Chronic hepatitis B patients with high liver fibrosis levels should receive antiviral treatment

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Abstract. The present study aimed to evaluate improvements in liver stiffness (LS) measured by transient elastography (TE) and associated factors in Chinese patients with chronic hepatitis B (CHB) treated with entecavir (ETV). A total of 190 consecutive CHB patients who received entecavir therapy and two LS measurements (LSMs) were enrolled in this retrospective study (average age, 47 years; 137 males [72.1%]), including 111 patients without liver cirrhosis (group 0) and 79 patients with liver cirrhosis (group 1). Each patient received LSM twice with an interval of six months. Normalized aspartate aminotransferase (AST) levels were accompanied by a significant reduction in LSM values (P<0.001) in each group. Multivariate analysis revealed that a higher initial LS value in groups 0 and 1, and a higher prothrombin time activity in group 1 was associated with a greater decline of the LS value. Higher initial quantitative hepatitis B surface antigen (qHBsAg) levels were correlated with a greater decline of the qHBsAg value in the two groups. In conclusion, LS values in CHB patients significantly improved after 24 weeks of entecavir therapy. The results suggested that higher LSM values at baseline contributed to a greater regression of LSM, and higher initial qHBsAg values could lead to greater qHBsAg reduction during ETV therapy. Extrapolating our results, we might be able to consider CHB patients who have higher initial LSM values or have higher levels of qHBsAg values when enrolled would have more benefit during ETV treatment.

Introduction

Hepatitis B virus (HBV) chronically infects 240 million people worldwide and remains a severe threat to public health. Chronic hepatitis B (CHB) can advance to cirrhosis and hepatocellular carcinoma. CHB-associated complications account for ~700,000 mortalities per year. The ultimate goal for treating CHB is to block the advancement of chronic liver injury to the stages of cirrhosis, hepatic decompensation and/or hepatocellular carcinoma (HCC). Thus, an early and accurate diagnosis of fibrosis stages is important for assessing prognosis (1-3).

Liver biopsy provides tissue for assessing liver pathology, but its applications are limited due to its invasiveness, patient discomfort, sampling errors, inter-observer variation and risk for internal bleeding complications.

In recent years, there has been increasing interest in estimating liver fibrosis using transient elastography (TE), a non-invasive method. TE utilizes an ultrasound (US) transducer attached to the axis of the vibrator that generates pulsation featured with a mild amplitude and low frequency (50 Hz). This resultant elastic shear wave transmits through the liver. Detection based on US pulse-echo tracks the dissemination of the shear wave and computes its velocity, which is proportional to liver tissue stiffness. The stiffer the tissue, the quicker the shear wave is transmitted (4,5). TE is a noninvasive, timesaving and reproducible method for assessing liver stiffness (LS) and it is well tolerated by most patients (6,7).

Entecavir (ETV), a new-generation nucleoside analogue, profoundly suppresses HBV DNA replication and has been widely prescribed for treating CHB due to its high efficacy. Clinical evidence suggested that fibrosis, particularly in the early stage, may in fact be reversed by effective ETV therapy. However, the efficacy of ETV therapy in blocking the progression of liver injury and reversing fibrosis in CHB in Chinese populations has only been evaluated by few studies.

The present study evaluated the effects of ETV treatment on viral replication, liver injury and hepatic fibrosis in 190 Chinese CHB patients who received LS measurement (LSM) twice using fibroscan at baseline and week 24 of the treatment. LSM values in patients significantly improved after 24 weeks of ETV therapy.

Patients and methods

Patients. A total of 218 consecutive Chinese CHB patients, who had been hepatitis B surface antigen-positive for ≥6 months, were enrolled in the present study from November 2013 to March 2015. The Child Pugh Score of all of the enrolled

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patients was <9 and the patients were aged 18-65 years. These patients received at least two LSMs while being administered oral ETV at the First Hospital of Jilin University (Changchun, China).

The exclusion criteria adopted were as follows: i) Co-infection with human immunodeficiency virus or hepatitis C virus (HCV); ii) excessive alcohol consumption or drug abuse; iii) alanine transaminase (ALT) >100 IU/l or aspartate transaminase (AST) >100 IU/l at baseline; iv) hepatocellular carcinoma suggested upon the first abdominal ultrasound; v) history of ascites, upper gastrointestinal hemorrhage, hepatic encephalopathy, infection, electrolyte disturbances or Child Pugh Score ≥9; vi) history of diabetes, hypertension or other metabolic conditions. Finally, 190 patients with CHB were enrolled.

Upon enrollment, each patient was subjected to an initial LSM and a second one followed ~6 months later. Liver cirrhosis was diagnosed based on US.

The recruitment of human subjects and the study protocol were approved by the Independent Institutional Review Board of the First Hospital of Jilin University (Changchun, China). Written informed consent was signed by each participant prior to enrollment.

Laboratory tests. All biochemical, serological and virological examinations were performed within five days prior to LSM. The ARCHITECT hepatitis B surface antigen (HBsAg) assay (Abbott, Chicago, IL, USA) was used to assess quantitative (q) HBsAg. Serum HBV DNA levels were examined by using the COBAS TaqMan HBV test with the High Pure System (Roche Molecular Systems, Inc., Pleasanton, CA, USA) at a lower detection limit of 15 IU/ml. Serum HBV DNA levels were expressed as log10 units. qHBsAg and serum HBV DNA levels were established using blood samples collected upon admission.

LSM. Patients who had fasted overnight were subjected to LSM by transient elastography (TE) with an M-probe (FibroScan; Echosens, Paris, France). A minimum of 10 valid measurements were acquired from each patient. LSM values were considered valid and entered into the final analysis only if the success rate of LSM reached >60%. Calculated median values of the valid measurements (expressed in kPa) reflected the relative LS for each patient at a specific time-point.

Statistical analysis. Quantitative differences in LSM value changes between two points were analyzed by Student's t-test. Percentages were weighed by Chi-square test. Continuous variables were expressed as the mean ± standard deviation. Independent factors associated with LS were individually ascertained through stepwise multiple linear regression models. All tests were two-sided, and P<0.05 was considered to indicate a statistically significant difference between values. SPSS v.23.0 (International Business Machines Corp., Armonk, NY, USA) was used for all statistical analyses.

Results

Patient characteristics at baseline. Clinical and laboratory characteristics of participants at baseline and follow-up are shown in Table I. A total of 190 CHB patients treated with ETV were enrolled in the present study, including 137 male and 53 female patients, and the mean age was 47 years. The mean duration of antiviral treatment prior to initial LSM was 484 days. Patients were assigned to group 0 when liver cirrhosis was absent (n=111) and to group 1 when liver cirrhosis was present (n=79). No significant difference was detected in the demographic characteristics, including gender, HBeAg-negative rate and family history of HBV infection between the two groups before baseline LSM. In addition, no significant difference was detected in the baseline levels of ALT, α-fetoprotein (AFP), serum creatinine (Cr), blood urea nitrogen (BUN) and triglycerides between the two groups. Furthermore, the mean age in group 1 was higher than that in group 0. At baseline, group 0 showed higher qHBsAg and HBV DNA titers, platelet count (PLT), albumin (ALB) and prothrombin time activity (PTA) than group 1, while initial AST and total bilirubin (TBIL) were higher in group 1. In addition, LSM values in group 1 were higher compared to those in group 0. Furthermore, the therapy course in group 0 was longer than that in group 1.

Changes in liver biochemical markers and LS value. Biochemical markers significantly improved after patients in group 0 underwent ETV therapy (Table I). For instance, initial and follow-up levels were 32.83±14.30 and 24.20±9.27 IU/l for AST (P<0.001), 18.09±60.50 and 3.26±1.94 ng/ml for AFP (P=0.010), 89.60±11.12 and 93.49±12.60% for PTA (P=0.001), 26.13±19.89 and 26.69±15.82 IU/l for ALT (P=0.763), 20.10±11.55 and 18.29±7.87 µmol/l for TBIL (P=0.063), 2.07±1.59 and 1.12±1.51 log IU/l for HBV DNA (P<0.001), and 2,991.54±5247.24 and 2,597.24±5846.97 IU/ml for qHBsAg (P=0.488), respectively. The mean LS value at baseline was 14.84±9.42 kPa, which decreased to 8.36±4.88 kPa.

Initial and follow-up levels in group 1 were 39.91±15.08 and 32.34±11.04 IU/l for AST (P<0.001), 31.91±17.01 and 33.97±17.45 IU/l for ALT (P=0.257), 24.39±12.63 and 24.91±11.26 µmol/l for TBIL (P=0.675), 76.39±15.03 and 80.90±16.42% for PTA (P<0.001), 11.75±29.64 and 11.72±68.30 ng/ml for AFP (P=0.998), 2.20±1.38 and 0.88±1.19 log IU/l for HBV DNA (P<0.001) and 1,240.17±1387.61 and 1,066.22±1184.79 IU/ml for qHBsAg (P=0.067), respectively. LS values significantly decreased from 21.08±8.55 to 16.01±10.60 kPa (P<0.001) during the 24 weeks of ETV therapy.

Parameters correlated with the improvement of LS. Univariate analysis suggested that factors indicating a greater decline of the LS value in group 0 included higher initial LS values (P<0.001), higher initial AFP values (P=0.001), lower initial serum ALB (P=0.029), lower initial BUN (P=0.031) and shorter duration of antiviral therapy prior to initial LSM (P=0.006). Furthermore, there was a positive correlation between the changes of LS values and the changes of HBV DNA after 24 weeks of ETV therapy (P=0.005). The above-mentioned factors were considered for entry in multivariate analysis. After adjusting for potential confounders, higher initial LS values were independently associated with a significant reduction in LS values (P<0.001; Table II).

Table I. Clinical and laboratory findings in the two groups.

Characteristic	Group 0 (n=111)	Group 1 (n=79)	P-value
Age, years	45.94±9.76	49.61±9.66	0.011
Male gender, n (%)	79 (71)	58 (73)	0.734
HBeAg (positive/negative)	54/57	32/47	0.266
Family HBV infection history (yes/no)	56/55	36/43	0.507
Initial AST (IU/l)	32.83±14.30	39.91±15.08	0.001
Follow-up AST (IU/l)	24.20±9.27	32.34±11.04	<0.001
Initial ALT (IU/l)	26.13±19.89	31.39±17.01	0.058
Follow-up ALT (IU/l)	26.69±15.82	33.97±17.45	0.003
Initial TBIL (μmol/l)	20.10±11.55	24.39±12.63	0.016
Follow-up TBIL (μmol/l)	18.29±7.87	24.91±11.26	<0.001
Initial PTA (%)	89.60±11.12	76.39±15.03	<0.001
Follow-up PTA (%)	93.49±12.60	80.90±16.42	<0.001
Initial AFP (ng/ml)	18.09±60.50	11.75±29.64	0.391
Follow-up AFP (ng/ml)	3.26±1.94	11.72±68.30	0.274
Initial HBV DNA (log IU/l)	2.07±1.59	2.20±1.38	<0.001
Follow-up HBV DNA (log IU/l)	1.12±1.51	0.88±1.19	<0.001
Initial qHBsAg (IU/ml)	2,991.54±5247.24	1,240.17±1387.61	0.001
Follow-up qHBsAg (IU/ml)	2,597.24±5846.97	1,066.22±1184.79	0.008
Initial LS (kPa)	14.84±9.42	21.08±8.55	<0.001
Follow-up LS (kPa)	8.36±4.88	16.01±10.60	<0.001
Therapy before initial LSM (days)	560.32±631.21	376.28±457.63	0.021
Initial platelet count (10^9/l)	169.11±64.19	110.99±70.15	<0.001
Initial serum Cr (μmol/l)	70.30±16.66	76.22±33.05	0.106
Initial BUN (mmol/l)	4.89±1.25	4.72±1.49	0.409
Initial ALB (g/l)	42.31±4.48	40.23±4.53	0.002
Initial triglycerides (mmol/l)	1.32±0.62	1.25±0.72	0.466

Values are expressed as the mean ± standard deviation. Normal ranges: AST, 15.0-40.0 IU/l; ALT, 9.0-50.0 IU/l; TBIL, 6.8-30.0 μmol/l; PTA, 80-120%; AFP, <20 ng/ml; serum Cr, 58-110 μmol/l; BUN, 3.2-7.1 mmol/l; ALB, 40.0-55.0 g/l; triglycerides, 0.28-1.80 mmol/l. qHBsAg, quantitative hepatitis B surface antigen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TBIL, total bilirubin; AFP, α-fetoprotein; PTA, prothrombin time activity; Cr, creatinine; BUN, blood urea nitrogen; ALB, albumin; HBV, hepatitis B virus; LSM, liver stiffness measurement.

In group 1, univariate analysis revealed that factors that may predict a significant reduction of the LS value included lower initial serum TBIL (P=0.038), higher initial PTA (P=0.034), higher initial BUN (P=0.026) and a higher initial LS (P=0.012), while multivariate analysis revealed that higher initial LS values (P<0.001) and a higher PTA (P=0.013) were correlated with a significant reduction of LS values after adjusting for potential confounders (Table III).

Parameters correlated with the decline of quantitative hepatitis B surface antigen (qHBsAg). In group 0, univariate analysis revealed that factors that may predict a significant reduction of the qHBsAg value included female gender (P=0.039), no family history of HBV infection (P=0.029) and higher initial qHBsAg (P<0.001), while multivariate analysis revealed that only the initial qHBsAg value was significantly correlated to the reduction of the qHBsAg values after adjusting for potential confounders (P<0.001; Table IV).

Univariate analysis suggested that factors indicating a greater decline of the LSM value in group 1 included higher initial qHBsAg (P<0.001) and higher initial triglycerides (P=0.020). After adjusting for potential confounders, multivariate analysis indicated that higher initial qHBsAg values were associated with a significant reduction in qHBsAg values (P<0.001; Table V).

Discussion

In the present study, the impact of 24 weeks of ETV therapy on LS in 190 CHB patients was investigated. Each patient was evaluated by TE at the beginning and the end of the 24-week period. After ETV treatment, liver injury was found to be significantly improved in each group. In parallel with normalized AST values, HBV DNA titers and LS scores also significantly declined in CHB patients with or without cirrhosis and reduced qHBsAg levels were observed in CHB patients after 24 weeks of ETV treatment.

LSM is one of the increasingly popular noninvasive methods for detecting and grading liver fibrosis (1). Numerous studies have revealed that this method has good reproducibility,

Table II. Factors associated with the decline of LS values in uni- and multivariate analyses in group 0.

Factor	Univariate coefficient	P-value	Multivariate coefficient	P-value
Gender	-1.055[a]	0.292		
Age, years	0.068	0.480		
Family HBV infection history	-0.236[a]	0.813		
Initial AST	0.154	0.106		
Initial ALT	0.166	0.082		
Initial TBIL	-0.019	0.845		
Initial LS	0.856	<0.001	0.862	<0.001
Initial qHBsAg	-0.130	0.173		
Initial AFP	0.320	0.001	0.007	0.901
HBeAg	-0.063	0.510		
Initial HBV DNA (log IU/ml)	0.126	0.187		
Initial PTA	-0.064	0.503		
Therapy before initial LSM	-0.258	0.006	0.016	0.772
Changes of HBV DNA	0.268	0.005	0.057	0.300
Initial platelets	-0.094	0.327		
Initial Cr	0.060	0.535		
Initial BUN	-0.205	0.031	-0.047	0.364
Initial ALB	-0.207	0.029	0.095	0.097
Initial triglycerides	0.128	0.182		

[a]Mann-Whitney U test. Values are expressed as the mean ± standard deviation. qHBsAg, quantitative hepatitis B surface antigen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TBIL, total bilirubin; AFP, α-fetoprotein; PTA, prothrombin time activity; Cr, creatinine; BUN, blood urea nitrogen; ALB, albumin; HBV, hepatitis B virus; LSM, liver stiffness measurement; LS, liver stiffness.

Table III. Factors associated with the decline of LS values in uni- and multivariate analyses in group 1.

Factor	Univariate coefficient	P-value	Multivariate coefficient	P-value
Gender	-1.570[a]	0.116		
Age (years)	-0.180	0.112		
Family HBV infection history	-0.148[a]	0.883		
Initial AST	0.021	0.885		
Initial ALT	0.006	0.960		
Initial TBIL	-0.233	0.038	-0.166	0.156
Initial LS	0.280	0.012	0.420	<0.001
Initial qHBsAg	-0.011	0.926		
Initial AFP	0.086	0.453		
HBeAg	-0.050	0.665		
Initial HBV DNA	0.032	0.779		
Initial PTA	0.239	0.034	0.315	0.013
Therapy before initial LSM	0.100	0.380		
Changes of HBV DNA	0.045	0.695		
Initial platelets	0.053	0.640		
Initial Cr	0.008	0.942		
Initial BUN	0.250	0.026	0.117	0.255
Initial ALB	-0.033	0.770		
Initial triglycerides	0.044	0.702		

[a]Mann-Whitney U test. qHBsAg, quantitative hepatitis B surface antigen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TBIL, total bilirubin; AFP, α-fetoprotein; PTA, prothrombin time activity; Cr, creatinine; BUN, blood urea nitrogen; ALB, albumin; HBV, hepatitis B virus; LSM, liver stiffness measurement, LS, liver stiffness.

Table IV. Factors associated with the decline of qHBsAg values in uni- and multivariate analyses in group 0.

Factor	Univariate coefficient	P-value	Multivariate coefficient	P-value
Gender	-2.064	0.039	-0.099	0.257
Age (years)	0.016	0.889		
Family HBV infection history	-2.180[a]	0.029	-0.105	0.227
Initial AST	-0.166	0.082		
Initial ALT	-0.092	0.337		
Initial Total bilirubin	-0.053	0.579		
Initial LS	-0.074	0.441		
Initial qHBsAg	0.462	<0.001	0.460	<0.001
Initial AFP	-0.045	0.639		
HBeAg	0.044	0.645		
Initial HBV DNA	0.158	0.099		
Initial PTA	0.049	0.611		
Therapy before initial LSM	0.017	0.857		
Changes of HBV DNA	0.011	0.910		
Initial platelets	0.008	0.932		
Initial Cr	0.062	0.519		
Initial BUN	0.097	0.310		
Initial ALB	0.100	0.294		
Initial triglycerides	0.005	0.962		

[a]Mann-Whitney U test. qHBsAg, quantitative hepatitis B surface antigen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TBIL, total bilirubin; AFP, α-fetoprotein; PTA, prothrombin time activity; Cr, creatinine; BUN, blood urea nitrogen; ALB, albumin; HBV, hepatitis B virus; LSM, liver stiffness measurement.

Table V. Factors associated with the decline of qHBsAg in uni- and multivariate analyses in group 1.

Factor	Univariate coefficient	P-value	Multivariate coefficient	P-value
Gender	-1.377[a]	0.169		
Age, years	0.002	0.985		
Family HBV infection history	-0.787[a]	0.431		
Initial AST	0.035	0.762		
Initial ALT	-0.064	0.573		
Initial Total bilirubin	-0.057	0.619		
Initial LS	-0.213	0.059		
Initial qHBsAg	0.526	<0.001	0.420	<0.001
Initial AFP	-0.018	0.878		
HBeAg	-0.076	0.506		
Initial HBV DNA (IU/ml)	0.019	0.871		
Initial PTA	0.083	0.467		
Therapy before initial LSM	-0.034	0.767		
Changes of HBV DNA	0.069	0.543		
Initial platelets	0.086	0.453		
Initial Cr	-0.108	0.344		
Initial BUN	-0.109	0.337		
Initial ALB	-0.075	0.513		
Initial triglycerides	0.261	0.020	0.138	0.165

[a]Mann-Whitney U test. qHBsAg, quantitative hepatitis B surface antigen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TBIL, total bilirubin; AFP, α-fetoprotein; PTA, prothrombin time activity; Cr, creatinine; BUN, blood urea nitrogen; ALB, albumin; HBV, hepatitis B virus; LSM, liver stiffness measurement.

relative reflection of histology and clinical utility (4,6,8,9). However, the stiffness in hepatic parenchyma may be caused by necroinflammation and/or fibrosis. LSM is not able to distinguish necroinflammation from fibrosis (1). In addition, the changes in LS values in severe inflammation at baseline did not reflect real reversal of fibrosis (8,10,11). Accordingly, patients with AST>100 IU/l or ALT>100 IU/l at baseline were excluded for minimizing the influence of inflammatory activity on LS values. Furthermore, it was identified that in parallel with normalized AST values, LS scores significantly declined in CHB patients with or without cirrhosis after 24 weeks of ETV treatment.

The present findings regarding the LS scores were principally consistent with previously published data. For instance, liver fibrosis has been reported to improve in 35-38% of lamivudine-treated CHB patients and 36-39% of ETV-treated CHB patients after one year (12,13). Long-term ETV treatment (>3 years) attenuated necroinflammatory activity in all patients and reduced liver fibrosis in 57-100% of patients (1,14). Furthermore, advanced liver fibrosis was shown to be reversed after long-term antiviral treatment (14,15). However, these previous studies always included patients with long-term antiviral treatment of at least >1 year. However, in clinical practice, patients with advanced fibrosis may not receive long-term antiviral treatment due to the occurrence of CHB-associated complications and the uncertainty of the survival time. However, according to our experience, short-term antiviral treatment may not show an obvious benefit. Based on the results of the present study, it may be concluded that hepatic fibrosis may regress in patients with liver cirrhosis after only 24 weeks of ETV treatment. As liver fibrosis can be reduced in a short time, CHB patients in different stages may all benefit from antiviral treatment. However, the present study had various limitations; for instance, the patients with a Child Pugh Score of ≥9 or ascites were not included as LS values may be influenced by ascites.

The present study found that the substantially reduced LS values in the two groups after 24 weeks of ETV treatment were associated with higher baseline LS scores, as has been previously reported (10,16). The reason for this may be that patients with higher initial LS values had a greater chance of reduction in LS values. In addition, it may be hypothesized that a significant decline in LS values may reflect an improvement in liver fibrosis after ETV treatment, as the influence of high ALT levels was excluded. Beyond that, patients with a shorter duration of antiviral treatment showed a larger decline of their LS value at follow-up, which may have been due to their comparatively worse liver condition when they were recruited. This noteworthy correlation was in agreement with the findings by Kuo *et al* (10). Therefore, the present study showed that patients with higher liver fibrosis levels should receive antiviral therapy, as it achieves a greater improvement in LS values.

Certain studies reevaluated the pathogenesis of HBV infection and suggested that a high level of HBV replication in infected cells leads to a high level of intracellular accumulation of viral products, which causes the destruction of infected cells. Inhibition of replication- and accumulation-mediated liver injury provides an explanation for the efficacy of nucleos(t)ide analogue therapy in mitigating liver injury and reducing liver

fibrosis in CHB patients. According to this mechanism, it is inferred that the decline of HBV DNA titers is associated with the reduction of LS values. However, the results of the present study did not identify any independent correlation between the changes of HBV DNA with the significant reduction in LSM values after adjusting for potential confounders in CHB patients receiving ETV treatment. This may be due to exclusion of patients with severe inflammation at baseline, which diminished the significance of a decline of liver fibrosis and inflammation induced by reduction of HBV DNA titers. In addition, the interval between the two LSMs in the present study was 24 weeks, while the effectiveness in reducing liver fibrosis caused by suppression of viral replication may be exerted over a longer period, which requires assessment in future studies. HBsAg was initially discovered and named 'Australia antigen' in 1968 (17) and is the hallmark of HBV infection. HBsAg levels have been reported to be in parallel with intra-hepatic HBV DNA and covalently closed circular DNA (cccDNA) levels. In the present study, the patient in the two groups did not achieve a significant decline of qHBsAg during 24 weeks of treatment with ETV. This may be due to a lack of a direct effect of nucleos(t)ide analogues on cccDNA and the fact that the intensity of host immunity to reduce the qHBsAg levels was low in the patients with ALT≤2 times the upper limit of normal. Furthermore, the mean duration of antiviral treatment before initial LS was 484 days in the present study, which is when the effect of the immune reaction decreases (18-20). Previous studies reported that the baseline qHBsAg predicts the treatment or virologic response in CHB patients with nucleos(t)ide treatment (18,19). In the present study, the substantially reduced qHBsAg values in the two groups after 24 weeks of ETV treatment were correlated with a higher initial qHBsAg but not with LS values. This suggested that the decline of qHBsAg was associated with HBV itself rather than the severity of patients' illness when the intensity of host immunity was low and patients with higher initial qHBsAg benefited more from antiviral treatment.

In conclusion, the present study evaluated changes in LS in 190 CHB patients who received ETV treatment and found a significant decrease in LSM scores in patients with or without cirrhosis only after 24 weeks of ETV treatment. The results suggested that higher LS values at baseline contributed to a greater LS regression and higher initial qHBsAg values led to a greater reduction of qHBsAg during ETV therapy. Based on these results, ETV treatment provided a greater benefit for CHB patients with higher initial LS values or qHBsAg levels at baseline.

Acknowledgements

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