DIURETIC DOPPLER ULTRASOUND FOR EVALUATING OBSTRUCTED AND NON-OBSTRUCTED KIDNEY

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ABSTRACT

Objective: *The objective of this study was to evaluate the implementation of diuretic Doppler Ultrasound (DDU) to differentiate the obstructed and non-obstructed kidney.* ***Material & Method:*** *From 28 patients, we gathered data of 48 kidneys in accordance with the inclusion criteria. We evaluated the Doppler Ultrasound Resistive Index (RI) before and after administration of diuretic, using the renogram as the comparison. The result of renogram was categorized into total obstruction (n = 19), partial obstruction (n = 18), and non-obstructive dilatation (n = 3). The statistical analysis was performed using Anova test followed by Tukey HSD test. We also performed diagnostic test, the total and partial obstruction were categorized within obstructed group (n = 37) whereas normal and non-obstructed dilated kidney categorized as non-obstructed group (n = 11).* ***Results:*** *Average change of RI (ΔRI) was 0,542 ± 0,0457 for total obstruction, 0,0428 ± 0,0439 for partial obstruction, 0,0275 ± 0,0392 for normal kidney, -0,0300 ± 0,0361 for non obstructed dilated kidney. The result of normality and homogeneity test indicated the data were normally distributed. One-way Anova test revealed significant differences of ΔRI between groups. The subsequent Tukey HSD test indicated that there were significant differences in total and partial obstruction groups, compared to non-obstructive dilated kidney group. Based on ΔRI cut-off point (0,035) the diagnostic characteristics were 88,5% sensitivity and 72,3% specificity.* ***Conclusion:*** *RI of Diuretic Doppler Ultrasound is a valuable examination to evaluate obstructed and non-obstructed kidney. The cut-off point of 0,035 indicated probability of obstructive kidney.*

Keywords: *Resistive index, renogram, obstructive kidney, non-obstructive kidney.*

ABSTRAK

Tujuan Penelitian: *Untuk mengkaji manfaat ultrasonografi Doppler dengan diuretik dalam membedakan ginjal obstruksi dan non obstruksi.* ***Bahan & Cara:*** *Dari 28 pasien yang diperiksa didapatkan 48 ginjal yang masuk kriteria inklusi untuk dievaluasi. Pasien tersebut dilakukan pemeriksaan Indeks Resistif dengan ultrasonografi Doppler sebelum dan sesudah pemberian diuretik (ΔRI) dengan pembandingnya adalah pemeriksaan Renogram. Berdasarkan hasil renogram ginjal diklasifikasikan sebagai obstruksi total (n = 19), obstruksi parsial (n = 18), ginjal normal (n = 8) dan dilatasi non obstruksi (n = 3). Uji yang digunakan adalah Anova yang bila belum didapatkan perbedaan dilanjutkan dengan Uji Tukey HSD. Disamping itu juga dilakukan uji diagnostik terhadap alat ini dengan klasifikasi obstruksi total dan obstruksi parsial menjadi kelompok obstruksi (n = 37) dan ginjal normal dan dilatasi non obstruksi menjadi kelompok non obstruksi (n = 11).* ***Hasil Penelitian:*** *Rerata ΔRI yang didapatkan adalah 0,542 ± 0,0457 untuk obstruksi total, 0,0428 ± 0,0439 untuk obstruksi parsial, 0,0275 ± 0,0392 untuk ginjal normal dan -0,0300 ± 0,0361 untuk dilatasi non obstruksi. Hasil uji normalitas dan homogenitas didapatkan data homogen dan berdistribusi normal. Uji statistik parametrik One way Anova dilakukan dengan hasil terdapat perbedaan signifikan ΔRI antar kelompok perlakukan, kemudian dilanjutkan dengan uji Tukey HSD dengan hasil berupa perbedaan yang signifikan hanya pada kelompok obstruksi total dan obstruksi parsial terhadap kelompok dilatasi non obstruksi. Berdasarkan nilai cut-off ΔRI (0,035) dilakukan uji diagnostik dengan hasil sensitifitas 88,5% dan spesifisitas 72,3%.* ***Simpulan:*** *Pemeriksaan RI Ultrasonografi Doppler dengan diuretik dapat menjadi pemeriksaan tambahan dalam mengevaluasi ginjal obstruksi dan non obstruksi dengan sensitifitas yang cukup tinggi tetapi spesifitas sedang dan nilai cut-off 0,035 dapat digunakan untuk indikasi adanya kemungkinan obstruksi pada ginjal.*

Kata kunci: *Indeks resistif, renogram, ginjal obstruksi, ginjal non obstruksi.*

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INTRODUCTION

Urinary tract obstruction can occur during fetal growth, child or adult. The cause of obstruction can be congenital or acquired and can be benign or malignant. Obstruction is influenced by the extent or degree of obstruction (partial or complete, unilateral or bilateral), chronicity (acute or chronic), renal underlying conditions, the potential for healing, and any other accompanying factors, such as urinary tract infections.[1]

Hydronephrosis is dilatation of renal pelvis or calyx that may be related with obstruction, but may also occur without obstruction. Obstructive uropathy is associated with functional or anatomic obstruction of urine flow at all levels of the urinary tract. Obstructive nephropathy occurs when the obstruction is caused by functional or anatomical renal impairment.[1]

Hydronephrosis in obstructive uropathy is the distension of urine-containing renal calyx and pelvis as a result of urine flow obstruction in the distal renal pelvis. Increasing renal pelvic pressure and reduction in renal blood flow are considered as the mechanism of cell injury and atrophy. Obstructive uropathy progressively inhibits all kidney functions except urinary dilution. The longer and more complete the obstruction, the more severe the pathophysiological changes.[2]

In diagnosing hydronephrosis due to obstructive uropathy many diagnostic tools can be used. Each tool has its advantages and disadvantages in both diagnosing renal anatomy and function. Renogram is one of obstructive uropathy diagnostic tools that are useful and non-invasive. This tool can replace intravenous pyelography (IVP) in patients at risk for contrast agents and patients with decreased kidney function. However, the limitations of the renogram are its limited availability and the expensive cost of the examination.

An alternative tool that can be used to see kidney function with hydronephrosis is Doppler ultrasonography (USG). However, this tool has not been a standard examination of kidney hydronephrosis with obstructive uropathy. Doppler ultrasound can be used to measure renal resistive index (RI), which had been used to assess the presence of obstruction of the kidney. RI is defined as peak systolic velocity (PSV) minus end-diastolic velocity (EDV) divided by PSV ([PSV- EDV]/PSV).

Several research groups have investigated the ability of Doppler ultrasound to diagnose kidney obstruction, but its use has not been established. Platt et al suggest that the resistive index of 0,7 as the upper limit of the normal kidney, RI values of more than 0,7, indicates an increase in resistance to blood flow, indicating the presence of obstructive uropathy. In subsequent studies, Platt et al also reported his experience using Doppler ultrasound in 23 patients with acute unilateral obstruction. Three patients obtained false negative results, two of them experienced pyelosinus extra vasation and one of them had obstruction for more than 5 hours. They concluded that the determination of the resistive index on Doppler ultrasound can support routine ultrasound evaluation of urinary tract obstruction. In contrast, other studies by Tublin et al (1994) found that Doppler ultrasound is not sensitive enough to detect obstruction. He reported that of 32 patients with colic, 12 of 19 patients with obstruction had a normal RI and 5 of 13 patients without obstruction has abnormal RI. One of the differences in those studies may be the degree of renal obstruction.[3-5]

Chen et al evaluated 27 patients with suspicion of obstruction. They used Doppler ultrasound and Intraveous Pyelography (IVP). In general, the use of resistive index of 0,7 is the critical value for the obstruction, the sensitivity is only 52%. However, related to the degree of IVP obstruction, the RI can distinguished kidneys with mild obstruction from those with severe obstruction. In mild obstruction, the mean RI is only 0,64, while in severe obstruction the mean RI is 0,74. Sensitivity of RI of greater than 0,7 for a significant obstruction was 9,3%. Fung et al also assessed Doppler ultrasound to evaluate obstruction. They measured the RI of the nine patients who underwent Whitaker examination for hydronephrosis grade 3 or 4. They found that the resistive index is directly related to the pressure of the renal pelvis. They determined that normal renal perfusion pressure is less than 0,82. The major drawback of this study to assess the Doppler ultrasound is inconsistent definition of obstruction and degree of obstruction. Although the presence of hydronephrosis associated with abnormally increased RI may indicate severity of obstruction, it is necessary to know the limitations of these and other clinical information and the use of functional assessment of the kidney for the action plan of the treatment. Intravenous furosemide may be used to increase the sensitivity of Doppler ultrasound in the diagnosis of obstructive uropathy by increasing pressure within the kidney. Yokohama H and Tsuji Y in their study on dogs found that, compared to

mannitol and sodium iothalamate, furosemide showed no significant differences in its diuretic effects, but furosemide increases the difference between the intrarenal RI in unilateral renal obstruction and normal kidney, so that it can improve the detection of unilateral urinary tract obstruction in humans. This has been confirmed by Mallek R et al. who stated that the Doppler ultrasound with diuresis could accurately distinguish between the obstructed and non-obstructed kidney.[6-10]

Rawashdeh YF et al., in their review article on the research of Doppler ultrasound related to obstructive uropathy, concluded that the resistive index is still in the development phase, so we need further study before this technique can be used for the diagnosis of obstructive uropathy.[11] In this regard it is necessary to research on the ΔRI on Doppler ultrasound compared to renogram results to determine whether a kidney has obstructive uropathy or not, as well as to test Doppler ultrasound diagnostic tool to diagnose patients with obstructive uropathy.

OBJECTIVE

Assessing the benefits of diuretic Doppler ultrasound to determine kidney with obstructive and non-obstructive uropathy.

MATERIAL & METHOD

This was an observational analytic study to prove the existence of differences in the results of Doppler ultrasound before and after diuresis in the obstructed kidney, which was conducted from January to May 2011.

The study population was 28 patients in Urology Outpatient Clinic with unilateral or bilateral hydronephrosis for over a month due to stones or malignancy that had been operated and had not been operated.

The inclusion criteria in this study were 1) patients with a clinical history of renal obstruction over a month based on recent history and ultrasound results, 2) patients with unilateral or bilateral hydronephrosis by urology ultrasound whose function was proven with renogram, 3) patients with obstructive uropathy due to urethral stones, cervix uterine cancer, and other abnormalities down the ureter, 4) patients who have obstructive uropathy surgery, therefore, patients with hydronephrosis but without obstruction.

Data were analyzed descriptively and analytically. Before testing the hypothesis, first we tested for normality and homogeneity of the data. Data from the evaluation of resistive index difference (ΔRI) of the Doppler ultrasound before and after furosemide on kidney with obstruction, partial obstruction, non-obstructive dilatation, and normal kidney used paired t test. Comparison of the results of ΔRI between kidney with obstruction, partial obstruction, non-obstructive dilatation and normal kidney used Anova test. When the Anova test showed no difference, the test was followed-up with Tukey HSD test. Data were analyzed with commercial software.

RESULTS

Twenty-eight patients became samples in this study, each patient had two kidneys, so the total kidneys examined were 56. From these results, 48 kidneys met the inclusion criteria, while eight kidneys were not included in studied variables because renogram results showed that they belonged to failure category. Among the 28 patients, eight showed unilateral renal impairment and 20 showed bilateral renal impairment.

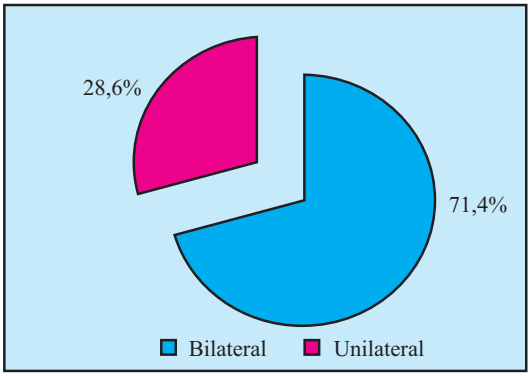

Figure 1. Distribution of renal obstruction.

Figure 1 shows most of the patients' renograms with bilateral renal impairment had a percentage of 71,4%, while 28,6% were unilateral.

Among the 28 patients, 17 were female and the remaining 11 were male. The 48 kidneys examined (table 1) were categorized into four groups based on the results of the renogram, kidney with total obstruction was 19 (39,6%), partial obstruction 18 kidneys (37,5%), 8 normal kidneys (16,7%), and 3 kidneys with non-obstructive dilatation (6,3%).

Table 1. Description of RI data of Doppler ultrasound.

Renogram Results		RI Pre	RI Post	Δ RI
Total obstruction	Mean	0,6611	0,7111	0,0542
	N	19	19	19
	Std. Deviation	0,07164	0,07310	0,04574
	Median	0,6800	0,6900	0,0600
	Minimum	0,54	0,63	-0,04
	Maximum	0,79	0,88	0, 11
	Range	0,25	0,25	0,15
Partial obstruction	Mean	0,6828	0,7256	0,0428
	N	18	18	18
	Std. Deviation	0,08574	0,06119	0,04390
	Median	0,6650	0,7300	0,0450
	Minimum	0,52	0,63	-0,03
	Maximum	0,84	0,84	0,12
	Range	0,32	0,21	0,15
Normal	Mean	0,6250	0,6525	0,0275
	N	8	8	8
	Std. Deviation	0,07151	0,09438	0,03919
	Median	0,6300	0,6550	0,0150
	Minimum	0,50	0,50	-0,01
	Maximum	0,75	0,79	0, 11
	Range	0,25	0,29	0,12
Non-obstructive dilatation	Mean	0,6267	0,5967	-0,0300
	N	3	3	3
	Std. Deviation	0,06807	0,10116	0,03606
	Median	0,6500	0,6500	-0,0200
	Minimum	0,55	0,48	-0,07
	Maximum	0,68	0,66	0,00
	Range	0,13	0,18	0,07

Table 2. Description of ΔRI data based on obstruction groups.

Groups	Mean	Std. Deviation	Lower	Upper
Total obstruction	0,0542	0,04574	0,0322	0,0763
Partial obstruction	0,0428	0,04390	0,0209	0,0646
Normal	0,0275	0,03919	-0,0053	0,0603
Non-Obstructive Dilatation	-0,0300	0,03606	-0,1196	0,0596

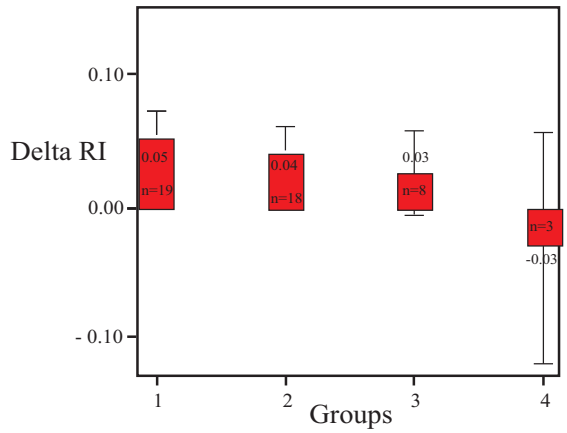

Figure 2. Comparison of mean ΔRI on each group.

Figure 2 shows the difference in the greatest RI in the total obstruction group, followed by partial obstruction and then normal group. For non-obstructive dilatation group, negative results were obtained, which means that the data after diuresis were lower than before the diuresis.

Table 3 shows relatively no significant difference between male and female in each group. From the chi-square test results, we found 0,791 level of significance, which means there is no significant difference based on sex in obstruction group.

Normality test data show (Table 4) that all four groups have normal distribution with a significance value of more than 0,05.

Table 3. Cross tabulation of sex in all groups.

Sex	Groups				Total
	Total obstruction	Partial obstruction	Normal	Non-Obstructive Dilatation	
Males	9 42,9%	7 33,3%	3 14,3%	2 9,5%	21 100,0%
Females	10 37,0%	11 40,7%	5 18,5%	1 3,7%	27 100,0%
Total	19 39,6%	18 37,5%	8 16,7%	3 6,3%	48 100,0%

Table 4. Normality test data.

Groups	Sig.	Notes
Total obstruction	0,204	Normal
Partial obstruction	0,816	Normal
Normal	0,112	Normal
Non-Obstructive Dilatation	0,537	Normal

Table 5. Results of homogenecity test.

Statistical tests	Results	Notes
Levene's test	0,336	Homogeneous
Significance	0,799	

Table 6. One way Anova test results.

F	Sig.	Note
3,488	0,023	Significant difference

Homogeneity test showed significance values higher than 0,05, so variants of data between homogeneous groups can be concluded (Table 5).

From the calculation of One Way Anova (Table 6), RI difference between the groups before and after treatment were significantly different ($p < 0,05$). With this result, it can be concluded that there is a difference between RI of Doppler ultrasound before and after the administration of furosemide on obstructed and partially obstructed kidneys, and normal kidney, and kidney with non-obstructive dilatation. Because no difference between groups were observed, further tests using Tukey HSD was performed.

Table 7 showed significant difference between total obstruction and non-obstructive dilatation and there is difference between partial obstruction and non-obstructive dilatation with significance value of less than 0,05, whereas the other group pairs do not show any significant difference.

The second hypothesis tested was the sensitivity and specificity of ΔRI. Total and partial obstruction was considered obstructed (n = 37) and normal and non-obstructive dilatation included in non obstructed group (n = 11).

Table 8 shows sensitivity = 23 : 26 (88,5%), specificity = 8 : 11 (72,3%), positive predictive value = 23 : 37 (62,2%), negative predictive value = 8 : 22 (36,4%), positive likelihood ratio 3,2, and negative likelihood ratio 12 : 16.

Table 7. Further or Post hoc test with Tukey HSD.

Groups	Total obstruction	Partial obstruction	Normal	Non Obstructive Dilatation
Total obstruction	-	0,856	0,474	0,017*
Partial obstruction	-	-	0,843	0,049*
Normal	-	-	-	0,224
Non Obstructive Dilatation	-	-	-	-

Note: * = significantly different

Table 8. ΔRI on renogram based on cut-off value.

		Renogram results		
		Obstructed	Non Obstructed	
ΔRI (cut-off value)	> 0,035	23 (88,5%)	3 (11,5%)	26 (54,2%)
	≤0,035	14 (63,6%)	8 (36,4%)	22 (45,8%)
		37 (77,1%)	11 (22,9%)	48 (100%)

Table 9. ROC curves in ΔRI.

Cut off	Area under the curve	Std. Error(a)	Asymptotic Sig.(b)	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
0,035	0,731	0,087	0,021	0,561	0,901

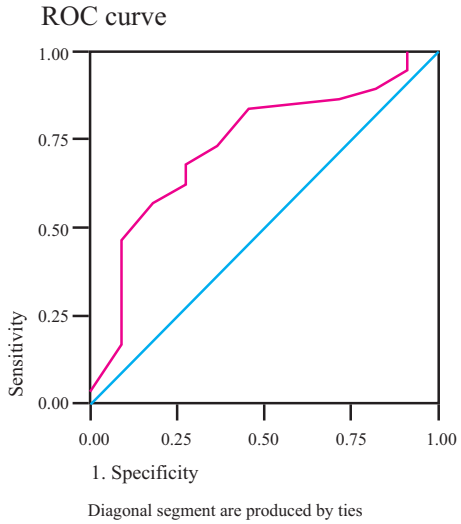

Figure 3. ROC curves in ΔRI.

DISCUSSION

Several studies have determined that mean RI value in normal kidneys is 0,60. For the upper limit of normal kidney, the value is generally 0,70, as determined by the most experts, except in children where mean RI may exceed 0,70 until age of 4 years. In older people without renal abnormalities, RI value may exceed 0,70.[12]

In this study the mean age was 48 years with an age range between 23 to 78 years. RI values before diuretics in total obstruction group was 0,66 ± 0,07, partial obstruction group 0,68 ± 0,08, normal kidney group 0,62 ± 0,07, and non-obstructive dilatation group 0,63 ± 0,07.

Mean RI before furosemide in total and partially obstructed kidneys was higher than the mean in normal kidneys and in kidneys with non-obstructive dilatation. This is consistent with the results obtained by Yokoyama H and Tsuji Y who examined the value of RI with diuretics in dogs with chronic unilateral partial obstruction. They found that the mean value of RI in obstructed kidney was higher than that in normal kidneys before being given with diuretics.[9]

Mean RI in normal kidney (0,62) and in kidney with non-obstructive dilatation (0,63) in this study are not much different from the mean in other studies, which is 0,60.

Many studies have found that furosemide provocation can increase RI in obstructed kidney and no effect on non-obstructive kidney in adults and children. However, there was also another study showing that administration of saline plus furosemide provocation produced different response, where the value of the renal RI increases and in non-obstructed of the kidneys the value reduced.[11]

In this study, there are four categories of kidney with total obstruction that has the greatest value of ΔRI (0,05 ± 0,04), followed by partial obstructed kidney (0,04 ± 0,04), normal kidney (0,03 ± 0,04) and kidney with non-obstructive dilatation (-0,03 ± 0,04).

The obtained value of ΔRI has considerable standard deviation and the difference between the ΔRI in each group is very small, making it difficult to determine standard values to distinguish kidneys with total and partial obstruction and normal kidneys. Only in total obstructed kidneys and kidney with non-obstructive dilatation a significant difference was found. However, total samples found in kidney with non-obstructive dilatation are very few (three kidneys). The results of statistical tests show that the ΔRI in groups tested had significant differences ($p < 0,05$).

Many studies have concluded that the difference in RI in Doppler ultrasound have significant differences between obstructed and non-obstructed kidneys, especially in children.[13] Yokoyama H and Y Tsuji also found that the resistive index after the administration of furosemide in obstructed kidney was increasing, as compared to normal kidney.[9]

Obstructive uropathy is usually associated with the dilatation of the upper urinary tract. However, not all kidney dilatation is obstruction. Differences in obstructed and non-obstructed dilatation were important and have significant meaning related to treatment, especially in children,

in whom unnecessary surgery can be avoided. Regular ultrasound and IVP are sensitive tools for the detection of pelvicalyectasis. However, a more detailed examination of the etiology cannot always be made only by examination.[11]

Gilbert R et al. in their study measured the RI compared with the results of renogram to evaluate children with hydronephrosis. Obstruction detected with RI had sensitivity of 100%, and specificity of 87% when considering 0,70 as the upper limit of normal values. In another study, Chen JH et al. examined 33 kidneys with various degrees of obstruction compared with 56 normal control kidneys. The sensitivity was 57% and specificity 98%. Subsequent grouping to obstructed dilatation group into mild and severe obstruction based on criteria IVP increased the sensitivity to 93%.[14]

Garcia-Pena et al reported that the difference of inter-renal RI, and the index difference pre and post diuretic are the most powerful indicators of Doppler ultrasound for the presence of renal obstruction in children. They combined the results of Doppler ultrasound RI and RI ratio before and after diuretics administration with conventional ultrasound parameters to create a scoring system that aims to differentiate obstructed kidneys and kidneys with non-obstructive dilatation. By using this scoring system, they classified kidneys into groups of low, moderate, and high obstruction risk. Low score ruled out the presence of obstruction with specificity of 99% and false negative rate of 9%, while high score detects obstruction with 91% sensitivity and false-positive rate was only 1%. The main limitation of this study was its retrospective nature. However, this study could be used as the basis of a prospective study to evaluate a scoring system for the diagnosis of obstructive uropathy.[15]

In this research, the sensitivity of RI was 97,3% and the specificity of RI was 9,1%. The resulting sensitivity value was not much different from that of previous studies, but with different specificity. In this study, the specificity produced is very low. Perhaps this is due to the variation in age of the examined patients. Previous studies concentrated more on children. Whereas, this study enrolled only adults, whose vascular compliance were more varied, although most USG experts assign the value of 0,7 as normal RI limit in adults.[16]

Cut-off value of the ΔRI in obstructed kidney obtained in this study was 0,035. In another study by Akata D et al who evaluated 28 renal hydronephrosis in children, the ΔRI increased at least 10% of the pre diuretic RI (baseline).[17]

CONCLUSION

RI examination of Doppler ultrasound of diuretics can be used as an additional examination in evaluating obstructed and non-obstructed kidney with a high sensitivity but moderate specificity and the cut-off value of 0,035 can be used to indicate the possibility of obstruction of the kidney.

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