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Novel predictors of response to therapy with terlipressin and albumin in hepatorenal syndrome–acute kidney injury

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Abstract

Background A combination of terlipressin and albumin is the first-line pharmacologic treatment for hepatorenal syndrome–acute kidney injury (HRS-AKI). We assessed the response rates to terlipressin–albumin therapy in patients with HRS-AKI and determined early predictors of treatment response and survival.

Methods A total of 84 patients with HRS-AKI (International Club of Ascites definition 2015) treated with terlipressin–albumin were included. Predictors of HRS reversal were identified by logistic regression analysis. Survival analysis was performed using the Kaplan-Meier method, and Cox regression models were used to determine independent predictors of mortality.

Results Complete response to therapy was observed in 54.8%, partial response in 14.3%, and no response in 31% of patients. The factors associated with complete treatment response were the presence of systemic inflammatory response syndrome (SIRS), baseline serum creatinine, a rise in mean arterial pressure by day 3, and a reduction in the renal resistive index (ΔRRI) by day 3 of treatment. Independent predictors of HRS reversal were the presence of SIRS at baseline (P=0.022; odds ratio [OR] 15.74, 95% confidence interval [CI] 1.47-167.82) and ΔRRI ≥5% by day 3 of treatment (P=0.048; OR 6.67, 95%CI 1.021-43.62). Mean transplant-free survival at 6 months was significantly better in treatment responders (148 vs. 90 days, P<0.001). Independent predictors of 6-month mortality were response to treatment (P=0.004) and model for end-stage liver disease–sodium >23 (P=0.018).

Conclusions SIRS and ΔRRI are simple parameters to predict treatment response in HRS-AKI. Non-responders have higher mortality and should be identified early to expedite liver transplantation.

Keywords Acute kidney injury, hepatorenal syndrome, terlipressin, systemic inflammatory response syndrome, renal resistive index

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Introduction

Hepatorenal syndrome (HRS) is defined as renal failure developing in patients with advanced cirrhosis of the liver, in the absence of significant structural abnormalities in the kidneys, due to vasoconstriction of the renal circulation [1]. There are 2 types of HRS [2]: (i) HRS with acute kidney injury (AKI; earlier called Type 1 HRS), characterized by a rapidly progressive impairment in renal function, associated with high mortality but with a potential for reversibility. The most common precipitants for HRS-AKI are bacterial infections [3], followed by drugs, gastrointestinal bleeding and severe alcoholic hepatitis; and (ii) HRS-non-AKI (earlier called Type 2 HRS), characterized by a moderate renal impairment with a progressive course that steadily evolves over weeks to months. HRS-non-AKI is further subclassified as HRS-acute kidney disease (renal dysfunction lasting for less than 3 months but not meeting the AKI criteria) and HRS-chronic kidney disease

(estimated glomerular filtration rate <60 mL/min/1.73 m^2 for >3 months).

The pathogenesis of HRS involves marked splanchnic vasodilatation due to portal hypertension and activation of systemic vasoconstrictors, both of which result in a significant reduction in the effective circulating blood volume and lead to marked impairment of renal blood flow [4].

Untreated HRS-AKI has an extremely dismal prognosis, with a median survival of weeks to months [5]. The transplant-free survival can, however, be improved by the identification and removal of the precipitating factor of AKI and appropriate pharmacologic treatment. Various studies have shown that the best available pharmacologic therapy for HRS is a combination of intravenous terlipressin (splanchnic vasoconstrictor) and intravenous albumin [6,7]. Terlipressin counteracts the splanchnic arterial vasodilatation, while albumin is a volume expander that further improves effective circulating volume and cardiac contractility. The safety and efficacy of terlipressin in patients with HRS-AKI have previously been evaluated in randomized trials, with response rates varying from 40-60% [8-10]. A meta-analysis of clinical trials [11] found that the pooled rate of patients with a complete response to terlipressin and albumin was 52%. In view of the modest rates of response to pharmacologic therapy, it is crucial to identify those patients with a low likelihood of treatment response early in the course, so that they can be offered other modalities of treatment, and workup for liver transplantation can be expedited.

The majority of studies assessing the response rates to vasoconstrictor therapy were performed in patients in whom Type 1 HRS was defined according to the old International Club of Ascites (ICA) criteria [1]. However, the definition of AKI in cirrhosis was recently modified [12] to align with Kidney Disease: Improving Global Outcomes (KDIGO) criteria [13]. Very few studies have evaluated the impact of the new AKI definition on treatment response rates. This study aimed to assess response rates to terlipressin based on the new definition of HRS-AKI and to identify novel predictive factors of improved renal function and survival.

Patients and methods

Patients

This prospective single-center study was carried out at a University Hospital in Kerala, South India, from October 2020 to December 2021. All patients diagnosed with HRS-AKI (based on ICA criteria) [12] and treated with terlipressin and albumin were included. Patients who developed an intolerance to terlipressin or were treated with other vasoconstrictors during the episode of HRS-AKI were excluded. The demographic, clinical, and laboratory variables obtained at baseline, and their changes during treatment, were analyzed as predictors of HRS reversal. All patients were then followed up for 6 months for the development of other complications, to check the need for renal replacement therapy (RRT), and to assess predictors of mortality.

Procedure

Terlipressin was administered at a starting dose of 2 mg/day as a continuous intravenous infusion. The dose of terlipressin was modified depending on the response to treatment. The same dose was continued if the serum creatinine was reduced by at least 25% after 48 h. In patients whose serum creatinine did not decrease by at least 25% within the first 3 days, or whose serum creatinine increased above pre-treatment values, the dose was gradually increased in increments of 2 mg every 48 h upto a maximum of 12 mg/day as an infusion. Terlipressin was given until serum creatinine decreased to a final value within 0.3 mg of the patient's baseline serum creatinine, or for a maximum of 14 days. Terlipressin administration was withheld if patients developed an intolerance to terlipressin or symptoms/electrocardiographic changes compatible with ischemic complications. Albumin was given at a dose of 40 g/day for the first 24 h, followed by 20-40 g/day. Clinical, hemodynamic, and renal parameters were monitored throughout the duration of treatment.

Renal vasoconstriction was assessed using Doppler ultrasound of the renal arteries by measuring the renal resistive index (RRI). Patients were made to lie in the supine, right and left lateral positions. Arcuate arteries (at the corticomedullary junction) and interlobar arteries (adjacent to medullary pyramids) were identified. Doppler evaluation of the renal arteries was performed by 2 independent examiners, using a 3.5 MHz convex transducer. RRI was determined using the formula (Peak systolic flow - Peak diastolic flow)/Peak systolic flow. Three to 5 waveforms were obtained from each kidney, and RRIs from these waveforms were averaged to obtain the mean RRI value for each kidney [14-16]. RRI was monitored throughout the duration of treatment at specified intervals.

Outcome definitions

Complete response was defined as a reduction in serum creatinine to a final value within 0.3 mg/dL of the patient's baseline level [12]. Partial response was defined as a regression of the AKI stage, but to a final serum creatinine >0.3 mg/dL from the baseline value. Non-responders were those with a rise in creatinine or a less than 25% decline in baseline creatinine, with a maximum possible dose of terlipressin over a maximum treatment duration of 14 days. systemic inflammatory response syndrome (SIRS) was defined as the presence of 2 of the following criteria: fever >38.0°C or hypothermia <36.0°C, tachycardia >90 beats/min, tachypnea >20 breaths/min, leukocytosis $>12\times10^9$/L, or leukopenia $<4\times10^9$/L [17,18]. The model for end-stage liver disease sodium score (MELD-Na) is a scoring system for assessing the severity of chronic liver disease and predicting survival, calculated usind serum bilirubin, serum creatinine, the international normalized ratio for prothrombin time and serum sodium values.

Statistical analysis

Quantitative data were expressed using mean (with standard deviation), median (with interquartile range), and categorical data as proportions and percentages. Comparisons of variables between study groups were made using the Student's *t*-test for normally distributed data, the Mann-Whitney *U* test for non-parametric data, and the chi-squared test for analysis of categorical variables. A multivariate analysis, including variables with predictive value in the univariate analysis, was performed using stepwise logistic regression to determine the variables with independent predictive value. The best cutoffs for prediction were obtained from analysis of receiver operating characteristic (ROC) curves and Youden's index. Survival analysis was performed using the Kaplan-Meier method, using a log-rank test to compare the groups. Cox regression models were used to assess the association of clinical characteristics with overall survival, and P values <0.05 were considered statistically significant.

Results

During the study period, we identified 90 patients diagnosed with HRS-AKI and started on treatment with terlipressin and albumin. Six were excluded as they had adverse responses to terlipressin requiring discontinuation of therapy.

Baseline characteristics

Patients had a mean age of 56.37±6.96 years. The etiology of cirrhosis was alcohol in 62% (n=52), followed by nonalcoholic steatohepatitis in 34.5% (n=29) and hepatitis B in 3.5% (n=3). The severity of cirrhosis, as defined by the Child-Pugh score, was Class B in 21.5% (*n*=18) and Class C in 78.5% (*n*=66). The most frequent precipitant of HRS-AKI was infections in 49% (n=41), of which 25% (n=21) had spontaneous bacterial peritonitis, while other infections (cellulitis, urinary tract infection, pneumonia, gastroenteritis, osteomyelitis) accounted for 24% (n=20). Drugs as a precipitating factor were identified in 44% of cases (n=31). The frequent culprit drugs identified were diuretics, β-blockers, nonsteroidal anti-inflammatory drugs, and alternative medicines. At baseline, 29% (n=24) had stage 1 AKI, 38% (n=32) were in stage 2 AKI, and 33% (n=28) had stage 3 AKI.

Response to treatment

Complete response of HRS-AKI to terlipressin/albumin was seen in 54.8% (n=46); 14.2% (n=12) had a partial response, while 31% of patients (n=26) had no response to treatment. Among complete responders, the mean time to achieve a complete response was 4.6±2.4 days, and the mean daily dose of terlipressin required was 3.3±1.51 mg.

Effects of terlipressin on systemic and renal hemodynamics

Terlipressin and albumin showed beneficial effects on systemic and renal hemodynamics in treatment responders. Complete responders showed improvement in systemic and renal hemodynamics by day 3 of treatment, with significant increases in both mean arterial pressure (P<0.001) and glomerular filtration rate (P<0.001), whereas RRI decreased significantly (P<0.001).

Predictors of treatment response

The clinical and demographic variables of patients with a complete response to treatment were compared with non-responders to identify predictors of successful treatment (Table 1). The factors associated with complete treatment response to treatment on univariate analysis were the presence of SIRS at baseline, serum creatinine, rise in mean arterial pressure by day 3 of treatment, stage of AKI, and a reduction in the renal resistive index (ΔRRI) by day 3 of treatment (P<0.001 for all). Forty-five patients had features of SIRS (≥2 SIRS components) at baseline, and in 76% of these patients (n=34) there was a complete response to treatment. In patients without SIRS, HRS reversal was seen only in 31% (12/39). Among the various stages of AKI (as defined by KDIGO), the rates of complete response to treatment were 91.3% (21/23), 71.4% (20/28), and 23.8% (5/21) for AKI stages 1, 2 and 3, respectively.

According to the multivariate analysis, the independent predictors of treatment response were the presence of SIRS at baseline (P=0.022; odds ratio [OR] 15.749, 95% confidence interval [CI] 1.478-167.82) and ΔRRI by day 3 (P=0.048; OR 6.67, 95%CI 1.021-43.625) (Table 2). The cutoff level for ΔRRI that best predicted response to treatment was ≥5% by day 3 (area under the curve, 0.803; P<0.001; sensitivity 83%; specificity 69%). Fig. 1 shows the ROC curve for the correlation of ΔRRI with treatment response. In those with ΔRRI ≥5% by day 3, there was a complete response to treatment in 85.4% (41/48), while in those with a ΔRRI <5% by day 3, only 20.8% (5/24) showed a complete treatment response.

Survival

Mortality was higher in non-responders compared to responders at 1 month (27% vs. 9%) and 6 months (73% vs. 45%). Response to treatment was significantly associated with transplant-free survival at 6 months (log-rank P<0.001) (Fig. 2). Mean transplant-free survival was significantly longer in the complete responders than in non-responders (148 days vs. 90 days). Response to terlipressin treatment was an independent predictor of transplant-free survival at 6 months (hazard ratio [HR] 0.527, 95%CI 0.342-0.810; P=0.004, while a higher MELD-sodium score was independently associated with 6-month mortality (HR 1.071, 95%CI 1.012-1.135; P=0.018) (Table 3). The cutoff level of MELD-sodium that best

Table 1 Comparison of sociodemographic and clinical characteristics of complete responders and non-responders

Characteristics	Non-responders (n=26)	Complete responders (n=46)	P-value
Age (years)	58.88±7.75	54.96±6.61	0.056
Sex (M/F)	23/3	43/3	0.457
Etiology (n, %)			
Alcohol	13 (50%)	32 (69.6%)	0.087
NASH	13 (50%)	12 (26.1%)	
HBV	0 (0%)	2 (4.3%)	
Precipitating factor (n, %)			0.632
SBP	6 (23.1%)	14 (30.4%)	
Other bacterial Infections	8 (30.8%)	9 (19.6%)	
Drugs	14 (53.8%)	16 (34.8%)	
Alcoholic hepatitis	1 (3.8%)	2 (4.3%)	
Child-Pugh score	10.73±1.61	11.04±1.48	0.406
MELD-Na score	27.62±6.59	26.98±5.36	0.657
KDIGO stage of AKI			
Stage 1 AKI	2 (7.7%)	21 (45.7%)	<0.001
Stage 2 AKI	8 (30.8%)	20 (43.5%)	
Stage 3 AKI	16 (61.5%)	5 (10.9%)	
Corrected BMI	21.78±1.99	22.82±2.49	0.073
Sarcopenia (Y/N)	24/2	34/12	0.058
SIRS (Y/N)	8/18	34/12	<0.001
Hemoglobin (g/dL)	10.47±1.91	11.19±2.03	0.141
WBC count ($\times 10^9$/L)	6.34±5.18	9.05±5.59	0.088
Platelets ($\times 10^9$/L)	69.03±36.76	77.86±46.68	0.410
ESR (mm/h)	29.77±33.31	44.85±34.20	0.074
Bilirubin (mg/dL)	3.50±4.60	5.16±5.00	0.169
SGOT (IU/L)	55.77±32.10	63.35±35.03	0.367
SGPT (IU/L)	36.62±31.47	34.39±23.19	0.733
Serum albumin (g/dL)	2.53±0.54	2.66±0.51	0.302
Urea (mg/dL)	83.35±42.53	81.22±32.45	0.812
Serum creatinine (mg/dL)	3.38±1.08	2.24±0.83	<0.001
Sodium (mEq/L)	131.92±6.03	129.78±6.19	0.160
Potassium (mEq/L)	4.40±0.74	4.44±0.71	0.835
Ascitic fluid protein (g/dL)	1.31±0.55	1.15±0.49	0.224
SAAG (g/dL)	2.08±0.54	1.94±0.42	0.238
Liver stiffness by 2D-SWE (kPa)	38.42±11.90	38.69±11.25	0.926
Renal resistive index	0.78±0.04	0.77±0.02	0.146
Change in MAP (day 3)	-1.50±9.40	10.43±4.48	<0.001
Change in creatinine (day 3)	0.65±0.85	0.43±0.33	0.115
ΔRRI (day 3) (%)	2.90±2.33	8.11±3.90	<0.001

M, male; F, female; NASH, nonalcoholic steatohepatitis; HBV, hepatitis B virus; SBP, spontaneous bacterial peritonitis; MELD-Na, model for end-stage liver disease-sodium score; KDIGO, Kidney Disease: Improving Global Outcomes; AKI, acute kidney injury; BMI, body mass index; SIRS, systemic inflammatory response syndrome; WBC, white blood cells; ESR, erythrocyte sedimentation rate; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamate-pyruvate transaminase; SAAG, serum-ascites albumin gradient; 2D-SWE, 2-dimensional shear wave elastography; MAP, mean arterial pressure; ΔRRI, change in the renal resistive index

Table 2 Binary logistic regression analysis to determine variables with independent predictive value for treatment response

Variables	P-value	OR	95%CI
SIRS day 1	0.022	15.749	1.478-167.824
Rise in MAP	0.093	4.971	0.766-32.270
Baseline serum creatinine	0.257	0.899	0.155-5.228
ΔRRI	0.048	6.673	1.021-43.625
AKI stage	0.388	2.556	0.303-21.553

SIRS, systemic inflammatory response syndrome; MELD, model for end-stage liver disease; MAP, mean arterial pressure; ΔRRI, change in the renal resistive index; AKI, acute kidney injury; OR, odds ratio; CI, confidence interval

Table 3 Cox proportional hazards regression analysis and independent predictors of 6-month mortality in HRS-AKI

Predictors	P-value	HR	95%CI
Hepatic encephalopathy	0.208	1.500	0.798-2.820
MELD-Na score	0.018	1.071	1.012-1.135
Serum creatinine	0.507	0.847	0.519-1.383
SIRS day 3	0.326	1.589	0.631-4.003
AKI stage	0.844	1.061	0.589-1.912
Response to treatment	0.004	0.527	0.342-0.810

SIRS, systemic inflammatory response syndrome; MELD-Na, model for end-stage liver disease-sodium score; HRS, hepatorenal syndrome; AKI, acute kidney injury; HR, hazard ratio; CI, confidence interval

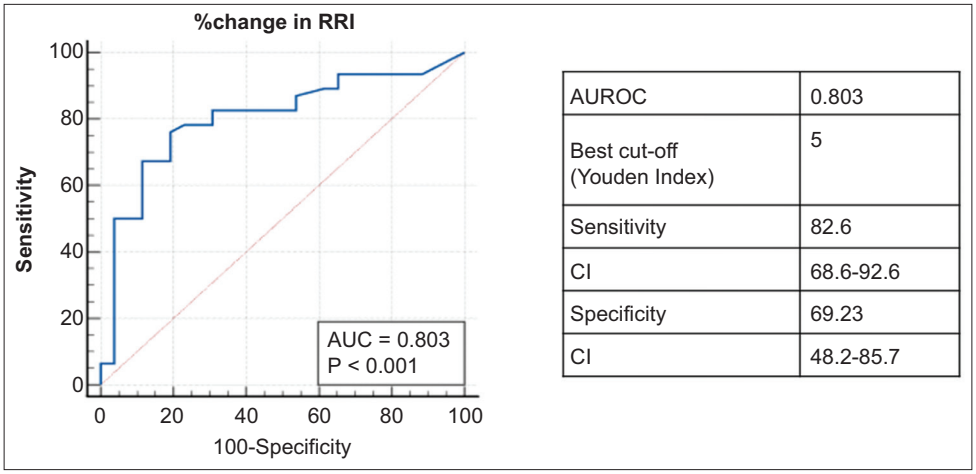
predicted 6-month mortality was ≥23 (area under the curve, 0.664; P=0.019; sensitivity, 84%; specificity, 43%).

Discussion

HRS is one of the most challenging complications of advanced liver disease and is associated with extremely high mortality. Successful treatment of HRS-AKI with pharmacologic therapy has the potential to improve short-term transplant-free survival and reduce the need for RRT. A combination of terlipressin and albumin is the first-line pharmacologic therapy to counteract splanchnic arterial vasodilation and improve renal perfusion in HRS-AKI.

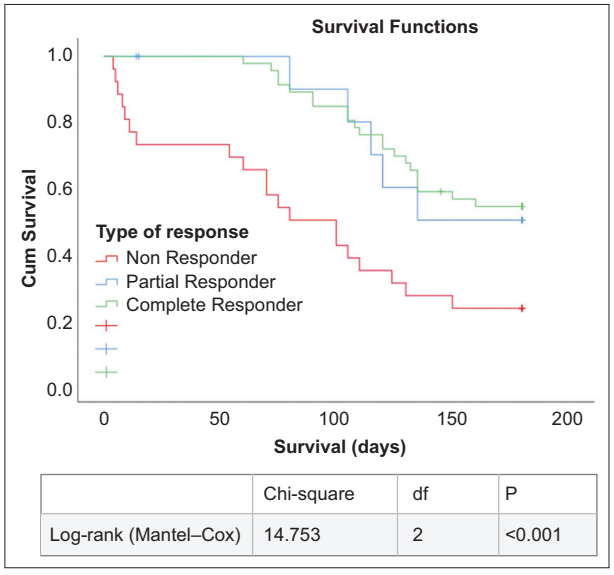
Various studies have evaluated the efficacy of pharmacologic therapy in HRS-AKI. However, most studies involved patients in whom type 1 HRS was defined according to the old ICA criteria [1]. This study used the new AKI definition to define response status and compared it with existing studies to assess whether the change in the definition of AKI in cirrhosis has an impact on the response rates to therapy.

Among the 84 patients with HRS-AKI included in this study, a response to treatment was observed in 69.1% (complete response in 54.8% and partial response in 14.3%.). The overall response rates were better with the new definition of HRS compared to existing studies, where response rates varied between 40-60% [8-10]. However, the rate of complete response to treatment observed in this study (54.8%) was



AUROC	0.803
Best cut-off (Youden Index)	5
Sensitivity	82.6
CI	68.6-92.6
Specificity	69.23
CI	48.2-85.7

Figure 1 Correlation of ΔRRI with treatment response (AUROC 0.803)
ΔRRI, change in the renal resistive index; CI, confidence interval; AUROC, area under the receiver operating characteristic curve



	Chi-square	df	P
Log-rank (Mantel–Cox)	14.753	2	<0.001

Figure 2 Kaplan-Meier survival analysis of the patient cohort
df, degrees of freedom

similar to that observed in previous studies [10,11,19,20]. Despite being the first-line pharmacologic treatment of HRS, it was observed that less than 60% of patients have a complete response to therapy with terlipressin. Therefore, it is crucial to identify non-responders early so they can be fast-tracked for liver transplantation. We compared the clinical and sociodemographic variables between complete responders and non-responders to identify predictors of successful treatment of HRS.

In this study, the factors associated with a complete response to treatment on univariate analysis were serum creatinine, the presence of SIRS on day 1, a rise in mean arterial pressure by day 3, the stage of AKI, and a reduction in RRI by day 3. Pre-treatment serum creatinine and a rise in mean arterial pressure as predictors of HRS reversal were also noted in various studies [21-23]. Other predictive factors of treatment response reported in previous studies [8,20,24-26] included age, alcohol etiology of cirrhosis, leucocyte count, serum bilirubin, serum albumin, Child-Pugh and MELD scores. However, these were not found to be statistically significant in our study. The independent predictors of treatment response on multivariate analysis were the presence of SIRS on day 1 and a reduction in the RRI (ΔRRI) ≥5% by day 3.

The fact that the presence of SIRS improved the renal response to terlipressin in patients with HRS-AKI is an interesting observation. Even in the absence of a clinically apparent infection, SIRS occurs frequently in patients with decompensated cirrhosis because of an increase in gut bacterial translocation, leading to a persistent inflammatory state that can be exacerbated during acute decompensations [27-29]. Terlipressin, by reducing the portal pressure, may lead to decreased gut bacterial translocation, which in turn reduces endotoxemia and the production of proinflammatory cytokines [30,31]. Terlipressin is also thought to have a direct anti-inflammatory action, independent of its effect in reducing portal hypertension [32]. Thus, in the presence of SIRS there is an exaggerated response to terlipressin, which leads to an enhanced renal response and resolution of HRS-AKI. Therefore, in patients with HRS-AKI, the presence of SIRS helps to identify a subset of patients that may not respond to volume expansion with albumin alone and could have a better response to terlipressin. In our study, the presence of SIRS on day 1 was found to have an independent predictive value for complete treatment response in cirrhosis patients with HRS-AKI. Very few studies have evaluated the impact of SIRS as a determinant of treatment response to terlipressin in HRS-AKI. Wong *et al* noted that HRS reversal with terlipressin was observed in 42.9% of subjects with SIRS, as compared to 24.6% in patients without SIRS [33].

The major pathophysiology of HRS is splanchnic arterial vasodilatation, leading to pooling of blood in the splanchnic vascular bed with associated renal artery vasoconstriction and hypoperfusion of the kidneys. This intrarenal arterial vasoconstriction causes an increase in the resistive index of

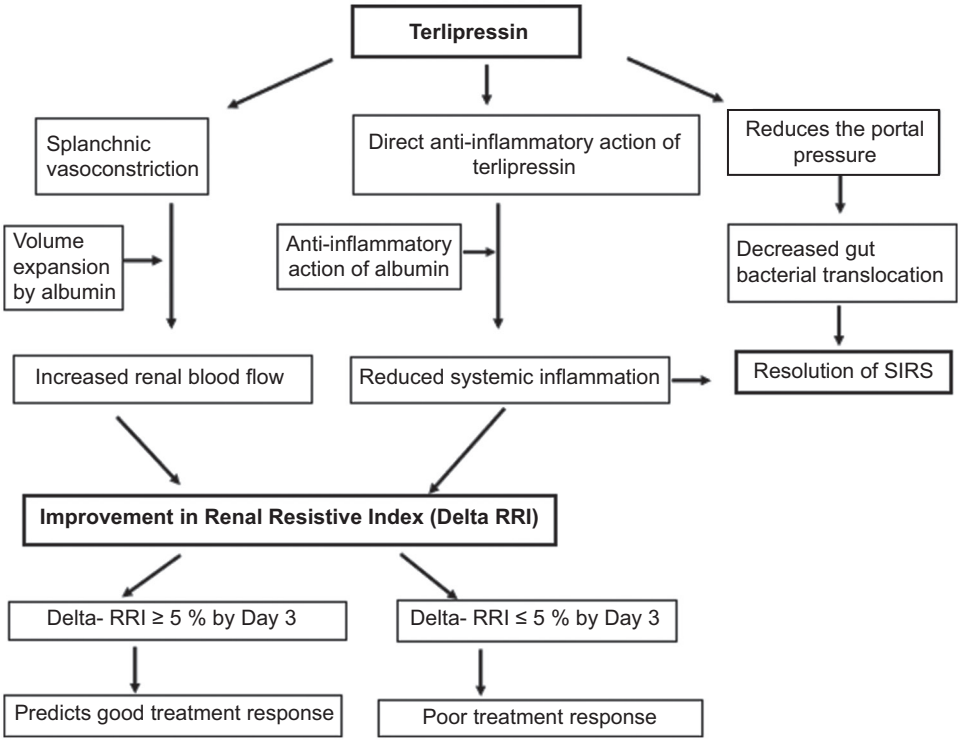


Figure 3 The postulated relationship between Renal Resistive Index, SIRS and the renal response to terlipressin in HRS-AKI
HRS, hepatorenal syndrome; AKI, acute kidney injury; ΔRRI, change in the renal resistive index; SIRS, systemic inflammatory response syndrome

the renal arterial system, which can be assessed by Doppler ultrasound [14-16]. Terlipressin causes selective vasoconstriction of splanchnic arterial vessels, which tends to reverse alterations in renal hemodynamics. RRI is a useful index for quantifying renovascular resistance in cirrhotic patients before HRS develops [34], but its utility in predicting treatment response in HRS has not been evaluated. We made serial measurements of RRI in patients with HRS-AKI who were started on terlipressin. The baseline RRI did not differ significantly between responders and non-responders. However, a change in RRI in the interlobar artery of ≥5% by day 3 of treatment predicted a complete treatment response. This was a novel finding in our study, and it will require validation in larger multicenter studies to assess its reproducibility across different settings (Fig. 3).

The results of the current study confirm data from previous reports indicating that patients with type 1 HRS who respond to treatment with terlipressin and albumin have longer survival compared with non-responders Both the long-term and short-term mortality were significantly higher in non-responders as compared to responders at 1 month (27% vs. 9%) and 6 months (74% vs. 45%). The mean transplant-free survival at 6 months was significantly longer in the responder group compared with non-responders to terlipressin therapy (148 vs. 90 days). Non-response to pharmacologic treatment and model for end-stage liver disease-sodium score ≥23 were found to be independent predictors of 6-month mortality in HRS-AKI. This highlights the fact that non-responders should be identified early and fast-tracked for liver transplantation.

The independent predictors of transplant-free survival at 6 months by Cox regression analysis were a response to treatment and MELD-sodium, which is consistent with the findings of Nguyen-Tat *et al* [9] and Heidemann *et al* [10].

Our study had certain limitations. The study was conducted on subjects from a single center, and the duration of follow up was 6 months. In the future, multi-center studies will be needed with larger sample sizes and a longer duration of follow up to assess long-term survival. Another limitation of our study is that in the absence of a placebo group, we cannot causally attribute survival advantage to the terlipressin response alone.

In conclusion, the rates of response to terlipressin and albumin in HRS-AKI are limited, even though this is the first-line pharmacologic therapy. Response to treatment is an independent predictor of transplant-free survival at 6 months. Non-responders have higher mortality and should be identified early to expedite liver transplantation. SIRS and ΔRRI are simple parameters to predict treatment response in HRS-AKI. In HRS-AKI, the RRI is a measure of the intrarenal vasoconstriction, and SIRS reflects exaggerated systemic inflammation, both of which are reversed by terlipressin, leading to an enhanced treatment response.

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Summary Box

What is already known:

- Hepatorenal syndrome (HRS) is one of the most challenging complications of advanced liver disease and is associated with extremely high mortality
- Successful treatment of HRS-acute kidney injury (AKI) with pharmacologic therapy has the potential to improve short-term transplant-free survival and reduce the need for renal replacement therapy
- A combination of terlipressin and albumin is the first-line pharmacologic treatment for HRS-AKI, but the treatment response rates vary between 40% and 60%

What the new findings are:

- Systemic inflammatory response syndrome (SIRS) at baseline and the change in the renal resistive index at day 3 are simple parameters that predict treatment response in HRS-AKI
- In HRS-AKI, the renal resistive index is a measure of the intrarenal vasoconstriction and SIRS reflects the exaggerated systemic inflammation, both of which are reversed by terlipressin, leading to an enhanced treatment response
- Non-response to pharmacologic treatment and model for end-stage liver disease-sodium are independent predictors of 6-month mortality in HRS-AKI

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