



# Prediction of Tubulo-interstitial Injury by Doppler Ultrasound in Glomerular Diseases: Value of Resistive and Atrophic Indices

MR Prabahaar+, R Udayakumar\*\*, Jamila Rose\*, EM Fernando++, R Venkatraman++, V Balaraman++, R Manorajan++, RE Amalraj#, M Jayakumar+++

## Abstract

**Background :** Doppler ultrasound is increasingly used in Nephrology for diagnosis of renovascular hypertension and evaluation of allograft dysfunction. However, its utility in glomerular disease remains controversial.

**Objectives :** Using Doppler Ultrasound, we prospectively tested the role of resistive and atrophic indices in predicting tubulointerstitial lesions in patients with glomerular disease as demonstrated by renal biopsy.

**Methods :** Seventy one patients with primary or secondary glomerular diseases were examined by Doppler ultrasonography immediately before renal biopsy. The resistive and atrophic indices (RI & AI) were calculated and compared with histologic changes in biopsy specimen.

**Results :** Receiver Operator Characteristics analysis showed RI of 0.60 as an optimal value for discriminating tubulointerstitial changes with sensitivity of 82.7% and specificity of 92%. An AI of 0.65 was shown to be optimal for discriminating tubulointerstitial injury with sensitivity of 69.2% and specificity of 85%. The combination of the two indices had not been found to be superior to either index alone. There was a significant correlation between atrophic and resistive indices. ( $r=0.358$ ,  $p<0.01$ ). It was observed that older age, smoking, elevated AI and RI, low GFR, high serum cholesterol and Hypertension were found to be significantly associated with the presence of tubulointerstitial injury in the univariate analysis whereas only elevated AI and RI were found to predict tubulointerstitial injury in multivariate analysis.

**Conclusion :** Measurement of RI by Doppler ultrasound can be considered as a supplementary diagnostic tool in glomerular diseases to predict the severity of tubulointerstitial injury. ©

## INTRODUCTION

Applications of Doppler Ultrasound in Nephrology are increasing day by day. Gray scale sonography is often routinely performed to evaluate a patient with suspected or known renal disease. Although this provides anatomic information, it lacks the ability to provide significant physiologic data. Duplex Doppler ultrasound has the potential to provide physiologic information concerning the renal arterial blood flow and resistance.<sup>1</sup>

Studies published in the last two decades indicated that Doppler can be used reliably in several types of intrinsic

renal diseases,<sup>2</sup> obstructive uropathy,<sup>3</sup> acute renal failure<sup>4</sup> and renovascular hypertension.<sup>5</sup> The diagnostic utility of Doppler in glomerular disease is under debate. Some studies show encouraging results,<sup>6,7</sup> whereas others are disappointing.<sup>8</sup> Different renal parenchymal diseases may present with distinct features on Doppler despite similar conventional ultrasound appearance. Renal vasculitis and tubulo-interstitial nephropathies are more frequently identified than glomerulonephritis since glomerular component accounts for only eight percent of renal parenchyma, whereas the highest percentage is occupied by the vascular and tubulointerstitial compartment.<sup>6</sup>

Among the Doppler derived indices, Resistive index(RI) is the most studied parameter for quantifying the alterations in renal blood flow that may occur with glomerular disease.<sup>9</sup> The RI seems to be related to the site of the disease in renal parenchyma. In patients with simultaneous glomerular and interstitial disease the RI was found to be higher than in patients with isolated glomerular disease.<sup>2</sup>

+Post graduate, ++Assistant professor, +++Professor & HOD, Department of Nephrology, Pathology\*, Madras Medical College and Government General Hospital Chennai. \*\*Radiologist, Genesis Scans, Chennai. #Dept of Epidemiology, The Tamil Nadu Dr.MGR Medical University, Chennai.

Received : 3.10.2006; Revised : 11.5.2007;  
Re-Revised : 25.10.2007; Accepted : 1.12.2007

At present accurate evaluation of tubulointerstitial lesions requires renal biopsy which is an invasive procedure. Although Doppler can't substitute renal biopsy, the measurement of resistive index which reflects renal vascular resistance has been found to be useful in detecting tubulointerstitial disease severity.<sup>10</sup> Tubulointerstitial lesions were proven to be the best histologic correlate of long term renal survival in various glomerular diseases.<sup>11,12</sup>

Atrophic index (AI) was a new parameter proposed by Sugiyura et al<sup>10</sup> for quantifying the atrophic changes in renal parenchyma. Retrospectively a combination of RI and AI has been found to predict the presence of tubulointerstitial lesion in glomerular disease with high sensitivity and specificity.<sup>10</sup>

## MATERIALS AND METHODS

In this prospective study, seventy five consecutive patients underwent Doppler examination of both kidneys immediately before percutaneous needle biopsy. The study has been approved by the Institutional ethics committee and written informed consent was obtained from all patients who participated in this study. The criteria adopted for biopsy were presence of any one of the following: Proteinuria >1 g/day, Proteinuria >0.5g/day with hematuria, Hematuria with RBC casts, rapidly worsening renal function.

Renal biopsies were done under ultrasound guidance with biopsy gun needle (C.R.BARD 22 mm 16 G) from the lower pole of the left kidney. All biopsies were successful and adequate glomeruli defined as more than seven glomeruli were obtained in sixty eight patients. Seventy one patients had glomerular disease in the biopsy and were included in the study. Rest had interstitial nephritis or hypertensive nephrosclerosis and was excluded from the study.

Data regarding age, gender, serum creatinine, 24 hr urine protein, Body Mass Index, presence of hypertension and renal failure were noted. Glomerular Filtration Rate (GFR) was calculated by the Cockcroft-Gault formula. Hypertension was defined as blood pressure >140/90 mm of Hg or use of antihypertensive drugs and renal failure was defined as serum creatinine >1.5 mg (>132 μmol) for this study purpose.

Doppler ultrasound study was performed just before the renal biopsy. A real time ultrasound device with 3.5 MHz convex probe and color Doppler capacity was used (SSH 140 A Toshiba medical Inc, Japan). The highest frequency that gave the measurable wave form was used and supplemented by the color or the power Doppler as and when required for vessel localization. Anti hypertensive drugs were stopped and dialysis deferred on the day of examination to avoid their potential effects on RI. Oral nifedipine was administered prior to biopsy if blood pressure is more than 140/90 mm of Hg.

After observation of intra renal arteries, arcuate arteries located on cortico medullary junction were insonated using

a 2-4 mm Doppler gate. Wave forms then optimized for the measurement using lowest pulse repetition frequency without aliasing (to maximize wave form size), highest gain without obscuring background noise and lowest wall filter. 3- 5 measurable wave forms from each kidney were obtained and RI was measured from the mean of above values. We used the data from the left kidney but no statistical difference was noted between the right and the left kidney (Data not shown). RI was calculated as follows = Peak Systolic Velocity-End Diastolic Velocity/Peak Systolic Velocity<sup>10</sup> using the in built software from the ultrasound unit.

To measure AI, the maximum longitudinal axis of the kidney was considered as the renal length (L). The major axis of the outer boundary of renal sinus was taken as the sinus length(S). The AI was calculated as S/L to quantitate the atrophic changes in the renal parenchyma.<sup>9</sup> As with RI 3-5 measurements from each kidney were taken and atrophic index was calculated from the mean of the above values. We used the data from the left kidney but no statistical difference was noted between the right and the left kidney. (Data not shown). To find out the RI in normal subjects a group of 109 healthy age matched voluntary kidney donors underwent ultrasound examination and measurement of RI. The mean RI of our healthy population was 0.58± 0.03. All measurements were made by a single experienced sonographer (radiologist) unaware of the study protocol.

The biopsy specimens were studied by light and immunofluorescence microscopy to determine the pathologic diagnosis and to quantify the severity of the histologic damage. For light microscopy tissues were fixed in Bouin solution and embedded in paraffin. Tissues were cut as 2 μm sections and stained with Hematoxylin and Eosin, Periodic acid Schiff and the Silver. For Immuno Fluorescence antisera against IgG, IgM, IgA, C1q, C3 were used.

A semiquantitative score was used to determine the extent of glomerulosclerosis and tubulo interstitial injury as studied previously.<sup>13</sup> Scoring was done by a single pathologist unaware of the study protocol. Tubulo interstitial injury was scored semi quantitatively on 30 cortical fields of Hematoxylin and Eosin stained specimens with a 20 x objective. Glomerulo sclerosis was defined as glomeruli exhibiting segmental or global collapse of glomerular capillaries with or without associated hyaline deposition and adhesion of capillary tuft to Bowman's capsule. To find out the independent role of RI and AI in predicting tubulointerstitial injury, the value of these elevated indices along with age, gender, proteinuria and hypertension were investigated between patients who had and who did not have tubulointerstitial injury.

## STATISTICAL ANALYSIS

Statistical analysis was carried out using the SPSS software (SPSS version 10.0, SPSS Inc). Descriptive statistics were obtained for factors considered in this study. Mean ± SD was obtained for continuous factors and frequency

distribution for discrete factors. Student t-test was used to find out whether the difference in means between groups was statistically significant. Chi-square test or Fisher's exact test whenever appropriate was used to find out whether the distribution of frequencies was equal among the groups. Results were shown as mean  $\pm$  SD. Sensitivity and specificity were determined from a series of 2x2 tables in which tubulo interstitial injury and no injury represented in one axis, RI and AI represented in the other. Tubulo interstitial score of 0 represent no injury and 1-4 were considered as its presence. ROC (Receiver Operator Characteristics) method<sup>14</sup> was used to determine whether the RI could discriminate between no tubulo interstitial injury and its presence. In ROC analysis sensitivity and the specificity were calculated for every score and ROC curve was plotted with ordinate indicating sensitivity, abscissa representing 1-specificity. The resultant ROC curve described the diagnostic efficacy of the test. An ideal test has an ROC that rises at critical score (indicating high sensitivity and specificity) and maintains plateau for higher values. Correlation coefficient was calculated between tubulointerstitial injury and RI. Linear regression equation was obtained for tubulointerstitial injury on RI. RI score was grouped into three categories based on the result from the present study (<0.6, 0.61-0.69,  $\geq$ 0.7). Kruskal-Wallis chi square test was obtained to find out whether the tubulo interstitial score and glomerular score were found to be significantly different in three different categories of the group based on RI score. AI score was grouped into two categories based on the result from the study (< 0.65 and  $\geq$ 0.65). Mann-whitney U test was applied to find out whether the tubulo interstitial score and glomerular score were found to be significantly different in two categories of the group based on AI score. All factors were independently associated with dichotomous category of tubulointerstitial injury and progression of the renal disease. The best cut off obtained from this study was used for AI and RI. Those factors found to be significant in the univariate analysis were used in multivariate logistic regression to find out the best combination of factors significantly associated with tubulointerstitial injury. In order to avoid multicollinearity problem, one of the factors among the correlated independent factors was considered to be dropped in the multivariate analysis. A p-value of less than 0.05 was considered to be significant.

## RESULTS

Seventy one subjects diagnosed to have glomerular disease were included in the study. The baseline characteristics of the patients are given in Table 1. The histopathology results of the study subjects are summarised in Table 2. The entire range of RI in the study (0.47-0.83) was evaluated for predictive ability by the ROC analysis. The resultant ROC curve is given in Fig. 1. The ROC curve indicated that RI value of 0.60 as the optimal value for discriminating tubulo interstitial injury with sensitivity of 82.7% and specificity of 92%. As the cut off point was raised the sensitivity improved at the expense of specificity.

The mean RI of our population in healthy people was  $0.58 \pm 0.03$  (109 subjects). In general it was widely accepted that RI of 0.7 was distinctly high.<sup>9</sup> Based on this the study group were divided into <0.6 – normal, 0.6-0.69 - high normal,  $\geq$  0.7- high. This was correlated with the degree of tubulo interstitial injury and glomerular injury. The degree of tubulo interstitial injury was significantly different among RI categories (high normal, high than in normal group) ( $p=0.001$ ). In contrast little relationship existed between RI and Glomerular score ( $p=0.307$ ).

Table 1 : Baseline characteristics of the study population

	Mean $\pm$ SD
1. Age	34.49 $\pm$ 5.68 yrs
2. Gender – Males	31 (43.7%)
3. 24 hr urine protein	2.63 $\pm$ 0.99 g/day
4. Serum creatinine	198.88 $\pm$ 73.92 $\mu$ mol/L
5. Glomerular filtration rate	0.83 $\pm$ 0.41 ml/sec
6. Serum albumin	31 $\pm$ 7 g/L
7. Serum cholesterol	5.50 $\pm$ 1.34 mmol/L
8. Follow up in months	18.53 $\pm$ 6.59
9. Hypertension at presentation	40.8%
10. Nephrotic syndrome	33.6%
11. Renal failure at onset	33.8%
12. Resistive index	0.64 $\pm$ 0.08
13. Atrophic index	0.65 $\pm$ 0.05

Table 2 : Biopsy results of the study subjects

Minimal change nephropathy	5
Membranous nephropathy	8
Mesangial proliferative glomerulonephritis	10
IgA nephropathy	10
Focal segmental glomerulo sclerosis	8
Diffuse proliferative glomerulonephritis	8
Membrano proliferative glomerulonephritis	4
Class IV lupus nephritis	9
Class III lupus nephritis	2
Class II lupus nephritis	2
Crescentic glomerulonephritis	5

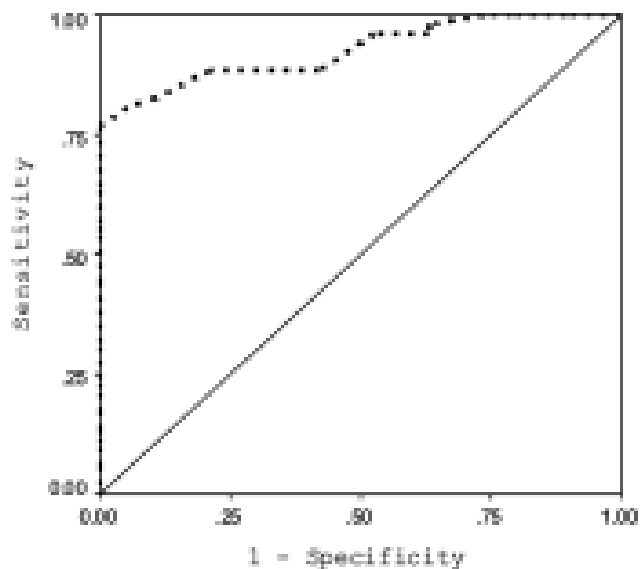


Fig. 1 : ROC Curve of the predictive value of RI

AI was a new parameter proposed to evaluate the degree of atrophic changes in renal parenchyma.<sup>10</sup> As with RI the full range of AI (0.53-0.76) was evaluated for the predictive ability in discriminating tubulointerstitial injury by ROC. The ROC indicated that AI of 0.65 had 69.2% sensitivity and 85% specificity. The ROC curve for AI is given at Fig. 2. As with RI, the correlation of AI with histologic changes was assessed. In contrast to RI, both tubulointerstitial (p=0.001) and glomerular score (p=0.001) were different in two categories of AI based on categories AI < 0.65 and AI ≥ 0.65.

To determine whether RI and AI indices were independent parameters, the correlation between them was examined. As shown below the correlation between them was statistically significant (r=0.358, p<0.01) (Fig. 3). The linear equation for AI based on RI is AI = 0.226 RI + 0.502 and R square for the regression equation is 0.358). This suggested that both are dependent variables in detecting tubulointerstitial injury. To confirm the above said observation subjects were divided into two groups where both RI and AI were normal and one or the other high. In this sensitivity and specificity remained low 62%, 76% respectively.

It was observed that older age, smoking, elevated AI and RI, low GFR, high serum cholesterol and Hypertension were found to be significantly associated with the presence of tubulointerstitial injury in the univariate analysis (Table 3) whereas only elevated AI and RI were found to predict tubulointerstitial injury in the multivariate analysis (Table 3).

## DISCUSSION

The usefulness of Doppler ultrasound in medical renal disease seems to be underestimated. This may be attributed

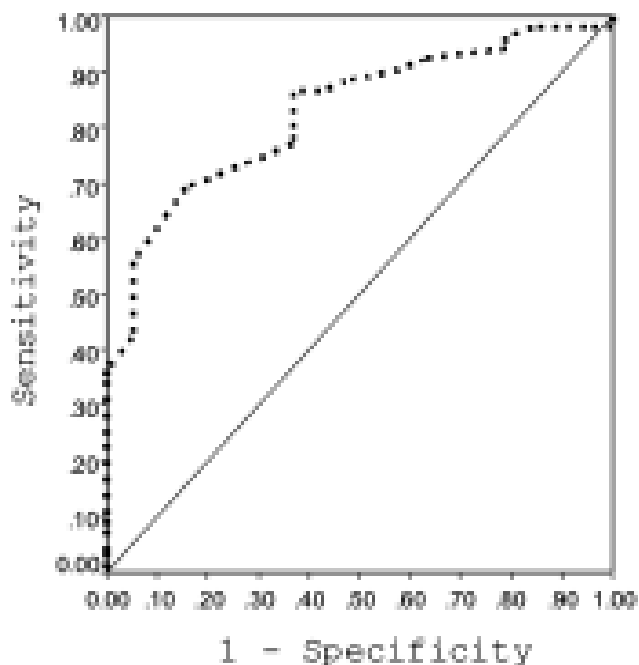


Fig. 2 : ROC Curve of the predictive value of AI

to contradictory reports from previous studies and the lack of ability to distinguish different renal diseases.<sup>9</sup> Renal parenchymal resistance as measured by RI represent the global resistance offered to blood flow by different parenchymal structures vascular, interstitial or glomerular compartments either separately or all together. This is especially true of vasculointerstitial compartment because when the damage is confined to glomeruli the RI does not seem to increase.<sup>15</sup> Few studies reported that RI correlated with tubulointerstitial changes.<sup>2,10</sup> The mechanism of raised RI in tubulointerstitial disease is probably the interstitial fibrosis surrounding the vessels increasing the vascular impedance.<sup>16</sup>

This prospective study demonstrated that extent of the tubulointerstitial injury can be predicted by measurement of RI and AI. Combination of these two have not been proven to be useful than either index alone in contrast to similar study<sup>10</sup> This study has also shown significant correlation between RI and AI which may be the reason for the above finding. RI correlated well with tubulointerstitial injury than with the glomerular injury whereas AI correlated both with glomerular as well as tubulointerstitial injury. This could account for lack of good correlation (r= 0.358) between them although it is statistically significant.

We used RI 0.60 as a cut off point instead of 0.7. Several studies have shown that a mean RI of people without preexisting renal disease was 0.60± 0.01.<sup>2,9,17</sup> Exceptions to this are children <4 yrs, adults >60 yrs. The mean RI of our healthy population (109 subjects) was 0.58± 0.03. Our ROC curve found 0.6 as the best discriminatory value. The present study shows that RI of 0.6 should be accepted as a cut off value in glomerular disease in Indian population.

The relationship between age and RI could have influenced the results but there was no statistically significant difference between patients with high, high normal or low RI (Data not shown). More over as stated earlier, a different value may be more appropriate in individual diseases.<sup>9</sup> For example in obstruction, to differentiate obstructive from unobstructed pelvicalyceal system RI of 0.7 was found to be the most appropriate with sensitivity of 92% and specificity of 88%.<sup>3</sup> On the other hand in Reno vascular hypertension, a value of >0.8 or more strongly predicted

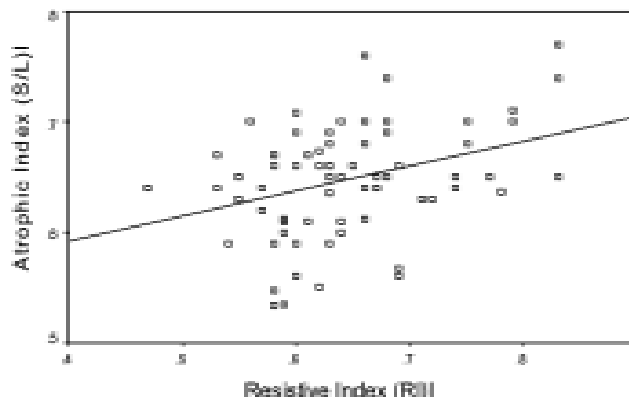


Fig. 3 : Correlation of the resistive index and the atrophic index

Table 3 : Association between various factors and tubulointerstitial injury

Factors	Tubulointerstitial injury Score				Test statistics	p-value
	0		≥ 1			
	Mean	SD	Mean	SD		
Age	23.05	9.98	34.96	14.12	3.37	0.01
24 hour urine protein 2.72	0.97	2.61	1.01	0.41	0.61	
GFR	64.36	18.92	45.03	25.62	2.99	0.01
BMI	20.31	3.17	21.26	3.63	1.00	0.32
Cholesterol	238.53	66.57	204.7	44.27	2.47	0.02
Gender*	Male	7 (36.8)	24 (46.2)		0.49	0.48
	Female	12 (63.2)	28 (53.8)			
RI*	< 0.60	18 (94.7)	10 (19.2)		33.2	0.01
	≥ 0.60	1 (5.3)	42 (80.8)			
AI*	< 0.65	18 (94.7)	23 (44.2)		14.5	0.01
	≥ 0.65	1 (5.3)	29 (55.8)			
Smoking	Yes	0 (0)	17 (32.7)			0.01*
	No	19 (100)	35 (67.3)			
Hypertension	Yes	4 (21.0)	25 (48.1)		4.21	0.04
	No	15 (78.9)	27 (51.9)			

\*Factors are expressed as number (percentages). Test statistics is chi-square (Fisher's Exact test) to test the distribution of subjects for the categories of these factors were equally distributed between tubulointerstitial score 0 versus tubulointerstitial score ≥ 1. For other factors, t- test was used to find out whether the mean of these factors are equal between tubulointerstitial score 0 versus tubulointerstitial score ≥ 1.

lack of improvement after revascularisation.<sup>18</sup>

We have also tested the value of AI which can be easily measured at bed side. This index was introduced to reduce the error while measuring the renal length alone to identify the atrophic changes of the kidneys as renal length can be normal with thin parenchyma in some cases. By ROC analysis the optimal discriminatory value was 0.65 which was again lower than in comparison with similar study.<sup>10</sup> The significance of AI in glomerular diseases requires further research.

Our study had few potential limitations. The Doppler and pathologic analyses were carried out by a single observer. It is well known fact that both are observer dependent parameters, hence significant intra observer variability does exist. This should be borne in mind while interpreting the results of this study. We administered antihypertensive drugs until a day before the Doppler study for patient safety. There was a possibility that drugs might decrease RI because of inadequate washout period. It is well known that converting enzyme inhibitors decrease RI whereas calcium channel blockers do not reduce RI.<sup>19</sup> But this finding is disputed by recent observations that converting enzyme inhibitors reduce RI only in diabetic subjects not in patients without diabetes.<sup>20</sup> Our study had no diabetic patients.

## CONCLUSIONS

We conclude that resistive and atrophic indices can be used to predict the presence of tubulointerstitial lesion in glomerular disease with high sensitivity and specificity. RI fared better than AI to predict the presence of tubulointerstitial disease. The combination of the two has not been found to be superior to either index alone. There was a significant correlation between atrophic and resistive indices. Elevated RI and AI independently predict

the tubulointerstitial injury. Hence measurement of resistive index can be considered as a supplementary diagnostic tool in glomerular diseases to assess severity of tubulointerstitial injury.

## REFERENCES

- Platt JF. Doppler Ultrasound of the kidney Seminars ultrasound CT 1997;18:22-32.
- Platt JF, Rubin JM, Ellis JH, Dipetro MA, Sedman AB. Intra renal arterial sonography in patients with non obstructive renal disease. Correlation of resistive index with biopsy findings. AJR Am J Roentgenol 1990;154:1223-7.
- Platt JF, Rubin JM, Ellis JH. Distinction between obstructive and non obstructive pyelocaliectasis with duplex Doppler Ultrasound. AJR Am J Roentgenol 1989;153:997-1000.
- Izumi M, Sugiura T, Nakamura H, Nagatoya K, Imai E, Masatsugu H. Differential diagnosis of pre renal azotemia from acute tubular necrosis and prediction of recovery by Doppler Ultrasound. Am J Kid Dis 2000;35:713-9.
- Greene ER, Avasthi PS, Hodges J. Non invasive Doppler assessment in renal artery stenosis and haemodynamics. J Clin Ultrasound 1987;15:653-9.
- Quaia E, Bertolotto M. Renal parenchymal diseases is characterisation feasible with ultrasound. Eur Radiol 2002;12:2006-20.
- Platt JF, Rubin JM, Ellis JH. Lupus Nephritis- predictive value of conventional and Doppler ultrasound in comparison with serology and biopsy findings. Radiology 1997;203:82-6.
- Mostbeck GH, Kain R, Mallek R, Derfler K, Walter R, Havelec L, Tscholakoff D. Duplex Doppler Ultrasound in renal parenchymal diseases : Histopathologic correlation. J Ultrasound Med 1991;10:189-94.
- Tublin ME, Bude RO, Platt JF. The resistive index in renal Doppler; where do we stand AJR. Am J Roentgenol 2003;180:885-92.
- Sugiura T, Nakamori A, Wada A, Fukuhara Y. Evaluation of tubulointerstitial injury by Doppler ultrasound in glomerular diseases. Clin Nephrol 2004;61:119-26.
- Nath KA. Tubulo interstitial damage as a major determinant of renal disease progression. Am J Kid Dis 1992; 20: 1-17
- Muller GA, Zeisberg M, Strutz F. The importance of tubulo interstitial

damage in progressive renal disease Nephrol. Dial Transplant 2000;15:76-7.

2003;26:132-7.

13. Nangaku M, Pippin J, William G. Couser C6 mediates chronic progression of tubulointerstitial damage in rats with remnant kidneys. J Am Soc Nephrol 2002;13:928-36.
14. Hanley JA, McNeil BJ. Meaning and use of ROC curve Radiology 1982;143:29-36.
15. Splendiani G, Parolini C, Fortunato T, Sturniolo A, Costanzi S. Resistive index in progressive nephropathies Clin Nephrol 2002;57:45-50.
16. Ikee R, Kobayashi S, Hemmi N, Imakiire T, Kikuchi Y, Moriya H, Suzuki S, Miura S. Correlation between the resistive index by Doppler ultrasound and kidney function and histology. Am J Kid Dis 2005;46:603-9.
17. Keogan M. Renal resistive indices: variability in Doppler US measurement in healthy population. Radiology 1996;199: 165-9.
18. Radermacher J, Chavan A, Bleck J, Vitzthum A, Stoess B, Gebel MJ, Galanski M, Koch KM, Haller H. Use of Doppler to predict the outcome of therapy in renal artery stenosis. N Engl J Med 2001;344:410-7.
19. Leoncini G, Martolini C, Viazzi F, Ravera M, Parodi M, Ratto E, Vettovetti S, Tomillo C, Derchi LE, Detenari G, Potremoli R. Changes in renal resistive index and urinary albumin excretion in hypertensive patients under longterm treatment with lisinopril or nifedipin GITS. Nephron 2002;90:169-73.
20. Taniwaki H, Ishimura E, Kawagishi T, Matsumoto N, Hosoi M, Emoto M, Shoj T, Shoji S, Nakatani T, Inaba M, Nishizawa Y. Intrarenal haemodynamic changes after captopril test in patients with type 2 diabetes : A duplex Doppler sonography study. Diabetes care

### Announcement

Indian Academy of Echocardiography is holding one of its kind event "XIII Annual International Conference on Clinical Echocardiography" from 8<sup>th</sup> – 10<sup>th</sup> Feb. 2008, at Hotel Ashok , New Delhi.

For details contact : Dr. Rakesh Gupta, Secretary General / President IAE, IAE India Headquarter, C – 1/ 16, Ashok Vihar – Phase - II , Delhi -110052.

Tele : 011-27415646 , 011-27419505 , 011-27134839; Mobile : 0-98110-13246 , 0-93110-13246 , 0-93111-13246

Email: [iaecon2008@gmail.com](mailto:iaecon2008@gmail.com) Website : [www.iaecho.org](http://www.iaecho.org)

### Announcement

Hypertension, Berlin 2008, 22<sup>nd</sup> Meeting of the International Society of Hypertension, June 14-19, 2008, Berlin, Germany.

Contact : C/o KIT GmbH, Association and Conference Management Group, Kurfurstendamm 71, D-10709, Berlin, Germany [www.hypertension2008.com](http://www.hypertension2008.com)

### Announcement

Vlth Annual Conference of the Maharashtra Chapter of ISG on February 23<sup>rd</sup>-24<sup>th</sup>, 2008 at Tata Hospital Auditorium, Mumbai. The theme of meeting is "Gastroenterology and Hematology- The Interface".

For details contact : [mahaisg2008@gmail.com](mailto:mahaisg2008@gmail.com) or Organising secretaries - Dr Aabha Nagral at 9820156834, Dr Samir Shah 9821131181 or Dr Harvinder Palaha 9869706825.

Limited registrations available