obstructive renal disease are probably associated with active tubulointerstitial, as opposed to glomerular disease. However, increased intrarenal RI alone does not rule out the presence of glomerular disease. Renal Doppler evaluation of intrarenal RI is useful as an ancillary diagnostic technique in azotemic dogs and cats with non-obstructive renal disease. This is particularly the case when gray-scale US findings are not definitive. Increased intrarenal RI can only be of restricted use in evaluating the severity of concurrent renal dysfunction. Intrarenal RI may subsequently return to normal following the administration of appropriate treatment in dogs with non-obstructive renal disease and in cats with both non-obstructive and obstructive disease (Rivers et al., 1997a).

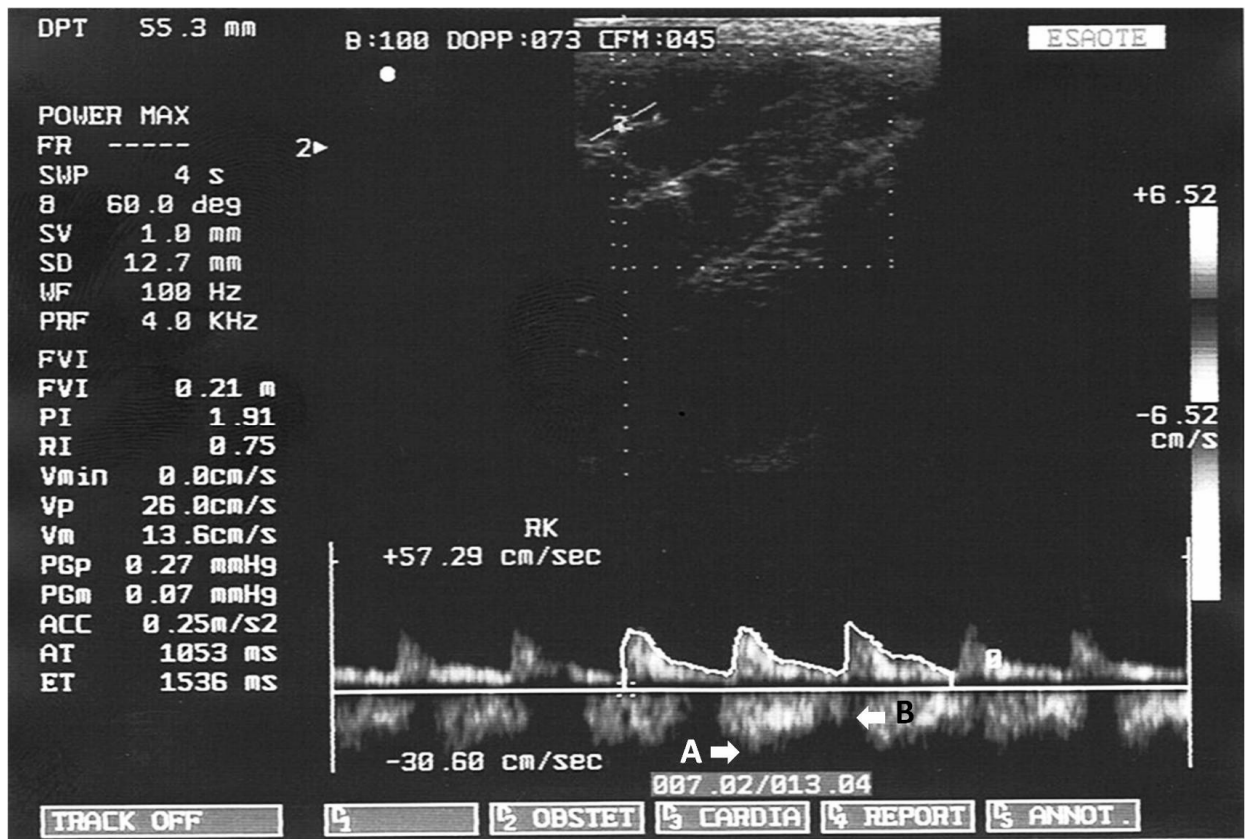


Fig. 3. Arterial and venous flow patterns in the right kidney of a dog with acute pyelonephritis. The peak venous flow signal (A) and the least flow signal (B), used in intrarenal venous impedance index, as well as elevated intrarenal arterial indexes are shown.

4.6 Renal neoplasias

Renal Doppler US does not contribute anything to gray-scale US in the diagnosis of simple cysts representing the great majority of renal masses. In contrast, the blood flow spectrum cannot be determined in septum cysts or in the presence of other solid components using Doppler US. In malign renal neoplasias, a high-velocity and low-resistance arterial flow spectrum associated with the hemodynamic characteristics of neovascularization originating from arteriovenous relations and the high pressure difference caused by them can be

observed. In benign neoplasia, on the other hand, no specific and measurable Doppler flow spectrum has been reported. Blood flow velocities similar to those in the abdominal aorta were reported in blood flow specimens obtained from renal cell carcinomas. Malign renal neoplasia, and particularly renal cell carcinoma, exhibit vascular and especially venous invasion. Thrombus in the renal vein or lumen of the inferior vena cava prevents the formation of blood flow-associated colorization. In contrast to benign hemorrhagic thrombus, blood flow signals can be determined by Doppler US in neoplastic thrombus. When the renal vein is completely obstructed by thrombosis, the finding to be determined with Doppler US is low, zero or below baseline diastolic volume in the intrarenal arterial structures, in other words, elevated blood flow. Renal Doppler US is also useful in the evaluation of masses inside the collecting system, such as renal parenchymal masses. Determination of the vascular flow spectrum or Doppler signals obtained from such neoplasia tumoral masses permits differentiation of non-neoplasia lesions such as coagulum or debris, from collecting system neoplasias. However, Doppler signals may not be observed in cases of deep localization or in which the lesions are small, or because the device or transducer are not set at the optimal level (Kier et al., 1990; Ramos et al., 1988).

5. Renal pathologies affecting renal hemodynamics

5.1 Renal vascular pathologies

5.1.1 Renal artery stenosis and occlusion

Renal artery stenosis is most commonly caused by either fibromuscular dysplasia or atherosclerosis. It may develop alone or in association with hypertension, renal insufficiency (ischemic nephropathy), or both. As a cause of hypertension and renal ischemia, renal artery stenosis resulting from atherosclerotic changes in the renal artery is now a serious concern, as it often leads to end-stage renal failure (Scoble, 1999). Hemodynamically, significant narrowing of the renal artery (a decrease in renal artery diameter $\geq 60\%$) leads to treatable hypertension. Since renal angiography is invasive and requires the use of contrast material, it is not widely used. In recent years, research has been focused on non-invasive diagnostic techniques, which might reliably predict the outcome of blood pressure and renal function after revascularization of renal artery stenosis. Renal artery stenosis is one of the most frequent indications for renal Doppler ultrasonographic examination, and renal Doppler US with a considerable reliability has been used in the diagnosis of renal artery stenosis and occlusion since 1984 (Avasthi et al., 1984).

An elevated flow rate is one of the hemodynamic findings in renal artery stenosis. Studies have shown that blood flow velocity is greater in the point of stenosis than normal renal artery velocities. In addition to blood flow velocity, turbulence in the blood flow spectrum post-stenosis is another important finding. The first studies regarded a blood flow velocity of 100 cm/s as the upper limit, while later research suggested the limit should be 170 - 200 cm/s. In these studies sensitivity was 81% - 92% and specificity was 87% - 96% (Gottlieb et al., 1995; House et al., 1999; Krumme et al., 1996; Miralles et al., 1996). However, the renal-aortic ratio obtained by dividing the renal artery flow velocity by the abdominal aorta flow velocity can be used to eliminate individual differences. A level ≥ 3.5 is regarded as diagnostic for renal artery stenosis, and has a sensitivity of 92% and specificity of 76% in renal artery stenosis diagnosis (Miralles et al., 1996). Various factors, such as the experience of the physician performing the examination, patient cooperation, meteorism and obesity

improve the practicality of the technique. Because of these limitations, technical imaging is easier in the diagnosis of renal artery stenosis, hemodynamic changes in the intrarenal arteries are used. Changes in the acceleration parameters of the blood flow spectra obtained from the level of the renal hilus can be used in the diagnosis of renal artery stenosis. Accordingly, a delayed rise in peak systolic velocity, low flow velocity and a blunt peak (pulsus tardus et parvus) and renal hemodynamic change in this vascular pathology make the Doppler spectrum diagnostically important (Handa et al., 1986). Intrarenal Doppler parameters such as decreased flow velocity, low RI (<0.50) and PI values, decreased acceleration ($<3 \text{ m/s}^2$) and increased acceleration time ($>70 \text{ m/s}$) are also considered in renal artery stenosis (Bude and Rubin 1995). Comparison of intrarenal RI and PI values on the side with pathology with the contralateral kidney also improves diagnostic success in unilateral renal artery stenosis (Krumme et al., 1996; Riehl et al., 1997). Another study suggested that the normal early systolic peak that should normally be observed disappears (Stavros et al., 1992). The sensitivity of intrarenal Doppler parameters declines in cases with high vascular resistance ($\text{RI} > 0.70$) (Stavros & Harshfield, 1994). Renal Doppler indices return to normal following treatment of renal artery stenosis (Ozbek et al., 1993). When renal artery and intrarenal Doppler parameters are considered together, sensitivity in the diagnosis of renal artery stenosis is 89%, and specificity of 92% (Krumme et al., 1996).

Various renal pathologies, such as atherosclerosis, and trauma or iatrogenic causes may lead to renal artery occlusion. In renal artery occlusions exhibiting acute development or with insufficient collateralization, blood flow in the renal arteries cannot be imaged with color or power Doppler, and the Doppler spectrum cannot be determined. At the same time, either a very weak blood flow spectrum is obtained from the intrarenal arteries, or else arterial flow cannot be established at all. For these reasons, the use of ultrasonographic contrast material in the diagnosis of renal artery stenosis enhances the success of renal Doppler US. The ultrasonographic contrast materials may make it easier to distinguish the renal arteries by increasing the Doppler signal intensity and that the inadequacy stemming from the inability to identify these arteries can thus be eliminated. Claudon et al. (2000) reported the sufficient investigation level rose from 64 to 84% with the use of ultrasonographic contrast material. Missouriis et al. (1996) reported that with the use of SH U 508 A (Levovist®), sensitivity in diagnosis of renal artery stenosis rose from 85 to 94%, and specificity from 79 to 88%. At the same time, while a shortening in investigation time has been reported with the use of these contrast materials, the high price of ultrasonographic contrast materials means they are not economical. Moreover, ultrasonographic contrast materials make a positive contribution in the presence and evaluation of accessory arteries, which represent a significant limitation in renal Doppler ultrasonographic examination and levels of observation of renal artery stenosis rose to 77% (Melany et al., 1997).

5.1.2 Renal vein thrombosis

Renal vein thrombosis is a known cause and complication of renal diseases. The acute form of this vascular pathology may arise in association with such causes as sudden water loss, hypercoagulopathies, trauma, malignancy and sepsis in children. One specific finding in gray-scale ultrasonographic examination of renal vein thrombosis is an increased thickness in renal parenchymal thickness. Decreased echogenicity in the renal cortex or a heterogeneous appearance observed together with cystic areas are other findings determined in gray-scale US. Increased renal cortex echogenicity is a finding that can appear in advance stages of

pathology. Despite not being specific, increased dimension in the renal vein is regarded as a non-specific finding. Thrombus inside the vein can be monitored in this pathology using gray-scale US. No blood flow findings being determined at renal Doppler US is sufficient for a diagnosis of renal vein thrombosis. Blood flow in the renal vein however may not be to established due to faulty devices or settings. All device settings must therefore be optimal for diagnosis. In addition, factors such as collapse of the renal vein due to inappropriate Doppler angle or probe pressure or blood flow being too decreased to measure due to valsalva can also have a negative impact on flow hemodynamics obtained from the renal vein. In cases in which no results can be obtained from Doppler examination of the renal vein, for reasons such as obesity or meteorism or in which direct imaging needs to be supported, intrarenal Doppler examinations can be performed. Elevated flow resistance is noteworthy among the intrarenal Doppler US findings for acute renal vein thrombosis. This develops in association with insufficient venous drainage and/or intrarenal edema. This, in turn, leads to high intrarenal RI and PI values. With a decrease in diastolic flow component, or it being below the baseline, forward and backward blood flow specimens may arise in the Doppler spectrum. These findings may lose specificity as a result of venous collaterals, such as capsular veins in the native kidney, becoming involved. Diagnosis of chronic renal vein thrombosis is more difficult than that of acute renal vein thrombosis. As with acute renal vein thrombosis, the observation of thrombus inside the vein at gray-scale US, or no or only partial blood flow findings from Doppler US can establish pathology. However, the kidney and renal vein frequently being normal size and intrarenal Doppler findings not emerging due to collateralization are factors complicating the diagnosis of chronic renal vein thrombosis (Chen et al., 1998; Helenon et al., 1995; Zubarev, 2001)

5.1.3 Arteriovenous fistulas

Renal arteriovenous fistulas frequently arise as a result of renal biopsy or other medical procedures. Renal Doppler US is quite successful in determining this pathology. Arteriovenous fistulas of clinically insignificant size may even be identified in a noninvasive form as a result of hemodynamic effects established by renal arteriovenous fistulas. High velocity flow at the fistula level, a consequent color artifact in the surrounding tissue, high-velocity and low-resistance arterial flow in the artery, and high-velocity and pulsatile (observed with arterial spectrum) flow in the vein are some Doppler US findings of arteriovenous fistulas. The focus of the high blood flow velocities determined from the level of the arteriovenous fistula itself is a prominent finding (Helenon et al., 1995; Ozbek et al., 1995). In color Doppler, adjustment of the color filter to high velocities and the elimination of low velocities facilitate the diagnosis of arteriovenous fistulas (Edwards & Beggs 1987).

5.1.4 Aneurism and pseudoaneurism

Renal arterial aneurisms can easily be diagnosed in cases where the lesion is determined with gray-scale ultrasound. A Doppler wave form is determined within the cystic structure identified. Like arteriovenous fistulas, pseudoaneurisms are frequently of iatrogenic origin and generally co-exist. Pseudoaneurisms are generally seen as cystic cavities within the renal parenchyma that cause an arterial spectrum at Doppler analysis. Cystic structures may gradually thrombose, either partly or completely (Chen et al., 1998; Zubarev, 2001).

5.2 Ureteral obstruction (obstructive uropathy)

Ureteral obstruction is one of the most important pathologies of the urinary system. Caused by a number of factors, it may lead to kidney failure and is characterized by irreversible and reversible destruction in the kidneys and ureter. Etiological factors include congenital, acquired, and predisposing elements. As well as distinguishing between obstructive and non-obstructive dilatation, the localization and extent of the obstructed area must also be determined in order to avoid unnecessary surgery. The early diagnosis and release of obstruction are essential if irreversible damage in the affected kidneys is to be prevented. Various imaging methods are used in the diagnosis of ureteral obstruction, including radiography, excretory urography, gray-scale US, Doppler US, computed tomography, magnetic resonance imaging and percutaneous antegrade pyelography. The majority of studies regarding renal Doppler US have concentrated the potential role of Doppler US in evaluating ureteral obstruction.

5.2.1 Complete obstruction

Gray-scale examination for potential acute and chronic obstruction has been known to have attendant limitations since the mid-'80s. Ultrasonography provides purely anatomical data, and these may be incomplete or absent: non-obstructive conditions (residual dilatation from previously existing relieved obstruction, pyelonephritis, congenital malformation, reflux and diuresis) may also give rise to collecting system dilatation. While conventional gray-scale US only supplies an anatomical image of the changes (e.g., pelviureteric dilatation) in ureteral obstruction, it may not be possible to distinguish between these potential causes using gray-scale US alone. In other words, there may be non-obstructive dilatations, while collective system dilatation may not be observable despite the presence of obstruction. Moreover, in an acute context, obstruction may persist for several hours prior to collecting system dilatation. A number of teams in the early 1990s hypothesized that urinary obstruction pathophysiology could be reliably revealed by changes in arterial Doppler spectra (Platt et al., 1989a; 1989b; Platt, 1992; Rodgers et al., 1992). This was the result of exhaustive animal studies demonstrating unique biphasic hemodynamic response to complete ureteral obstruction.

5.2.1.1 Acute obstruction

Immediately after obstruction, renal blood flow increases in response to the elevation in ureteric pressure. This generally lasts less than 1.5–2 h. It is thought to be the result of preglomerular vasodilatation. This period of likely prostaglandin-mediated vasodilatation, lasting less than 2 h, occurs immediately after obstruction. The following 2–4 h sees a gradual fall in renal blood flow with continued elevation of pelvic and ureteric pressures, which are probably the result of postglomerular vasoconstriction. Kim et al. (1997) used unilateral lamb model an acutely obstructed and reported 29% decrease in total blood flow in the obstructed side, compared to an increase in total blood flow in the unobstructed kidney. Karaguzel et al. (2011) obtained similar findings using power Doppler in a study of partial unilateral ureteral obstruction in rabbits (Fig. 4.). This implies that resistance is increased on the obstructed side and reduced on the unobstructed side and that contralateral obstruction on the unobstructed kidney produces a notable effect. Renal blood flow thus declines, while renal vascular resistance increases. Initial research suggested that this vasoconstriction response was to a large extent a mechanical one, the result of increases in collecting system pressures. However, more recent studies suggest that complex

interactions between several regulatory pathways (renin-angiotensin, kallikrein-kinin, and prostaglandin-thromboxane) are in fact responsible for intense, postobstructive renal vasoconstriction. Whatever the mediation involved, this vasoconstriction response appeared ideal for by changes in the RI. Researchers from University of Michigan obtained RIs from 21 hydronephrotic kidneys prior to nephrostomy. The mean RI levels in 14 kidneys with confirmed obstruction (0.77 ± 0.04) were higher compared to those from seven kidneys with non-obstructive pelvicaliectasis (0.64 ± 0.04). Additionally, intrarenal RI values returned to normal post-nephrostomy (Platt et al., 1989a). A subsequent larger study involving 229 kidneys largely corroborated these results. That study employed a discriminatory RI threshold of 0.70; sensitivity and specificity of the Doppler diagnosis of obstruction were determined as 92 and 88%, respectively (Platt et al., 1989b).

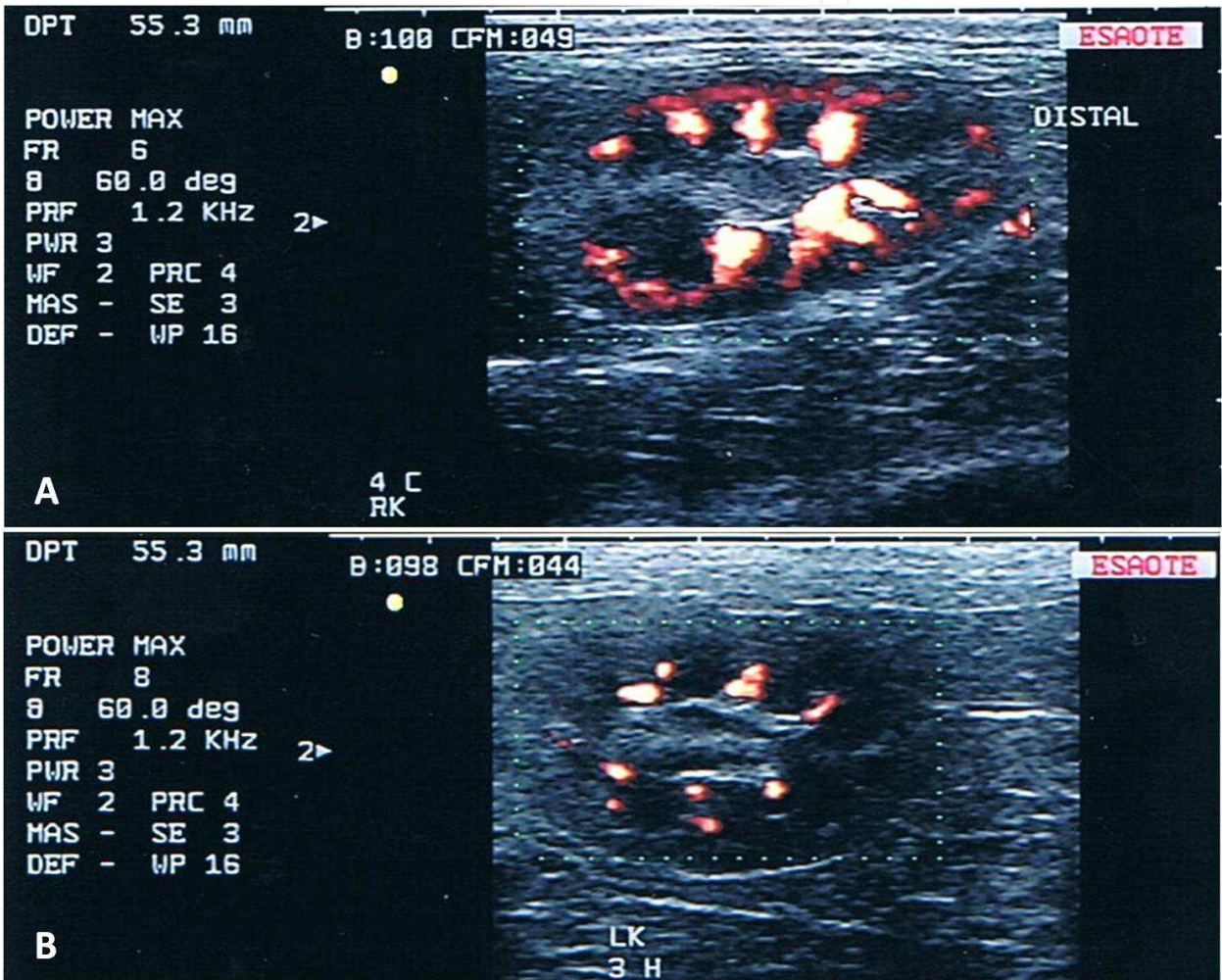


Fig. 4. Power Doppler ultrasound images of experimentally induced unilateral ureteral obstruction in a rabbit. Colorization in the non-obstructed right kidney (A) is clear, whereas in colorization of the interlobar vessels decreased and cortical colorization is absent in the obstructed left kidney (B) at 3 hr post-obstruction.

5.2.1.2 Ureteral obstruction severely dilating the collecting system

Severe hydronephrotic kidney was shown to not exhibit any elevation in intrarenal RI, despite the presence of what the authors regarded as obvious urinary obstruction (Platt et

al., 1989b). The lack of response might have been due to a marked decrease in absolute blood flow in chronic high-grade obstruction, decreased filtration pressure produced by a renal cortex functioning at a minimal level or elevated compliance in a capacious dilated collecting system (Ulrich et al., 1995).

5.2.2 Partial ureteral obstruction

A number of reports (Brkljacic et al., 1994; Opdenakker et al., 1998; Rodgers et al., 1992; Shokeir & Abdulmaaboud, 2001) have encourage various institutions to include RI analysis in the sonographic evaluation of collecting system dilatation. However, anecdotal reports, follow-up clinical trials, and animal studies have all had a negative effect on the clinical impact of Doppler US (Chen et al., 1993; Cole et al., 1997; Coley et al., 1995; Deyoe et al., 1995; Rawashdeh et al., 2001; Tublin et al., 1994). Doppler US was found to be of especially limited use in the evaluation of partial ureteral obstruction. Chen et al. (1993), for example, reported a sensitivity of Doppler US for the diagnosis of obstruction of only 52%. Although the results of the examination were often positive with high-grade obstruction, most patients with partial obstruction had normal RIs. Doppler US's failure to reliably detect low-grade obstruction was confirmed later in pig and rabbit models (Cole et al., 1997; Coley et al., 1995; Kaya et al., 2010).

5.2.3 Comparison with the contralateral kidney without diuresis in obstructive uropathy

The accuracy of the discriminatory value of RI (0.70) can be improved by evaluating the contralateral kidney. This is particularly the case in acute obstruction in which RI may still be below the limit of 0.70. A difference of ≥ 0.10 between the obstructed and the contralateral kidney further suggests the accuracy of the diagnosis (Platt et al., 1991a). Sensitivity rose from 57 to 71% in acute obstruction with comparison of RI in the two kidneys in one study (Rodgers et al., 1992). The obstructed to normal kidney RI ratio can also be helpful. Ulrich et al. (1995) cited a ration of 1.15 as a diagnostic criterion of acute obstruction. Keller et al. (1989) showed that with the RI ratio of ≥ 1.11 , the sensitivity for determining obstruction was 77%, while the specificity for excluding obstruction was 81%, in a study involving 48 patients with unilateral obstruction and 34 healthy controls. Comparison with the contralateral kidney is not naturally used an option in patients with bilateral renal obstruction or with only one kidney (Shokeir et al., 1997a).

5.2.4 Diuresis in obstructive uropathy (diuretic Doppler US)

A number of researchers have shown that it is possible to enhance the sensitivity of Doppler US for the detection of partial obstruction by performing the evaluation after forced diuresis (diuretic Doppler US) (Akata et al., 1999; Lee et al., 2001; Ordorica et al., 1993). Experimental research has provided a theoretical basis for the use of diuretic Doppler US in the evaluation of obstructive uropathy. An increase of RI of $\geq 15\%$ after furosemide injection is regarded as a diagnostic criterion of obstruction (Ordorica et al., 1993). Infusion of normal saline and administration of furosemide have been shown to significantly enhance the sensitivity, specificity and general accuracy of the use of RI in the diagnosis of obstructed kidneys in children (Shokeir et al., 1996). Following induction of complete left-side ureteral obstruction,

left intrarenal RI increased significantly over the course of five consecutive days. Mannitol has reduced intrarenal RI in the non-obstructed contralateral kidneys (Choi et al., 2003). The RI difference and ratio obtained in unilateral cases by comparison with the non-obstructive kidney further reinforces the diagnosis of obstructive uropathy. Fluid and diuretic procedures raise intrarenal RI values in the obstructed kidney. In this way, the further increase in RI difference and ratio that result are renal hemodynamic parameters that can be used in the diagnosis of unilateral ureteral obstruction. (Kaya et al., 2010)

Palmer et al. (1991) investigated Doppler US in children before and after the administration of intravenous furosemide. They demonstrated that this leads to an increase in RI above baseline in obstructed kidneys, but that it has no significant impact on RI compared to baseline in normal and non-obstructed pyelocliectasic kidneys. Bude et al. (1994) showed that infusion of normal saline and administration of furosemide reduced intrarenal RI of non-obstructed renal units to a significant extent compared with baseline values. In the wake of such positive, further series indicated the potential of Doppler US to differentiate renal transplant obstructive and non-obstructive pelvicaliectasis (Platt et al., 1991c) and to determine ureteral stent patency (Platt et al., 1993).

5.2.5 Changes in renal resistive index following relief of obstruction

Platt et al. (1989a) reported that 2–9 days after the relief of obstruction RI decreased in nine out of 10 adult patients. Ordorica et al. (1993) showed that RI decreased to <0.75 in all nine kidneys evaluated 3 months after operation. Shokeir et al. (1997b) also confirmed that RI reversed after relief of mild and severe degrees of obstruction in an experimental model. An experimental study in dogs reported that elevated intrarenal RI value in complete bilateral ureteral obstruction was not affected by peritoneal dialysis, but this high level again decreased with relief of the obstruction (Kirmizigul et al., 2007). On the other hand, Chen et al. (1993) reported that RI remained elevated in two out of five adult patients after the release of obstruction. Future studies might usefully determine those factors interfering with the reversal of RI after the relief of obstruction, such as the age of the patient, the type and duration of obstruction, and the extent of vascular and parenchymal damage.

5.2.6 The effect of certain drugs on renal resistive index in obstructive uropathy

Patients who present with renal colic with are often administered with non-steroidal anti-inflammatory drugs (NSAIDs) for pain relief prior to undergoing a comprehensive diagnostic evaluation. NSAIDs reduce prostaglandin synthesis, and are therefore involved in hemodynamic changes within the kidney, with resultant changes in the renovascular resistance. This can thus impact on intrarenal RI. These drugs can reverse both the early vasodilatation and later vasoconstriction that accompany acute renal obstruction and hence lower renal blood flow, renal vascular resistance and glomerular filtration rate. Low urine production causes lower intraluminal pressure, one of the major causes of renal obstruction (Kmetec et al., 2002). Shokeir et al. (1999) reported that NSAIDs significantly decreased the RI of acutely obstructed kidneys, but did not affect RI in normal contralateral kidneys. However, although their patients were administered ketoprofen, mean RI levels for the obstructed kidneys remained above the discriminatory threshold (>0.70) during the first 71 h of obstruction (Kmetec et al., 2002). The mean RI on the obstructed side was only slightly below the threshold in kidneys obstructed for > 72 h, though the difference between the

kidneys was significant. On the basis of their findings, the measurement of RI is a trustworthy diagnostic method for detecting acute renal obstruction.

In a study on rabbits, Ayyıldız et al. (2009) stated that tadalafil had a low effect on intrarenal RI and PI in partial ureteral obstruction. They suggested that their findings might lead to this drug being used to minimize the negative effects of obstruction in clinical practice. Another study suggested that ginkgo glycosides may protect and restore renal perfusion in partial unilateral ureteral obstructions, as shown by a decrease in RI and the enhanced colorization obtained with power Doppler US in the obstructed kidney. That study further suggested that ginkgo glycosides might also be employed to minimize renal parenchymal damage and maintain kidney function (Karaguzel et al., 2011).

5.2.7 Changes in venous impedance caused by obstructive uropathy

The intrarenal venous impedance index determined by the use of Doppler US is associated with compliance in the vein and can assist in assessing renal parenchymal compliance (Karabulut et al., 2003). Researchers have observed a dampening of the hepatic vein signal in cases of acute and chronic liver disease, and have ascribed this to reduced hepatic compliance (Bolondi et al., 1991). It has been suggested that, because of the resulting changes in compliance, disease in the liver can be identified by measuring the pulsatility of the venous signal in the hepatic veins. Compliance of the liver tissue is reflected by the pulsatility of the hepatic venous signal since the majority of pathologies expand the liver parenchyma within its confining capsule. This, in turn, reduces compliance and leads to dampening of the hepatic venous signal (Britton et al., 1992). It is believed that there is an equivalent phenomenon in the kidney. It has been suggested that the increased pressure causing a decrease in renal parenchymal compliance in acute renal obstructions may also alter Doppler signals obtained from the intrarenal veins (Bateman & Cuganesen, 2002; Karabulut et al., 2003). Right-sided atrial pressure changes result in a triphasic waveform. In this situation, the atrial and sometimes the ventricular venous pulse components produce a reversed flow in the inferior vena cava (Appleton et al., 1987). The reversal of flow at the end of diastole (from atrial contraction) progresses into the renal vessels. The arterial data also show a high flow of blood into the kidney throughout diastole and that enlargement of the veins (compliance) has to compensate for a temporary decrease in outflow. If the veins are made non-compliant due to raised interstitial pressure, this end diastolic flow reduction declines. Similarly, venous pulsatility rises if compliance is increased (Bateman and Cuganesen 2002). Once peak venous flow signal (A) and least flow signal (B) (Fig. 3) have been measured venous impedance index $(A-B/A)$ is calculated (Bateman and Cuganesen 2002, Karabulut et al. 2003). The venous impedance indices (0.44 ± 0.06 for the right kidney, 0.41 ± 0.07 for the left kidney) determined for the normal kidney by Karabulut et al. (2003) were compatible with those from an earlier study by Bateman and Cuganesen (2002), who reported mean impedance indices of 0.45 ± 0.18 for the right kidney and 0.43 ± 0.19 for the left kidney. Bateman & Cuganesan (2002) further reported venous impedance indices of 0.38 ± 0.25 for the obstructed side and 0.80 ± 0.25 for the unobstructed side. The peak venous flow signal in the obstructed kidney was 69% higher than the flow in the unobstructed kidney and 86% higher than the signal in the control group. They suggested that renal obstruction produces a greater change in venous flow than arterial flow, and concluded that a comparison between venous flow levels in the obstructed and unobstructed kidneys might result in enhanced diagnostic accuracy.

6. Doppler ultrasonographic examination of renal allograft

Kidney transplant is the treatment of choice for patients with end-stage renal disease. These patients are susceptible to complications with the potential to threaten the transplant kidney, especially immediately after transplant. The main allograft complications are vascular pathology (renal artery stenosis or occlusion, renal vein thrombosis, arteriovenous fistulas and pseudoaneurism), collecting system pathology and medical allograft dysfunctions (rejection, acute tubular necrosis, cyclosporine toxicity, and infection). These complications are routinely differentiated using renal biopsy, though the procedure is invasive and poses inherent morbidity risks. The usefulness of renal Doppler US as a noninvasive technique in the evaluation of these complications has been established. The RI value is a sensitive index in predicting renal allograft dysfunction.

6.1 Vascular system pathologies in renal transplantation

6.1.1 Renal artery stenosis or occlusion

Doppler US findings for transplant kidney in the main renal artery stenosis or occlusions are to a great extent similar to those for the native kidney. However, transplant kidneys possess a number of advantages making Doppler ultrasonographic diagnosis more definitive. The first of these is that the transplant kidney and its arterial structures can be more clearly visualized sonographically. The absence from the transplant kidney of collateral arterial structures present in the native kidney and a knowledge of the artery number and localizations of anastomoses means that the main renal arteries can be distinguished and evaluated easily and reliably. The presence of intrarenal Doppler findings such as late elevation of systolic peak, low flow velocity, pulsus tardus *et* parvus, a decrease in flow velocity, low RI (<0.50) and PI values, decreased acceleration ($<3 \text{ m/s}^2$), and increased acceleration time ($>70 \text{ m/s}$) will suggest renal artery pathologies (Bude and Rubin 1995; Handa et al. 1986). Following the determination of these Doppler findings the renal artery has to be evaluated with Doppler US. Renal artery systolic velocity needs to be correlated with the systolic velocity of the iliac artery in the proximal direction (renoiliac ratio) as a renal artery stenosis finding. A ratio greater than 2 has been proposed as a diagnostic criterion in renal artery stenosis (Gottlieb et al., 1995; McGee et al., 1990). Helenon et al. (1994) reported that although Doppler ultrasonographic diagnosis had a more limited success rate in stenosis in the segmental branches it had an almost 100% diagnostic success rate in renal artery stenosis.

6.1.2 Renal vein thrombosis

Renal vein thrombosis, one of the early complications of the transplant kidney, can lead to loss of the transplant kidney if diagnosis is delayed. Because the transplant kidney has advantages over the native kidney with regard to sonographic imaging, renal Doppler US is quite successful in revealing this pathology. In contrast to the native kidney, because the transplant kidney has no collateral vascular structures and possibility of drainage, renal vein and intrarenal Doppler US findings are more dramatic (Helenon et al., 1995). If the diastolic flow component is below the baseline (reversed flow form), this spectral image is a non-specific finding in acute rejection and acute tubular necrosis (Schwerk et al., 1994). Renal vein thrombosis may be present when diastolic flow is reversed and no renal venous flow is detected (Dodd et al., 1991b).

6.1.3 Arteriovenous fistulas and pseudoaneurisms

Transplant kidneys are frequently subjected to biopsy during or after transplantation. Arteriovenous fistulas and pseudoaneurisms that generally arise in association with renal biopsy are evaluated in terms of the criteria used in Doppler ultrasonographic diagnosis of arteriovenous fistulas and pseudoaneurisms in the native kidney. For example, focal high velocity, low-impedance intrarenal arterial flow might suggest an arteriovenous fistula. At the same time, because of the imaging advantages attendant upon the transplant kidney diagnosis can easily be established.

6.2 Collecting system pathologies in renal transplantation

Since the transplant kidney is removed together with the ureters during surgery and anastomosed to the recipient bladder at a different level (ureteroneocystostomy), mild pelvicaliectasis and ureter dilatation may be determined in the anastomosis region in the early postoperative period. Another possible cause of these ultrasonographic findings is that the kidney and ureters are significantly denervated and the collective system loses natural tonus. In contrast, obstructive pathologies may cause significant pelvicaliectasis and/or ureter dilatation. One finding in respect of obstructive transplant kidney pathologies that must not be underestimated is the possibility of renal colic in the denervated kidneys. Obstruction in these kidneys, where urine output is at the threshold limit, prevents the collecting system being dilated with urine as a cause of a sudden drop in output. Repeated rejection attacks cause the walls of the collecting system and ureter to thicken and lose elasticity. Therefore, collecting system dilatation may not be observed in transplant kidneys with obstructive pathology (Bude & Rubin, 1995). In contrast to these ultrasound findings in obstruction, an abnormal rise may be seen in Doppler indices during the early postoperative period. However, the rise in these indices may also be seen in medical pathologies (*e.g.*, rejection) (Platt et al., 1991c).

6.3 Medical allograft dysfunctions

These patients must be properly monitored and screened in the early postoperative period for management of early onset renal complications and dysfunctions. It is important to begin a work-up to establish the precise nature of the problem and determine the optimal management as soon as possible. The use of a non-invasive technique capable of accurately establishing and identifying the causes of renal transplant dysfunction is also important. While renal biopsy is the standard means of distinguishing between these complications, it is nevertheless invasive and involves inherent risks of morbidity. Conventional US is able to determine anatomical changes in the allograft (hydronephrosis, hematoma and urinoma, for instance), but it is less successful in evaluating functional abnormalities, such as acute tubular necrosis, acute rejection, and drug toxicity (Radmehr et al., 2008). Initial enthusiasm gradually gave way to skepticism over a number of articles investigating the role of Doppler US in transplant dysfunction analysis (Allen et al., 1998; Buckley et al., 1987; Choi et al., 1998; Rifkin et al., 1987; Rigsby et al., 1987; Trillaud et al. 1998).

6.3.1 Rejection

Acute rejection represents the most common need for special attention. Elevated RI used to be regarded as specific for rejection (Allen et al., 1998; Buckley et al., 1987; Rifkin et al., 1987).

A number of studies have subsequently revealed the lack of specificity inherent in an elevated RI (Choi et al., 1998; Trillaud et al., 1998). Perrella et al. (1990), for example, reported that sensitivity and specificity of Doppler US for the diagnosis of rejection was 43 and 67%, respectively, with a threshold RI of 0.90. The complex and heterogeneous nature of rejection physiopathology may be regarded as responsible for this discrepancy. One study showed that Doppler indices may be initially normal, and even low, at the beginning of the pathology in mild-moderate intensity acute rejection (Ponziak et al., 1992). Because of these discouraging results, most physicians regard an elevated RI as a nonspecific marker of transplant dysfunction. It has been maintained that renal vascular resistance is not static, in acute rejection, but exhibits a dynamic picture depending on such variables as the immunosuppressive drugs used and the degree of rejection. Accordingly, reports have stated that values from Doppler examinations obtained at different times in cases of acute rejection may be of greater use in diagnosis (Hollenbeck, 1994; Mizrahi et al., 1993). Although RI analysis is not helpful in differentiating the typical causes of transplant dysfunction (acute tubular necrosis, rejection, and immunosuppression toxicity), it is still useful for identifying vascular complications associated with transplantation.

6.3.2 Acute tubular necrosis

Acute tubular necrosis is common in transplant kidneys from cadaver donors. It is a primary allograft dysfunction. Diuresis either never develops, or else is soon halted. Although these preliminary clinical findings are supported by elevated renal Doppler indices, no typical finding has been described for acute tubular necrosis in practice (Lee & Newstead, 1993; Taylor & Marks, 1990).

6.3.3 Other allograft complications

In the late postoperative period, a series of allograft dysfunctions, such as chronic rejection, cyclosporine toxicity and glomerulonephritis, developing in the allograft kidney present a similar pathological picture. Success levels in studies regarding definitive diagnosis and differentiation of these pathologies with Doppler US are not at all high (Pelling & Dubbins, 1992; Taylor & Marks, 1990).

7. Conclusion

As a noninvasive technique, renal Doppler US allows evaluation of renal hemodynamics, which helps to diagnose and monitor renal pathologies. Based on earlier clinical and experimental studies, Doppler ultrasonographic parameters have today been identified and defined as diagnostic indices for determining renal hemodynamic changes in response to renal vascular pathologies. When diuretic procedures together with RI difference and ratio are used in unilateral ureteral obstruction, renal Doppler US may be enough to make an accurate diagnosis. However, this technique should be combined with other radiological methods in patients with bilateral renal obstruction. Moreover, in the evaluation of both native and transplant kidneys, renal Doppler US has assumed the important function of concentrating suspicions on renal medical pathologies by successfully excluding vascular and obstructive pathologies.

8. References

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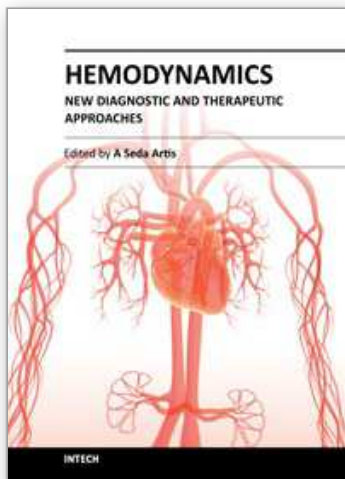
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