



Study of Renal Haemodynamics Assessed by Renal Colour Doppler Ultrasound in Liver Cirrhosis

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Abstract

Background: Liver cirrhosis patients are complicated by different pathological processes leading to increased mortality and morbidity among them. Renal hemodynamic alteration leads to development of hepatorenal syndrome. Renal arterial Doppler study can be an effective screening modality for liver cirrhosis patients. Resistivity and Pustality indices are parameters measured by renal Doppler which reflects renovascular impedance. There is good correlation between these parameters and severity of liver cirrhosis assessed by Child-Pugh scoring system.

Materials and Methods: This study included 50 cirrhotic patients divided into three groups according to Child-Pugh classification, and fifteen healthy controls. All the patients were subjected to clinical, laboratory and ultrasound evaluation to confirm the diagnosis of cirrhosis. The renal arterial duplex ultrasound examination was conducted on patients as well as controls to measure Pustality and Resistivity index in main, segmental and cortical renal arteries.

Results: Pustality and Resistivity index were found to be elevated in the patients of Child class B and C as compared to class A and controls in the main and segmental renal arteries. Both indices were highest in class C than B. The Child class A and controls were not showing statistically significant difference in the main and segmental renal arteries. Resistivity index of the cortical arteries showed significant difference with that of controls. Both Pustality and Resistivity indices were highest in class C than B and A in cortical arteries. Oesophageal varices also showed significant correlation to elevated Pustality and Resistivity indices in relation to Child classes.

Conclusion: Both renal Pustality and Resistive index increase with the degree of the severity of the liver cirrhosis assessed by Child-Pugh classification. Renal duplex ultrasound is a safe, non-invasive and effective screening modality to study the renal hemodynamics and may predict renal dysfunction in different stages of the liver cirrhosis.

Introduction

Liver cirrhosis patients are complicated by different pathological processes leading to increased mortality and morbidity among them. This is in fact attributed to altered hemodynamics in cirrhosis patients. Renal hemodynamic alteration leads to development of hepatorenal syndrome. The morbidity and mortality associated

with it is very high and few therapeutic options to the patients. Hepatorenal syndrome is functional form of renal failure secondary to intrinsic renal vasoconstriction¹.

At present, there are no clinical or laboratory tests which are available to help in screening of such patients to detect at risk category of patients in subset of liver cirrhosis. Recently investigators

have suggested role of cystatin C and exogenous excretory markers such as inulin, to monitor for development of renal dysfunction^{2,3}. But these methods are costly and cannot be applied as screening tests for these patients.

Renal arterial Doppler study can be an effective screening modality for liver cirrhosis patients. It helps to detect intrarenal vasoconstriction associated altered renal hemodynamics due to circulatory changes in liver cirrhosis⁴. Resistivity and Pulsatility indices are parameters measured by renal Doppler which reflects renovascular impedance. There is good correlation between these parameters and severity of liver cirrhosis assessed by Child-Pugh scoring system⁵.

Present study was carried out to evaluate role of renal arterial Doppler to study altered renal hemodynamics in liver cirrhosis patients.

Materials and Methods

This descriptive study has been carried out in Department of Radiodiagnosis, Andhra Medical College, Visakhapatnam. A total of 50 patients of liver cirrhosis based on clinical, laboratory and ultrasonography were included in the study. The study period was from March 2017 to December 2018.

The protocol of the study was approved by the research council and ethical committee of the institute. Informed consent was taken from all patients who participated in the study.

Inclusion Criteria

1. Age group-All cirrhotic patients of age group >15years will be included.
2. Diagnosis of cirrhosis will be based on clinical, laboratory and/or ultrasound findings.

Exclusion Criteria

1. Known renal diseases such as Diabetic nephropathy, Hypertensive nephropathy other medical renal disorders.
2. Serum creatinine >1.5mg/dl.
3. Marked hepatic encephalopathy, recent episode of gastrointestinal bleed (within 1-2 days).

Results

The present study focuses on two important indices of renovascular impedance namely, Pulsatility Index and Resistivity Index. These two indices were measured in three different artery levels such as main renal artery, segmental renal artery and cortical renal artery respectively. The total number of samples in the study are 65 of which the number of individuals under Child class A is 23(35.4%), B is 9(13.8%), C is 18(27.7%) and Controls 15(23.1%). The number of males over females are 55(84.4%) and 10(15.6%) respectively. The main objective of the study is to observe the above two indices and their average variations with respect to 3 categories of Child class. Along with this comparison summary statistics such as mean, S.D, minimum, maximum, and range are to be reported for 3 categories of Child class as well as sex.

Table 1- Child Class Distribution

CHILD Class	Frequency	Percent
A	23	35.4
B	9	13.8
C	18	27.7
Controls	15	23.1
Total	65	100.0

Figure 1- Grey Scale Features Liver Cirrhosis with Ascites



Table 2- Main Renal Artery Pulsatility and Resistivity Index

	Parameters	Statistics	Child Class				F-statistic (p-value)
			A	B	C	Controls	
Main Renal Artery	Pulsatility Index	Mean	1.042 ^a	1.198 ^b	1.439 ^c	1.083 ^a	111.430 (0.000*)
		Std. Deviation	0.062	0.037	0.110	0.043	
		Minimum	0.910	1.130	1.270	1.000	
		Maximum	1.130	1.260	1.680	1.140	
		Range	0.220	0.130	0.410	0.140	
	Resistivity Index	Mean	0.615 ^a	0.679 ^b	0.751 ^c	0.627 ^a	64.980 (0.000*)
		Std. Deviation	0.034	0.033	0.038	0.024	
		Minimum	0.520	0.630	0.670	0.580	
		Maximum	0.680	0.720	0.800	0.660	
		Range	0.160	0.090	0.130	0.080	

In the table 2, the statistics along with the ANOVA results are reported for 2 indices. Statistical significance was observed in both the indices (P<0.05) and under Pulsatility index, the Child class C was possessing the highest average Pulsatility Index and the least was observed in Child class A. With the aid of Multiple Comparison Test, it was clear that Child class B and C were differing significantly with A and

Controls as well as between them. Further, one fact was revealed that there was no difference between the Child class A and Controls.

The alphabets a, b and c as super scripts indicates to the mean values of 3 categories of Child class. The same super scripts indicate that there is no difference between the classes and different super scripts indicates significantly different between the classes.

Figure 2- Renal Artery at Hilum Doppler

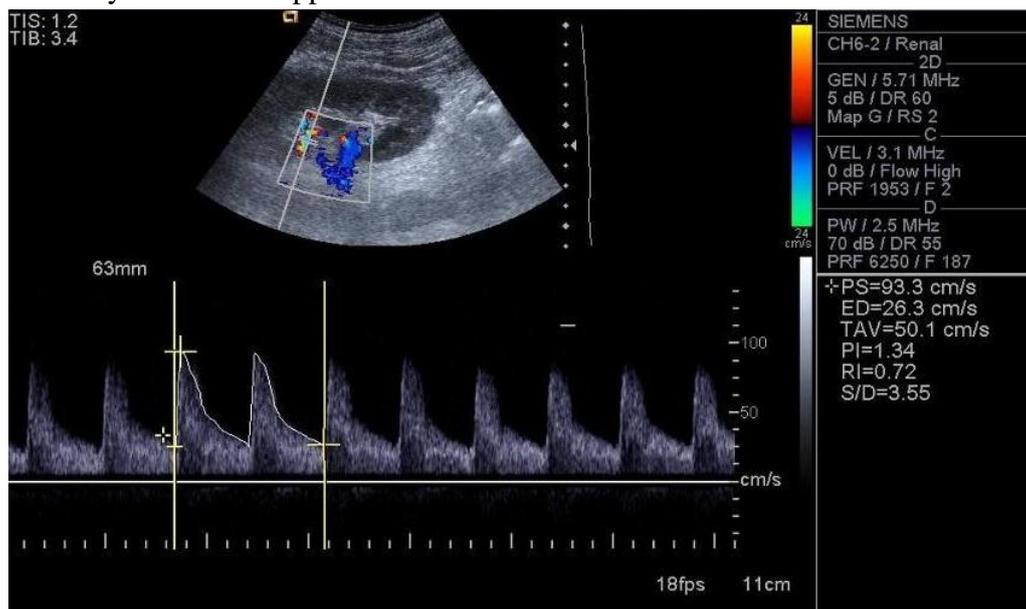


Table 3- Segmental Renal Artery

	Parameters	Statistics	Child Class				F-statistic (p-value)
			A	B	C	Controls	
Segmental Renal Artery	Pulsatility Index	Mean	0.967 ^a	1.130 ^b	1.337 ^c	0.988 ^a	89.746 (0.000*)
		Std. Deviation	0.073	0.059	0.099	0.062	
		Minimum	0.800	1.000	1.190	0.830	
		Maximum	1.090	1.190	1.590	1.070	
		Range	0.290	0.190	0.400	0.240	
	Resistivity Index	Mean	0.581 ^a	0.649 ^b	0.706 ^c	0.563 ^a	72.021 (0.000*)
		Std. Deviation	0.036	0.025	0.031	0.031	
		Minimum	0.500	0.610	0.660	0.510	
		Maximum	0.630	0.700	0.760	0.600	
		Range	0.130	0.090	0.100	0.090	

In table 3, the statistical significance was observed in both Pulsatility Index and Resistivity Index of segmental renal artery ($P < 0.05$). The Child class C was having the highest mean, P.I and R.I, and was

differing significantly with mean Pulsatility index and Resistivity index with A, B and Controls. But the Child classes A and Controls were not statistically significant

Figure 3- Segmental Renal Artery Doppler

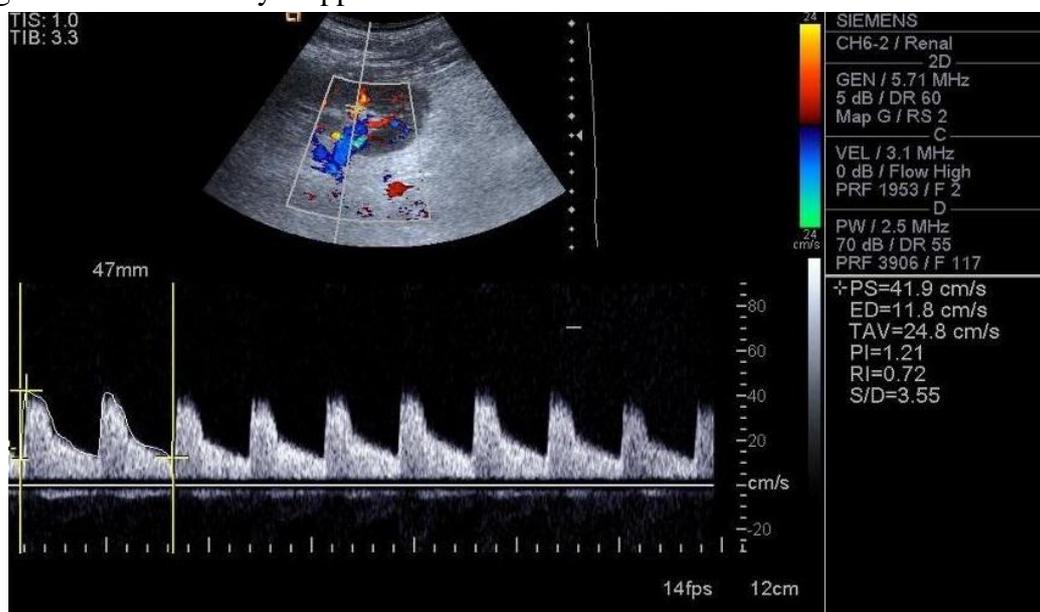


Table 4 - Cortical Renal Artery

	Parameters	Statistics	Child Class				F-statistic (p-value)
			A	B	C	Controls	
Cortical Renal Artery	Pulsatility Index	Mean	0.890 ^a	1.031 ^b	1.234 ^c	0.863 ^a	99.409 (0.000*)
		Std. Deviation	0.075	0.067	0.073	0.068	
		Minimum	0.710	0.900	1.090	0.760	
		Maximum	1.000	1.090	1.330	0.960	
		Range	0.290	0.190	0.240	0.200	
	Resistivity Index	Mean	0.536 ^a	0.604 ^b	0.667 ^c	0.498 ^d	81.533 (0.000*)
		Std. Deviation	0.038	0.037	0.027	0.033	
		Minimum	0.460	0.530	0.620	0.450	
		Maximum	0.600	0.650	0.720	0.550	
		Range	0.140	0.120	0.100	0.100	

In table 4, statistical significance was observed in both P.I and R.I of Cortical Renal Artery ($P < 0.05$). Under Pulsatility Index, the Child class C was differing significantly with A, B and controls. But the child classes A and controls were statistically insignificant. An interesting fact was observed in R.I that all the categories of Child

class were statistically significant and were differing to each other. Here, the Child class C possessed the highest mean Resistivity Index and the least was observed in controls. In this Resistivity Index of cortical renal artery, the Child classes A and Controls were also differing significantly.

Figure 4- Cortical Renal Artery Doppler

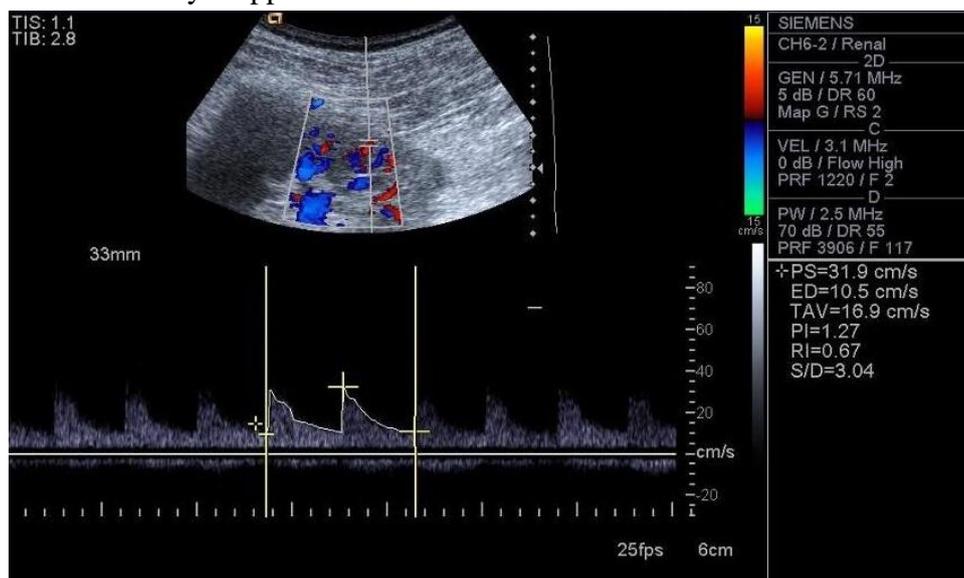


Table 5- Comparison of All Data in Male and Female

SEX		AGE	MRA PI	MRA CI	SRA PI	SRA RI	CRA PI	CRA RI
Male	Mean	46.51	1.2011	.6707	1.1102	.6289	1.0225	.5838
	N	55	55	55	55	55	55	55
	Std. Deviation	9.682	0.19133	0.06914	0.18740	0.06882	0.17308	0.07465
	Minimum	24	0.91	0.52	0.80	0.50	0.71	0.45
	Maximum	65	1.68	0.80	1.59	0.76	1.33	0.72
	Range	41	0.77	0.28	0.79	0.26	0.62	0.27
Female	Mean	38.30	1.0830	0.6280	1.0220	0.5760	0.8670	0.5120
	N	10	10	10	10	10	10	10
	Std. Deviation	10.955	0.04620	0.02440	0.04315	0.02591	0.07258	0.03225
	Minimum	18	1.00	0.60	0.94	0.54	0.76	0.46
	Maximum	50	1.14	0.66	1.07	0.62	0.96	0.57
	Range	32	0.14	0.06	0.13	0.08	0.20	0.11

Table 5 depicts the summary information of all the parameters with respect to sex. The results show that in all the Pulsatility Index and Resistivity Index of main renal artery, segmental renal artery

and cortical renal artery, the means were at higher level when compared to females. The mean age of males (46.51) was also greater than females (38.3).

Table 6- Child Class Correlation with Serum Urea and creatinine

Parameters	Child Class	Mean	Std. Deviation	F-value (p-value)
Serum Urea	A	23.391	5.655	2.401 (0.102 ^{NS})
	B	23.111	7.201	
	C	27.611	7.555	
Serum Creatinine	A	0.735	0.170	2.838 (0.069 ^{NS})
	B	0.667	0.132	
	C	0.828	0.199	

From above table it is clear that there is no significant correlation between Child’s class and elevation of both serum urea and creatinine values.

Discussion

This prospective cross-sectional study was performed in Department of Radiodiagnosis, Department of Radiodiagnosis, Andhra Medical College, Visakhapatnam, from March 2017 to

December 2018. This study was carried out on 50 patients of liver cirrhosis divided into three groups on the basis of Child-Pugh classification and 15 healthy controls. There were 10 from female and 55 male in present study. The age of the patients ranged from 18 to maximum of 65 years. There were 23 patients belonging to Child's class 'A', 9 to class 'B' and 18 to class 'C'. Present study was done to observe changes in renal hemodynamics in main, segmental and cortical renal arteries in terms of elevated Pulsatility and Resistivity indices in different stages of liver cirrhosis. Early identification of these changes will be helpful to identify the nonazotemic patients who are at risk developing renal dysfunction and hepatorenal syndrome and may be beneficial in directing or modifying their the clinical management.

Hepatorenal syndrome is well recognized complication of liver cirrhosis that often develop acutely in previously nonazotemic patients. Earliest stage of apparently functional form of hepatorenal syndrome often do unrecognized because Creatinine elevation is late feature⁶. Hepatorenal syndrome related mortality in advanced cirrhosis is very high. Early identification of prognostic predictors remains to be topic of debate. Presently Child Pugh classification of liver cirrhosis severity is most commonly used by clinicians for classification of patients, but it has certain limitations such as subjective nature of ascites and proportionate correlation with prediction of mortality and prognosis for hepatorenal syndrome⁷.

Clinical manifestations and laboratory abnormality in terms of elevated urea and Creatinine are associated with very poor outcome and therefore limiting effective therapeutic outcome⁸. Liver Doppler parameters such as peak systolic velocity, Resistivity and Pulsatility index of hepatic artery were not correlating with Child classification system probably due to buffer role of hepatic artery with advanced liver cirrhosis and pseudonormalisation of Doppler parameters⁹.

Doppler renal arterial parameters such as Resistivity and Pulsatility index measurement not

only indicate abnormal renovascular hemodynamic derangement in liver cirrhosis but can give information about early markers of cortical ischemia secondary to intrinsic renal vasoconstriction in patients with normal serum urea and creatinine¹⁰.

The results obtained in present study are in good agreement with the results from literature. Elevated Pulsatility and Resistivity index values are more commonly found in patients with advanced clinical stage of liver cirrhosis, but can be present in Child A and B stage also as shown by various previous studies. Platt and coworkers performed a long term follow up of 180 patients of liver cirrhosis without azotemia showing that initial elevated intrarenal Resistivity and Pulsatility index correlate with future development of renal dysfunction and hepatorenal dysfunction on their clinical follow up. They found that within 76 patients of elevated intrarenal Resistivity index more than 0.7, 55% of patients developed renal dysfunction and 26% of patients developed hepatorenal syndrome whereas only 6% of patients with normal Resistivity index developed renal dysfunction¹¹.

Our study result showed that elevated values of Pulsatility and Resistivity index in both Child group B and C in main and segmental renal artery compared to class A and controls. Cortical artery is showing elevated Pulsatility and Resistivity index in class A, B and C compared to controls. We didn't follow up the patients to monitor changes of renal dysfunction or hepatorenal syndrome.

Yaseer M Fraud and co-investigators showed in their study that Pulsatility and Resistivity index values were higher for main, segmental and cortical arteries in all Child's A, B and C compared to controls. Furthermore they observed elevated values were highest in class C suggesting severity of ascites correlate with renovascular impedance¹². Our study showed similar results, but elevated pulsatility and Resistivity index in Child's class A were observed only in cortical artery compared to controls. We didn't find

statistically significant difference in main and segmental renal artery Pulsatility and Resistivity index values in Child A compared to controls. This finding has not been described in available literature.

Our results are further supported by Maroto et al who demonstrated elevation of Resistivity index was significantly higher in decompensatory stage with refractory ascites than responsive ascites and compensatory stage¹³. Koda and their coworkers also showed that both Pulsatility and Resistivity index elevation were significantly higher in cirrhosis than controls and correlated with severity of cirrhosis assessed by Child-Pugh scoring system¹⁴.

Rivolta et al observed in their clinical study of 57 cirrhosis patients, elevated Resistivity index correlate with severity of cirrhosis and ascites. They observed that elevated Resistivity index of cortical arteries only in Child group C patients with normal values in group A and B compared to controls¹⁵. On the basis of this observation, they suggested that cortical ischemia is feature of decompensated stage with refractory ascites. In our study we observed elevation of these values in cortical arteries of all the groups compared to controls, highest elevation in group C patients compared to A and B. This is in contradiction to above observation of cortical ischemia.

Y Wang et al showed that elevated intrarenal Resistive index correlated with stage of liver cirrhosis. Their study also showed the gradient of arterial Resistivity index across main, segmental and cortical renal artery was retained in patients even at decompensatory stage with non-refractory ascites but loss of this gradient in patients of refractory ascites. So, they suggested loss of this gradient can be important and characteristic prognostic factor in development of hepatorenal syndrome¹⁶. In our study we didn't find this observation as this gradient was retained even in patients of refractory ascites.

In our study these elevated parameters Pulsatility and Resistivity index were also showed correlation with presence of esophageal varices on

upper gastrointestinal endoscopy examination. This fact was observed in Popov et al in their study 4. Colli et al in their study of 50 liver cirrhosis of Child's class A found that presence of esophageal varices correlate significantly in patients of elevated resistivity index of intrarenal artery. They suggested pathophysiological correlation between development of portal hypertension and renovascular impedance in non-ascites cirrhosis patients¹⁷. Our study didn't show presence of esophageal varices on endoscopy on any of the Child's class A patients. This may be attributed to absence of significantly elevated main and segmental renal artery Pulsatility and Resistivity index in Child group A patients compared to our healthy controls.

In our study we didn't observe significant correlation between any trend of serum urea and Creatinine values with changing intrarenal resistance parameters in various stages of Child's classification of liver cirrhosis.

In this study, patients with diabetes mellitus or hypertension were excluded because of impact of these diseases on renal hemodynamics and leading to altered parameters^{18,19}.

The following are the limitations of the present study:

- 1) No clinical follow up of the patients studied
- 2) Child's criteria was taken as sole criteria for the assessment of liver cirrhosis, which is not a perfect system due to subjective evaluation of ascites and encephalopathy⁹.
- 3) Interobserver variability of Doppler examination, which was minimized by standard protocol of renal Doppler examination.
- 4) Few other clinical conditions such as kidney obstruction, acute tubular necrosis, renal vein thrombosis and hemolytic uremic syndrome can affect renal resistive indices⁶. This was minimized by available clinical, laboratory and imaging data of the patients.

Conclusion

This prospective cross-sectional study was conducted in the Department of Radiodiagnosis, Andhra Medical College, Visakhapatnam. The study period was between the March 2017 to December 2018. A total of 15 controls and 50 patients of the liver cirrhosis were recruited in study based on clinical, laboratory and imaging findings, after obtaining written informed consent. The present study was done to evaluate the role of duplex ultrasound in detecting early renal hemodynamic changes seen in the liver cirrhosis patients. Pulsatility and Resistivity index were taken as parameters to assess renovascular impedance.

All 50 patients of the liver cirrhosis with normal renal profile were divided into three groups according to Child-Pugh staging system. These patients and fifteen controls underwent both grey scale and duplex ultrasound examination of renal arteries to determine Pulsatility and Resistivity indices in main, segmental and cortical renal arteries. All continuous variables were presented with its summary statistics (mean, standard deviation, range) for both patients and controls. The entire statistical analysis has been conducted with IBM SPSS 19.0 version.

The result of our study showed that changes in Pulsatility and Resistivity index evaluated using renal arterial duplex ultrasound shows good correlation with severity of the ascites and disease status assessed by Child-Pugh staging system. We found good correlation between increased renovascular impedance and presence of esophageal varices. The patients with normal renal profile and abnormal results of renal arterial duplex study can be identified before the development of clinical renal dysfunction and hepatorenal syndrome.

From our study we concluded that renal duplex ultrasound is safe and effective screening modality in liver cirrhosis patients to detect the patients who are at risk of developing renal dysfunction and hepatorenal syndrome which contribute to increased morbidity and mortality. Also, renal

duplex ultrasound can be used in order to apply therapeutic interventions in these patients to reduce morbidity and mortality. Further studies are necessary to investigate the role of renal duplex ultrasound in monitoring these therapeutic interventions in liver cirrhosis patients.

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