ISSN 1949-8470 (online)

World Journal of *Radiology*

World J Radiol 2024 June 28; 16(6): 139-240

Published by Baishideng Publishing Group Inc

World Journal of Radiology

Contents

Monthly Volume 16 Number 6 June 28, 2024

REVIEW

MINIREVIEWS

ORIGINAL ARTICLE

Retrospective Study

Observational Study

CASE REPORT

World Journal of Radiology

Monthly Volume 16 Number 6 June 28, 2024

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Radiology*, Xian-Li Lv, MD, Associate Professor, Department of Neurosurgery, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University, Beijing, China. lvxianli000@163.com

AIMS AND SCOPE

The primary aim of *World Journal of Radiology* (*WJR*, *World J Radiol*) is to provide scholars and readers from various fields of radiology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJR mainly publishes articles reporting research results and findings obtained in the field of radiology and covering a wide range of topics including state of the art information on cardiopulmonary imaging, gastrointestinal imaging, genitourinary imaging, musculoskeletal imaging, neuroradiology/head and neck imaging, nuclear medicine and molecular imaging, pediatric imaging, vascular and interventional radiology, and women's imaging.

INDEXING/ABSTRACTING

The *WJR* is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 Edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJR* as 1.4; JIF without journal self cites: 1.4; 5-year JIF: 1.8; JIF Rank: 132/204 in radiology, nuclear medicine and medical imaging; JIF Quartile: Q3; and 5-year JIF Quartile: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Radiology

ISSN
ISSN 1949-8470 (online)

LAUNCH DATE
January 31, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Thomas J Vogl

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1949-8470/editorialboard.htm

PUBLICATION DATE
June 28, 2024

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Radiology

Submit a Manuscript: https://www.f6publishing.com

World J Radiol 2024 June 28; 16(6): 221-231

DOI: 10.4329/wjr.v16.i6.221

ISSN 1949-8470 (online)

ORIGINAL ARTICLE

Observational Study

Renal resistive index measurements by ultrasound in patients with liver cirrhosis: Magnitude and associations with renal dysfunction

Himanshu Surya, Ramesh Kumar, Rajeev Nayan Priyadarshi, Sabbu Surya Prakash, Sudhir Kumar

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B
Novelty: Grade B
Creativity or Innovation: Grade B
Scientific Significance: Grade B

P-Reviewer: Popovic DD, Serbia

Received: March 7, 2024
Revised: May 17, 2024
Accepted: June 3, 2024
Published online: June 28, 2024
Processing time: 110 Days and 17.4 Hours

Himanshu Surya, Ramesh Kumar, Sabbu Surya Prakash, Sudhir Kumar, Department of Gastroenterology, All India Institute of Medical Sciences, Patna 801507, India

Rajeev Nayan Priyadarshi, Department of Radiodiagnosis, All India Institute of Medical Sciences, Patna 801507, India

Corresponding author: Ramesh Kumar, MBBS, MD, Additional Professor, Department of Gastroenterology, All India Institute of Medical Sciences, Phulwari Sharif, Patna 801507, India. docrameshkr@gmail.com

Abstract

BACKGROUND

The hemodynamic alterations seen in liver cirrhosis lead to renal vasoconstriction, ultimately causing acute kidney injury (AKI). The renal resistive index (RRI) is the most common Doppler ultrasound variable for measuring intrarenal vascular resistance.

AIM

To evaluate the association of the RRI with AKI in patients with liver cirrhosis and to identify risk factors for high RRI.

METHODS

This was a prospective observational study, where RRI was measured using Doppler ultrasound in 200 consecutive hospitalized patients with cirrhosis. The association of RRI with AKI was studied. The receiver operating characteristic (ROC) curve analysis was utilized to determine discriminatory cut-offs of RRI for various AKI phenotypes. Multivariate analysis was conducted to determine the predictors of high RRI.

RESULTS

The mean patient age was 49.08 ± 11.68 years, with the majority (79.5%) being male; the predominant etiology of cirrhosis was alcohol (39%). The mean RRI for the study cohort was 0.68 ± 0.09, showing a progressive increase with higher Child-Pugh class of cirrhosis. Overall, AKI was present in 129 (64.5%) patients. The mean RRI was significantly higher in patients with AKI compared to those without it (0.72 ± 0.06 *vs* 0.60 ± 0.08; $P < 0.001$). A total of 82 patients (41%) had hepatorenal syndrome (HRS)-AKI, 29 (22.4%) had prerenal AKI (PRA), and 18 (13.9%) had acute tubular necrosis (ATN)-AKI. The mean RRI was significantly

higher in the ATN-AKI (0.80 ± 0.02) and HRS-AKI (0.73 ± 0.03) groups than in the PRA (0.63 ± 0.07) and non-AKI (0.60 ± 0.07) groups. RRI demonstrated excellent discriminatory ability in distinguishing ATN-AKI from non-ATN-AKI (area under ROC curve: 93.9%). AKI emerged as an independent predictor of high RRI (adjusted odds ratio [OR]: 11.52), and high RRI independently predicted mortality among AKI patients (adjusted OR: 3.18).

CONCLUSION
In cirrhosis patients, RRI exhibited a significant association with AKI, effectively differentiated between AKI phenotypes, and predicted AKI mortality.

Key Words: Renal resistive index; Cirrhosis; Acute kidney injury; Hepatorenal syndrome; Renal Doppler

Core Tip: Renal resistive index (RRI) is the most common Doppler ultrasound variable for measuring intrarenal vascular resistance. Higher RRI indicates renal vascular constriction in patients with advanced cirrhosis due to hemodynamic and neurohormonal alterations. This study evaluated the association of RRI with acute kidney injury (AKI) in patients with liver cirrhosis, assessed the diagnostic accuracy of RRI in distinguishing between different phenotypes of AKI, and identified predictors of high RRI. RRI correlated well with AKI, predicted its occurrence, differentiated between AKI phenotypes, and predicted mortality among AKI patients, and thus may be useful for evaluating renal dysfunction in cirrhosis patients.

Citation: Surya H, Kumar R, Priyadarshi RN, Surya Prakash S, Kumar S. Renal resistive index measurements by ultrasound in patients with liver cirrhosis: Magnitude and associations with renal dysfunction. *World J Radiol* 2024; 16(6): 221-231
URL: https://www.wjgnet.com/1949-8470/full/v16/i6/221.htm
DOI: https://dx.doi.org/10.4329/wjr.v16.i6.221

INTRODUCTION

Acute kidney injury (AKI) is a prevalent complication affecting approximately 30%–50% of hospitalized patients with cirrhosis, correlating with a high mortality rate[1]. The most common AKI phenotypes in cirrhosis patients include prerenal AKI (PRA), acute tubular necrosis (ATN), and hepatorenal syndrome (HRS)[2]. These phenotypes and the stage of AKI play crucial roles in determining outcomes for cirrhosis patients with AKI[3]. The 3-mo survival rates for cirrhosis patients with PRA, HRS, and ATN are 89%, 39%, and 38%, respectively[4].

The assessment of kidney function in cirrhosis patients poses numerous challenges[5]. Serum creatinine level, often used to gauge renal impairment in cirrhosis patients, is unreliable because factors such as sarcopenia and increased tubular secretion of creatinine falsely lower the serum creatinine levels, thereby leading to an underestimation of renal dysfunction. Furthermore, hyperbilirubinemia can interfere with creatinine measurement in certain assays. Commonly used formulas for estimating glomerular filtration rate (GFR), such as the Modification of Diet in Renal Disease, Chronic Kidney Disease Epidemiology Collaboration, and the Cockroft-Gault formulas, which rely on serum creatinine, tend to overestimate renal function in cirrhosis patients[6]. Alternative methods for assessing renal function pose challenges related to cost, availability, complexity, and the risk of radiation exposure.

The hemodynamic alterations observed in cirrhosis result in vasoconstriction of renal vessels, causing a significant reduction in GFR, azotemia, and AKI[1,5]. The renal resistive index (RRI) is the most common Doppler ultrasound variable to estimate intrarenal vascular resistance. It is also the most widely applicable and accepted tool due to the easy availability and non-invasive nature of ultrasonography. Patients with advanced cirrhosis often exhibit elevated RRI due to renal vascular constriction. Some studies have explored the utility of RRI in assessing renal dysfunction in cirrhosis patients, particularly in determining whether AKI is structural or functional[7,8]. Fang *et al*[7] observed higher RRI values in patients with HRS compared to those with ATN. However, there is limited research on RRI's ability to distinguish between ATN-AKI and other phenotypes[9].

In our current study, we investigated the relationship between RRI and AKI in hospitalized cirrhosis patients. We evaluated the diagnostic accuracy of RRI in differentiating various AKI phenotypes and identified predictors of high RRI and AKI-related mortality.

MATERIALS AND METHODS

This prospective observational study was conducted at the Department of Gastroenterology, All India Institute of Medical Sciences (Patna, Bihar, India), a tertiary care medical center in India. The protocol received approval from the Institute's Research Board and Ethics Committee (Reference No: AIIMS/Pat/IEC/PGTh/July21/10), and all investigations were carried out according to the principles outlined in the Declaration of Helsinki. Prior to enrollment in the

study, written informed consent was obtained from all patients or their first-degree relatives.

Selection of study participants

Between March 2022 and December 2023, consecutive adult patients with liver cirrhosis admitted to the Department of Gastroenterology were evaluated for the inclusion and exclusion criteria. The inclusion criteria were patients with cirrhosis between the ages of 18 years and 75 years, diagnosed on the basis of clinical features, imaging characteristics, and endoscopic findings. Exclusion criteria included: (1) Critically ill cirrhosis patients requiring intensive care unit treatment; (2) patients with active variceal bleeding or advanced hepatic encephalopathy; (3) those with advanced cardiovascular disease; (4) patients diagnosed with intraabdominal malignancies, including hepatocellular carcinoma; (5) pregnant individuals; (6) patients with urinary tract infections; (7) patients on vasoconstrictors or renal replacement therapy (RRT); and (8) individuals lacking informed consent.

Definitions

AKI: An increase in serum creatinine value ≥ 0.3 mg/dL within 48 h or an increase of ≥ 50% from baseline was defined as AKI. According to the International Club of Ascites criteria, AKI was staged as follows: stage 1 AKI indicated an increase in serum creatinine by ≥ 0.3 mg/dL or ≥ 1.5-fold to 2-fold from baseline; stage 2 AKI was defined as an increase in serum creatinine > 2-fold to 3-fold from baseline; and stage 3 AKI indicated an increase in serum creatinine > 3-fold from baseline or serum creatinine ≥ 4.0 mg/dL or initiation of RRT[10,11].

HRS-AKI: The diagnosis of HRS-AKI in patients with ascites was made when there was no response after 2 d of albumin infusion and withdrawal of diuretics when none of the following were present: (1) Recent use of nephrotoxic drugs; (2) microhematuria with > 50 red blood cells per high-power field and/or proteinuria > 500 mg/d; (3) radiographic abnormalities; and (4) shock[11].

PRA: This was diagnosed when there was a history of excessive fluid loss due to gastrointestinal bleeding, diarrhea, or diuretic therapy, as indicated by weight loss > 500 g/d or 1000 g/d in patients without and with edema, and when there was renal function improvement following intravenous fluid administration with a > 25% decline in serum creatinine from baseline[9].

ATN-AKI: This was diagnosed if any three of six following criteria were met: (1) Presence of shock or nephrotoxic drug use; (2) granular/muddy-brown casts in urine sediment; (3) renal tubular epithelial cells in urinary sediment; (4) sodium excretion fraction > 2%; (5) urinary sodium > 40 mEq/L; and (6) urinary osmolarity < 400 mOsm/L[12].

Acute on chronic liver failure: Acute on chronic liver failure (ACLF) was defined as per Asia Pacific Association for the Study of the Liver criteria[13].

Patients' evaluation, RRI estimation, and management

Demographic information including age, sex, comorbidities, etiology, and duration of cirrhosis, diabetes mellitus (DM), and anthropometric parameters was collected at baseline. Estimates of dry weight were made for corrected body mass index (BMI) calculations by deducting 5%, 10%, or 15% of the actual weight in the cases of mild, moderate, or severe ascites, respectively, as well as an additional 5% in the case of pedal edema. Liver function tests, complete hemogram, kidney function tests, complete urine analysis, coagulation profiles, and serum lipids profiles were conducted for all patients. The severity of cirrhosis was assessed using Child-Turcotte-Pugh (CTP) classification and model for end-stage liver disease-sodium (MELD-Na) scores.

RRI measurements were taken for all patients after enrolment, regardless of AKI presence. Non-selective beta blockers and diuretics were halted for 48 h and 24 h, respectively, before RRI estimation. To achieve accurate RRI measurement of both kidneys, a duplex Doppler ultrasound machine (RS80 EVO; Samsung, Ridgefield Park, NJ, United States) with a 3.5 to 5.0 MHz convex probe was used. Furthermore, ascites was mobilized through paracentesis, and albumin infusion was used as per the guidelines. Duplex wave forms of main and interlobar arteries at upper, mid, and lower parts; peak systolic velocity; end diastolic velocity; and resistive indices of both kidneys were measured. RRI was calculated automatically by the machine as (peak systolic velocity - end diastolic velocity)/peak systolic velocity (Figure 1). The resistive index on both sides at the aforementioned places averaged a value that was reported as RRI. Based on the average cut-off of previous studies, an RRI value > 0.73 was considered high[8,14].

Standard medical therapy was provided for all patients as per their needs, and AKI management followed the established guidelines for cirrhosis patients[11]. Clinical monitoring occurred daily during hospitalization, with serum creatinine levels checked every 48 h. Outcomes were measured as alive at discharge or dead during hospitalization.

Statistical analysis

Descriptive analysis was performed to summarize the socio-demographic, clinical, and laboratory characteristics of the study participants. The continuous variables are reported as the mean ± standard deviation, while categorical data are expressed as proportions. For the comparison of continuous variables between subgroups, the Student's *t*-test, Mann-Whitney *U* test, one-way analysis of variance, or Kruskal-Wallis test was used as appropriate. Categorical variables were compared using the χ^2 test of association or Fisher's exact test when applicable. The discriminatory power of RRI for differentiating among PRA, ATN-AKI, and HRS AKI was assessed using the area under the receiver operating characteristic (AUROC) curve, with clinical adjudication as the gold standard. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of high RRI and in-hospital mortality. Odds ratio (OR) and

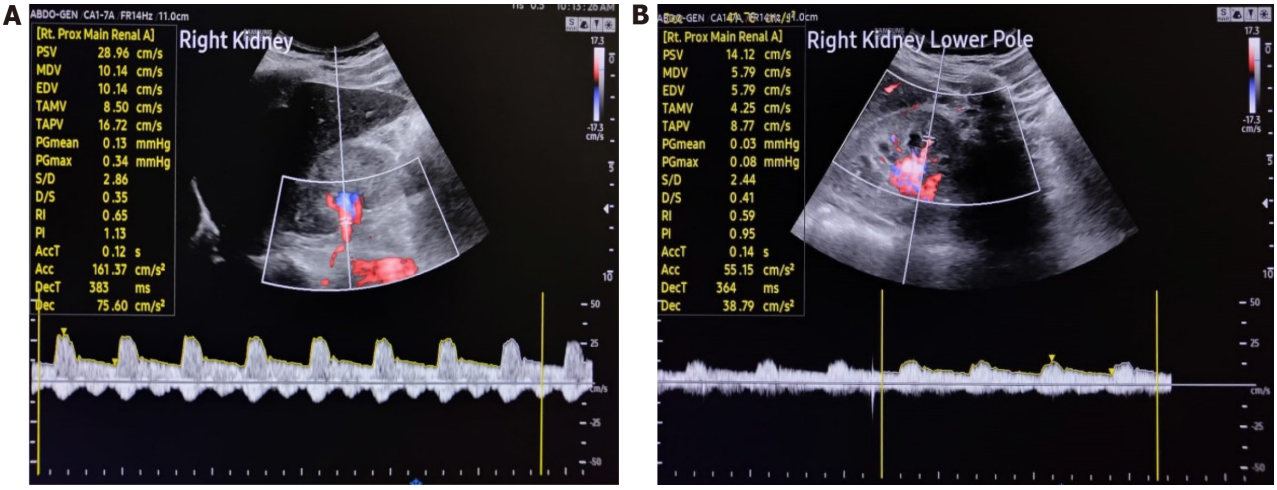

Figure 1 Measurements of the renal resistive index. A and B: Using a duplex Doppler ultrasound machine at right renal artery at hilum (A) and right lower interlobar artery (B).

95% confidence intervals (CIs) were reported for all significant variables in the regression analysis. Given the high prevalence of AKI in our study (64%), the sample size remained well above the estimated size of 152, based on previous studies. $P < 0.05$ was considered statistically significant throughout the analyses. The statistical analyses were conducted using Jamovi version 2.3.28.

RESULTS

Of the 557 cirrhosis patients admitted during the study period, 357 patients were excluded based on various exclusion criteria (Figure 2). Ultimately, 200 cirrhosis patients were included in the study.

Baseline characteristics of study cohort

The mean age of the patients (n = 200) was 49.08 ± 11.68 years, with the majority (79.5%) being male. The predominant etiologies of cirrhosis were alcohol (39%), non-alcoholic fatty liver disease (24.5%), and viral (18.5%). Cirrhosis distributions by Child-Pugh classes A, B, and C were 11.5%, 33%, and 55.5%, respectively. The median MELD-Na score of the cohort was 21 (7-40). Forty-four patients (22%) had hypertension and thirty-four (17%) had DM. The mean duration of DM and HTN was 23.94 ± 13.3 mo and 24.09 ± 11.84 mo, respectively. ACLF was present in 27 patients (13.5%), with the majority having Grade II (37%) or Grade III (40.7%) ACLF. Among the 200 patients, 153 (76.5%) had ascites, 70 (45.7%) had Grade II ascites, and 83 (54.2%) had Grade III ascites. Diuretic-responsive ascites was observed in 90 patients (59%), while 63 (41%) had diuretic-resistant ascites (Table 1).

AKI and its phenotypes

Of the 200 patients, AKI was seen in 129 (64.5%) patients, with 43 patients presenting AKI upon admission and 86 developing it during hospitalization. Sepsis, accounting for 48.8% of cases, was the most common AKI precipitator, with spontaneous bacterial peritonitis being the most common form of infection present in 60 patients (46.5%). The distribution of AKI stages was as follows: stage 1 in 51 patients (39.53%), stage 2 in 48 patients (37.2%), and stage 3 in 30 patients (23.25%) (Table 2). Regarding AKI phenotypes, HRS-AKI was observed in 82 patients (63.56%), PRA in 29 patients (22.48%), and ATN-AKI in 18 patients (13.95%). Among the HRS-AKI patients, 32 (39.02%) were in stage 1, 30 (36.58%) in stage 2, and 20 (24.39%) in stage 3. Of the 86 patients who developed AKI during hospitalization, 59 (72%) had HRS-AKI, 13 (72.2%) had ATN-AKI, and 14 (48.2%) had PRA.

Table 2 compares the characteristics between patients in the non-AKI and AKI phenotype groups. The severity of liver disease, indicated by the mean CTP score, was significantly higher in the ATN-AKI (11.89 ± 1.08), HRS-AKI (10.44 ± 1.87), and PRA (9.83 ± 1.61) groups compared to the non-AKI group (7.93 ± 2.08; $P \leq 0.001$). The mean MELD-Na score was significantly higher in the ATN-AKI (29.60 ± 7.19) group compared to the HRS-AKI (22.10 ± 7.10), PRA (21.50 ± 5.54), and non-AKI (17.70 ± 5.70) ($P < 0.001$) groups. Sepsis as an AKI precipitator was most prevalent in the 49 (59.75%) HRS-AKI patients and 12 (66.67%) ATN-AKI patients. By contrast, only 2 patients (6.9%) in the PRA group had sepsis, and no sepsis cases were observed in the non-AKI group ($P \leq 0.001$).

RRI measurements

RRI in the whole cohort: The mean RRI of our study cohort was 0.68 ± 0.09. RRI showed a significant increase with escalating CTP classes: CTP-A (0.56 ± 0.08), CTP-B (0.65 ± 0.08), and CTP-C (0.71 ± 0.07) (Supplementary Table 1). Additionally, RRI was notably higher in patients with a high median MELD-Na score (≥ 21) compared to those with a low median MELD-Na score (< 21). Moreover, significantly different RRI values were observed between patients with ascites

Table 1 Baseline clinical characteristics of the study population, *n* = 200

Parameter	Frequency
Age in yr, mean ± SD	49.08 ± 11.68
Male, *n* (%)	159 (79.5)
Etiology of cirrhosis, *n* (%)	
Alcohol	78 (39.0)
NAFLD	49 (24.5)
Viral	37 (18.5)
Others	36 (18.0)
CTP Class, *n* (%)	
A	23 (11.5)
B	66 (33.0)
C	111 (55.5)
Cirrhosis duration in mo, median (IQR)	6.00 (2.001-4.40)
CTP score, mean ± SD	9.59 ± 2.27
MELD-Na score, median	21 (7-40) ± 7.19
BMI, mean ± SD	19.79 ± 3.05
Comorbidity, *n* (%)	
None	121 (60.5)
Type 2 DM	34 (17.0)
HTN	44 (22.0)
Hypothyroidism	1 (0.5)
Duration of type 2 DM in mo, mean ± SD	23.94 ± 13.3
Duration of HTN in mo, mean ± SD	24.09 ± 11.84
ACLF presence, *n* (%)	27 (13.5)
ACLF grade among *n* = 27, *n* (%)	
I	6 (22.2)
II	10 (37.0)
III	11 (40.7)
Abdominal circumference in cm, mean ± SD	95.64 ± 16.28
Ascites among *n* = 153, *n* (%)	
Grade II	70 (45.7)
Grade III	83 (54.3)
Diuretic responsive	90 (59.0)
Diuretic resistant	63 (41.0)
MAP in mmHg, mean ± SD	76.16 ± 5.39
Heart rate in bpm, median (IQR)	80.00 (60.00-130.00)

ACLF: Acute-on-chronic liver failure; CTP: Child Turcotte Pugh; DM: Diabetes mellitus; HTN: Hypertension; IQR: Interquartile range; MAP: Mean arterial pressure; MELD: Model for end-stage liver disease; NAFLD: Non-alcoholic fatty liver disease; SD: Standard deviation.

Table 2 Baseline clinical characteristics according to the type of acute kidney injury, *n* = 200

Parameter	PRA, *n* = 29	ATN-AKI, *n* = 18	HRS-AKI, *n* = 82	No-AKI, *n* = 71	[a]*P* value
Age in yr, mean ± SD	53.9 ± 10.1	43.3 ± 10.8	50.7 ± 11.3	46.8 ± 12.0	0.003
Sex as male/female	26/3	16/2	64/18	53/18	0.268
Etiology of cirrhosis: Alcohol/NAFLD/viral/others	15/9/4/1	14/1/2/1	25/21/25/11	24/18/17/12	0.012
Hepatic encephalopathy, *n* (%)	4 (13.7)	1 (5.5)	5 (6.1)	7 (9.8)	0.568
GI bleed, *n* (%)	1 (3.4)	0 (0.0)	2 (2.4)	55 (69.6)	< 0.001
Sepsis, *n* (%)	2 (6.9)	12 (66.6)	49 (59.7)	0 (0.0)	< 0.001
Shock, *n* (%)	0 (0.0)	18 (100.0)	0 (0.0)	0 (0.0)	< 0.001
ACLF, *n* (%)	0 (0.0)	13 (72.2)	14 (17.0)	0 (0.0)	< 0.001
CTP score, mean ± SD	9.83 ± 1.61	11.89 ± 1.08	10.44 ± 1.87	7.93 ± 2.08	< 0.001
MELD-Na score, mean ± SD	21.50 ± 5.54	29.60 ± 7.19	22.10 ± 7.10	17.70 ± 5.70	< 0.001
Stage of AKI: Stage 1/stage 2/stage 3	16/13/0	3/5/10	32/29/21	0/0/0	< 0.001
Ascites: No/diuretic responsive/refractory	1/26/2	0/7/11	0/34/48	46/23/2	< 0.001
Hemoglobin in g/dL, mean ± SD	7.78 ± 1.58	8.79 ± 2.27	8.87 ± 1.75	7.97 ± 2.54	0.010
Total leukocyte count as cells/mm^3, mean ± SD	7410 ± 5750	13760 ± 6760	7290 ± 3990	5640 ± 3290	< 0.001
Platelet count as cells/mm^3, mean ± SD	89700 ± 31600	97100 ± 27600	98000 ± 32700	98200 ± 38400	0.654
Bilirubin in mg/dL, mean ± SD	1.76 ± 1.13	10.11 ± 8.70	3.62 ± 3.35	2.20 ± 1.82	< 0.001
ALT in U/L, mean ± SD	40.5 ± 23.1	53.1 ± 24.6	57.1 ± 77.9	38.6 ± 28.9	0.078
AST in U/L, mean ± SD	64.3 ± 41.2	130.7 ± 59.1	109.4 ± 63.2	68.4 ± 66.9	< 0.001
INR, mean ± SD	1.64 ± 0.42	2.43 ± 0.66	1.83 ± 0.57	1.57 ± 0.45	< 0.001
Albumin, mean ± SD	2.80 ± 0.41	2.48 ± 0.34	2.62 ± 0.43	2.98 ± 0.47	< 0.001
Urea in mg/dL, mean ± SD	90.10 ± 20.24	33.40 ± 6.85	44.3 ± 29.68	44.0 ± 26.31	< 0.001
Creatinine in mg/dL on Day 1, mean ± SD	1.68 ± 0.191	0.911 ± 0.264	1.335 ± 0.778	0.940 ± 0.276	< 0.001
Creatinine in mg/dL on Day 3, mean ± SD	1.53 ± 0.315	3.10 ± 1.165	2.81 ± 1.537	0.975 ± 0.212	< 0.001
CRP in mg/L, mean ± SD	38.6 ± 28.1	42.2 ± 25.7	37.7 ± 32.7	23.4 ± 19.9	< 0.001
Serum sodium in mEq/L, mean ± SD	126 ± 23.52	128 ± 6.26	130 ± 6.66	133 ± 4.89	0.001
Serum potassium in mEq/L, mean ± SD	4.42 ± 0.611	4.35 ± 0.604	4.25 ± 0.668	4.14 ± 0.552	0.155
RRI, mean ± SD	0.63 ± 0.07	0.80 ± 0.02	0.73 ± 0.0	0.60 ± 0.07	< 0.001

[a]*P* value: $P < 0.05$ was considered statistically significant between the groups. ACLF: Acute on chronic liver failure; AKI: Acute kidney injury; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ATN: Acute tubular necrosis; CRP: C-reactive protein; CTP: Child Turcotte Pugh; GI: Gastrointestinal; HRS: Hepatorenal syndrome; INR: International normalized ratio; MELD-Na: Model for end-stage liver disease-sodium; NAFLD: Non-alcoholic fatty liver disease; PRA: Prerenal AKI; RRI: Renal resistive index; SD: Standard deviation.

(0.71 ± 0.07) and without ascites (0.58 ± 0.07), with $P \leq 0.001$.

RRI According to AKI: The mean RRI was significantly higher in patients with AKI than those without it (0.72 ± 0.06 *vs* 0.60 ± 0.08; $P \leq 0.001$). Furthermore, patients with stage III AKI exhibited significantly higher RRI values (0.75 ± 0.04) compared to patients with stage II (0.71 ± 0.06) and stage I (0.70 ± 0.07) AKI ($P < 0.001$). Amongst AKI phenotypes, RRI was notably higher in patients with ATN-AKI (0.80 ± 0.02) compared to the HRS-AKI (0.73 ± 0.03), PRA (0.63 ± 0.07), and non-AKI (0.60 ± 0.07) groups ($P \leq 0.001$). RRI was greatly elevated in patients with HRS-AKI compared to those with PRA ($P \leq 0.001$). However, there was no statistically significant difference in RRI values between the PRA and non-AKI groups ($P = 0.061$). Moreover, RRI was significantly higher in patients with low mean arterial pressure (MAP) and tachycardia compared to their counterparts ($P < 0.001$). Patients who died during hospitalization had significantly higher RRI values than those who survived (0.74 ± 0.04 *vs* 0.64 ± 0.09; $P < 0.001$). Interestingly, RRI values did not vary significantly across different age groups, sex, BMI categories, and various etiologies of cirrhosis (Supplementary Table 1).

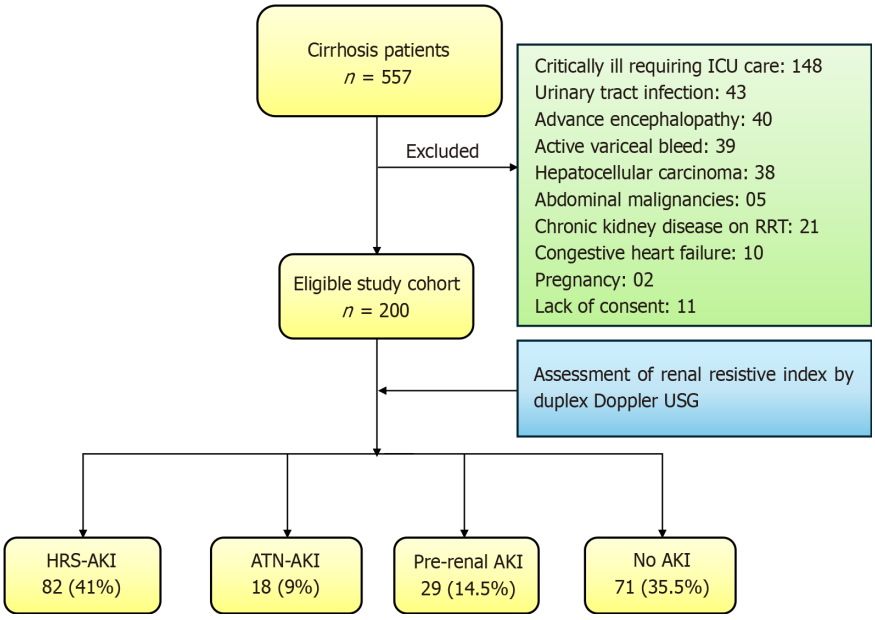

Figure 2 Selection of study participants. A total of 557 hospitalized cirrhosis patients were evaluated during study period. On the basis of various exclusion criteria, 357 patients were excluded. Finally, 200 cirrhosis patients were found eligible for the inclusion. AKI: Acute kidney injury; ATN: Acute tubular necrosis; HRS: Hepatorenal syndrome; ICU: Intensive care unit; PRA: Pre-renal AKI; RRT: Renal replacement therapy; USG: Ultrasound.

High vs low RRI

Among the 200 patients, high RRI (> 0.73) was found in 82 (41%) patients. Of these, 96.3% (n = 79) had AKI either at presentation or during hospitalization. By contrast, only 50 (42.4%) of 118 patients in the low RRI group had AKI ($P \leq 0.001$). High RRI predicted the occurrence of AKI during hospitalization, with 54 of 82 patients (65.8%) with high RRI developing AKI during hospitalization compared to 32 of 118 patients (27.1%) in the low RRI group ($P < 0.001$). Overall, 17 patients (94.4%) with ATN-AKI, 59 (72%) with HRS-AKI, and 3 (10.3%) with PRA had high RRI ($P \leq 0.001$). Table 3 provides a comparison of different parameters between patients with high and low RRI. On conducting multivariate analysis, low MAP (adjusted OR [aOR] = 0.86, 95%CI = 0.76–0.98; P = 0.02) and AKI (aOR = 11.52, 95%CI = 2.12–62.49; P = 0.005) were identified as independent predictors of high RRI (Supplementary Table 2).

RRI in differentiating AKI phenotypes

To differentiate ATN-AKI from non-ATN-AKI, the diagnostic accuracy (AUROC) of RRI was 94%. Additionally, an RRI cut-off value of 0.77 had a sensitivity of 89%, specificity of 96%, positive predictive value (PPV) of 80%, and negative predictive value (NPV) of 98% for predicting ATN-AKI. However, the diagnostic accuracy of RRI in differentiating HRS-AKI from non-HRS-AKI was poor, with an AUROC curve of only 56%. RRI showed good accuracy in differentiating PRA from both HRS-AKI (AUROC: 87%) and ATN-AKI (AUROC: 93%). Nonetheless, diagnostic accuracy of RRI for differentiating PRA from non-AKI was poor. The sensitivity, specificity, PPV, and NPV for various discriminatory cut-offs are shown in Table 4.

RRI and mortality

The in-hospital mortality rate of the study cohort was 30.50% (61 of 200 patients), with all patients except one dying with AKI. RRI was significantly higher in those who died during hospitalization as compared to those who remained alive (0.75 ± 0.04 *vs* 0.64 ± 0.090, $P \leq 0.001$). Among the AKI patients, 60 (48.06%) of 129 died during hospitalization. High RRI (aOR 3.18, 95%CI = 1.35–7.49; P = 0.008) emerged as an independent predictor of mortality among AKI patients (Supplementary Table 3).

DISCUSSION

AKI is common among hospitalized cirrhosis patients, and early prediction of AKI along with accurate differentiation between different AKI phenotypes can have significant therapeutic implications. The results of this study suggest that RRI is a reliable tool for evaluating renal hemodynamics in cirrhosis patients. In our cohort of 200 cirrhosis patients, RRI showed strong correlations with AKI, predicted AKI occurrence, differentiated between ATN and HRS-AKI from PRA, and independently predicted mortality in AKI patients.

Traditionally, the use of RRI has been advocated for cirrhosis patients to distinguish between structural and functional forms of AKI. Such differentiation is crucial not only for guiding optimal treatment decisions but also for avoiding unnecessary volume expansion and the adverse effects of vasoconstrictor medication. While many studies have shown higher RRI values in HRS patients compared to non-AKI patients, there is a lack of studies focusing on RRI's performance

Table 3 Comparison of clinical parameters in patients with and without high RRI, *n* = 200

Parameters	High RRI, > 0.73, *n* = 82	Low RRI, ≤ 0.73, *n* = 118	[a]*P* value
Age in yr, mean ± SD	47.98 ± 11.01	50.40 ± 12.37	0.810
Sex			
Male, *n* (%)	69 (84.1)	90 (76.2)	0.170
Comorbidity, *n* (%)			
Present	19 (23.2)	60 (50.8)	0.110
ACLF among *n* = 27	20 (24.3)	7 (5.9)	< 0.001
ACLF grade, *n* (%)			
Grade I	5 (25)	1 (0.8)	0.002
Grade II	7 (35)	3 (2.5)	
Grade III	8 (40)	3 (2.5)	
AKI, *n* (%)	79 (96.3)	50 (42.4)	< 0.001
AKI stage among *n* = 129, *n* (%)			
Stage I	27 (32.9)	24 (20.3)	
Stage II	28 (34.1)	19 (16.1)	
Stage III	24 (29.2)	7.0 (5.9)	
AKI phenotype among *n* = 129, *n* (%)			
ATN-AKI	17 (94.4)	1 (0.8)	< 0.001
HRS-AKI	59 (72)	23 (19.4)	
PRA	3 (10.3)	26 (22.0)	
BMI in kg/m²	19.70 ± 3.06	19.87 ± 3.06	0.169
Abdominal circumference in cm	102.98 ± 10.2	90.54 ± 17.6	< 0.001
Duration of cirrhosis in mo	10.96 ± 11.5	10.55 ± 12.18	0.574
Etiology, *n* (%)			
Alcohol	31 (37.8)	47 (39.8)	0.907
NAFLD	19 (23.2)	30 (25.4)	
Viral	22 (26.8)	15 (12.7)	
Others	10 (12.2)	26 (22.1)	
CTP class, *n* (%)			
A	1 (1.2)	22 (18.6)	< 0.001
B	17 (20.7)	49 (41.5)	
C	64 (78.1)	47 (39.8)	
MELD-Na Score	23 (7-33)	19 (7-28)	< 0.001
Ascites among *n* = 153, *n* (%)			
Grade-II	26 (32.5)	44 (37.2.3)	< 0.001
Grade-III	54 (67.5)	29 (24.5)	
MAP in mmHg	73.50 ± 6.77	78.2 ± 2.61	< 0.001
Heart rate	90.8 ± 16.55	80.8 ± 7.35	< 0.001

[a]*P* value: $P < 0.05$ was considered statistically significant between the groups. ACLF: Acute on chronic liver failure; AKI: Acute kidney injury; ATN: Acute tubular necrosis; BMI: Body mass index; CTP: Child Turcotte Pugh; HRS: Hepatorenal syndrome; MAP: Mean arterial pressure; MELD-Na: Model for end-stage liver disease-sodium; NAFLD: Non-alcoholic fatty liver disease; PRA: Prerenal AKI; RRI: Renal resistive index; SD: Standard deviation.

Table 4 Discriminatory performance of renal resistive index for different phenotypes of acute kidney injury

Parameters	AUROC curve	RRI cut-off	Sensitivity	Specificity	PPV	NPV
ATN-AKI *vs* non-ATN AKI	94%	0.77	89%	96%	80%	98%
ATN-AKI *vs* HRS-AKI	94%	0.77	89%	98%	94%	97%
ATN-AKI *vs* PRA	93%	0.73	100%	89%	85%	100%
HRS-AKI *vs* non HRS-AKI	56%	0.72	94%	55%	78%	84%
HRS-AKI *vs* PRA	87%	0.71	95%	89%	96%	86%
PRA *vs* no-AKI	59%	0.59	76%	45%	36%	81%

AKI: Acute kidney injury; ATN: Acute tubular necrosis; AUROC: Area under receiver operating characteristic curve; HRS: Hepatorenal syndrome; NPV: Negative predictive value; PPV: Positive predictive value; PRA: Prerenal AKI; RRI: Renal resistive index.

in ATN-AKI scenarios[7-9]. For instance, a small study by Maroto *et al*[8] reported significantly higher RRI in AKI patients compared to non-AKI patients (mean RRI: 0.74 *vs* 0.64). However, this study considered all AKI patients as having HRS, which may not reflect real-world scenarios accurately. In another study by Fouad *et al*[15], RRI was notably greater in HRS patients than in those with non-AKI cirrhosis. However, the study did not specifically address ATN. In our research, we measured RRI in patients with all three AKI phenotypes. The highest RRI values were observed in patients with ATN-AKI. Moreover, RRI was excellent at discriminating ATN-AKI from non-ATN-AKI (AUROC: 94%). Patients with PRA showed significantly lower RRI values compared to those with ATN-AKI and HRS-AKI. These findings are consistent with a recent study by George *et al*[9], which also observed elevated RRI values in patients with ATN-AKI and HRS-AKI and lowest RRI values in patients with PRA. This suggests that intrarenal vascular resistance remains markedly high in patients with ATN-AKI. Several factors, including a marked arteriolar vasoconstriction, tissues edema, endothelial dysfunction, and micro-thrombosis, may contribute to high RRI values in ATN-AKI patients[16]. These changes are not observed in HRS-AKI patients, making a high RRI value (0.77 or more) indicative of ATN-AKI over HRS-AKI (Table 4).

RRI demonstrated good accuracy in differentiating PRA from both HRS-AKI (AUROC: 87%) and ATN-AKI (AUROC: 93%). This finding holds important therapeutic and prognostic implications in clinical practice. In our study, the optimal RRI cut-off value to differentiate HRS-AKI from PRA was 0.71, which was higher than the corresponding 0.62 cut-off reported by George *et al*[9]. The exclusion of patients with DM and hypertension in their study may explain the lower RRI cut-off value. Studies by Bruno *et al*[14] have indicated that the presence of DM and hypertension can elevate RRI values, suggesting increased arterial stiffness in these patients.

The mean RRI in our study cohort increased significantly with higher grades of CTP class in cirrhosis (CTP class A: 0.56; class B: 0.65; class C: 0.71). This observation aligns with findings from previous studies by Sacerdoti *et al*[17] and Ćulafić *et al*[18]. Furthermore, RRI was higher in cirrhosis patients with ascites than those without it. It must be noted that RRI dynamics do not change linearly with changes in renal vascular resistance in advanced cirrhosis. Several variables, including intra-abdominal pressure, heart rate, arterial blood pressure, and vascular compliance, can influence RRI. In our study, the presence of SBP and lower MAP were also found to be associated with high RRI values.

Assessing renal function in cirrhosis patients presents multiple challenges. Serum creatinine levels often underestimate the degree of renal dysfunction due to factors such as sarcopenia. While urine neutrophil gelatinase-associated lipocalin shows promise in differentiating ATN-AKI from other AKI types, it is not currently available in clinical practice in most countries[19]. RRI, measured by Doppler ultrasound, is a sensitive marker of renal vasoconstriction and can identify patients at risk of developing AKI. In our study, 65.8% of patients with high RRI developed AKI during hospitalization compared to 27% of those with RRI below the cut-off ($P < 0.001$). In a study by Bardi *et al*[20], cirrhosis patients with RRI of 0.70 or higher had a 3.32 relative risk of developing HRS. Thus, detecting high RRI could be crucial for early intervention and prevention of renal disease progression, as they have been linked with poor outcomes in cirrhosis patients with AKI. In another study, an RRI value of 0.78 predicted poor outcomes in patients with HRS[20]; this is also seen in our study where RRI independently predicted mortality in cirrhosis patients with AKI. In hospitalized cirrhosis patients, AKI has been independently associated with mortality with OR of 3.80[21].

Our study aimed to investigate the relevance of RRI measurement by using a Doppler ultrasound, an underutilized but affordable, accessible, safe, and reproducible tool for assessing renal impairment in cirrhosis patients. Nevertheless, our study has limitations. The results might not be generalizable because the study only involved one center. RRI's dynamicity with respect to outcome factors could not be evaluated because it was only measured once at baseline. Moreover, the small proportion of ATN-AKI patients and reliance on ancillary tests rather than biomarkers of tubular damage or renal biopsy for ATN diagnosis were additional limitations[22].

CONCLUSION

In conclusion, our study highlighted the importance of RRI measurements in patients with cirrhosis. RRI exhibited a significant association with AKI, effectively differentiated between AKI phenotypes, and predicted AKI-related mortality

in cirrhosis patients. Further large scale studies, which also address the limitations of this study, are required to validate the findings of our study.

FOOTNOTES

Author contributions: Himanshu S and Kumar R contributed to the concept and design of the manuscript, data collection, and manuscript writing; Priyadarshi RN, Surya Prakash S, and Kumar S contributed to the data collection, critical input, and manuscript writing; All authors have made a significant contribution and approved the final manuscript.

Institutional review board statement: The study was reviewed and approved by the Institute research board (Reference No: AIIMS/Pat/IEC/PGTh/July21/10).

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrolment.

Conflict-of-interest statement: The authors have no conflicts of interest to declare.

Data sharing statement: All relevant data included. No additional data are available.

STROBE statement: The authors have read the STROBE Statement checklist of items, and the manuscript was prepared and revised according to the STROBE Statement checklist of items.

Country of origin: India

ORCID number: Ramesh Kumar 0000-0001-5136-4865; Rajeev Nayan Priyadarshi 0000-0003-2890-8910; Sabbu Surya Prakash 0009-0006-5117-5443; Sudhir Kumar 0000-0001-7117-1382.

S-Editor: Gong ZM
L-Editor: Filipodia
P-Editor: Che XX

REFERENCES

1 **Nadim MK**, Garcia-Tsao G. Acute Kidney Injury in Patients with Cirrhosis. *N Engl J Med* 2023; **388**: 733-745 [PMID: 36812435 DOI: 10.1056/NEJMra2215289]
2 **Allegretti AS**, Solà E, Ginès P. Clinical Application of Kidney Biomarkers in Cirrhosis. *Am J Kidney Dis* 2020; **76**: 710-719 [PMID: 32622560 DOI: 10.1053/j.ajkd.2020.03.016]
3 **Allegretti AS**, Parada XV, Eneanya ND, Gilligan H, Xu D, Zhao S, Dienstag JL, Chung RT, Thadhani RI. Prognosis of Patients with Cirrhosis and AKI Who Initiate RRT. *Clin J Am Soc Nephrol* 2018; **13**: 16-25 [PMID: 29122911 DOI: 10.2215/CJN.03610417]
4 **Huelin P**, Piano S, Solà E, Stanco M, Solé C, Moreira R, Pose E, Fasolato S, Fabrellas N, de Prada G, Pilutti C, Graupera I, Ariza X, Romano A, Elia C, Cárdenas A, Fernández J, Angeli P, Ginès P. Validation of a Staging System for Acute Kidney Injury in Patients With Cirrhosis and Association With Acute-on-Chronic Liver Failure. *Clin Gastroenterol Hepatol* 2017; **15**: 438-445.e5 [PMID: 27720915 DOI: 10.1016/j.cgh.2016.09.156]
5 **Kumar R**, Priyadarshi RN, Anand U. Chronic renal dysfunction in cirrhosis: A new frontier in hepatology. *World J Gastroenterol* 2021; **27**: 990-1005 [PMID: 33776368 DOI: 10.3748/wjg.v27.i11.990]
6 **Pena Polanco NA**, Martin P, Carrion AF. Advances in the Management of Renal Dysfunction in Patients With Cirrhosis. *Gastroenterol Hepatol (N Y)* 2021; **17**: 211-220 [PMID: 34924889]
7 **Fang Y**, Zhu H, Gao C, Gu Y, Liu Y, Yuan Y, Wu X. Value of shear wave elastography in predicting hepatorenal syndrome in patients with liver cirrhosis and ascites. *Int J Clin Pract* 2021; **75**: e14811 [PMID: 34490949 DOI: 10.1111/ijcp.14811]
8 **Maroto A**, Ginès A, Saló J, Clària J, Ginès P, Anibarro L, Jiménez W, Arroyo V, Rodés J. Diagnosis of functional kidney failure of cirrhosis with Doppler sonography: prognostic value of resistive index. *Hepatology* 1994; **20**: 839-844 [PMID: 7927224 DOI: 10.1002/hep.1840200411]
9 **George R**, Sonika U, Mahajan B, Sharma A, Dalal A, Sachdeva S, Kumar A. Diagnostic utility of urine neutrophil gelatinase-associated lipocalin and renal resistive index in patients of decompensated cirrhosis with acute kidney injury. *Dig Liver Dis* 2023; **55**: 1230-1235 [PMID: 37244788 DOI: 10.1016/j.dld.2023.03.002]
10 **Khwaja A**. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract* 2012; **120**: c179-c184 [PMID: 22890468 DOI: 10.1159/000339789]
11 **Angeli P**, Garcia-Tsao G, Nadim MK, Parikh CR. News in pathophysiology, definition and classification of hepatorenal syndrome: A step beyond the International Club of Ascites (ICA) consensus document. *J Hepatol* 2019; **71**: 811-822 [PMID: 31302175 DOI: 10.1016/j.jhep.2019.07.002]
12 **Perazella MA**, Coca SG, Kanbay M, Brewster UC, Parikh CR. Diagnostic value of urine microscopy for differential diagnosis of acute kidney injury in hospitalized patients. *Clin J Am Soc Nephrol* 2008; **3**: 1615-1619 [PMID: 18784207 DOI: 10.2215/CJN.02860608]

13 **Sarin SK**, Choudhury A, Sharma MK, Maiwall R, Al Mahtab M, Rahman S, Saigal S, Saraf N, Soin AS, Devarbhavi H, Kim DJ, Dhiman RK, Duseja A, Taneja S, Eapen CE, Goel A, Ning Q, Chen T, Ma K, Duan Z, Yu C, Treeprasertsuk S, Hamid SS, Butt AS, Jafri W, Shukla A, Saraswat V, Tan SS, Sood A, Midha V, Goyal O, Ghazinyan H, Arora A, Hu J, Sahu M, Rao PN, Lee GH, Lim SG, Lesmana LA, Lesmana CR, Shah S, Prasad VGM, Payawal DA, Abbas Z, Dokmeci AK, Sollano JD, Carpio G, Shresta A, Lau GK, Fazal Karim M, Shiha G, Gani R, Kalista KF, Yuen MF, Alam S, Khanna R, Sood V, Lal BB, Pamecha V, Jindal A, Rajan V, Arora V, Yokosuka O, Niriella MA, Li H, Qi X, Tanaka A, Mochida S, Chaudhuri DR, Gane E, Win KM, Chen WT, Rela M, Kapoor D, Rastogi A, Kale P, Rastogi A, Sharma CB, Bajpai M, Singh V, Premkumar M, Maharashi S, Olithselvan A, Philips CA, Srivastava A, Yachha SK, Wani ZA, Thapa BR, Saraya A, Shalimar, Kumar A, Wadhawan M, Gupta S, Madan K, Sakhuja P, Vij V, Sharma BC, Garg H, Garg V, Kalal C, Anand L, Vyas T, Mathur RP, Kumar G, Jain P, Pasupuleti SSR, Chawla YK, Chowdhury A, Alam S, Song DS, Yang JM, Yoon EL; APASL ACLF Research Consortium (AARC) for APASL ACLF working Party. Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific association for the study of the liver (APASL): an update. *Hepatol Int* 2019; **13**: 353-390 [PMID: 31172417 DOI: 10.1007/s12072-019-09946-3]

14 **Bruno RM**, Daghini E, Landini L, Versari D, Salvati A, Santini E, Di Paco I, Magagna A, Taddei S, Ghiadoni L, Solini A. Dynamic evaluation of renal resistive index in normoalbuminuric patients with newly diagnosed hypertension or type 2 diabetes. *Diabetologia* 2011; **54**: 2430-2439 [PMID: 21499674 DOI: 10.1007/s00125-011-2148-y]

15 **Fouad YM**, Mokarrab H, Elgebaly AF, El-Amin H, Abdel-Raheem EM, Sharawy MA, Shatat ME. Renal duplex Doppler ultrasound in patients with HCV related liver cirrhosis. *Trop Gastroenterol* 2009; **30**: 213-218 [PMID: 20426281]

16 **Bouglé A**, Duranteau J. Pathophysiology of sepsis-induced acute kidney injury: the role of global renal blood flow and renal vascular resistance. *Contrib Nephrol* 2011; **174**: 89-97 [PMID: 21921613 DOI: 10.1159/000329243]

17 **Sacerdoti D**, Bolognesi M, Merkel C, Angeli P, Gatta A. Renal vasoconstriction in cirrhosis evaluated by duplex Doppler ultrasonography. *Hepatology* 1993; **17**: 219-224 [PMID: 8428719]

18 **Ćulafić D**, Štulić M, Obrenović R, Miletić D, Mijač D, Stojković M, Jovanović M, Ćulafić M. Role of cystatin C and renal resistive index in assessment of renal function in patients with liver cirrhosis. *World J Gastroenterol* 2014; **20**: 6573-6579 [PMID: 24914379 DOI: 10.3748/wjg.v20.i21.6573]

19 **Allegretti AS**, Parada XV, Endres P, Zhao S, Krinsky S, St Hillien SA, Kalim S, Nigwekar SU, Flood JG, Nixon A, Simonetto DA, Juncos LA, Karakala N, Wadei HM, Regner KR, Belcher JM, Nadim MK, Garcia-Tsao G, Velez JCQ, Parikh SM, Chung RT; HRS-HARMONY study investigators. Urinary NGAL as a Diagnostic and Prognostic Marker for Acute Kidney Injury in Cirrhosis: A Prospective Study. *Clin Transl Gastroenterol* 2021; **12**: e00359 [PMID: 33979307 DOI: 10.14309/ctg.0000000000000359]

20 **Bardi A**, Sapunar J, Oksenberg D, Poniachik J, Fernández M, Paolinelli P, Orozco R, Biagini L. [Intrarenal arterial doppler ultrasonography in cirrhotic patients with ascites, with and without hepatorenal syndrome]. *Rev Med Chil* 2002; **130**: 173-180 [PMID: 11974530]

21 **Belcher JM**, Garcia-Tsao G, Sanyal AJ, Bhogal H, Lim JK, Ansari N, Coca SG, Parikh CR; TRIBE-AKI Consortium. Association of AKI with mortality and complications in hospitalized patients with cirrhosis. *Hepatology* 2013; **57**: 753-762 [PMID: 22454364 DOI: 10.1002/hep.25735]

22 **Russ KB**, Stevens TM, Singal AK. Acute Kidney Injury in Patients with Cirrhosis. *J Clin Transl Hepatol* 2015; **3**: 195-204 [PMID: 26623266 DOI: 10.14218/JCTH.2015.00015]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com