Article

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A Retrospective Study of Long-Term Clinical Outcomes in Patients with Chronic Hepatitis C Treated with Interferon and Ribavirin

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Background: The key endpoint for treatment efficacy in chronic hepatitis C (CHC) is the absence of a detectable virus at 24 weeks after treatment. This study aims to determine the long-term clinical outcomes in patients with CHC after interferon and ribavirin treatment and the factors that influence them.

Methods: A retrospective study was conducted on 259 patients with CHC between 2003 and 2021, and the patients were divided into treated (n = 159) and untreated (n = 100) groups. The median observation duration was four years for the treated group (range: 1–15 years) and four years for untreated groups (range: 1–14 years).

Results: The mean ages of the treated and untreated groups were 47.38 $\pm$ 9.07 and 51.17 $\pm$ 8.38 years, respectively. Regardless of whether antiviral therapy had been administered, patients with undetectable hepatitis C virus (HCV) load had a lower risk of developing liver cirrhosis and hepatocellular carcinoma (HCC) than patients with detectable HCV load ($p < 0.05$). Furthermore, patients with HCV genotype 1b were more likely to develop cirrhosis and HCC than patients with HCV non-genotype 1b ($p < 0.05$). Based on the results of multivariate analysis, age of 50 years and above (hazard ratio [HR] = 6.74, 95% confidence interval [CI] = 2.79–16.28) and infection with HCV genotype 1b (HR = 2.43, 95% CI = 1.06–5.56) were significant predictors of liver cirrhosis and HCC development, whereas undetectable HCV RNA load (HR = 0.14, 95% CI = 0.43–0.46) was a protective factor.

Conclusions: During the long-term follow-up, no cases of HCC were discovered in patients with undetectable HCV RNA load. Nevertheless, long-term monitoring is still required in patients with liver cirrhosis, since it increases the risk for developing liver cancer.

Keywords: chronic hepatitis C; cumulative incidence; liver cirrhosis; hepatocellular carcinoma

Introduction

Hepatitis C virus (HCV) infection is a major public health issue in some parts of the world [1]. HCV has infected about 3% of the world's population, and chronic hepatitis C (CHC) is developed in about 70% of HCV patients [2]. Nearly 400,000 people die of serious complications of CHC, including cirrhosis and hepatocellular carcinoma (HCC), on an annual basis worldwide [3]. The main goal of therapy for HCV infection is to eliminate the virus from the body and stop the progression of liver disease, thus blocking the progression of the disease to successive stages of its natural history [4]. Many multicenter studies have shown that patients with acquired sustained virological response (SVR) have a lower risk of liver decompensation and liver-related mortality when compared to non-SVR patients at post-interferon follow-up [5].

The present study sought to ascertain the long-term clinical outcomes in patients with CHC treated with interferon (IFN) and ribavirin, and to determine the factors that influence them.

Patients and Methods

Patients

In this retrospective study, 259 patients (Fig. 1) with CHC were selected from the First Affiliated Hospital of Guangxi Medical University from April 2003 to July 2021. The patients were selected based on the criteria stated in the hepatitis C prevention and treatment guidelines, 2019 edition [6]. Meanwhile, patients with hepatitis A, B, D, or E infection, human immunodeficiency virus infection, primary biliary cirrhosis, alcoholic liver disease, autoimmune liver disease, other serious systemic diseases, and liver diseases caused by pregnancy were excluded from this study.

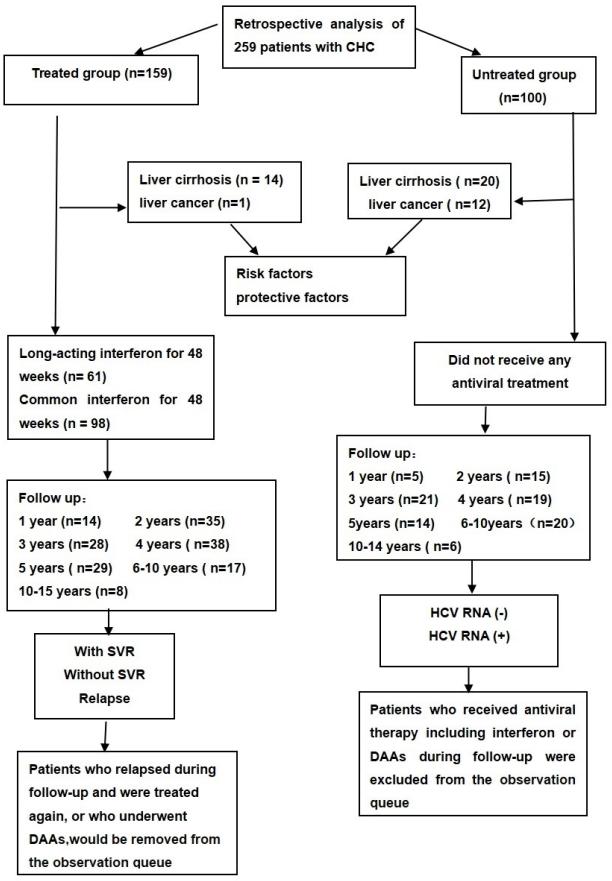

Fig. 1. A flow diagram of the study. Abbreviations: CHC, chronic hepatitis C; DAAs, direct-acting antiviral agents; HCV, hepatitis C virus; SVR, sustained virological response.

Treatment

Patients in the treated group received long-acting IFN therapy, including polyethylene glycol IFN-α-2a (180 mg) and polyethylene glycol IFN-α-2b (1.5 mg/kg), or the common IFN-α (300–600 w/u), which was administered thrice a week, and the dosage was adjusted according to the condition of the patient. The patients were treated for 48 weeks with antiviral therapy. Patients in the untreated group did not receive any antiviral therapy, such as IFN and direct-acting antiviral agents (DAAs), throughout the entire follow-up duration.

Follow-Up

All patients in the two groups were followed up for at least one year. Patients in the treated group who received antiviral therapy again or switched regimens because of recurrence during follow-up, and patients in the untreated group who received any antiviral therapy including IFN or DAAs during follow-up, were removed from the study. Follow-up was carried out every month, three months, or six months, depending on the patients. The follow-up entailed a list of procedures targeted at the patients, such as clinical evaluation, biochemical examination, and ultrasound screening for HCC. The patient was subjected to further examination by computed tomography (CT) or magnetic resonance imaging (MRI) if the ultrasound examination found a new space-occupying lesion.

Diagnosis

Before commencing the antiviral therapy, the serum samples of patients were sent to Guangzhou JinYu Medical Testing Center for HCV genotyping by polymerase chain reaction (PCR). The serum HCV RNA concentration was determined by real-time fluorescent quantitative polymerase chain reaction (qRT-PCR) based on the emitted fluorescence from the amplification of hepatitis virus nucleic acid (Shanghai Kehua Bioengineering Co. Ltd, Shanghai, China). The lowest detection value was 20 IU/L. Commercial kits were also used to determine the levels of total bilirubin (TBIL; the normal value is 3.4–20.5 µmol/L), direct bilirubin (DBIL; the normal value is 0–6.8 µmol/L), alanine transaminase (ALT; the normal value is 7–45 U/L), and aspartate transaminase (AST; the normal value is 13–40 U/L), with strict accordance to the manufacturers' instructions. Fatty liver, liver cirrhosis, and HCC were diagnosed with the detection of liver fibrosis, ultrasound, CT, or MRI examination.

Efficacy Evaluation

SVR is an efficacy endpoint referring to the time when serum HCV RNA is undetectable at the end of antiviral therapy and after a six-month follow-up [7]. Recurrence is considered when serum HCV RNA is undetectable after completing the antiviral therapy. However, serum HCV RNA could be detected again at 24 weeks after treatment [8].

Statistical Analysis

Continuous variables conforming to a normal distribution are expressed as mean $\pm$ standard deviation. Continuous variables not conforming to a normal distribution are expressed as median/interquartile range (IQR). Shapiro–Wilk test was used to assess the normal distribution of all variables. Student's *t*-test was used to compare the means of continuous variables with normally distributed data. Otherwise, Mann–Whitney *U*-test was used. The comparison of rates were tested using Chi-square. Kaplan–Meier method was used to analyze the cumulative incidence, which was compared using log-rank test. Finally, multivariate Cox regression analyses were used to identify the clinical predictors of liver cirrhosis and HCC development. All statistical analyses were conducted using IBM SPSS Statistical software (version 23.0, IBM, Armonk, NY, USA). $p < 0.05$ was considered statistically significant.

Table 1. Demographics and clinical features of the patients.

	Treated group (n = 159)	Untreated group (n = 100)	χ^2 or Z	p
Sex			0.13	0.72
Female [case (%)]	79 (49.7%)	52 (52.0%)		
Male [case (%)]	80 (50.3%)	48 (48.0%)		
Age			8.86	***
≥50 [case (%)]	56 (32.7%)	54 (62.0%)		
<50 [case (%)]	103 (67.3%)	46 (38.0%)		
Genotype			3.52	0.06
1b [case (%)]	70 (44.0%)	56 (56.0%)		
Non-1b [case (%)]	89 (56.0%)	44 (44.0%)		
Route of infection			1.15	0.28
Transfusion route [case (%)]	83 (52.2%)	59 (59.0%)		
Other infection [case (%)]	76 (47.8%)	41 (41.0%)		
Baseline HCV RNA load			14.05	***
≤20 (IU/mL) [case (%)]	64 (40.3%)	18 (18.0%)		
>20 (IU/mL) [case (%)]	95 (59.7%)	82 (82.0%)		
Child-Pugh score			25.77	***
Class A	146 (91.8%)	68 (68.0%)		
Class B	12 (7.5%)	24 (24.0%)		
Class C	1 (0.6%)	8 (8.0%)		
ALT baseline level [Median (IQR), in U/L]	48.0 (12.0)	45.5 (21.0)	1.69	0.92
AST baseline level [Median (IQR), in U/L]	49.0 (15.0)	45.0 (20.0)	0.87	0.38
Combined liver cirrhosis [case (%)]	6 (3.8%)	1 (1.0%)	0.90	0.34

Notes: ***$p < 0.001$. ALT, alanine transaminase; AST, aspartate transaminase; IQR, interquartile range.

Results

Characteristics of Patients at the Time of Admission

A total of 259 people, including 159 patients of the treated group who were treated with IFN and ribavirin and 100 patients of the untreated group who were treated with any antiviral therapy, were analyzed retrospectively. Furthermore, patients in the treated group were followed up for 1–15 years, with a median of four years, and the mean age of the patients in this group was 47.5 ± 9.1 years. Meanwhile, patients in the untreated group were followed up for 1–14 years, with a median of four years, and the mean age of the patients was 51.2 ± 8.4 years. Patients in the treated group were younger than those in the untreated group and had a lower liver score and HCV RNA level at baseline ($p < 0.05$) (Table 1).

Virological Response

Virological Response in Treated and Untreated Groups

In the treated group, 109 patients (68.6%) achieved SVR while 50 patients (31.4%) were unresponsive to the treatment. Of the 61 patients (38.4%) treated with long-acting IFN, 38 patients (62.3%) achieved SVR. In addition, 98 patients (61.6%) were treated with common IFN, and 41 of them (41.8%) achieved SVR. Patients treated with long-acting interferon were more likely to acquire SVR than those treated with common interferon (hazard ratio (HR) = 4.43, 95% confidence interval (CI) = (1.42–13.79), $p = 0.01$. In the untreated group, 18 patients (18.0%) demonstrated persistently undetectable HCV RNA load during follow-up. Patients in the treated group were more likely to be persistently negative for HCV RNA than those in the untreated group during the follow-up period ($\chi^2 = 34.29$, $p < 0.001$) (Fig. 2).

Hepatitis C Virus Genotype and the Patients with Undetectable HCV RNA

There were 18 cases, 124 cases, 24 cases, 25 cases, 36 cases, 23 cases, and 9 cases with HCV genotype 1a, genotype 1b, genotype 2a, genotype 3a, genotype 3b, genotype 6a, and genotype 6b, respectively, who had undetectable HCV RNA. The negative conversion rate of each HCV genotype, determined by dividing the number of cases with persistently undetectable HCV RNA in a genotype by the total number of cases with the genotype, is depicted in Fig. 3.

Relapse

Throughout the retrospective analysis, 109 patients (68.6%) with SVR after IFN and ribavirin treatment and 13 patients (11.9%) experienced relapse during follow-up (details are shown in Table 2). Of those 13 patients who relapsed, 7.7% (1/13) patients developed HCC and 30.8% (4/13) developed liver cirrhosis. Therefore, relapse can occur in patients as soon as one year and as late as eight years after follow-up. Furthermore, most patients who had recur-

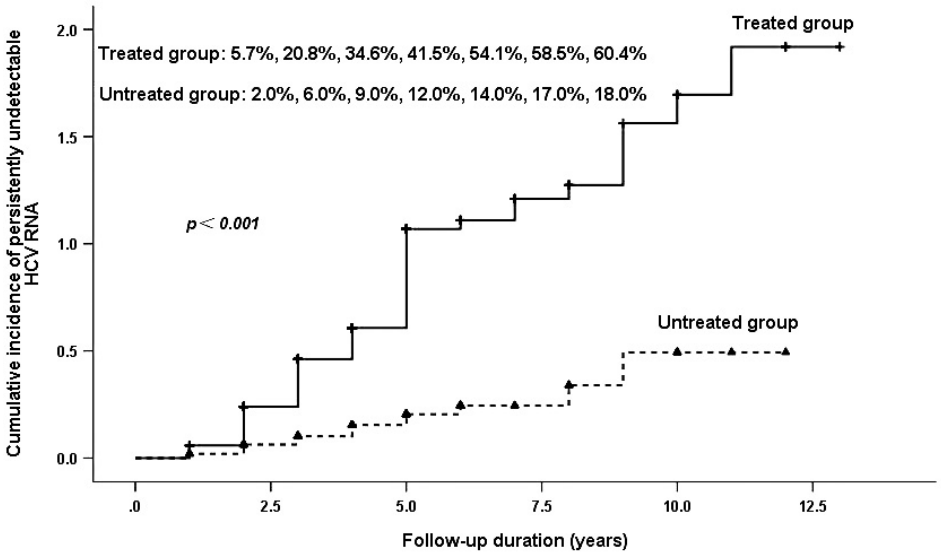

Fig. 2. Cumulative incidence of persistently undetectable HCV RNA during follow-up in the treated and untreated groups. $\chi^2 = 34.29$, $p < 0.001$.

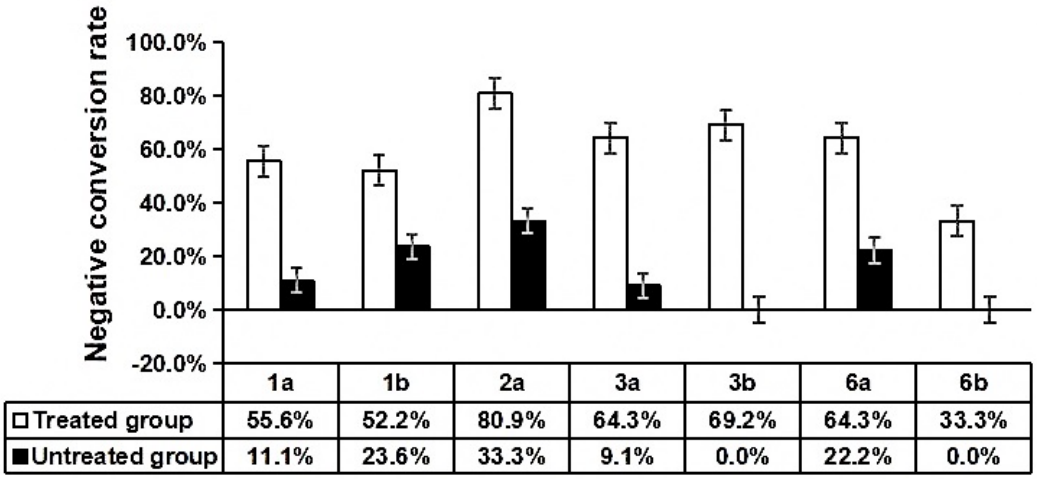

Fig. 3. Negative conversion rate of each HCV genotype in the treated and untreated groups.

Table 2. Relapse rate and cumulative relapse rate in the treated group.

Follow-up duration (years)	≥1	≥2	≥3	≥4	≥5	6–10	≥10
Number of patients	109	99	74	60	42	24	6
Number of relapse cases	1	4	2	4	-	2	-
Relapse rate (%)	0.9	4.1	2.7	6.7	-	8.3	-
Cumulative relapse rate (%)	0.9	4.6	6.4	10.1	10.1	11.9	11.9

rence were infected by genotypes 1 and 3 HCV, with relapse rates of 22.2% (2/9), 10.1% (7/69), 21.4% (3/14) and 3.8% (1/26) for the genotypes 1a, 1b, 3a and 3b, respectively, and there was no significant difference in patient relapse rate between the genotypes ($p > 0.05$).

Liver Cirrhosis and Hepatocellular Carcinoma Development

Overall Incidence of Liver Cirrhosis and HCC Development during the Follow-Up Period

A total of 47 patients (18.1%) from the cohort of 259 patients analyzed retrospectively developed liver cirrhosis and HCC. Of these patients, 34 patients (13.1%) developed liver cirrhosis and 13 patients (5.0%) developed HCC. The

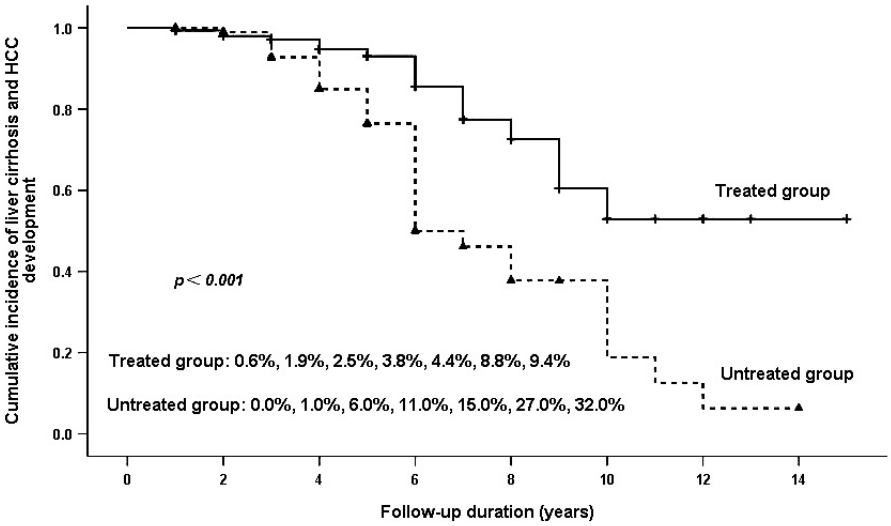

Fig. 4. Cumulative incidence of liver cirrhosis and hepatocellular carcinoma (HCC) development in the treated and untreated groups.

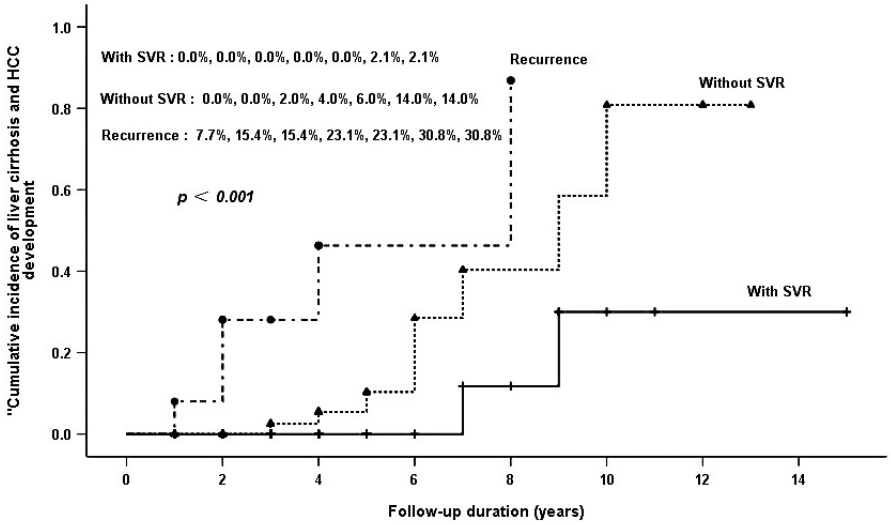

Fig. 5. Development of liver cirrhosis and HCC in treated patients with different virological states.

overall incidence of liver cirrhosis and HCC was significantly lower in the treated group (15/159, 9.4%) than in the untreated group (32/100, 32.0%) (χ^2 = 13.03, $p < 0.001$) (Fig. 4).

In the treated group, 15 patients (9.4%) developed liver-related diseases: 14 patients (8.8%) developed liver cirrhosis, and only one patient (0.6%) developed HCC. Patients in the treated group who achieved SVR had a lower risk of developing liver cirrhosis and HCC than those who did not achieve SVR or had a recurrence (χ^2 = 17.13, $p <$ 0.001) (Fig. 5). In the untreated group, 32 patients (32.0%) developed liver-related diseases, including 20 cases of liver cirrhosis (20.0%) and 12 cases of HCC (12.0%). Patients in the untreated group with undetectable HCV RNA had a lower risk of disease development than those with detectable HCV RNA (χ^2 = 4.14, p = 0.04) (Fig. 6).

Incidence of Liver Cirrhosis and HCC in the Treated Group

The cumulative incidence of liver cirrhosis was 2.1% (2/96) and 16.0% (8/50) in patients with SVR and those without SVR, respectively, during the follow-up period. Furthermore, the cumulative incidence of liver cirrhosis in recurrent patients was 30.8% (4/13). Only one patient in the treated group had a recurrence of liver cancer in the second year of follow-up. Details on liver cirrhosis in treated patients under different virological states are provided in Table 3.

Incidence of Liver Cirrhosis and Hepatocellular Carcinoma in the Untreated Group

The cumulative incidence rate of liver cirrhosis in patients with persistently negative HCV RNA in the untreated

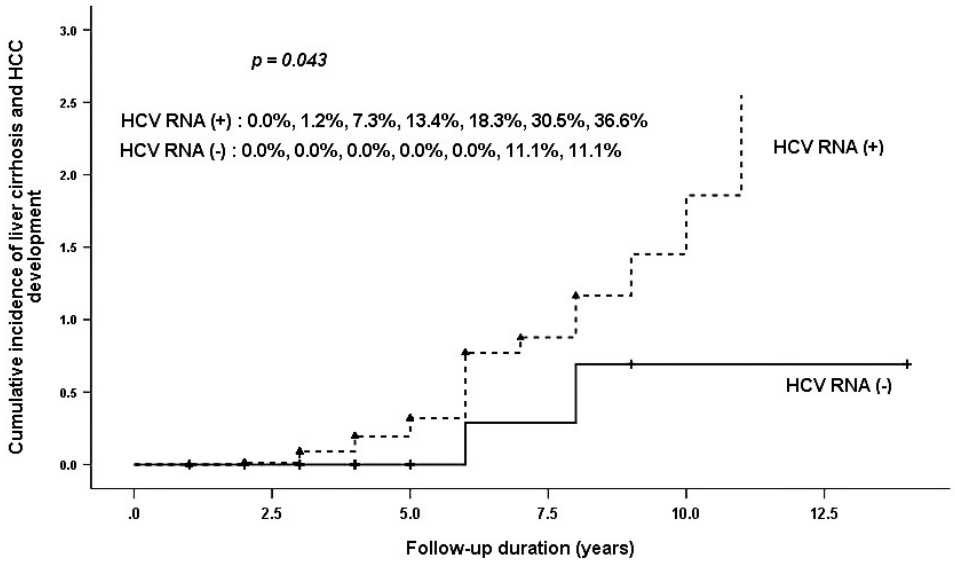

Fig. 6. Development of liver cirrhosis and HCC in untreated patients with different virological states.

Table 3. Incidence of liver cirrhosis in the treated group under different virological states.

	With SVR		Recurrence		Without SVR	
Follow-up duration (years)	Total patients	Liver cirrhosis	Total patients	Liver cirrhosis	Total patients	Liver cirrhosis
≥1	96	-	13	1 (7.7%)	50	-
≥2	87	-	11	1 (9.1%)	47	-
≥3	66	-	7	-	40	1 (2.5%)
≥4	54	-	6	1 (16.7%)	35	1 (2.9%)
≥5	39	-	6	-	21	1 (4.8%)
6–10	21	2 (9.5%)	4	1 (25.0%)	12	4 (33.3%)
≥10	3	-	3	-	5	1 (20.0%)

group was 11.1% (2/18), and no patient was found to develop liver cancer during the follow-up period. Moreover, in the patients with persistently positive HCV RNA, the cumulative incidence of liver cirrhosis was 21.9% (18/82), while the cumulative incidence of HCC was 14.6% (12/82). Details on liver cirrhosis and HCC in untreated patients with different levels of HCV load are given in Table 4.

Relationship of Hepatitis C Virus Genotype with the Development of Liver Cirrhosis and Hepatocellular Carcinoma

All patients included in this study (n = 259) were genotyped, with 124 being genotype 1b and 135 being non-genotype 1b. Liver cirrhosis developed in 16.9% (21/124) and HCC developed in 7.3% (9/124) of the patients with genotype 1b. Liver cirrhosis occurred in 9.6% (13/135) and HCC developed in 3.0% (4/135) of patients with non-genotype 1b. Patients infected with genotype 1b HCV were more susceptible to developing liver cirrhosis and HCC than those with non-genotype 1b HCV (χ^2 = 10.32, $p <$ 0.001). Table 5 shows the distribution of HCV genotypes in patients who developed liver cirrhosis and HCC.

Predictors of Liver Cirrhosis and Hepatocellular Carcinoma

In this retrospective analysis, we used Cox regression to identify the potential risk factors of liver cirrhosis and HCC (Table 6). The multivariate Cox regression analysis revealed that the significant predictors of liver cirrhosis and HCC development in CHC patients were age ≥50 years (HR = 6.74, 95% CI = 2.79–16.2) and genotype 1b (HR = 2.43, 95% CI = 1.06–5.56), and that the undetectable HCV load (HR = 0.14, 95% CI = 0.43–0.46) was the protective factor.

Discussion

The presence or absence of active HCV replication appears to have a significant impact on the risk of liver-related complications, with only a small proportion of patients experiencing recurrence despite acquiring SVR; patients with liver cirrhosis who have no prior history of liver decompensation are still at risk for decompensation and HCC [9]. Patients with HCV who had advanced liver fibrosis (FIB-4 ≥3.25) and did not achieve SVR after IFN therapy were more likely to develop liver-related complications. In con-

Table 4. Incidence of liver cirrhosis and HCC in the untreated patients with different levels of HCV load.

	HCV RNA (-)			HCV RNA (+)		
Follow-up duration (years)	Total patients	Liver cirrhosis	HCC	Total patients	Liver cirrhosis	HCC
≥1	18	-	-	82	-	-
≥2	16	-	-	78	1 (1.3%)	-
≥3	12	-	-	58	4 (6.9%)	1 (1.7%)
≥4	9	-	-	41	3 (7.3%)	2 (4.9%)
≥5	6	-	-	29	2 (6.9%)	2 (6.9%)
6–10	4	2 (50.0%)	-	16	7 (43.8%)	3 (18.8%)
≥10	1	-	-	5	2 (40.0%)	3 (60.0%)

Table 5. Distribution of HCV genotypes in patients who developed liver cirrhosis and HCC.

HCV genotype	1b	1a	2a	3a	3b	6a	6b
Total (cases)	124	18	24	25	36	23	9
Liver cirrhosis [case (%)]	21 (16.9%)	2 (11.1%)	2 (8.3%)	5 (20.0%)	2 (12.5%)	1 (4.3%)	1 (11.1%)
HCC [case (%)]	9 (7.3%)	1 (5.6%)	-	2 (8.0%)	1 (9.3%)	-	-

Table 6. Univariate and multivariate Cox regression analysis of risk factors for liver cirrhosis and HCC.

Factors	Progressive group	CHC group	Univariate Cox regression			Multivariate Cox regression		
	n = 47	n = 212	*p*	HR	95% CI	*p*	HR	95% CI
Sex (male/female)	25/22	103/109	0.57	1.21	0.64–2.28	0.74	0.87	0.39–1.93
Age (≥50 years/<50 years)	39/8	65/147	***	0.21	0.09–0.46	***	6.74	2.79–16.28
Genotype (1b/non 1b)	30/17	94/118	**	0.36	0.18–0.73	*	2.43	1.06–5.56
Route of infection (transfusion route/others)	32/15	110/102	0.41	0.76	0.39–1.47	0.61	2.19	0.97–4.99
Combined fatty liver (yes/no)	9/38	47/165	0.89	1.06	0.47–2.36	0.26	0.58	0.23–1.49
Baseline HCV RNA (-/+)	4/43	110/102	*	3.93	1.32–11.69	**	0.14	0.43–0.46
Baseline ALT levels (≤52/>52 U/L)	11/36	152/60	0.61	1.25	0.53–2.97	0.11	2.31	0.83–6.42
Baseline AST levels (≤52/>52 U/L)	7/40	148/64	0.18	0.60	0.29–1.26	0.60	0.78	0.30–2.01
Baseline TBIL levels (≤14/>14 μmol/L)	25/22	131/81	0.43	0.78	0.39–1.48	0.90	1.01	0.46–2.43
Baseline DBIL levels (≤5/>5 μmol/L)	25/22	124/88	0.86	0.94	0.49–1.81	0.60	0.81	0.36–1.80
Antiviral therapy (yes/no)	15/32	144/86	0.14	1.69	0.85–3.37	0.06	0.44	0.19–1.01

Notes: HR, hazard ratio; CI, confidence interval; TBIL, total bilirubin; DBIL, direct bilirubin. *$p < 0.05$; **$p < 0.01$, ***$p < 0.001$.

trast, HCV SVR significantly reduced the long-term risk of major liver-related complications in HCV-infected patients after IFN-based therapy [5]. Before the DAAs drugs were approved for treatment, the standard treatment for chronic HCV infection was a combination of ribavirin and polyethylene glycol interferon (PegIFN). This combination achieved SVR rates of 50% in HCV genotypes 1 and 4, and of 80% in genotypes 2 and 3 [10]. Treatment of CHC with IFN and ribavirin has also been reported to result in sustained virologic response rates ranging from 54% to 80% [2]. In addition, SVR rates for PegIFN/ribavirin (RBV) were in the range of 70%–90% in a Taiwanese study [11]. In patients treated with PegIFN/RBV, fibrosis resolved regardless of virologic response. This is especially true in patients who have achieved SVR [12]. In the current study, our results are not entirely consistent with these previously reported results. 68.6% of the patients achieved SVR in this study, and patients treated with long-acting interferon were more likely to acquire SVR than those treated with common interferon. The likeliness to achieve SVR could be related to the use of different types of IFN by the patients in this cohort.

A British prospective study on the HCV RNA-positive and untreated patients found that the fibrosis progression rate was 33% at 2.5 years and 42% at 4.4 years [13]. Patients who cleared HCV had significantly lower cumulative incidence and liver-related mortality from HCC compared with untreated patients, especially those with cirrhosis [14]. It has also been reported that patients who achieve SVR are more likely to delay the development of decompensated cirrhosis and HCC and thereby reduce mortality compared with those who achieve SVR [1]. In addition, achieving an SVR has been associated with a reduction in liver fibrosis and subsequent risk of complications. In contrast, patients with persistent viral infections have an increased risk of liver fibrosis progression due to persistent liver inflammation [12]. Achieving an SVR may reduce the risk of HCC occurrence but does not completely prevent it, and

long-term clinical testing is still required after SVR, particularly in patients with liver cirrhosis [9]. Our findings are congruent with previous studies, as in the patients with SVR have a significantly lower risk of liver cirrhosis and HCC development than those without SVR. However, we reckon that due to the small sample size and the method of detecting HCV RNA, the exact data we had could possibly deviate from the actual situation. Thus, more sensitive tests are required to detect low levels of HCV RNA load in patients.

Untreated chronic hepatitis or failure to clear harmful substances can lead to liver fibrosis and cirrhosis [12]. In this study, 38.6% of the patients did not receive antiviral therapy, and 32.0% of them developed liver cirrhosis and HCC, serious complications whose risk can be reduced by means of HCV eradication [3]. Applying early antiviral therapy is a cost-effective approach to treating patients with and without fibrosis. Previous researchers have recommended early antiviral therapy for CHC patients younger than 60 years of age, and the most recent guidelines recommend HCV therapy for all affected patients, regardless of the stage of fibrosis [11,13].

Age, sex, stage of liver fibrosis, serum ALT and AST levels, serum bilirubin levels, etc., were predictors of liver cirrhosis or HCC development [15]. It has been reported by Jung *et al*. [16] that pegylated interferon and ribavirin therapy can help patients achieve a high SVR rate, attaining 36.7% in patients with HCV genotype 1b and 86.0% in patients with non-genotype 1. A previous study found that the incidence of HCC development was significantly different between patients with HCV genotype 1b and non-genotype 1b [17]. This study discovered that the patients with HCV genotype 1b were more likely to develop liver cirrhosis and HCC than those with non-genotype 1b ($p < 0.05$). The sample size of this study needs to be increased if the future direction is to further investigate the relationship.

A previous meta-analysis found that the long-term low-dose PegIFN did not reduce the incidence of HCC in patients with advanced hepatitis C who did not achieve SVR [18]. In our study, patients who did not achieve SVR after IFN therapy had a 16.0% risk of developing cirrhosis. Other researchers reported that HCC still occurs in 22.1% (60/271) of patients who have successfully eradicated CV after IFN and ribavirin treatment, and the cumulative incidence of HCC at 5,10, and 15 years is 4%, 6%, and 12%, respectively [19]. However, there are better treatment options for CHC patients, for instance, the DAAs [18]. A DAA regimen has a curative rate of more than 95% in patients with chronic HCV infection. However, in some patients who fail to respond to the DAAs treatment, resistance-associated substitution may develop, greatly limiting the retreatment options and further driving the spread of resistant viruses [20]. Nevertheless, patients residing in remote or low-income regions do not have access to DAAs. According to national and international retreatment guidelines, patients who do not achieve SVR or relapse may be treated with second or even third-line therapy [21]. This means that a small number of patients may still require IFN therapy, whose long-term clinical effect is uncertain.

Conclusions

During the long-term follow-up, no cases of HCC were discovered among the patients with undetectable HCV RNA load. However, long-term clinical follow-up of patients with CHC is necessary, regardless of the treatment applied.

Availability of Data and Materials

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

Author Contributions

Conception and design: XTL, YZ and MHS. Acquisition of data: XTL, YZ, SYL, GZD, MS, JJL and YCW. Analysis and interpretation of data: XTL and YZ. Image interpretation: XTL, YZ, JNJ and MHS. Writing (original draft preparation): Joint implementation. Writing (review and editing): JNJ and MHS. Project administration: MHS. Funding acquisition: MHS. All authors contributed to the article and approved the submitted version. All authors agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (approval number: 2022-KY-E-182) and meets the criteria of the Helsinki Declaration. All patients signed informed consent forms.

Acknowledgment

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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