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Prevalence, risk factors, and short-term outcomes of postparacentesis acute kidney injury using revised criteria of the international club of ascites

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Abstract

Acute kidney injury (AKI) can become complicated after paracentesis due to extrarenal fluid loss and inadequate blood flow to the kidneys. The objective of this study was to explore the incidence and clinical implications of postparacentesis AKI.

A retrospective cohort of 137 liver cirrhosis patients (mean age: 61.3 ± 11.8 years, male: 100 [73.0%], viral hepatitis: 93 [67.9%]) who underwent paracentesis was analyzed. The incidence of AKI as defined by the international club of ascites (ICA) criteria, the risk factors, and its impact on early mortality were all assessed.

Thirty two patients (23.4%) developed AKI after paracentesis. In multivariate analysis, the Model for end-stage liver disease (MELD)-Na score was an independent factor associated with AKI development (odds ratio [OR], 1.14; 95% confidence interval [CI], 1.07–1.23) after paracentesis. The incidence of early mortality was significantly higher for those with AKI than without AKI (71.9% [23/32 patients] vs 11.4% [12/105 patients], $P < .001$). AKI (hazard ratio [HR], 7.56; 95% CI, 3.40–16.8) and MELD-Na score (HR, 1.08; 95% CI, 1.02–1.14) were independent factors associated with early mortality. In subgroup analysis, AKI after paracentesis was associated with significantly higher early mortality in both MELD-Na groups, that is, patients with a MELD-Na score >26 (87.5% vs 22.2%, $P < .001$) and those with a MELD-Na score ≤26 (56.3% vs 9.2%, $P < .001$).

Postparacentesis AKI occurred frequently in cirrhotic patients. Furthermore, it was associated with early mortality. Baseline MELD-Na score was associated with AKI, indicating that careful attention is required for those with a higher MELD-Na score who are being considered for therapeutic paracentesis.

Abbreviations: AKI = acute kidney injury, CI = confidence intervals, CT = computerized tomography, HCC = hepatocellular carcinoma, HR = hazard ratios, ICA = international club of ascites, IQR = interquartile range, MELD = model for end-stage liver disease, OR = odds ratio, PICD = paracentesis-induced circulatory dysfunction, WBC = white blood cell.

Keywords: acute kidney injury, ascites, liver cirrhosis, model for end-stage liver disease-Na, prognosis

Key Points

- Few studies have investigated the prevalence and outcome of AKI according to revised criteria of the International Club of Ascites
- The revised ICA-AKI criteria are useful in facilitating earlier diagnoses while broadening the population of cirrhotic patients considered to have AKI.
- Post-paracentesis AKI occurred frequently in cirrhotic patients. Furthermore, it was associated with early mortality.
- Baseline MELD-Na score was associated with AKI, indicating that careful attention is required for those with a higher MELD-Na score who are being considered for therapeutic paracentesis.

1. Introduction

Ascites, one of the most common manifestations of cirrhotic liver, is caused by a complex chain of pathophysiological events including portal hypertension and progressive vascular dysfunction. Adequate management of cirrhotic ascites and its complications can improve

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quality of life. The mainstay to managing patients with ascites is modest salt restriction and treatment with diuretic therapy. However, in patients with large grade 3 ascites, therapeutic paracentesis is usually required to rapidly remove tense ascites. In physiology, the maintenance of body fluid volume is crucial to normal kidney function as it is necessary for constant renal perfusion.[1] Therefore, after paracentesis, cirrhotic patients with ascites are highly vulnerable to acute kidney injury (AKI) due to extrarenal fluid loss and inadequate blood flow to the kidneys.[2] AKI is a potentially life-threatening complication in cirrhotic patients, and it can lead to further hepatic decompensation. Paracentesis-induced circulatory dysfunction (PICD), first described by Ginès et al, is a widely used syndrome-like concept represented by a decreased fluid-shifting compensatory response after paracentesis in the presence of cirrhosis.[3,4] PICD results from impaired circulating fluid volume, decreased systemic vascular resistance, and activation of the renin-angiotensin-aldosterone pathway, and is associated with faster re-accumulation of ascites, hyponatremia, renal impairment, and poor survival.[5] Previous studies suggest that AKI can be a simple surrogate marker for PICD because AKI is also largely associated with altered hemodynamics caused by fluid shifts and additional decreases in intravascular fluid volume.[6] Recently, the international club of ascites (ICA) announced revised AKI criteria, now defined as an increase in serum creatinine (sCr) $\geq$0.3 mg/dL within 48 hour or sCr $\geq$50% from baseline.[7] However, to date, few studies have investigated the prevalence and outcome of AKI according to these ICA criteria in cirrhotic patients who underwent paracentesis. This indicates a need to elucidate the association between paracentesis and AKI in a real clinical setting. Therefore, using the current AKI criteria, we developed this study to explore the incidence and clinical implications of postparacentesis AKI and to evaluate predictive risk factors for postparacentesis AKI.

2. Materials and methods

2.1. Study design and patients

This is a retrospective, single-center cohort study including patients with liver cirrhosis who underwent paracentesis between March 2016 and February 2017 in Samsung Medical Center, Seoul, South Korea. A diagnosis of liver cirrhosis was made in patients with underlying liver disease on evidence of portal hypertension by comprehensively compiling laboratory results for thrombocytopenia with a platelet count below 150,000/uL, endoscopic findings (e.g., esophageal varix or gastric varix), or imaging of cirrhotic features (irregular pattern of the liver surface or hypertrophied caudate lobe and/or splenomegaly) on abdominal ultrasound or abdominal computerized tomography (CT). First, we selected a total of 230 cirrhotic patients who underwent paracentesis for ascites, which was defined as free peritoneal fluid identified by abdominal ultrasound, CT, or magnetic resonance imaging, or as clinically evident ascites confirmed by paracentesis. Then, we excluded 93 patients who met any of the following criteria: patients who underwent liver transplantation (n=27); patients who had been diagnosed with chronic kidney disease (n=9); patients who were diagnosed with a malignant tumor other than hepatocellular carcinoma (HCC) (n=33); failed paracentesis (n=8); follow-up duration fewer than 7 days after paracentesis (n=16), and incomplete laboratory and clinical data (n=12). Ultimately, a total of 137 patients were included and analyzed for this study. The study protocol was approved by the Ethics Committee of Samsung Medical Center, and the study was conducted in accordance with the principles of the Declaration of Helsinki. Because the study was based on the retrospective analysis of existing administrative and clinical data, the requirement to obtain informed patient consent was waived by the Institutional Review Board.

2.2. Variables, data collection and measurement

The primary outcome variables of this study were incidence of AKI within 7 days following paracentesis and patient survival rate depending on AKI development in cirrhotic patients who underwent paracentesis. Secondary outcome measures included risk factors for postparacentesis AKI and mortality according to the presence of AKI in different prognostic subgroups stratified by Model for End-Stage Liver Disease (MELD)-Na score. The following data were collected and reviewed: age at diagnosis, gender, blood test results, etiology of cirrhosis, presence of portal vein thrombosis (defined as thrombosis that develops within the main portal vein and intrahepatic portal branches), volume of paracentesis, use of diuretics or beta blockers on the day of paracentesis, albumin infusion (yes/no), and volume of infusion. Liver functional reserve was assessed using baseline Child-Pugh, MELD, and MELD-Na scores, which were calculated at the time of diagnosis according to their respective formulas.[8–10] We used the aforementioned revised ICA-AKI criteria as the definition of paracentesis- induced AKI diagnosis. Baseline serum creatinine was defined as the last stable sCr value observed between 3 months prior to and 7 days following paracentesis. Values for serum creatinine on the day of paracentesis, again after 48 hours, and again after 7 days were also included in the analysis.

For this study, we additionally identified laboratory parameters and clinical variables that could affect early mortality within the 30 days after paracentesis. The follow-up period was the time elapsed between the date of diagnosis and the date of mortality or last follow-up. Patient survival data were collected from the National Statistics Service, ensuring that all deaths at the time of assessment were certified. Survival time was calculated from the date of diagnosis to the date of death or the date of the last follow-up observation.

2.3. Statistical analysis

Statistical analyses were carried out using SPSS, version 22 (IBM Corporation, Armonk, NY) and R version 3.1.0 (Vienna, Austria; http://www.Rproject.org/). Statistical analyzes were performed using the Chi-Squared test or the Fisher exact test for categorical variables and the Student *t*-test (or Mann–Whitney's test, if appropriate) for continuous variables. Data were summarized as mean and standard deviation, median with interquartile range (IQR), or number (%) as appropriate. Overall survival was compared using the Kaplan–Meier method and the log-rank test. Logistic regression models were used to identify risk factors associated with paracentesis-induced AKI. Variables found to be statistically significant by a univariate analysis were then entered into a multivariate logistic regression analysis to identify independent risk factors for the development of AKI. A Cox proportional hazards regression model was used to verify prognostic factors influencing early mortality within 30 days of paracentesis in cirrhotic patients, and hazard ratios (HR) and 95% confidence intervals (CI) were obtained. Univariate analysis was performed to determine whether any of the 14 historical predictors of interest were associated with early mortality. After

that, we constructed a multivariate model using the 4 variables that were statistically significant at the 0.025 level by univariate analysis. *P* values <.05 with a two-tailed test were considered statistically significant.

3. Results

3.1. Baseline characteristics

Thirty two patients (23.4%) developed AKI within 7 days following paracentesis. All patients were classified into 2 groups depending on their AKI results: the AKI group (n = 32) and the non-AKI group (n = 105). Baseline demographic and clinical characteristics of the 2 groups are summarized in Table 1. The mean patient age at the time of paracentesis was 61.3 ± 11.8 years, and males outnumbered females by 100 (73.0%) to 37 (27.0%). The main etiology was virus-related cirrhosis at 67.9% (93/137). There was no significant difference in patient demographics between the 2 groups, nor were there any differences in the proportions of HCC or portal vein thrombosis, paracentesis volume, albumin infusion dose, beta blocker use, baseline serum creatinine, prothrombin time, or C-reactive protein. Baseline serum sodium levels (median [IQR], 129 [124–134] vs 134 [129–137]; *P* = .005) were significantly lower in the AKI group than in the non-AKI group, whereas serum bilirubin levels (10.8 [1.9–18.6] vs 5.3 [1.4–6.3], *P* = .019) and white blood cell (WBC) count (9.04 [5.74–11.44] vs 6.84 [3.84–8.63], *P* = .013) in the AKI group were significantly higher. Patients in the non-AKI group had more often been prescribed diuretics on the day of paracentesis than were the AKI case patients (67.6% vs 43.8%, respectively; *P* = .026). The majority of study patients presented deterioration of liver function with Child-Pugh class C (62.8%). The proportion of patients belonging to either Child-Pugh class B or C was not significantly different. The median Child-Pugh, MELD, and MELD-Na scores were 10 (IQR, 9–11), 18 (IQR, 13–22), and 21 (IQR, 14–26), respectively. Patients in the AKI group had significantly higher MELD and MELD-Na scores compared to those in the non-AKI group, whereas Child-Pugh scores were not significantly different between the 2 groups. Almost half (47.4%) of the patients had drainage of 3 liters or more, and the volume proportion, dividing by 3L and 5L, was not different between the 2 groups. In most cases (84.7%), albumin was infused as a volume expander postparacentesis, and the dose was 20 g in 75.2% of cases. In this study, most (81/103, 78.6%) of the patients were at a relatively advanced stage of HCC (modified International Union Against Cancer (mUICC) stage III-IV). In cases where patients fell into mUICC stages III-IV, AKI was more prevalent compared to HCC patients

Table 1

Comparison of demographic and clinical characteristics according to presence of postparacentesis acute kidney injury.

Variables	All patients (n = 137)	AKI group (n = 32)	Non-AKI group (n = 105)	*P* value
Age (yr)	61.3 ± 11.8	61.7 ± 10.6	61.2 ± 12.2	.842
Male	100 (73.0)	22 (68.8)	78 (74.3)	.696
Etiology				1.000
Viral hepatitis-related	93 (67.9)	22 (68.8)	71 (67.6)	
Others	44 (32.1)	10 (31.2)	34 (32.4)	
HCC	103 (75.2)	26 (81.2)	77 (73.3)	.485
PVT	63 (46.0)	17 (53.1)	46 (43.8)	.470
Child-Pugh score	10 (9-11)	10 (9–11)	10 (8–11)	.211
Child-Pugh class				.154
B	51 (37.2)	8 (25.0)	43 (41.0)	
C	86 (62.8)	24 (75.0)	62 (59.0)	
MELD score	18 (13–22)	24 (17–29)	16 (12–20)	<.001
MELD-Na score	21 (14–26)	27 (23–31)	19 (12–24)	<.001
Volume of paracentesis				.256
<3 L	72 (52.6)	13 (40.6)	59 (56.2)	
3–5 L	52 (38.0)	16 (50.0)	36 (34.3)	
≥5 L	13 (9.5)	3 (9.4)	10 (9.5)	
Albumin infusion dose				.389
0 g	21 (15.3)	5 (15.6)	16 (15.2)	
20 g	103 (75.2)	22 (68.8)	81 (77.1)	
40 g	13 (9.5)	5 (15.6)	8 (7.6)	
Diuretics use*	85 (62.0)	14 (43.8)	71 (67.6)	.026
Beta blocker use*	25 (18.2)	4 (12.5)	21 (20.0)	.484
Sodium (mEq/L)	133 (128–137)	129 (124–134)	134 (129–137)	.005
Creatinine (mg/dL)	0.82 (0.67–1.10)	0.96 (0.69–1.32)	0.80 (0.66–0.98)	.121
Bilirubin (mg/dL)	6.6 (1.5–7.7)	10.8 (1.9–18.6)	5.3 (1.4–6.3)	.019
Albumin (mg/dL)	2.8 (2.5–3.1)	2.8 (2.6–3.1)	2.8 (2.4–3.2)	.991
ALT (U/L)	81 (21–70)	179 (23–100)	51 (21–53)	.247
AST (U/L)	186 (42–145)	484 (50–242)	96 (41–104)	.212
PT (INR)	1.64 (1.25–1.77)	1.80 (1.33–2.10)	1.59 (1.24–1.75)	.118
CRP (mg/dL)	4.01 (1.14–5.93)	4.68 (1.89–7.03)	3.81 (0.92–5.55)	.324
WBC count (x10^3/μL)	7.36 (4.02–9.49)	9.04 (5.74–11.44)	6.84 (3.84–8.63)	.013

AKI = acute kidney injury, ALT = alanine transaminase, AST = aspartic acid transaminase, CRP = C-reactive protein, HCC = hepatocellular carcinoma, MELD = model for end-stage liver disease, PT = prothrombin time, PVT = portal vein thrombosis, WBC = white blood cell.

* On the day of paracentesis.

Age is presented as mean ± standard deviation (SD); other variables are presented as median with interquartile range (IQR) or number (%).

Table 2

Risk factors for postparacentesis acute kidney injury.

Variables	Univariate OR (95% CI)	*P* value	Multivariate* OR (95% CI)	*P* value
Age (yr)	1.00 (0.97–1.03)	.841		
Female (vs male)	1.31 (0.55–3.12)	.538		
Etiology (viral vs others)	1.05 (0.44–2.47)	.90		
HCC (yes vs no)	0.63 (0.23–1.70)	.36		
PVT (yes vs no)	1.45 (0.65–3.21)	.35		
Child-Pugh class C (vs B)	2.08 (0.85–5.06)	.10		
MELD-Na score	1.16 (1.08–1.24)	<.001	1.14 (1.07–1.23)	<.001
Paracentesis volume (>3 L vs <3 L)	1.87 (0.83–4.18)	.12		
Albumin infusion (yes vs no)	0.97 (0.32–2.89)	.95		
Diuretics use† (yes vs no)	0.37 (0.16–0.83)	.01	0.48 (0.19–1.20)	.119
Beta blocker use† (yes vs no)	0.57 (0.18–1.80)	.34		
ALT (U/L)	1.00 (0.99–1.01)	.12		
CRP (mg/dL)	1.04 (0.95–1.13)	.32		
WBC count (x10^3/μL)	1.11 (1.01–1.21)	.01	1.03 (0.93–1.13)	.548

Abbreviations: See Table 1.

* The variables that were statistically significant by univariate analysis were included in a multivariate analysis.

† On the day of paracentesis.

at mUICC stages I-II. However, this difference was not statistically significant (stage III-IV vs stage I-II: 27.2% vs 18.2%, $P = .581$).

3.2. Risk factors for postparacentesis acute kidney injury

To explore potential risk factors associated with paracentesis-induced AKI, we performed multivariate analysis. Table 2 shows the odds ratios (ORs) and associated 95% CIs for AKI development in the patients who underwent paracentesis. In univariate analysis of 14 demographic and clinical predictors of interest, MELD-Na score, use of diuretics, and WBC count were statistically significant ($P < .05$). Of these, in multivariate analysis, only the baseline MELD-Na score was significantly associated with AKI development after paracentesis (OR, 1.14; 95% CI, 1.07–1.23).

3.3. Comparison of baseline characteristics according to early mortality after paracentesis

Of the 137 patients who underwent paracentesis, 35 (25.5%) patients died within 30 days of the procedure. These patients were classified as the early mortality group, and the remaining 102 (74.5%) were classified as the survivor group. A comparison of the baseline characteristics of the 2 groups is presented in Table 3. Patients in the early mortality group showed higher baseline Child-Pugh scores, MELD scores, MELD-Na scores, serum bilirubin levels, prothrombin time, C-reactive protein levels, and WBC count, and lower baseline serum sodium levels than those in the survivor group. Postparacentesis AKI was observed in 23 patients in the early mortality group, where there was a significantly higher rate of AKI than in the survivor group (65.7% vs 8.8%, $P < .001$).

3.4. Prognostic factors associated with early mortality after paracentesis

To identify prognostic factors influencing early mortality in patients who underwent paracentesis, Cox proportional hazards regression analysis was performed. Results of univariate and multivariate analysis using this model are shown in Table 4. Univariate analysis revealed the following unfavorable indicators of early mortality at the 0.025 level of *P* values: higher MELD-Na

Table 3

Comparison of baseline characteristics according to incidence of postparacentesis early mortality.

Variables	Early mortality group (n = 35)	Survivor group (n = 102)	*P* value
Age (yr)	61 ± 11	61 ± 12	.918
Male	26 (74.3)	74 (72.5)	1.000
Etiology			.465
Viral hepatitis-related	26 (74.3)	67 (65.7)	
Others	9 (25.7)	35 (34.3)	
HCC	29 (82.9)	74 (72.5)	.263
PVT	19 (54.3)	44 (43.1)	.344
Child-Pugh score	11 (10–12)	10 (8–11)	.006
Child-Pugh class			.066
B	8 (22.9)	43 (42.2)	
C	27 (77.1)	59 (57.8)	
MELD score	24 (17–30)	16 (12–19)	<.001
MELD-Na score	27 (24–33)	18 (12–24)	<.001
Volume of paracentesis			.412
<3 L	15 (42.9)	57 (55.9)	
3–5 L	16 (45.7)	36 (35.3)	
≥5 L	4 (11.4)	9 (8.8)	
Albumin infusion dose			.184
0 g	2 (5.7)	19 (18.6)	
20 g	29 (82.9)	74 (72.5)	
40 g	4 (11.4)	9 (8.8)	
Diuretics use*	18 (51.4)	67 (65.7)	.194
Beta blocker use*	2 (5.7)	23 (22.5)	.049
Sodium (mEq/L)	129 (124–134)	134 (129–137)	.006
Creatinine (mg/dL)	0.97 (0.63–1.29)	0.95 (0.66–1.00)	.892
Bilirubin (mg/dL)	11.1 (2.5–18.8)	5.0 (1.3–5.7)	.005
Albumin (mg/dL)	2.7 (2.5–3.0)	2.8 (2.5–3.2)	.171
ALT (U/L)	166 (28–99)	51 (20–55)	.259
AST (U/L)	472 (54–295)	89 (41–100)	.177
PT (INR)	2.02 (1.35–2.18)	1.51 (1.22–1.74)	.011
CRP (mg/dL)	5.29 (1.80–7.81)	3.58 (0.93–4.64)	.043
WBC count (x10^3/μL)	9.13 (5.97–11.59)	6.75 (3.84–8.76)	.005
AKI (Yes)	23 (65.7)	9 (8.8)	<.001

Abbreviations: See Table 1.

* On the day of paracentesis.

Values are expressed as mean ± standard deviation (SD), mean with interquartile range (IQR), or number (%).

Table 4

Prognostic factors associated with postparacentesis early mortality.

Variables	Univariate HR (95% CI)	*P* value	Multivariate* HR (95% CI)	*P* value
Age (yr)	0.99 (0.96–1.02)	.778		
Female (vs male)	0.95 (0.44–2.03)	.904		
Etiology (viral vs others)	0.69 (0.32–1.47)	.340		
HCC (yes vs no)	1.66 (0.69–4.01)	.255		
PVT (yes vs no)	155 (0.80–3.03)	.192		
Child-Pugh class C (vs B)	2.16 (0.98–4.78)	.055		
MELD-Na score	1.14 (1.09–1.20)	<.001	1.11 (1.02–1.20)	.009
Paracentesis volume (>3 L vs <3 L)	1.46 (0.75–2.86)	.261		
Albumin infusion (yes vs no)	1.67 (0.87–3.20)	.122		
Diuretics use† (yes vs no)	0.56 (0.29–1.10)	.096		
Beta blocker use† (yes vs no)	0.23 (0.05–0.96)	.044		
ALT (U/L)	1.00 (1.00–1.00)	.010	1.00 (0.99–1.00)	.789
CRP (mg/dL)	1.06 (1.00–1.12)	0.037		
WBC count (x$10^3/\mu$L)	1.09 (1.03–1.16)	0.002	1.03 (0.93–1.15)	.512
AKI (yes vs no)	13.6 (6.6–27.8)	<0.001	11.12 (3.92–31.53)	<.001

Abbreviations: See Table 1.

* The variables that were statistically significant by univariate analysis were included in a multivariate analysis.

† On the day of paracentesis.

score, alanine aminotransferase levels, WBC count, and development of AKI. To determine whether each of these predictors was significantly associated with early mortality, we performed multivariate analysis. Subsequently, we found that a higher MELD-Na score (HR, 1.11; 95% CI, 1.02–1.20) and development of AKI (HR, 11.12; 95% CI, 3.92–31.53) remained as independent predictors for early mortality.

3.5. Comparison of early mortality rate according to presence of acute kidney injury in MELD-Na subgroups

When comparing early mortality after paracentesis using Kaplan–Meier survival curves, patients who developed AKI demonstrated significantly worse survival compared with those who did not. (Fig. 1) We also investigated early mortality depending on whether the patients had postparacentesis AKI in different prognostic subgroups stratified by MELD-Na score. Based on ROC curve analysis, patients were classified into 2 groups by MELD-Na score (>26 and ≤26 points). Patients with MELD-Na score >26 showed significantly higher early mortality compared to those with MELD-Na score ≤26 (52.9% vs 16.5%, $P < .001$). However, patients who underwent paracentesis and then developed AKI, regardless of which MELD-Na subgroups the patients belonged to, exhibited significantly higher early mortality than patients who did not develop AKI (MELD-Na

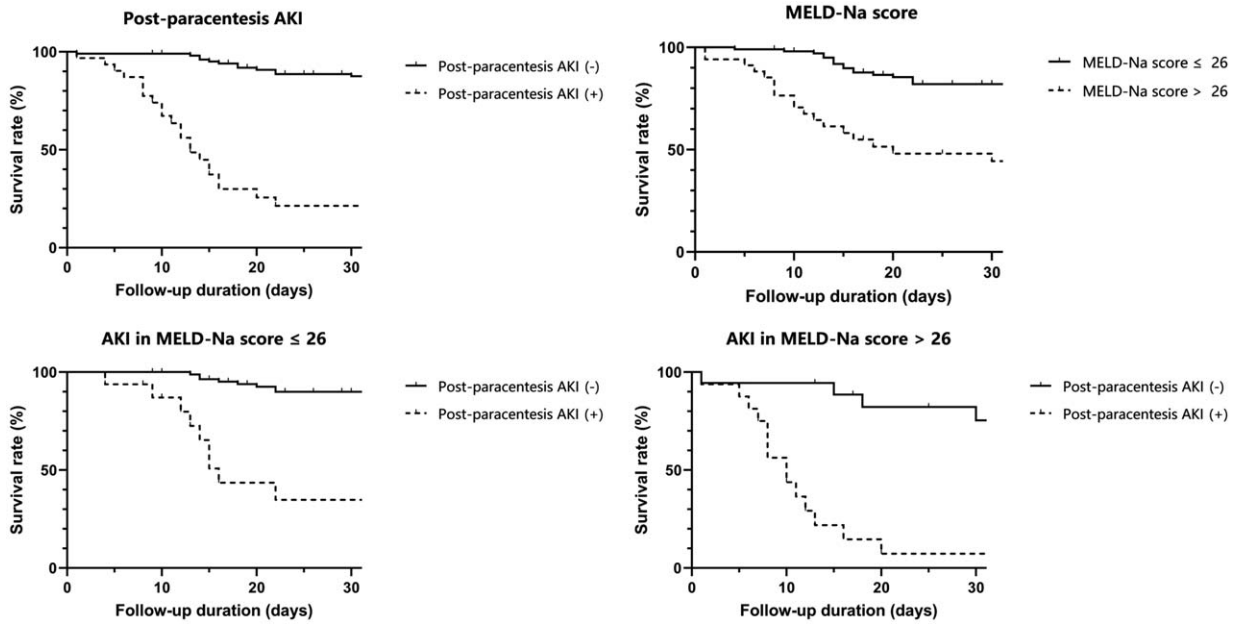

Figure 1. Comparison of early mortality rate according to presence of postparacentesis AKI in MELD-Na subgroup. Kaplan–Meier survival curves of patients with postparacentesis AKI or MELD-Na score >26 points show a significantly higher early mortality compared to those without. Patients who developed postparacentesis AKI, regardless of which MELD-Na subgroup they belonged to (>26 or ≤26 points), exhibited significantly higher early mortality than patients who did not develop AKI.

score >26: 87.5% vs 22.2%, $P < .001$; MELD-Na score ≤26: 56.3% vs 9.2%, $P < .001$).

4. Discussion

An initial objective of the present study was to investigate the prevalence and outcomes of postparacentesis AKI in cirrhotic patients. Hemodynamic abnormality usually occurs after the development of splanchnic and systemic vasodilatation in patients with portal hypertension. The vasodilatation results in a decrease in effective arterial blood volume. As cirrhosis progresses, compensatory mechanisms to maintain a reasonable arterial pressure do not work properly, and patients experience further decreased renal blood flow.[11] Patients with end-stage liver disease are both predisposed to renal hypoperfusion and ill-equipped to respond to it.[12] Therefore, AKI is one of the most frequently stated problems in patients with advanced cirrhosis and is mainly associated with a poor prognosis.[13] However, in clinical care of cirrhotic patients, presence and severity of postparacentesis AKI has often been underestimated due to unappreciated flaws in the current conceptualization of AKI. Despite improved understanding of the precipitants of and physiology underlying AKI in cirrhosis, considerable confusion continues to surround its diagnosis. Seeking to remedy this failing and bring the approach to acute renal dysfunction in cirrhosis in line with evolving conceptions of AKI, a working group composed of members of the IAC and the Acute Dialysis Quality Initiative (ADQI) network recommended adaptation of the Acute Kidney Injury Network (AKIN) criteria to redefine AKI, instead of using the traditional IAC definition which employs a fixed creatinine cutoff of >1.5 mg/dL.[14] In our study, we found an AKI incidence of 23.4% within 7 days following paracentesis among cirrhotic patients with ascites. The AKI incidence in this investigation was higher compared to that of Peron et al, who reported a 14% AKI incidence, where AKI was defined by serum creatinine >1.5 mg/dL.[15] Our finding is also contrary to a prospective study of 206 cirrhotic patients, which showed AKI development of 17% using the same definition of fixed creatinine.[12] However, there were similarities in prevalence with some previous studies.[16,17] The wide range in prevalence seems to be due to different study populations and varying definitions of renal dysfunction. We suggest that an increase in serum creatinine as small as 0.3 mg/dL or elevation more than or equal to 50% compared to the baseline value is a clinically meaningful definition of AKI. We also suggest that clinical prognosis can be classified differently according to this criterion. Our results demonstrate that the incidence of early mortality was significantly higher for patients with AKI than for those without AKI (71.9% [23/32 patients] vs. 11.4% [12/105 patients], $P < .001$). Additionally, postparacentesis AKI was an independent predictor of early mortality. This study confirms that an advanced MELD-Na score was found to be a significant risk factor for AKI development after paracentesis. These results are in accordance with recent studies indicating the contribution of MELD-Na scores in predicting AKI.[18,19] In contrast to earlier findings, no significant association was evident between paracentesis volume and AKI development. This inconsistency might be due to a relatively lower proportion of large-volume paracentesis (LVP) cases (exceeding 5L) in the current study, compared to that of Patil et al who reported that the median volume of fluid drained per paracentesis was 6L (range 1–20L).[6] A paracentesis volume exceeding 5L has been implicated as the cause of orthostatic hypotension and renal insufficiency, which may progress to AKI, as a part of PICD.[20] It has been reported that PICD occurs in up to 80% of cases when a LVP is performed without supplementation of an intravascular volume expander. Intravenous albumin is recommended as a volume expander, which can reduce the incidence of PICD as much as 15% to 35%.[5] For LVP of more than 5 L, infusion of 6 to 8 g of intravenous albumin per liter of drained ascites is recommended. When less than 5 liters of ascites are removed, dextran-70 (8 g/L of ascites removed) or polygeline (150 mL/L of ascites removed) show efficacy similar to that of albumin. Although the risk of postparacentesis circulatory dysfunction is relatively low in patients undergoing paracentesis of less than 5 L of ascites, intravenous albumin can be still considered in these patients because of concerns about use of alternative plasma expanders.[21] We classified patients into 3 groups based on paracentesis volume (<3, 3–5 and ≥5 liters), and the albumin was also infused differently at a dose of 0 g, 20 g, and 40 g. We recognized that a higher albumin infusion dose, over 40 g, is usually required in LVP cases exceeding 5L volume because a dose of 40 g would be the minimum when ascites of 5L is drained. However, the Korean National Health Insurance Service applies guidelines for reimbursement of albumin use at a dose of 20 g (20% solution, 100 mL 1 bottle) after 3 to 5-liter paracentesis. It also permits 40 g (2 bottles) albumin use after paracentesis of >5 liter. For this reason, in our cohort, only up to 40 g of albumin was administered in the patients undergoing LVP.

The current study has identified that even if the paracentesis volume was less than 5L, the incidence of paracentesis-induced AKI was not lower than expected, and there was no significant difference compared to the cases where paracentesis of 5L or more was performed (AKI group vs. non-AKI group: 9.4% vs 9.5%, $P = .01$). Additionally, this study found no significant difference in AKI incidence depending on whether or not albumin was administered (AKI group vs non-AKI group: 15.6% vs 15.2%, $P = .01$). Taken together, these findings suggest that in cases where a relatively small amount of ascites, less than 5 L, is drained, and even when the volume expander is administered, AKI does not occur less frequently. Contrary to expectations, use of diuretics was not an independent risk factor for AKI development when multivariate logistic regression analysis was performed. Questions have been raised about the effect of diuretics on postparacentesis AKI. In clinical practice, discontinuation or at least reduction of diuretics happens frequently due to electrolyte imbalances and progressive renal dysfunction.[22] However, it seems more likely that AKI onset is also related to aging, comorbid health conditions, dosage, or drug-drug interactions, rather than only to diuretics, although their use should be considered as an aggravating factor. Overall, the most important clinically relevant finding is that post-paracentesis AKI was associated with significantly higher early mortality when analyzed by observing 2 subgroups divided at a MELD score of 26. Hence, it could conceivably be suggested that paracentesis-induced AKI could be a possible predictive factor for early mortality even in patients with relatively preserved liver function.

The major limitation of this study stems from its retrospective design, which potentially introduced biases to patient selection and data measurement. Secondly, the study included a high proportion of HCC patients. This could affect the overall mortality of our cohort and make our findings less generalizable. However, this study did not find any significant difference in terms of early mortality according to the presence of HCC.

Notwithstanding these limitations, this study offers some insight into AKI diagnosis criteria that were recently adapted in clinical practice. The revised ICA-AKI criteria are useful in facilitating earlier diagnoses while broadening the population of cirrhotic patients considered to have AKI. The results of this study also confirmed that current AKI criteria could allow for critical distinction of prognoses in cirrhotic patients who have undergone paracentesis.

In conclusion, postparacentesis AKI occurred frequently in cirrhotic patients. Furthermore, it was associated with early mortality. Baseline MELD-Na score was associated with AKI, indicating that careful attention is required for those with a higher MELD-Na score who are being considered for therapeutic paracentesis. We also recognize that comprehensive and balanced future research is required to validate the diagnostic and prognostic efficacy of AKI criteria in this complex and precarious condition.

Author contributions

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