Clinical utility of the treatment eligibility score HEPSANET for chronic hepatitis B in Asia

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The availability of tools to assess treatment eligibility of chronic hepatitis B (CHB) is a significant barrier to treatment initiation in resource limited regions.[1] A simple score (HEPSANET) which included platelets, aspartate aminotransferase, and alanine aminotransferase was proposed to determine treatment eligibility in CHB patients in Africa with a high diagnostic accuracy.[2] The Asia–Pacific region has a huge burden of hepatitis B virus (HBV) infection with low treatment rate.[1] The HBV DNA quantification, as a core part of current treatment eligibility assessment, remains inaccessible for many resource-limited settings in Asia–Pacific region.[3] Thus, simplified algorithms based on inexpensive diagnostic tools for treatment eligibility might also benefit CHB patients in Asia–Pacific region.

We evaluated the performance of HEPSANET score in two large cohorts of Asian CHB patients, including a liver biopsy cohort (n = 1031) and a non-invasive test (NIT) cohort (n = 1066). Treatment-naïve patients with chronic HBV infection who received liver biopsy or non-invasive test by vibration-controlled transient elastography were included. Patients in the liver biopsy cohort were included from four medical centers (Nanjing Drum Tower Hospital [Nanjing, China], The Affiliated Infectious Diseases Hospital of Soochow University [Suzhou, China], Huai'an No. 4 People's Hospital [Huai'an, China], and The Fifth People's Hospital of Wuxi [Wuxi, China]) between 2004 and 2023, and patients in the NIT cohort were included from Nanjing Drum Tower Hospital (Nanjing, China) between 2019 and 2023. The main exclusion criteria were as follows: (1) coexisting of liver steatosis, other viral hepatitis, human immunodeficiency virus infection, immune-related liver diseases, hereditary and metabolic liver diseases; (2) coexisting of metabolic disorders, including diabetes, hypertension and hyperlipidemia; (3) coexisting of hepatocellular carcinoma or other malignancy; (4) alcohol abuse. This study was conducted following the Declaration of Helsinki and approved by the Institutional Review Board of Nanjing Drum Tower Hospital (Ethics number: 2008022). Due to a retrospective design, informed consent of patient was waived by the ethics committees.

Supplementary Fig. S1 shows the flow diagram describing the process of patient selection. The clinical features of the study population were showed in the Supplementary Table S1. The median age of patients in the NIT cohort and liver biopsy cohort were 36.0 years and 38.0 years, respectively. Patients in the liver biopsy cohort had higher proportions of male sex (65.1% vs. 50.2%, $P < 0.001$) and HBeAg positivity (46.5% vs. 21.4%, $P < 0.001$) as well as higher values of serum ALT (40.0 U/L vs. 23.0 U/L, $P < 0.001$), HBV DNA (5.0 $\log_{10}$ IU/ml vs. 3.0 $\log_{10}$ IU/ml, $P < 0.001$), and body mass index (BMI, 22.8 kg/m^2 vs. 21.9 kg/m^2, $P < 0.001$). The median values of liver stiffness measurement and controlled attenuation parameter were 6.0 kPa and 218.0 dB/m, respectively in the NIT cohort.

A total of 20.3% and 12.6% of patients were eligible for treatment based on the criteria of European Association for the Study of the Liver (EASL) 2017 guidelines[4] and American Association for the Study of Liver Diseases (AASLD) 2018 guidance[5] in the NIT cohort, while the corresponding proportions were 64.2% and 58.2% in the biopsy cohort, respectively (Supplementary Table S1). The area under the receiver operator curves (AUROCs) of HEPSANET score for determining treatment eligibility were 0.74 (95% CI 0.70–0.77) and 0.73 (95% CI 0.70–0.76) in the NIT cohort and biopsy cohort based on treatment criteria by EASL 2017 guidelines, with a sensitivity and specificity of 54.6% and 92.7%, 67.9% and 78.5%, respectively (Table 1). The diagnostic performance of HEPSANET

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	AUROC (95% CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	P value	P value[a]
EASL 2017 criteria							
Non-invasive test cohort (n = 1066)							
Tier-specific algorithms							
Tier 0–1	0.61 (0.58–0.65)	69.9	52.7	27.3	87.3	<0.001	<0.001
Tier 2 (HEPSANET score)	0.74 (0.70–0.77)	54.6	92.7	65.6	88.9	<0.001	–
Tier 3	0.82 (0.80–0.85)	82.4	82.4	54.3	94.9	<0.001	<0.001
TREAT-B	0.81 (0.78–0.84)	80.6	81.1	51.9	94.3	<0.001	<0.001
Liver biopsy cohort (n = 1031)							
Tier-specific algorithms							
Tier 0–1	0.55 (0.52–0.58)	71.8	39.0	68.0	43.3	<0.001	<0.001
Tier 2 (HEPSANET score)	0.73 (0.70–0.76)	67.9	78.5	85.1	57.5	<0.001	–
Tier 3	0.76 (0.74–0.79)	87.0	65.7	82.1	73.7	<0.001	0.006
TREAT-B	0.78 (0.75–0.80)	86.7	68.7	83.4	74.1	<0.001	0.002
AASLD 2018 criteria							
Non-invasive test cohort (n = 1066)							
Tier-specific algorithms							
Tier 0–1	0.59 (0.54–0.63)	67.2	50.3	16.3	91.4	<0.001	<0.001
Tier 2 (HEPSANET score)	0.78 (0.73–0.82)	64.9	90.0	48.3	94.7	<0.001	–
Tier 3	0.76 (0.73–0.80)	76.9	75.9	31.4	95.8	<0.001	0.464
TREAT-B	0.76 (0.72–0.80)	76.9	75.1	30.7	95.8	<0.001	0.446
Liver biopsy cohort (n = 1031)							
Tier-specific algorithms							
Tier 0–1	0.51 (0.48–0.54)	68.7	32.9	58.8	43.0	0.708	<0.001
Tier 2 (HEPSANET score)	0.68 (0.65–0.71)	66.5	69.6	75.3	59.9	<0.001	–
Tier 3	0.69 (0.66–0.72)	84.0	53.6	71.6	70.6	<0.001	0.526
TREAT-B	0.70 (0.67–0.73)	83.5	55.9	72.5	70.9	<0.001	0.260

AUROC, area under the receiver operator curve; NPV, negative predictive value; PPV, positive predictive value; TREAT-B, treatment eligibility in Africa for the hepatitis B virus. [a]Compared with HEPSANET score.

Table 1: **Accuracy of the HEPSANET score in determining hepatitis B treatment eligibility according to the EASL 2017 guidelines and AASLD 2018 guidance.**

score was inferior to another simple score free from HBV DNA (TREAT-B score)[6] and Tier 3 algorithm. Similar performance of HEPSANET score was observed when using the treatment criteria by the AASLD 2018 guidance. Moreover, we conducted a sensitivity analysis after excluding patients with overweight/obesity (BMI ≥ 25 kg/m^2) and the performance of HEPSANET score did not change significantly (Supplementary Table S2). Although the AUROCs of HEPSANET score were over 0.8 in the study by Minier et al.,[2] the HEPSANET score presented a moderate accuracy to determine treatment eligibility both in the NIT cohort and biopsy cohort in the present study. The differences in clinical features of patients such as age, HBV genotypes or comorbidities may lead to the inconsistent results.

In summary, the simple algorithm of HEPSANET score had a moderate accuracy to determine treatment eligibility for CHB in our cohorts of Asian patients with CHB. Given that the HEPSANET score only contained routine laboratory parameters, we believe that HEPSANET score remains a promising tool for eliminating hepatitis B in resource-limited settings in Asia–Pacific region. However, more studies are needed to validate the performance of HEPSANET score in more diverse populations and settings before widespread adoption.

Contributors

Jian Wang: Conceptualization; writing—original draft. Zhiyi Zhang: methodology. Chuanwu Zhu: data curation. Chao Wu: Conceptualization; writing—review and editing. Rui Huang: Conceptualization; writing—original draft; writing—review and editing; supervision.

Data sharing statement

The data that support the study findings are available upon reasonable request from the corresponding author.

Declaration of interests

Declaration of personal interests: None.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2024.101097.

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