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Original Article

A hemodynamic analysis of renal dysfunction in 79 patients with liver cirrhosis

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Abstract: Hemodynamic changes occur in cirrhosis patients with early renal damage. We retrospectively analyzed the data of 79 patients hospitalized with liver cirrhosis between June 2016 and January 2019 at the Chinese Rocket Force Characteristic Medical Center. According to their estimated glomerular filtration rate and urinary protein, the patients were divided into two groups: the renal dysfunction group and the non-renal dysfunction group. Univariate and multivariate logistic analyses were performed on the patients' sex, age, type of cirrhosis, complications, alanine aminotransferase, total bilirubin, serum albumin, creatinine, diameter of bilateral renal arteriovenous, diameter of the hepatic vein, diameter of the portal vein, and anatomical flow. The results of the univariate analysis showed that serum albumin (P=0.001) and the diameter of the left renal artery (P=0.03) were significantly different between cirrhotic patients with renal dysfunction and those without renal dysfunction (P < 0.05). The results of a binary logistic regression analysis showed that the serum albumin level (odds ratio=0.878, 95% confidence interval: 0.802-0.961) and the diameter of left renal artery (odds ratio=0.138, 95% confidence interval: 0.030-0.639) were protective factors for renal dysfunction in liver cirrhosis (odds ratio < 1, P < 0.05). Conclusions: The serum albumin level and the diameter of the right renal artery are protective factors for renal dysfunction in cirrhosis. Renal artery contraction and insufficient renal blood perfusion occur before the complications of hepatorenal syndrome occur in patients with advanced cirrhosis.

Keywords: Liver cirrhosis, renal dysfunction, computed tomography angiography, risk factors, hemodynamics

Introduction

The human liver is closely related to the kidneys. In traditional Chinese medicine there is a saying regarding "the same origin of the liver and kidney". In Western medicine, there is also the concept of "hepato-renal disorder" [1]. Clinically, patients with chronic liver disease can have multiple kidney injuries, which need to be vigilantly monitored by clinicians [2].

In this study, we retrospectively analyzed the data of patients with cirrhosis hospitalized in the Chinese Rocket Force Characteristic Medical Center. A hemodynamic analysis was carried out to provide guidance for the clinical diagnosis and treatment of liver cirrhosis patients with early renal dysfunction.

Materials and methods

Research subjects

We collected data from hospitalized patients who were diagnosed with liver cirrhosis from June 2016 to January 2019 at the Chinese Rocket Force Characteristic Medical Center and who underwent abdominal CTA or an enhanced CT examination. The data from these patients were retrospectively analyzed. The patients who had been hospitalized repeatedly were included in this study only once. All the patients were diagnosed with cirrhosis according to their medical history, symptoms, signs, laboratory examinations and imaging examinations. The exclusion criteria were as follows: (1) chronic kidney diseases; (2) liver or kidney transplantation; (3) essential hypertension or

diabetes; (4) a recent history of nephrotoxic drugs; (5) diseases causing myocardial infarction or cerebral infarction needing anticoagulation; (6) shock; (7) malignant tumors such as liver cancer; and (8) severe infection.

Methods

Blood and urine laboratory tests: We selected the first fasting blood sample after admission to test the following laboratory parameters: alanine aminotransferase, total bilirubin, albumin, fasting blood sugar, creatinine, white blood cells, percentage of neutrophils, and INR (international normalized ratio of prothrombin). We collected the first morning urine for the urine protein test. The above tests were completed by the Laboratory Department of the Chinese Rocket Force Characteristic Medical Center.

We calculated the Model for End-Stage Liver Disease (MELD) score with the formula R=9.6 × ln (creatinine mg/dl) + 3.8 × ln (bilirubin mg/dl) + 11.2 × ln (INR) + 6.4 × Pathogeny (Pathogeny: Biliary or alcoholic cirrhosis is 0, while other causes of cirrhosis, such as viruses, are 1) [3].

Imaging examinations: The abdominal CTA and enhanced CT examinations were performed by the Radiology Department of the Chinese Rocket Force Characteristic Medical Center. We read the CT films to determine whether there were spleen-kidney shunts or gastro-kidney shunts and measured the diameters of the bilateral renal arteries and veins, the hepatic vein, and the portal vein.

Determination of renal dysfunction

According to the serum creatinine level, we calculated the glomerular filtration rate using the Modification of Diet in Renal Disease (MDRD) formula as follows: eGFR [ml·min^{-1}·(1.73 m^2)$^{-1}$] =186 × [Scr (mg/dl)]$^{-1.154}$ × [Age (years)]$^{-0.203}$ × Sex (Male=1.000, Female=0.742). Based on the recommendations of the Kidney Disease Outcomes Quality Initiative (K/DOQI) Expert Group of the American Kidney Foundation, we included the patients with eGFR < 90 ml·min^{-1}·(1.73 m^2)$^{-1}$ in the group with renal dysfunction [4, 5].

We also included the patients with positive urinary protein in the group with renal dysfunction.

Statistical methods

SPSS 25.0 statistical software was used for statistical analysis.

Univariate analysis: The measurement data were analyzed by the Kolmogorov-Smirnov method to test for the normality of the distribution. Normally distributed data are expressed as the means ± standard deviation. A *t*-test was used to compare the data between two groups. The nonnormally distributed data are expressed as the medians and interquartile ranges. The comparison between the data of two groups was performed using the Mann-Whitney U test. The count data are expressed as percentages. The comparison between the data between two groups was tested using a chi-square test. A P value < 0.05 indicated that there was a statistically significant difference.

Multivariate analysis: The possible risk factors for renal dysfunction were analyzed by binary logistic regression. In the forward analysis, the likelihood ratio (LR) method was used for the analysis. The entry standard was 0.05 and the deletion criterion was 0.10. P < 0.05 indicated a correlation.

Results

General information

Data from a total of 79 patients with complete data were collected, including 52 males, 27 females, 62 patients younger than 60 years old, 17 older than 60 years old, 12 patients with viral hepatitis cirrhosis, 7 patients with alcoholic cirrhosis, 36 patients with Budd-Chiari syndrome, 9 patients with autoimmune cirrhosis, 1 patient with drug-induced cirrhosis, 1 patient with hepatolenticular degeneration, 1 patient with portal cavernous degeneration and 12 patients with unexplained cirrhosis. There were 15 patients with gastro-renal shunts and 28 patients with splenorenal shunts. With an eGFR < 90 ml·min^{-1}·(1.73 m^2)$^{-1}$ or positive urinary protein as the criteria for judging renal dysfunction, there were 31 patients with renal dysfunction and 48 patients without renal dysfunction.

Results of the univariate analysis

Sex, age, etiology of the cirrhosis, complications and other count data were analyzed using

Table 1. Chi-square test results of sex, age, and complications

Enumeration data		Case group (n=31)	Control group (n=48)	Statistic of chi-square test	*P* value
Sex, n (%)	Male	19 (61.29%)	33 (68.75%)	0.466	0.495
	Female	12 (38.71%)	15 (31.25%)		
Age, n (%)	< 60 years	24 (77.42%)	38 (79.17%)	0.034	0.854
	≥ 60 years	7 (22.58%)	10 (20.83%)		
Types of cirrhosis, n (%)	Budd-Chiari syndrome	14 (45.16%)	22 (45.83%)	0.003	0.953
	Others	17 (54.84%)	26 (54.17%)		
Hepatic encephalopathy, n (%)	Yes	13 (41.94%)	17 (35.42%)	0.34	0.56
	No	18 (58.06%)	31 (64.58%)		
Gastrointestinal hemorrhage, n (%)	Yes	16 (51.61%)	24 (50%)	0.02	0.889
	No	15 (48.39%)	24 (50%)		
Hypersplenism, n (%)	Yes	22 (70.97%)	34 (70.83%)	0.000165	0.99
	No	9 (29.03%)	14 (29.17%)		
Hydrocele, n (%)	Yes	17 (54.84%)	26 (54.17%)	0.003	0.953
	No	14 (45.16%)	22 (45.83%)		
Splenic and renal shunts, n (%)	Yes	8 (25.81%)	20 (41.67%)	2.071	0.15
	No	23 (74.19%)	28 (58.33%)		
Gastric and renal shunts, n (%)	Yes	7 (22.58%)	8 (16.67%)	0.428	0.513
	No	24 (77.42%)	40 (83.33%)		
	No	16 (51.61%)	20 (41.67%)		

a chi-square test, as shown in **Table 1**. The measurement data of the laboratory parameters, the diameters of the bilateral renal arteries and veins, and the diameters of the hepatic arteries and portal veins, were compared with T-tests or U-tests for two independent samples as shown in **Table 2**. The results showed that there were significant differences in serum albumin levels and the diameter of the left renal artery between the renal dysfunction group and the non-renal dysfunction group ($P < 0.05$), as shown in **Table 2**. There was no significant difference in sex, age, type of cirrhosis, hepatic encephalopathy, gastrointestinal hemorrhage, hypersplenism, peritoneal effusion, spleen-kidney and gastro-renal shunts, alanine aminotransferase levels, total bilirubin levels, fasting blood sugar levels, the INR, white blood cell counts, percentages of neutrophils, MELD scores, diameters of the right renal artery, diameters of the bilateral renal vein, diameters of the hepatic artery, or the diameters of the portal vein in the renal dysfunction group and the non-renal dysfunction group ($P>0.05$), as shown in **Tables 1** and **2**.

Multivariate analysis results

According to the criterion of whether renal dysfunction was present, the 79 patients with liver cirrhosis were divided into two groups: the group with renal dysfunction and the group without renal dysfunction. The serum albumin level, the presence of spleen-kidney and gastro-renal shunts, the bilateral renal artery diameter and other possible risk factors in the two groups were included as independent variable X, and the occurrence of renal dysfunction was the response variable Y (Y=0, Y=1) in the logistic regression model. The risk factors and assignments of the 79 patients with liver cirrhosis are shown in **Table 3**.

The results showed that the serum albumin level and the diameter of the left renal artery were protective factors against renal dysfunction in patients with cirrhosis.

In the 31 patients with liver cirrhosis and renal dysfunction, the level of serum albumin was 31.2548 ± 6.45243 g/L, while the serum albumin level in the 48 patients with cirrhosis without renal dysfunction was 36.4854 ± 5.65192 g/L. The *t*-test for the two independent samples showed that there was a significant difference (the statistic -3.798, and the *P* value close to 0. The T value was negative, indicating that the mean of the case group was smaller than the mean of the control group). The logistic regression model was adjusted for the diameter of

Table 2. The analysis results of the measurement data

Measurement data	Case group (n=31)	Control group (n=48)	Statistical method	Statistic	*P* value
Alanine aminotransferase	M=22.9, Q=16.4	M=27.5, Q=18.55	Mann-Whitney U test	588.5	0.118
Total bilirubin	M=29.85, Q=46.18	M=26.835, Q=35.035	Mann-Whitney U test	676	0.495
MELD score	12.8387 ± 4.06691	M=12, Q=5	Mann-Whitney U test	621	0.215
Fasting blood glucose	M=5.16, Q=1.69	M=5.135, Q=1.815	Mann-Whitney U test	710.5	0.737
INR	1.3471 ± 0.28531	M=1.26, Q=0.335	Mann-Whitney U test	714	0.763
White blood cells	5.3684 ± 3.25425	M=3.705, Q=2.4075	Mann-Whitney U test	550.5	0.52
Diameter of left renal vein	10.8581 ± 3.26188	M=10.8, Q=3.2	Mann-Whitney U test	676	0.495
Serum albumin	31.2548 ± 6.45243	36.4854 ± 5.65192	T-test	-3.798	0.000289
Percentage of neutrophils	61.5032 ± 18.26305	64.0042 ± 9.54748	T-test	-0.797	0.428
Diameter of right renal artery	4.9065 ± 1.01388	5.3023 ± 0.79541	T-test	-1.937	0.056
Diameter of left renal artery	5.0839 ± 1.08323	5.5875 ± 0.80889	T-test	-2.362	0.021
Diameter of right renal vein	9.929 ± 2.3953	9.2021 ± 2.34933	T-test	1.333	0.187
Diameter of hepatic artery	5.1387 ± 1.32431	5.0792 ± 1.41074	T-test	0.188	0.852
Diameter of portal vein	14.6296 ± 5.64193	14.2634 ± 2.54163	T-test	0.364	0.717

(Comments: INR: international standardized ratio of prothrombin; MELD: Model for End-Stage Liver Disease; M: median: Q: quartile spacing).

Table 3. Logistic regression analysis of the risk factors and assignment

Factors	Variable name	Assignment statement
Diameter of right renal artery	X1	
Diameter of left renal artery	X2	
Serum albumin	X3	
Shunt	X4	No=1, Yes=2
Renal dysfunction	Y	No=0, Yes=1

Table 4. Results of the logistic regression analysis

	OR (95% CI)	*P* value
Diameter of left renal artery	0.514 (0.281-0.938)	0.030
Serum albumin	0.862 (0.787-0.944)	0.001

the bilateral renal artery and the presence of a shunt. The results showed that the risk of renal dysfunction in patients with liver cirrhosis with higher serum albumin levels was reduced (OR=0.862, 95% CI: 0.787-0.944), as shown in **Table 4**.

In the 31 patients with renal dysfunction, the diameter of the left renal artery was 5.0839 ± 1.08323 mm. In the 48 patients without renal dysfunction, the diameter of the left renal artery was 5.5875 ± 0.80889 mm. The *t*-test for two independent samples showed that there was a significant difference (the statistic was -2.362, P=0.021 < 0.05. The T value was negative, indicating that the mean of the case group was less than the mean of the control group). The logistic regression model was adjusted for the presence of a shunt, the serum albumin level, and other factors. The results showed that in patients with liver cirrhosis, the risk of renal dysfunction was reduced in patients with wider diameters of the left renal artery (OR=0.514, 95% CI: 0.281-0.938), as shown in **Table 4**.

Discussion

Liver disease is closely related to nephropathy. In decompensated cirrhosis, there are many types of vasoactive factor imbalances in vivo, leading to changes in systemic hemodynamics and a decrease in renal blood flow [6, 7], and resulting in insufficient renal artery perfusion and a decrease in the glomerular filtration rate. The inactivation of active factors affecting vasoconstriction in the liver is reduced, which leads to vasoconstriction of the renal cortex and promotes a decrease in the glomerular filtration rate. If the disease continues to develop, hepatorenal syndrome may occur, which has a high mortality and a poor prognosis [8, 9]. In addition, renal dysfunction can also affect the use of drugs to treat liver cirrhosis [10, 11]. For example, the key points of the *Clinical Practice Guidelines* on the management of hepatitis B virus infection of the European Association for the Study of the Liver suggests that patients receiving tenofovir treatment should be monitored regularly for renal function, and the drugs

entecavir and tenofovir-alafenamide-fumaric acid should be replaced when necessary.

This study retrospectively analyzed the renal dysfunction data of 79 patients with cirrhosis and analyzed their hemodynamics. The results showed that the serum albumin level and the diameter of the left renal artery were protective factors against renal dysfunction in patients with cirrhosis.

1. Serum albumin can maintain the plasma colloid osmotic pressure, maintain the circulating blood volume, improve the renal blood flow, and maintain the glomerular filtration rate [12].

2. At present, the study of renal hemodynamics in patients with liver cirrhosis is mostly based on a comparison of CT examinations between normal people and patients with liver cirrhosis, but our research objective was to compare liver cirrhosis between the renal dysfunction group and the non-renal dysfunction group. In this study, the imaging data of 79 patients with cirrhosis who underwent abdominal CTA or enhanced CT were analyzed. In a univariate analysis, the diameters of the bilateral renal arteries in patients with renal dysfunction were smaller than those in patients without renal dysfunction. In a multivariate binary logistic regression study, we found that patients with a wider diameter of the left renal artery had a lower risk of renal dysfunction. This finding was considered to be related to blood perfusion. People with wider arterial diameters have better kidney blood perfusion, and the risk of renal dysfunction is lower. According to the results of our univariate and multivariate analyses, hemodynamic changes occurred in patients with cirrhosis, and blood flow shunting to the kidney decreased, resulting in bilateral renal artery contraction. This finding is consistent with previous studies on the redistribution of blood flow in the late stage of cirrhosis resulting in insufficient renal blood perfusion, and the pathogenesis of hepatorenal syndrome. None of the 79 patients in this study had hepatorenal syndrome, indicating that renal artery contraction and insufficient renal blood perfusion had occurred before the complications of hepatorenal syndrome in patients with advanced cirrhosis. Clinically, attention should be paid to maintaining the effective blood volume in patients and preventing renal vasoconstriction induced by large amounts of ascites and excessive diuresis.

When portal hypertension reaches a certain level in patients with cirrhosis, shunts may occur from the portal vein to the inferior vena cava, such as spontaneous spleno-gastric-renal shunts. These can reduce portal vein pressure and the ascites volume, but it may also lead to hepatic encephalopathy [13]. In this study, 79 patients were studied, with 31 patients in the renal dysfunction group, 15 of whom had gastro-renal or spleen-kidney shunts, and 48 patients in the non-renal dysfunction group, 28 of whom had shunts. A chi-square test was performed on the data from the two groups. The result showed that the *P* value was 0.386, which means there was no significant difference between the renal dysfunction group and the non-renal dysfunction group. This may be caused by too few samples. We can perform a further study with a larger sample size to clarify whether anatomical flow has an impact on renal function.

Changes in renal perfusion may precede abnormal laboratory test results [14]. This study is a retrospective study. The abdominal CTA and enhanced CT examinations of the patients were completed. We could only analyze the data of the anatomical flow, the diameters of the bilateral renal arteries and veins, and the diameters of the hepatic arteries and portal veins. We intend to carry out a prospective study to analyze the real-time renal hemodynamics during abdominal CTA and enhanced CT examinations to provide a basis for the early detection, clinical diagnosis, and treatment of patients with liver cirrhosis and related renal dysfunction.

Acknowledgements

This study was approved by the medical ethics examination of China Rocket Force Characteristic Medical Center.

Disclosure of conflict of interest

None.

Abbreviations

CT, Computed Tomography; CTA, Computed Tomography Angiography; CI, confidence interval; eGFR, estimated glomerular filtration rate; INR, international standardized ratio of prothrombin; K/DOQI, Kidney Disease Outcomes Quality Initiative; LR, likelihood ratio; MELD, Model for End-Stage Liver Disease; MDRD,

Modification of Diet in Renal Disease; OR, odds ratio; Scr, Serum creatinine.

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