

Cardiac health in patients with hepatitis B virus-related cirrhosis

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Abstract

Not only alcoholic cirrhosis related to cardiac dysfunction, cirrhosis caused by nonalcoholic etiology including hepatitis B virus (HBV) infection also related to impaired cardiac health. The aims of present study were to perform a noninvasive evaluation of cardiac function and to evaluate exercise performance in HBV related cirrhotic patients without typical symptoms of cardiac disease.

Seventy-nine HBV related cirrhotic patients and 103 matched subjects without a previous history of cardiac involvement were recruited. Clinical examination and cardiac health evaluation were performed. The incidence, risk factors of cardiac dysfunction and exercise tolerance were investigated.

A correlation between QTc interval and model for end-stage liver disease score ($R=0.239$, $P=.018$) was detected, however, the connection between QTc prolongation and the severity of liver disease was uncertain. Patients with HBV related cirrhosis had a tendency toward left ventricular wall thickening ($P=.007$). Forty-one patients (51.90%) were in accordance with the definition of cirrhotic cardiomyopathy, and a significant increase in the incidence of cardiac diastolic dysfunction (CDD) could be found with increasing Child-Pugh grade ($P=.004$). HBV related cirrhotic patients with CDD had a higher level of pro-brain natriuretic peptide ($P=.025$), international normalized ratio ($P=.010$) Child-Pugh score ($P=.020$), and a higher proportion of ascites ($P<.001$). The higher Child-Pugh score (odds ratio = 1.662, $P=.010$) was an independent diagnostic predictor of CDD. The cardiac depression and exercise tolerance also got worse with increasing Child-Pugh score ($P<.001$).

Impaired cardiac health was common in HBV related cirrhotic patients. Cardiogenic factors must be carefully considered in the integral therapy of cirrhosis. Hepatology physicians should lay emphasis on exercise training in daily life.

Abbreviations: ALT = alanine aminotransferase, AST = aspartate transaminase, BNP = brain natriuretic peptide, CDD = cardiac diastolic dysfunction, CHB = chronic hepatitis B, CK = creatine kinase, EF = ejection fraction, HBV = hepatitis B virus, INR = international normalized ratio, IVST = interventricular septum thickness, LVEDD = left ventricular end-diastolic diameter, LVESD = left ventricular end-systolic diameter, LVPWT = left ventricular posterior wall thickness, MELD = model for end-stage liver disease.

Keywords: cardiac health, cirrhotic cardiomyopathy, hepatitis B virus, liver cirrhosis

1. Introduction

Hepatitis B virus (HBV) infection is the most common cause of liver cirrhosis in the Asian-Pacific region. Patients with either

compensated or decompensated liver cirrhosis may face several complications including impaired cardiac health. It was ever believed that cardiac dysfunction was more common in patients with alcoholic cirrhosis.^[1] However, recent studies arrived at the conclusion that potential cardiac complications are also connected to nonalcoholic cirrhosis.^[2,3] Patients with liver cirrhosis are under the condition of hemodynamic disorder, including decreased systemic vascular resistance, volume redistribution, and impaired cardiac function.^[1-5] Meanwhile, impaired cardiac function may also induce further liver injury.^[6] The cross-talk between cardiac and hepatic dysfunction can lead to high mortality, as the data showed that impaired heart function resulted in up to 25.8% of cirrhotic patients' deaths.^[7]

According to the diagnostic criteria by the Working Party for cirrhotic cardiomyopathy (CCM), chronic heart dysfunction can be defined as abnormal systolic responses to stress and/or diastolic dysfunction at rest without primary cardiac disease.^[5] However, cirrhotic patients with cardiac dysfunction always present a serious of untypical symptoms. At the same time, the medical treatment like nonselective beta-blockers, which could impact systemic hemodynamics, was often prescribed for cirrhotic patients with portal hypertension. Based on this fact, cardiac health should be paid attention in the integral treatment of liver cirrhosis. Currently, little is known about the exact incidence and risk factors of cardiac dysfunction in the cirrhotic populations. Therefore, the primary aim of this study is to evaluate the cardiac function, by serum markers, electrocardiogram (ECG) and ultrasound cardiogram (UCG), in the patients

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with HBV related cirrhosis, which is most common in Asian-Pacific region. Additionally, we further assessed the exercise tolerance and cardiac depression in patients with HBV related cirrhosis, as few studies on physical activity, which is associated with quality of life and reduced cardiac mortality,^[8] were ever reported in cirrhotic patients.

2. Methods

2.1. Patients and study design

From January 1, 2017 to October 31, 2017, the data from 158 HBV related cirrhotic patients with atypical cardiac manifestations were reviewed. Atypical cardiac manifestations referred to the absence of typical symptoms (breathlessness, orthopnea, paroxysmal nocturnal dyspnea) and specific signs (elevated jugular venous pressure, third heart sound, and laterally displaced apical impulse).^[9] Diagnosis of liver cirrhosis was based on clinical observations, laboratory parameters, and imageology examination. The fibrosis scores of aspartate aminotransferase-to-platelet ratio index and Fibrosis 4 Score, tissue stiffness or liver biopsy if necessary was used to evaluate the morphology of liver.^[10] For the present analysis, 79 patients were excluded from the study, including 12 patients with evidence of primary liver cancer, 32 patients with a history of hypertension, diabetes mellitus or primary cardiovascular disease, 15 patients with a history of long-term alcohol use, 7 patients suffering with uncontrolled extrahepatic diseases (severe infection, hemorrhage, and anemia), and 13 patients with incomplete data on cardiac function or lost for follow-up. The Child-Pugh score and the model for end-stage liver disease (MELD) score were used to evaluate the severity of liver.

The 103 matched chronic hepatitis B (CHB) patients who followed up in our institute during the corresponding period were enrolled as controls. CHB was defined as:

- (1) HbsAg seropositive ≥ 6 months;
- (2) Active HBV replication (positive HBeAg with HBV DNA $\geq 20,000$ IU/ml or negative HBeAg with HBVDNA ≥ 2000 IU/ml);
- (3) Raised alanine aminotransferase (ALT) level.^[11] Antiviral treatment, nucleos(t)ide analogs or peg-IFN, respectively was prescribed according to APASL guideline in CHB patients.^[11]

In order to choose the best antiviral treatment, a series of examinations including mental health, thyroid function, 6-minutes walking test and cardiac depression scale were evaluated before starting antiviral treatment.

Recruited CHB patients as control group, by contrast, achieved sustained virological response without evidence of advanced fibrosis. The Child-Pugh score and the MELD score were used to evaluate the severity of liver disease.

This research project was performed in accordance with principles of the Helsinki Declaration and approved by the Human Ethics Committees of Shanghai Public Health Clinical Center, Fudan University.

2.2. ECG examination

The standard 12-lead ECG was performed on all of the enrolled subjects. The resting heart rate and the QT interval were recorded by the cardiologist. The QT interval was corrected by R-R interval and recorded in the form of QTc. QTc prolongation was defined as QTc value >440 milliseconds (ms) for men or QTc

value >460 ms for women. The electrolytes were in the normal range when ECG was performed.

2.3. UCG examination

The UCG was also performed on all of the enrolled subjects by ultrasound physician. Heart wall thickness, such as left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), interventricular septum thickness (IVST), and left ventricular posterior wall thickness (LVPWT), was assessed by 2-dimensional ultrasound. The left ventricular systolic and diastolic function, such as peak velocities of early diastolic filling (E wave)/late diastolic filling (A wave), E/A ratio, early diastolic annular velocity (E' wave), E/E' ratio, deceleration time (DT), ejection fraction (EF), and pulmonary artery systolic pressure, were evaluated by M-mode echocardiography and tissue doppler imaging.

Cardiac systolic dysfunction in cirrhotic patients connects to EF $<55\%$ and regional wall motion abnormality.^[5,12] The definition of cardiac diastolic dysfunction (CDD) is as follows^[13]:

- (1) Impaired relaxation refers to E/A ratios <1.0 and DT >250 ms;
- (2) Pseudonormalization refers to E/A ratios >1.0 , E/E' ratios >10 , and DT >150 ms;
- (3) Severe diastolic dysfunction refers to E/A ratios >1.5 , E/E' ratios >10 , and DT <150 ms.

2.4. Cardiac depression and exercise tolerance

The Chinese version of Cardiac Depression Scale (C-CDS) was used to evaluate the exercise confidence.^[14] It is a self-report questionnaire consisted of 25 items to assess the domains of sleep, anhedonia, uncertainty, mood, cognition, hopelessness, and inactivity.^[14]

Exercise tolerance was assessed by the 6-minute walk test (SMWT). SMWT was not performed on cirrhotic patients with Child-Pugh grade C due to the high incidence of complications, such as refractory ascites, mild-to-moderate encephalopathy, and coagulopathy. The SMWT was carried out according to American Thoracic Society guidelines.^[15] Briefly, patients were asked to walk at their usual pace along a straight 50-meter flat-way. The distance was recorded at the end of the 6 minutes. The patients were encouraged to walk as much as possible, but also allowed to quit if there were intolerance symptoms.

2.5. Statistical analysis

Statistical analysis was performed with SPSS 16.0 software. Continuous variables with normal distributions are reported as medians (quartiles) and analyzed by *t* test or 1-way ANOVA analysis of variance. Continuous variables with non-normal distributions are reported as medians (quartiles) and analyzed by Mann-Whitney *U* test or Kruskal-Wallis test. Categorical variables are expressed as frequencies, analyzed by chi-square test or Fisher exact test. Correlation between variables was determined by the Spearman rho test. Binary logistic regression was used for modeling the relationships between CDD and clinical parameters.

3. Results

3.1. General characteristics

Baseline characteristics including demographics and clinical parameters were recorded as shown in Table 1. All selected patients of HBV related cirrhosis were prescribed with nucleos(t)ide analogs according to the clinical practice. Seventy-nine cirrhotic

Table 1
Baseline characteristics of patients in controls and HBV related cirrhosis group.

Characteristics	Controls (N = 103)	HBV-cirrhosis (N = 79)	P-value
Age, yr	59 (41–67)	53 (41–62)	.763
Gender (Male/female)	57/46	50/29	.280
Platelet count (10 ⁹ /L)	133 (99–188)	80 (57–175)	<.001
ALT, U/L	55 (19–363)	43 (21–125)	.193
AST, U/L	50 (31–339)	75 (39–191)	.119
sCr, μmol/L	62.0 (52.9–70.4)	64.3 (49.8–79.9)	.826
TBil, μmol/L	26.7 (13.4–192.3)	69.2 (32.6–235.5)	<.001
TC, mmol/L	3.74 (2.91–4.10)	2.87 (1.83–3.36)	<.001
TG, mmol/L	1.31 (0.81–2.15)	0.92 (0.60–1.20)	<.001
CK, U/L	62 (41–82)	78 (46–99)	.444
Pro-BNP, pg/ml	262.69 (168.87–496.01)	1129.02 (339.81–1861.90)	.001
INR	1.10 (1.02–1.39)	1.48 (1.34–2.01)	<.001
HBeAg (Positive/negative)	51/52	34/45	.454
MELD score	NA	11.65 (8.53–17.87)	NA
Child-Pugh score	NA	8 (7–9)	NA

ALT = alanine aminotransferase, AST = aspartate transaminase, BNP = brain natriuretic peptide, CHB = chronic hepatitis B, CK = creatine kinase, HBV = hepatitis B virus, INR = international normalized ratio, MELD = model for end-stage liver disease, NA = not applicable, sCr = serum creatinine, TBil = total bilirubin, TC = total cholesterol, TG = triglyceride.

patients were enrolled in the cohort of this study. Meanwhile, 103 matched CHB patients were enrolled as controls. To avoid the bias between the 2 groups, the age, gender, status of e antigen, and viral loads were analyzed, there were no significant differences of age (53 [41–62] vs 59 [41–67] years, $P = .763$), gender (male/female [50/29] vs [57/46], $P = .280$), e antigen status (positive/negative [34/45] vs [51/52], $P = .454$) between HBV related cirrhotic patients and the control group. Viral loads of all patients in both groups were lower than 100 IU/ml.

3.2. ECG manifestations

There was no significant difference of rest HR between HBV related cirrhotic patients and the control group (75 [68–92] vs 74 [62–84] beats per minute, $P = .076$). However, HBV related cirrhotic patients had a longer QTc interval duration than the control group (437 [414–457] vs 420 [403–435] ms, $p < .001$). There was a weak correlation between QTc interval and MELD score ($R = 0.239$, $P = .018$, Fig. 1). However, the proportions of QTc prolongation in controls, Child-Pugh grade A, grade B, and

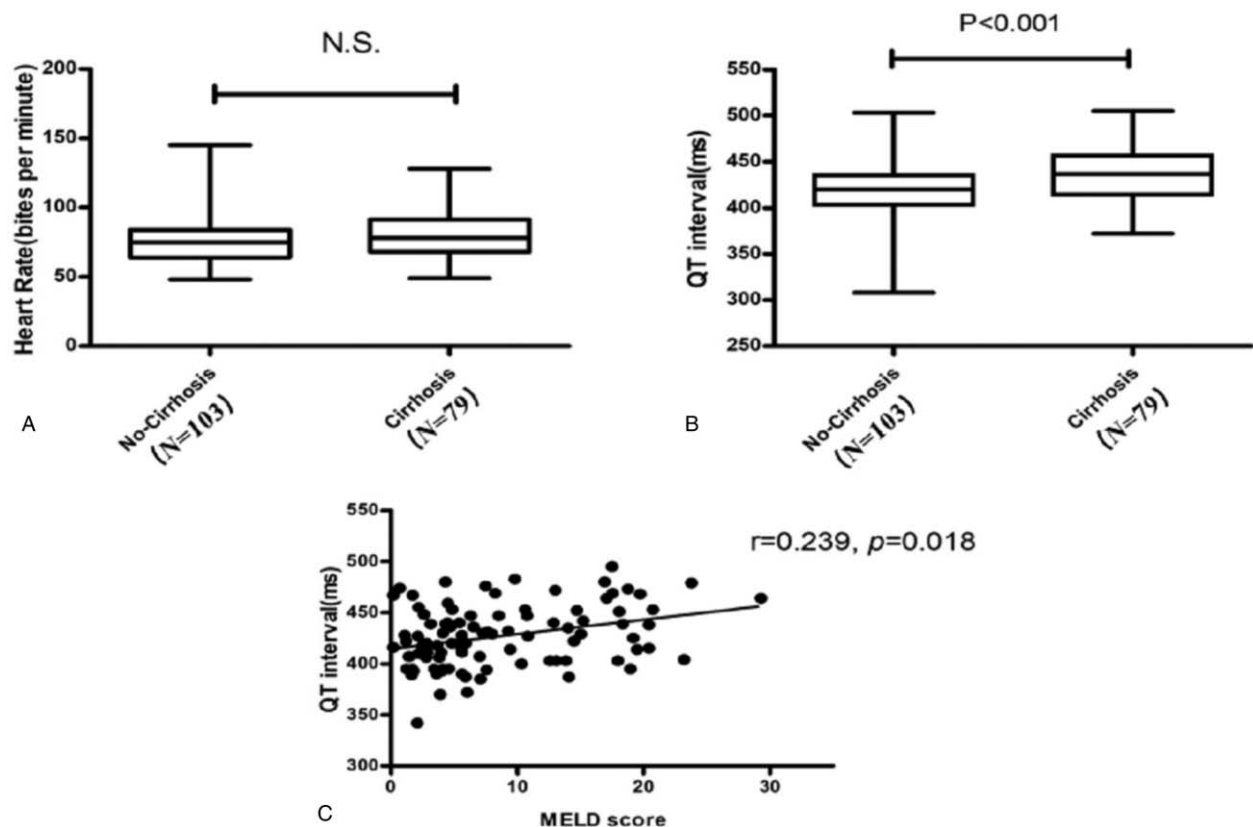


Figure 1. Electrocardiogram manifestation in patients with cirrhosis and no-cirrhosis groups. (A) Heart rate ($P = .076$), (B) QTc interval ($P < .001$), (C) Correlations between QTc interval and MELD score ($r = 0.239$, $P = .018$). MELD = model for end-stage liver disease.

Table 2**Ultrasound cardiogram findings.**

Items	Controls (N = 103)	HBV-cirrhosis (N = 79)			P-value
		Child A (N = 25)	Child B (N = 33)	Child C (N = 21)	
LVEDD, mm	46 (43–50)	46 (44–50)	48 (45–51)	48 (44–54)	.547
LVESD, mm	29 (26–32)	30 (28–34)	31 (28–32)	32 (30–35)	.007
IVST, mm	9 (8–10)	9 (9–10)	9 (9–10)	9 (9–10)	.602
LVPWT, mm	9 (9–10)	10 (9–11)	9 (8–10)	9 (9–10)	.138
PASP, mm Hg	31 (28–35)	32 (29–34)	30 (28–37)	32 (27–36)	.301
EF (%)	67 (64–70)	65 (61–69)	68 (64–68)	65 (59–70)	.298
CDD in total (N, %)	30, 29.13		38, 48.10		.008
		37, 28.91		31, 57.41	<.001
Impaired relaxation	22, 21.40	4, 16.00	17, 51.52	9, 42.86	
Pseudonormalization	4, 3.88	1, 3.03	0, 0.00	2, 9.52	.005*
Severe diastolic dysfunction	4, 3.88	2, 8.00	3, 9.09	0, 0.00	

CDD = cardiac diastolic dysfunction, CHB = chronic hepatitis B, EF = ejection fraction, HBV = hepatitis B virus, IVST = interventricular septum thickness, LVEDD = left ventricular end-diastolic diameter, LVESD = left ventricular end-systolic diameter, LVPWT = left ventricular posterior wall thickness, PASP = pulmonary artery systolic pressure.

* Fisher exact test.

grade C groups were 8.73%, 13.66%, 32.0%, and 31.25%, respectively ($P = .069$).

3.3. UCG manifestations

The UCG manifestations of the patients with both HBV-related cirrhosis and noncirrhosis, were summarized in Table 2. No statistical significances of LVEDD, IVST, and LVPWT were observed between the 2 groups. Compared with controls, however, LVESD was thicker in patients with cirrhosis (Table 2).

Forty-one patients (51.90%) of HBV-related cirrhotic patients were in accordance with the definition of CCM. As to EF value, which is associated with cardiac systolic function, there was no significant difference among all groups. A total of 68 enrolled patients (37.57%) had some degree of CDD: 30 patients (29.13%) in the control group, 7 patients (28.00%) in Child-Pugh grade A, 20 patients (60.61%) in Child-Pugh grade B, and 11 patients (52.38%) in Child-Pugh grade C. Further analysis showed that patients with HBV-related cirrhosis (38, 48.10%) had a higher incidence of CDD than controls (30, 29.13%) ($P = .008$). The patients with Child-Pugh grade B and C (31, 57.41%), which indicated advanced liver cirrhosis, had a higher incidence of CDD than the control and Child-Pugh grade A group (37, 28.91%) ($P < .001$). Nevertheless, there was no statistical

significance between the Child-Pugh B group and Child-Pugh C group (60.6% and 52.3%, $P = .551$).

3.4. Risk factors for CDD in patients with HBV infection

As shown in Table 3, the individuals with CDD had a high level of pro-brain natriuretic peptide (pro-BNP) ($P = .025$), international normalized ratio (INR) ($P = .010$), and Child-Pugh score ($P = .020$), in contrast, platelet count was lower in the CDD group ($P = .046$). Furthermore, patients with CDD had a higher proportion of ascites complication ($P < .001$). However, there were no differences between the groups in serum ALT, serum creatine, total bilirubin, total cholesterol, troponin I, and MELD score levels (Table 1). To control the confounding effects between the variables, binary logistic regression modeling was performed. The platelet count, pro-BNP, INR, Child-Pugh score, and the proportion of ascites were analyzed. The results showed the high Child-Pugh score (odds ratio = 1.662, $P = .010$) was an independent diagnostic predictor of CDD in patients with HBV infection.

3.5. Cardiac depression and exercise tolerance

One hundred twenty-five patients (68.68%) completed C-CDS questionnaire. The C-CDS indexes of controls, HBV related cirrhotic patients with Child-Pugh grade A, Child-Pugh grade B,

Table 3**Risk factors for CDD in patients with HBV related cirrhosis.**

Items	No-CDD (N = 114)	CDD (N = 68)	P-value
Platelet count, $10^9/L$	123 (82–192)	116 (72–139)	.046
ALT, U/L	94 (34–626)	37 (22–92)	.213
sCr, $\mu\text{mol/L}$	59.6 (49.6–73.1)	62.0 (50.4–75.9)	.606
TBil, $\mu\text{mol/L}$	113.9 (21.0–202.6)	51.2 (13.1–169.8)	.343
TC, mmol/L	3.05 (2.48–3.98)	3.29 (2.69–3.63)	.128
CK, U/L	63 (45–98)	52 (39–98)	.296
Pro-BNP, pg/ml	298.83 (180.55–460.75)	978.28 (357.36–1882.00)	.025
TNI, ng/ml	0.025 (0.003–0.036)	0.012 (0.001–0.0335)	.387
INR	1.29 (1.06–2.01)	1.41 (1.22–1.61)	.010
Child-Pugh score	7 (6–9)	8 (6–10)	.020
MELD score	6.55 (3.55–12.89)	10.39 (4.44–16.21)	.139
Ascites (N, %)	14 (12.28)	33 (48.53)	<.001

ALT = alanine aminotransferase, AST = aspartate transaminase, BNP = brain natriuretic peptide, CDD = cardiac diastolic dysfunction, CK = creatine kinase, INR = international normalized ratio, MELD = model for end-stage liver disease, sCr = serum creatinine, TBil = total bilirubin, TC = total cholesterol, TG = triglyceride, TNI = troponin I.

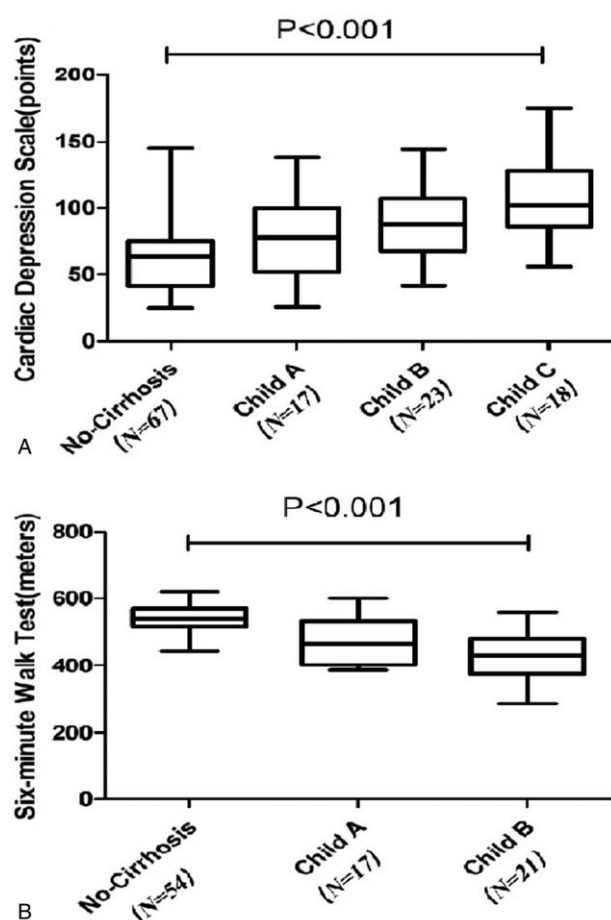


Figure 2. The indexes of cardiac depression scales and score of 6-minute walking test in patients with controls and HBV related cirrhotic patients. HBV= hepatitis B virus.

and Child-Pugh grade C were 64 (42–75), 78 (55–96), 87 (70–110), 102 (86–133), respectively (Fig. 2). There was a statistically significant increase in C-CDS indexes along with increasing Child-Pugh grade ($P < .001$).

To evaluate the exercise tolerance, 92 patients (50.55%) were enrolled in SMWT: 54 (58.70%) patients in the control group; 17 patients (18.48%) in Child-Pugh grade A; and 21 (22.83%) patients in Child-Pugh grade B. Compared to the walking distance of the control group (545 [520–575] meters), the walking distance of patients with Child-Pugh grade A (495 [425–550] meters) and grade B (455 [400–510] meters) were significantly shorter ($P < .001$) (Fig. 2).

4. Discussion

HBV infection, especially in the Asian-Pacific area, is a main cause for advanced liver diseases such as cirrhosis, liver failure and HCC.^[16,17] Not only alcoholic cirrhosis, it became clear that cirrhosis per se was also an independent factor of cardiac dysfunction. However, in patients with asymptomatic clinical manifestations in early stage, few studies on the cardiac health and its risk factors in HBV-related cirrhotic patients were reported to our knowledge. Most of the previous studies either evaluated cardiac function only with UCG or did not focus on physical activity in cirrhotic patients. In this study, cardiac health

including cardiac depression and exercise tolerance, ECG and UCG manifestations were focused.

A significant longer QTc interval duration could be detected in cirrhotic patients when compared with the control group, which was in line with previous researches.^[18–20] A longer QTc interval duration could result from delayed repolarization of cardiac muscle, which was possibly associated with volume overload, sympathoadrenergic activity and portal hypertension in cirrhotic patients.^[18,20] On the other hand, Li et al also showed that the prolonged QTc interval duration became normal in 17 of 20 patients undergoing liver transplantation,^[19] indicating the impact of liver cirrhosis on heart function.^[21,22] Additionally, QTc interval was found weakly associated with MELD score. The proportion of QTc prolongation had an upward tendency with the increase of Child-Pugh grade. However, no significant difference was detected. With the inconsistency of above results, although electrophysiological changes were common in patients with HBV-related cirrhosis, we could hardly establish the connection between QTc prolongation and the severity of HBV related cirrhosis. QTc interval might be affected by some other decisive factors independent of cirrhosis, such as alcohol consumption, hepatic venous pressure gradient (HVPG) and plasma calcium level.^[23]

There are many ways to evaluate heart function, including UCG and cardiac magnetic resonance (CMR).^[9] CMR is known as the gold standard for the measurements of volumes and EF of the heart, but is limited by higher costs and lower availability.^[9] UCG, which is considered feasible and precision, was used to access the heart function in our study. Ventricular wall thickening occurred in patients with liver cirrhosis according to the data of our study. Patients with liver cirrhosis had a thicker LVSEd than noncirrhotic patients. The exact pathogenesis between heart wall thickness and liver cirrhosis is still uncertain. The possible explanation could be as follows:

- (1) volume redistribution and cardiac overload might lead to cardiac hypertrophy^[21];
- (2) hyperactivity of renin-angiotensin-aldosterone system could result in an increase in both the number and size of cardiac cells in the animal model.^[24]

In our study, we found a similar incidence of systolic function between the cirrhotic and non-cirrhotic group, and the EF value showed no significant difference between different groups. Meanwhile, 30 patients (29.13%) in the noncirrhotic group and 38 patients (48.10%) in the cirrhotic group had evidence of CDD. The proportion of CDD increased significantly with the severity of liver disease. Most of the enrolled subjects, both cirrhotic group (30 subjects, 81.08%) and the control group (22 subjects, 73.33%), had impaired cardiac relaxation (mild CDD). Child-Pugh grade B group had highest incidence of CDD. Similar results were ever reported, and the mechanism of CDD in liver cirrhosis was possibly associated with hyperdynamic circulation.^[25] In total, 51.90% of HBV-related cirrhotic patients without significant manifestations were diagnosed as CCM. Due to the heavy use of non-selective beta-blocker and diuretics, which could affect the system hemodynamics, cardiac condition should be taken into account in the treatment of cirrhosis.

Only a few studies have focused on the risk factors of CDD in liver disease. Compared with no-CDD group, patients with CDD showed higher levels of INR, pro-BNP and Child-Pugh score and lower level of platelet count. The increase of INR and decrease of platelet count resulted in an advanced liver condition. Pro-BNP is a reliable biomarker to evaluate cardiac dysfunction in early

stage.^[26] In our study, patients with CDD had a higher level of pro-BNP. The elevation of pro-BNP might be linked with volume overload, and the persistent existence of CDD might further elevate the level of pro-BNP. Furthermore, the presence of ascites had a high incidence in CDD group, because cirrhotic patients with complication of ascites might be under a worse condition of volume overload and HVP. ^[22] However, in the regression model, only Child-Pugh score was an independent predictor of CDD incidence. In other words, the severity of liver disease itself was closely related to cardiac dysfunction, as well as the hyperdynamic circulating state.

The SMWT is a low-cost and easy-to-conduct assessment for exercise tolerance. It is generally safe for patients with liver disease.^[27] Previous study showed distance of the SMWT was associated with nutritional status and mortality in patients with severe liver disease.^[28,29] As the data shown in Figure 2, patients in Child-Pugh grade B had the least exercise confidence, while the distance of SMWT decreased with the severity of liver disease. Although the UCG has not shown impairment of cardiac function, the cirrhotic complications, including volume overload (ascites) and myodystrophia, resulted in poor exercise tolerance. In line with the previous findings, this observation suggested distance of SMWT was associated with the severity of liver disease. However, the reliability and validity of SMWT in liver disease are relatively weak. A study on SMWT in patients with liver transplantation suggested though the SMWT was a simple test of physical functioning, it was difficult to apply because of a low level of fitness in this population.^[27] In our study, a proportion of cirrhotic patients with Child-Pugh Grade C were excluded due to the severity of illness, thus, sampling bias might not be avoided. The results of SMWT could only be considered as a helpful hint to indicate an advanced condition. According to the practical management of chronic heart failure, the physical exercise is the cornerstone to improve functional status and survival rate.^[30,31] It might be necessary to stress the importance of exercise training in cirrhotic patients.

There are some limitations to the study. First, this was a single-center retrospective study and was limited by small sample size. Further work should include a follow-up work designed to evaluate whether cardiac function is connected with the severity of liver and concomitant medication, such as nonselective beta-blocker and diuretics. Quantitative analysis of liver cirrhosis, such as apparent diffusion coefficient value and cirrhosis risk score, should be enrolled in the future study.^[32,33] Second, stress ECG or UCG was not further performed to evaluate the compensatory capacity of the heart. Third, patients with cirrhosis are often under the condition of portopulmonary hypertension, it needs further study on right cardiac function in cirrhotic patients. Finally, functional tests such as SMWT and C-CDS are not liver specific, a certain degree of bias might be occurred. The result of exercise tolerance and confidence might only work as a cue for clinical management.

5. Conclusion

Electrophysiological changes and cardiac dysfunction were common in patients with HBV related cirrhosis. Cardiac condition must be carefully considered in the integrated therapy of liver cirrhosis. Hepatology physicians should lay emphasis on exercise training in daily life to improve exercise confidence and exercise tolerance.

Author contributions

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