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Original Article

Entecavir provides favorable virological control but minimal metabolic benefit in patients with Chronic Hepatitis B and MAFLD

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Abstract: Objective: To systematically evaluate the multidimensional efficacy of entecavir in patients with Chronic Hepatitis B (CHB) complicated with metabolic-associated fatty liver disease (MAFLD), with a focus on virological response, liver function, and metabolic parameters. Methods: A retrospective analysis was conducted on 285 patients with CHB and concurrent MAFLD who received entecavir treatment at Minzu Hospital of Guangxi Zhuang Autonomous Region between January 2022 and May 2024 (MAFLD with comorbidities group). During the same period, 310 CHB patients without MAFLD served as the viral-only group. Both groups were treated with entecavir. Baseline characteristics, treatment efficacy at week 35, virological response, liver function parameters, fibrosis progression, metabolic indicators, and safety profiles were compared between the two groups. Results: Compared with the viral-only group, patients in the MAFLD with comorbidities group exhibited significantly higher body mass index (BMI), waist circumference (WC), homeostasis model assessment of insulin resistance (HOMA-IR), fasting insulin (FINS), and triglyceride (TG) levels, as well as lower high-density lipoprotein cholesterol (HDL-C) levels, alanine aminotransferase (ALT)/aspartate aminotransferase (AST) normalization rates, hepatitis B virus (HBV) deoxyribonucleic acid (DNA) negativity rates, and hepatitis B e-antigen (HBeAg) seroconversion rates ($P < 0.05$). AST and GGT levels were also significantly lower in the viral-only group than in the MAFLD with comorbidities group ($P < 0.05$). Post-treatment fibrosis staging was more advanced in the MAFLD with comorbidities group ($P < 0.05$). After treatment, patients with MAFLD maintained higher HOMA-IR and TG levels and lower HDL-C levels than those without MAFLD ($P < 0.05$). During follow-up, the overall incidence of adverse events was 2.11% in the MAFLD with comorbidities group and 1.94% in the viral-only group, with no statistically significant difference between the groups ($P > 0.05$). Conclusion: Entecavir can effectively control viral replication in patients with CHB combined with MAFLD. However, the recovery of liver function, improvement of steatosis and improvement of metabolic indicators were all slightly inferior to those of the non-MAFLD population, suggesting that the coexistence of MAFLD may weaken the comprehensive benefits of antiviral treatment.

Keywords: Entecavir, Chronic Hepatitis B, MAFLD, retrospective analysis

Introduction

Chronic Hepatitis B (CHB) is a common chronic inflammatory liver disease caused by persistent infection with the hepatitis B virus (HBV). Without effective treatment, CHB may progress to liver fibrosis, cirrhosis, or even hepatocellular carcinoma, resulting in increased treatment complexity and poor prognosis [1]. Metabolic-associated fatty liver disease (MAFLD) is characterized by excessive lipid accumulation in hepatocytes and is strongly associated with metabolic dysfunction and insulin resistance. With its rising global prevalence, MAFLD has become one of the leading causes of chronic liver disease [2]. Notably, the coexistence of CHB and MAFLD is increasingly observed in clinical practice. The interaction between CHB and MAFLD is not a simple additive process but a mutually reinforcing one. Persistent HBV repli-

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cation triggers immune-mediated hepatocellular injury, whereas MAFLD-related lipid metabolism disorders, insulin resistance, and oxidative stress further exacerbate hepatic inflammation and fibrosis, accelerating disease progression [3, 4]. Moreover, the presence of metabolic abnormalities may not only aggravate hepatic injury but also impair antiviral efficacy, thereby influencing treatment outcomes in CHB patients with concomitant MAFLD [5]. Therefore, managing patients with CHB complicated by MAFLD poses a new clinical challenge.

Entecavir, a potent nucleoside analogue against HBV, effectively suppresses viral DNA replication by inhibiting HBV polymerase activity and is currently recommended as a first-line therapeutic agent in both domestic and international guidelines. Its efficacy and safety have been extensively validated in patients with uncomplicated CHB [6]. However, most previous studies have excluded patients with significant metabolic abnormalities or fatty liver, resulting in a limited understanding of the actual therapeutic efficacy of entecavir in CHB patients complicated by MAFLD. In this context, evaluating the clinical outcomes in these comorbid patients is of considerable clinical importance. Further comprehensive studies are needed to clarify the therapeutic value of entecavir in such complex cases [7]. Real-world evidence provides valuable insight into the effectiveness and safety of antiviral agents in heterogeneous patient populations under routine clinical practice, thereby compensating for the limited external validity of randomized controlled trials. Therefore, this study retrospectively analyzed the impact of MAFLD on the therapeutic efficacy of entecavir in patients with CHB, aiming to provide evidence-based guidance for optimizing combination treatment strategies. The findings are summarized as follows.

Materials and methods

Case selection

This study was approved by the Ethics Committee of the Minzu Hospital of Guangxi Zhuang Autonomous Region. A retrospective analysis was conducted on 285 CHB patients with concomitant MAFLD who received entecavir treatment at our hospital between January 2022 and May 2024 (MAFLD with comorbidities group). During the same period, 310 CHB patients without MAFLD were included as the viral-only group.

Inclusion criteria: Patients were included if they met the following criteria: (1) Diagnosed with CHB according to the "Guidelines for Primary Care of Chronic Hepatitis B (Practice Edition, 2020)" [8]; (2) Positive for hepatitis B surface antigen (HBsAg) for at least 6 months and fulfilling the diagnostic criteria for CHB (HBV DNA ≥ 2000 IU/mL or ALT exceeding the upper limit of normal); (3) For the MAFLD with comorbidities group, diagnosis with MAFLD according to the 2020 APASL Clinical Practice Guidelines for the Diagnosis and Management of MAFLD [9]; (4) Entecavir treatment with good medication adherence; (5) Complete baseline and follow-up clinical data available.

Exclusion criteria: Patients were excluded if they met any of the following conditions: (1) Presence of other liver diseases, including alcoholic liver disease or autoimmune hepatitis; (2) Decompensated liver cirrhosis, where entecavir monotherapy may be insufficient; (3) Concurrent hepatocellular carcinoma or other malignancies; (4) Co-infection with human immunodeficiency virus (HIV) or other immunosuppressive disorders; (5) Use of medications that may affect metabolism or liver function (e.g., SGLT2 inhibitors, statins); (6) Baseline HBV DNA < 20 IU/mL (complete viral suppression).

Treatment method

According to disease progression, all patients received liver-protective therapy and were instructed to abstain from alcohol and follow a low-fat diet. Patients with concomitant comorbidities were given appropriate symptomatic treatment. Both groups were administered oral entecavir (Chia Tai Qing Tian, China National Medicine Standard H20100019) at a dose of 0.5 mg once daily for a continuous treatment period of 35 weeks.

Data collection and outcome measurements

Primary indicators: (1) Assessment of liver fibrosis: Liver stiffness (E value) and the controlled attenuation parameter (CAP value) were measured using a FibroScan® 502 device. All patients fasted for at least 8 hours and were examined in the supine position. Measurements

were taken more than 10 times through the right intercostal space, and the median value was recorded as the final result.

Fibrosis progression was defined as an increase in E value by ≥ 1 fibrosis stage or by an absolute increase of ≥ 1.5 kPa compared with baseline during follow-up. Fibrosis stage was graded according to the METAVIR scoring system [10]: F0: No fibrosis; normal liver architecture; F1: Mild fibrosis; minimal fibrous expansion confined to portal tracts without septa formation; F2: Moderate fibrosis; fibrous expansion of portal areas with a few septa, preserved lobular architecture; F3: Severe fibrosis; numerous fibrous septa with architectural distortion but no cirrhosis; F4: Cirrhosis; extensive fibrosis with pseudolobule formation and complete architectural destruction.

(2) Evaluation of metabolic parameters: Five milliliters of fasting venous blood were collected in the morning, allowed to stand for 30 minutes, and centrifuged at 3,000 rpm for 15 minutes to obtain serum.

Fasting blood glucose (FBG) was measured using the glucose oxidase method; triglycerides (TG) by the GPO-PAP method; and high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) by direct enzymatic assays, all performed on a Mindray BS-800 automatic biochemical analyzer. Fasting insulin (FINS) was determined using a chemiluminescence immunoassay (CLIA). The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using the following formula: FBG × FINS/22.5. All reagents were supplied by Guangzhou Orida Biotechnology Co., Ltd., and all tests were conducted in strict accordance with the manufacturer's standard operating procedures.

Secondary indicators: (1) Baseline data collection: Baseline characteristics were retrieved from the hospital's electronic medical record (EMR) and laboratory information system (LIS), including demographic variables (age, sex, height, weight), body mass index (BMI), and waist circumference (WC, measured at end-expiration midway between the lower rib margin and the iliac crest), as well as virological, biochemical, and metabolic indicators.

(2) ALT/AST normalization rate: Defined according to the American Association for the Study of Liver Diseases (AASLD) criteria, with normalization thresholds of ALT ≤ 30 U/L for males and ≤ 19 U/L for females [11].

(3) Virological response: The rate of HBV DNA negativity was determined using a highly sensitive PCR assay with a detection limit of < 20 IU/mL; negativity was defined as HBV DNA < 20 IU/mL. HBeAg seroconversion was measured using an electrochemiluminescence immunoassay and defined as HBeAg loss with the simultaneous appearance of anti-HBe antibodies. The assay kits were supplied by Shanghai WYTSCI Biotech CO., LTD. (catalog number WL-H02471), and all tests were performed in strict accordance with the manufacturer's standard operating procedures.

(4) Liver function indicators: Fasting venous blood samples (3-5 mL) were collected from patients in the morning. After standing for 30 minutes, the samples were centrifuged at 3,000 rpm for 15 minutes to obtain serum. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and γ-glutamyltransferase (GGT) levels were measured using an automated biochemical analyzer.

Statistical analysis

Data were analyzed using SPSS 27.0 and GraphPad Prism software. Continuous variables were expressed as mean ± standard deviation (SD). Between-group comparisons were conducted using the independent sample t-test, while paired t-tests were used for within-group comparisons. Categorical data were expressed as percentages and analyzed using the chi-square (χ^2) test. Ordinal data were assessed using the rank-sum test. A *p*-value less than 0.05 was considered statistically significant.

Results

Comparison of baseline characteristics between groups

There were no statistically significant differences between the two groups in terms of age, sex distribution, ALT levels, HBV DNA load, HBV genotype, FBG, total cholesterol (TC), or LDL-C (P > 0.05), indicating good baseline comparability in demographic and virological characteristics. Regarding metabolic indicators, patients

Table 1. Comparison of baseline characteristics between the two groups

Variable	MAFLD with comorbidities group (n = 285)	Viral-only group (n = 310)	t/χ^2	*P*-value
Age (years)	39.30±10.30	39.61±10.87	0.354	0.723
Sex				
Male (n)	155	189	2.637	0.104
Female (n)	139	121		
BMI (kg/m^2)	26.29±3.99	22.50±2.85	13.412	< 0.001
WC (cm)	89.88±11.25	79.84±9.99	11.529	< 0.001
ALT (U/L)	179.87±78.50	187.95±79.88	1.243	0.214
HBV-DNA (lg copies/mL)	6.24±0.78	6.20±0.64	0.686	0.493
Genotype				
HBV genotype B (%)	168	174	0.374	0.540
HBV genotype C (%)	117	136		
HOMA-IR	3.67±3.89	2.07±1.98	6.397	< 0.001
FINS (mU/L)	15.46±10.93	9.03±7.36	8.477	< 0.001
FBG (mmol/L)	5.11±0.85	4.99±0.80	1.774	0.077
TG (mmol/L)	1.80±0.95	1.33±0.64	7.128	< 0.001
TC (mmol/L)	3.78±1.07	3.72±0.97	0.717	0.473
HDL-C (mmol/L)	0.86±0.34	1.07±0.35	7.412	< 0.001
LDL-C (mmol/L)	2.31±0.72	2.19±0.88	1.811	0.071

Notes: BMI, body mass index; WC, waist circumference; ALT, alanine aminotransferase; HBV, hepatitis B virus; HOMA-IR, homeostasis model assessment of insulin resistance; FINS, fasting insulin; FBG, fasting blood glucose; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

in the MAFLD with comorbidities group exhibited significantly higher BMI and WC than those in the viral-only group ($P < 0.05$), reflecting more pronounced obesity. In addition, HOMA-IR values and FINS levels were significantly elevated in the MAFLD with comorbidities group ($P < 0.05$), indicating greater insulin resistance. Furthermore, TG levels were elevated, while HDL-C levels were significantly lower in the MAFLD with comorbidities group ($P < 0.05$), consistent with characteristic features of metabolic syndrome. Overall, patients in the MAFLD with comorbidities group demonstrated more pronounced metabolic abnormalities, supporting their classification as individuals with Chronic Hepatitis B complicated by MAFLD (**Table 1**).

Comparison of treatment efficacy after 35 weeks of entecavir between groups

After 35 weeks of entecavir therapy, the rates of ALT/AST normalization, HBV DNA negativity, and HBeAg seroconversion were significantly lower in the MAFLD with comorbidities group compared with the viral-only group, whereas the corresponding non-normalization and non-seroconversion rates were significantly higher in the MAFLD with comorbidities group ($P < 0.05$) (**Figure 1**). These results suggest that concomitant metabolic dysfunction may attenuate the antiviral efficacy of entecavir.

Comparison of liver function indicators between groups

AST and GGT levels were significantly lower in the viral-only group compared to the MAFLD with comorbidities group (**Figure 2A** and **2B**). Specifically, AST levels in the viral-only group were notably reduced, and GGT levels also demonstrated a substantial decrease. These findings suggest milder hepatocellular injury and cholestasis in the viral-only group, indicating better recovery of liver function (**Figure 2**).

Comparison of fibrosis progression between groups

After treatment, the distribution of new fibrosis stages in the MAFLD with comorbidities group was: F0/F1, 166 cases (58.2%); gray zone F2, 92 cases (32.3%); F3, 18 cases (6.3%); and F4, 9 cases (3.2%). In the viral-only group, the distribution was: F0/F1, 210 cases (67.7%); gray

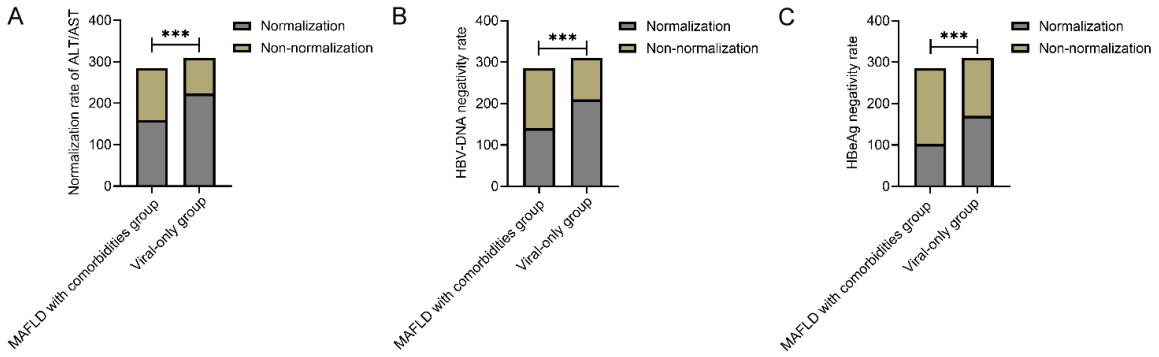


Figure 1. Comparison of Therapeutic effect of entecavir at 35 weeks. A: ALT/AST Normalization rate; B: HBV-DNA Negativity rate; C: HBeAg Seroconversion rate. ***P < 0.001. Note: ALT, serum alanine aminotransferase; AST, aspartate aminotransferase; HBV, hepatitis B virus; HBeAg, hepatitis B surface antigen.

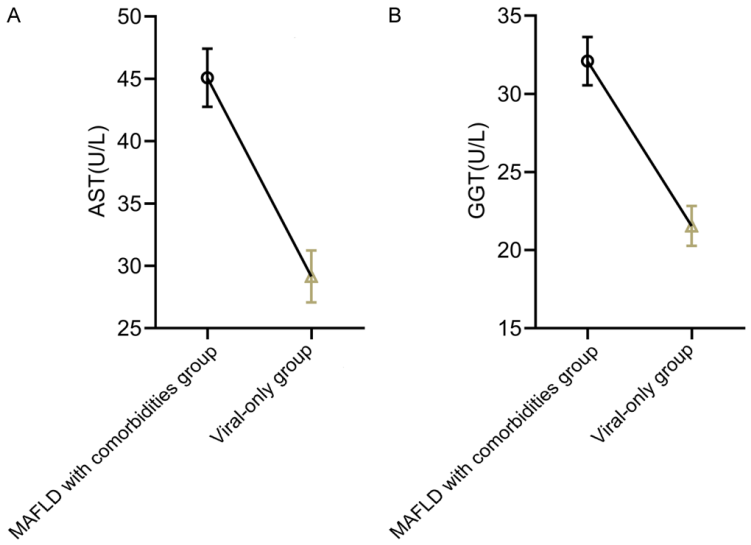


Figure 2. Comparison of liver function indicators between groups. A: AST; B: GGT. Note: AST, aspartate aminotransferase; GGT, γ-glutamyltransferase.

zone F2, 80 cases (25.8%); F3, 12 cases (3.9%); and F4, 8 cases (2.6%). Compared with the virus-only group, the proportion of mild fibrosis in the MAFLD with comorbidities group was lower, while the proportion of moderate to severe fibrosis (F2-F4) was higher. The difference between the two groups was statistically significant (P = 0.022, **Figure 3A**). FibroScan® results illustrated the variability in fibrosis and steatosis: Case 1 (male): E value 10.6 kPa, CAP 163 dB/m, indicating advanced liver fibrosis (F3) without significant steatosis and not meeting cirrhosis criteria (F4) (**Figure 3B**). Case 2 (female): E value 53.7 kPa, CAP 217 dB/m, suggesting severe cirrhosis (F4) combined with moderate steatosis (**Figure 3C**). These findings indicate a significantly increased risk of cirrhosis among patients with fatty liver, highlighting the importance of close monitoring of fibrosis progression in this population. Both cases warrant standardized follow-up and therapeutic interventions, with particular vigilance for Case 2 due to the coexistence of fatty liver, cirrhosis, and potential complications.

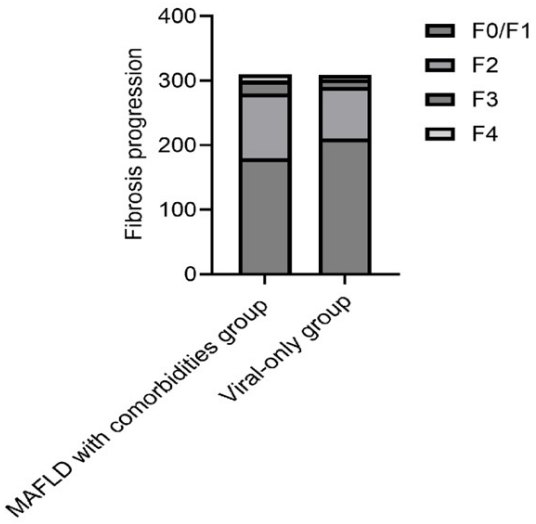
Comparison of metabolic indicators between groups

Compared with the baseline, there were certain fluctuations in the metabolic indicators of the two groups of patients after treatment, but the overall trend remained consistent. The MAFLD with comorbidities group still showed higher HOMA-IR and TG levels and lower HDL-C levels after treatment (all P < 0.05), suggesting that antiviral treatment alone was insufficient to significantly improve the metabolic disorders related to MAFLD. There was no significant difference in the changes of FBG and LDL-C between the two groups (P > 0.05) (see **Figure 4**).

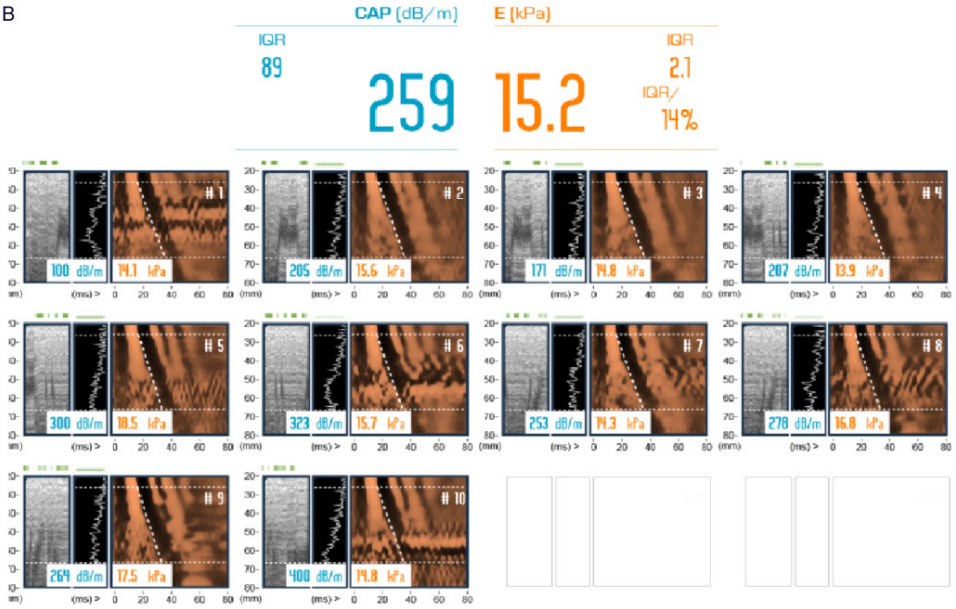
Safety evaluation

During the follow-up period, the overall incidence of adverse events was 2.11% in the MAFLD with comorbidities group and 1.94% in the viral-only group, with no statistically significant difference between the two groups (P >

A


400
300
200
100
0
Fibrosis progression
F0/F1
F2
F3
F4
MAFLD with comorbidities group
Viral-only group

B


CAP [dB/m]
IQR
89
259
E [kPa]
IQR
2.1
IQR/
14%
15.2
1
100 dB/m
14.1 kPa
2
205 dB/m
15.6 kPa
3
171 dB/m
14.8 kPa
4
207 dB/m
13.9 kPa
5
300 dB/m
18.5 kPa
6
323 dB/m
15.7 kPa
7
253 dB/m
14.3 kPa
8
278 dB/m
16.8 kPa
9
264 dB/m
17.5 kPa
10
400 dB/m
14.8 kPa

C

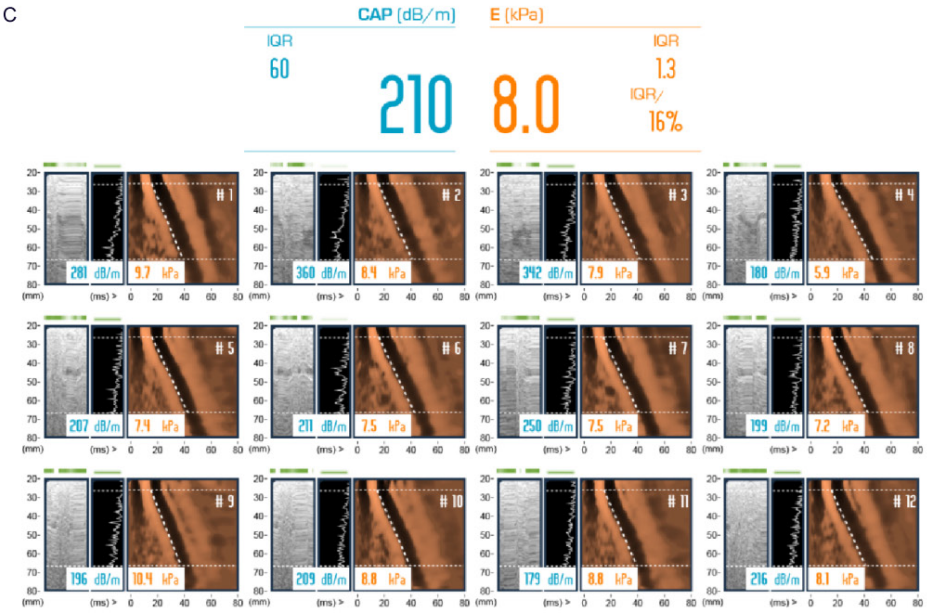

CAP [dB/m]
IQR
60
210
E [kPa]
IQR
1.3
IQR/
16%
8.0
1
281 dB/m
9.7 kPa
2
360 dB/m
8.4 kPa
3
342 dB/m
7.9 kPa
4
180 dB/m
5.9 kPa
5
207 dB/m
7.4 kPa
6
211 dB/m
7.5 kPa
7
250 dB/m
7.5 kPa
8
199 dB/m
7.2 kPa
9
196 dB/m
10.4 kPa
10
209 dB/m
8.8 kPa
11
179 dB/m
8.8 kPa
12
216 dB/m
8.1 kPa

Figure 3. Liver fibrosis progression and liver stiffness measurements. A: Distribution of Fibrosis Stages; B: FibroScan® report of a representative case of severe fatty liver with Concurrent Hepatitis B; C: FibroScan® report of a representative case of fatty liver complicated with liver cirrhosis.

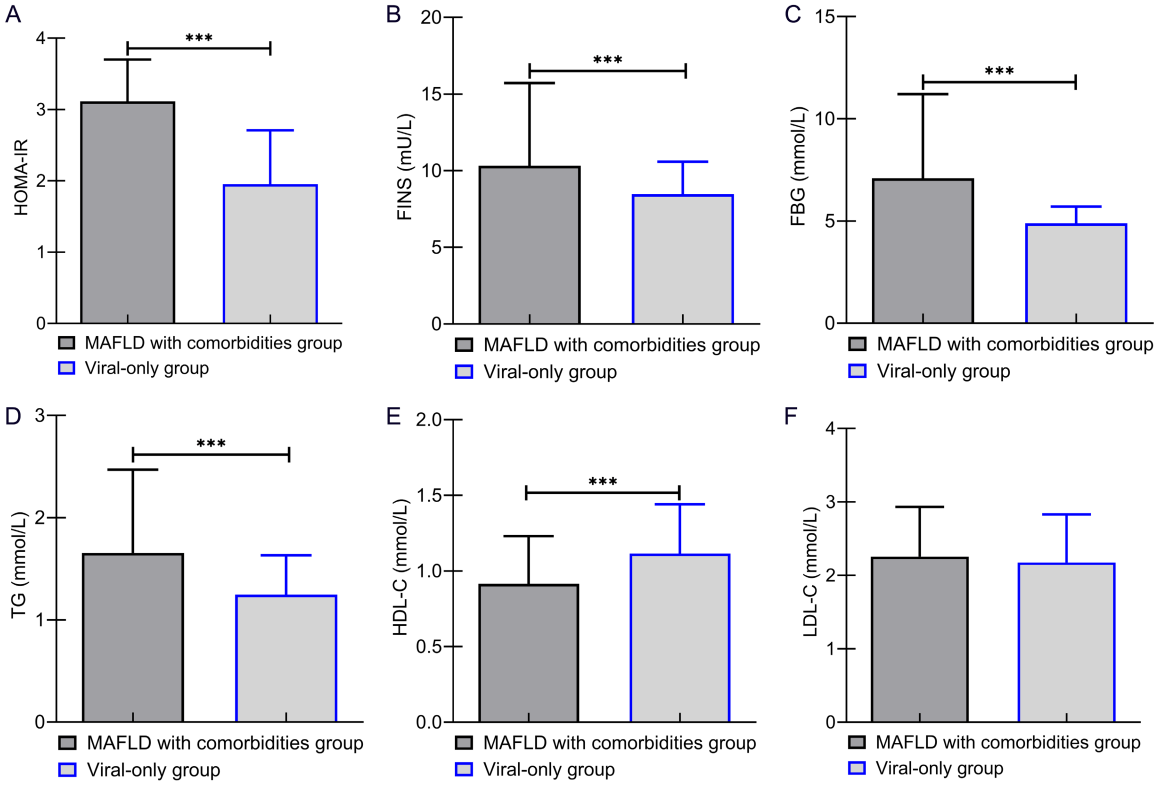


Figure 4. Metabolic indexes of patients in different groups. Comparison of metabolic indicators between groups. A. HOMA-IR; B. Fasting Insulin (FINS); C. Fasting Blood Glucose (FBG); D. Triglycerides (TG); E. High-Density Lipoprotein Cholesterol (HDL-C); F. Low-Density Lipoprotein Cholesterol (LDL-C); Compared with the MAFLD with comorbidities group, ***$P < 0.001$.

0.05), indicating a favorable safety profile for entecavir in both populations (**Table 2**).

Discussion

CHB is a liver disease caused by persistent infection with HBV and can progress to cirrhosis and even hepatocellular carcinoma [12]. MAFLD is characterized by hepatic steatosis and is closely associated with insulin resistance and metabolic dysfunction [13]. Patients with CHB are at increased risk of developing MAFLD, and the presence of insulin resistance and metabolic abnormalities in MAFLD further exacerbates liver inflammation and fibrosis. Consequently, CHB patients with concurrent MAFLD experience a more complex disease state compared to those with CHB alone, which can diminish the efficacy of antiviral therapy and accelerate disease progression [14]. Therefore, evaluating the antiviral efficacy of CHB treatment in the context of coexisting MAFLD is of urgent clinical importance for optimizing patient management strategies.

Entecavir, a first-line nucleoside analogue for the treatment of CHB, has been shown to effectively suppress HBV DNA replication and delay disease progression [15]. Although entecavir does not directly target metabolic pathways, the presence of MAFLD may influence drug metabolism and pharmacokinetics, potentially attenuating the therapeutic efficacy of entecavir [16]. However, it remains unclear whether MAFLD significantly interferes with the antiviral treatment efficacy of entecavir in CHB patients with concurrent MAFLD [17]. To address this knowledge gap, we conducted a retrospective analysis based on non-intervention real-world clinical data, consistent with the principles of

Table 2. Comparison of Adverse Events Between Groups [n (%)]

Group	Total Incidence Rate	Headache	Fatigue	Gastrointestinal Reactions (Nausea/Diarrhea)	Rash
MAFLD with comorbidities group (n = 285)	6 (2.11%)	2 (0.70%)	1 (0.35%)	2 (0.70%)	1 (0.35%)
Viral-only group (n = 310)	6 (1.94%)	1 (0.32%)	2 (0.65%)	2 (0.65%)	1 (0.32%)
χ^2	0.022	-	-	-	-
P	0.883	-	-	-	-

real-world studies (RWS). Unlike randomized controlled trials (RCTs), which are performed under highly controlled and standardized conditions, RWS rely on routine clinical practice data, better reflecting patient heterogeneity and disease complexity [18]. In this study, real-world data (RWD) were leveraged to assess the impact of MAFLD on entecavir efficacy in CHB treatment, thereby providing evidence to fill gaps in current knowledge.

The results showed no significant differences between the two groups in baseline demographic or virological parameters, indicating good comparability and minimizing confounding factors. Therefore, subsequent findings more accurately reflect the impact of MAFLD on treatment outcomes. The MAFLD with comorbidities group exhibited higher BMI, WC, HOMA-IR, FINS, and TG levels, along with lower HDL-C, reflecting more pronounced metabolic abnormalities consistent with the CHB population complicated by MAFLD. This distinction ensures that differences in subsequent treatment efficacy can be more confidently attributed to the coexistence of MAFLD.

Patients with MAFLD typically have increased visceral fat, which is highly metabolically active and promotes the secretion of large amounts of free fatty acids (FFAs). Elevated FFAs lead to greater hepatic lipid deposition, exacerbating hepatocellular steatosis and contributing to increased BMI and WC [19]. Insulin plays a crucial role in regulating glucose and lipid metabolism. Patients with MAFLD may develop insulin resistance, which results in reduced insulin sensitivity; this metabolic disturbance is consequently reflected in elevated biomarkers, specifically increased HOMA-IR values and higher FINS levels [20]. Additionally, dysregulated lipid metabolism is common in MAFLD, with elevated TG levels and decreased HDL-C levels serving as direct indicators of metabolic dysfunction [21].

The results of this study showed that, after treatment, the MAFLD with comorbidities group exhibited lower rates of ALT/AST normalization, HBV DNA negativity, and HBeAg seroconversion compared to the viral-only group, while AST and GGT levels remained significantly higher. Post-treatment fibrosis staging was more severe than that of the virus-only group. This may be attributed to the concomitant metabolic dysfunction in these patients, including hyperglycemia and elevated FFA levels, which can induce mitochondrial dysfunction in hepatocytes. Such dysfunction impairs oxidative phosphorylation, reduces ATP production, disrupts cellular energy metabolism, and consequently diminishes hepatocyte repair and regeneration capacity [22]. Moreover, elevated FFAs can activate inflammatory signaling pathways, disrupt immune function, and cause imbalances in T cell subsets, thereby impairing the body's ability to recognize and eliminate HBV. This immune dysregulation can compromise antiviral treatment efficacy and potentially accelerate liver fibrosis progression. As a result, normalization of liver function markers such as ALT and AST is delayed, and HBV DNA clearance is hindered [23]. Additionally, insulin resistance in MAFLD patients disrupts hepatic insulin signaling, further altering the activity of metabolic enzymes in hepatocytes. This facilitates persistent HBV replication and compromises the effectiveness of antiviral therapy [24]. Collectively, MAFLD diminishes the virological and biochemical responses to entecavir and accelerates liver fibrosis progression through multiple mechanisms, including energy metabolism disorders, chronic inflammation, and hepatocyte immune imbalance.

Additionally, this study found that, after treatment, the MAFLD with comorbidities group continued to exhibit higher HOMA-IR and TG levels, along with lower HDL-C. These findings indicate that entecavir monotherapy does not directly regulate glucose or lipid metabolism and has

limited efficacy in improving metabolic disorders. No significant changes were observed in FBG or LDL-C before and after treatment in either group, suggesting that entecavir itself does not exert a detectable adverse effect on glucose and lipid metabolism. During the follow-up period, the overall incidence of adverse events was 2.11% in the MAFLD with comorbidities group and 1.94% in the viral-only group, with no significant difference. This favorable safety profile may be due to entecavir's good tolerability and its primary hepatic metabolism, which does not significantly affect key metabolic enzyme systems or directly interfere with glucose and lipid metabolic pathways [25]. These observations suggest that while entecavir effectively suppresses HBV replication in patients with CHB complicated by MAFLD, it is insufficient to reverse underlying metabolic dysfunction, highlighting the need for coordinated metabolic interventions in this population.

However, several limitations should be acknowledged. This study is retrospective, which may introduce information loss or data entry errors, and potentially lead to bias. Although MAFLD may accelerate liver fibrosis progression, the relatively short follow-up duration limits the ability to assess the long-term effects of entecavir on clinical outcomes. Therefore, large-scale prospective studies are needed to further explore these issues and provide stronger evidence for optimizing management strategies in CHB patients with MAFLD.

In summary, entecavir provides effective virological suppression in CHB patients with concomitant MAFLD. However, the recovery of liver function, improvement of steatosis and metabolic improvement were all inferior to those of patients without MAFLD. For this population, comprehensive management strategies - including targeted metabolic interventions, vitamin supplementation, and exercise - should be integrated to optimize long-term outcomes.

Disclosure of conflict of interest

None.

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