

A Noninvasive Model to Predict Liver Histology for Antiviral Therapy Decision in Chronic Hepatitis

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Description

Hepatitis B Virus (HBV) infection is a worldwide epidemic and remains a serious global public health problem. According to the World Health Organization, about 2 billion people worldwide infected with HBV, 240 million of them are Chronic Hepatitis B (CHB) [1], there is an increased risk of cirrhosis and Hepatocellular Carcinoma (HCC) [2]. Therefore, early appropriate antiviral therapy can effectively inhibit virus replication and prevent disease progression [3].

Treatment of CHB is based on serum HBV-DNA level, serum ALT level and hepatic histological severity ($G \geq 2$ or $S \geq 2$) [4]. Several guidelines recommend antiviral therapy for CHB patients with an Alanine Aminotransferase (ALT) level two folds higher than the Upper Limit of Normal (ULN) range. Early reasonable antiviral therapy can significantly reduce the necro-inflammatory of liver cells, even reverse liver fibrosis and early cirrhosis, and reduce the occurrence of HCC and other complications [1,4]. However, most studies have shown severe liver damage in some CHB patients with normal ALT level [5,6]. Previous studies have shown that 28%-37% patients with mild elevation of ALT or normal CHB liver biopsy suggested moderate and severe inflammation and/or significant fibrosis, requiring antiviral therapy [7-9], which is consistent with our findings. Our previous results also showed that some CHB with ALT<2ULN patients had significant liver pathological changes. We think that ALT level insufficient to assess the severity of liver necro-inflammation and may affect the timing of antiviral therapy for CHB with ALT<2ULN. In addition, active significant liver inflammation is a major risk factor for CHB to progress cirrhosis and HCC [1,10]. Therefore, it is of great importance to establish a non-invasive model or find non-invasive biomarkers that can effectively reflect the pathological state of liver to guide antiviral therapy.

At present, liver biopsy remains the gold standard for evaluating liver histology. However, as an invasive test, it has certain limitations and its clinical application is limited [11]. In recent years, most studies have focused on the development and evaluation of non-invasive model to identify liver pathological status in CHB patients, guiding early antiviral therapy. Through clinical retrospectively analysis, our team group established a non-invasive model to evaluate the severity of liver histology for the decision-making of antiviral therapy for CHB patients with ALT $\geq$ 2ULN. In this study, 577 patients with CHB who underwent liver biopsy and ALT $\geq$ 2ULN were analyzed retrospectively [12].

We analyzed the data using univariate and multivariate analyses and receiver operating characteristic curves (ROC), and found that Aspartate Aminotransferase (AST), Anti-hepatitis B virus core antibody (Anti-HBC) and Glutamyl Transpeptidase (GGT) were independent predictors for antiviral therapy, with areas under ROC curves of 0.649, 0.647 and 0.616, respectively. Combined with AST, Anti-HBC and GGT, the new model (AGH) index was constructed, and the ROC in the training set and validation set were 0.700 and 0.742 respectively (Figure 1), which had better diagnostic performance than the single variable.

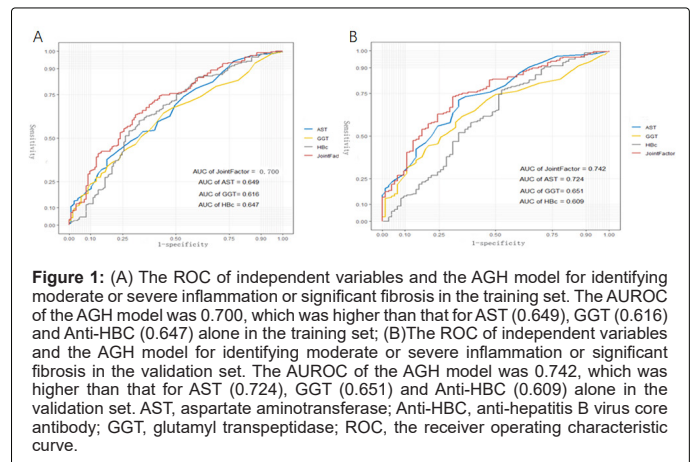


Figure 1: (A) The ROC of independent variables and the AGH model for identifying moderate or severe inflammation or significant fibrosis in the training set. The AUROC of the AGH model was 0.700, which was higher than that for AST (0.649), GGT (0.616) and Anti-HBC (0.647) alone in the training set; (B) The ROC of independent variables and the AGH model for identifying moderate or severe inflammation or significant fibrosis in the validation set. The AUROC of the AGH model was 0.742, which was higher than that for AST (0.724), GGT (0.651) and Anti-HBC (0.609) alone in the validation set. AST, aspartate aminotransferase; Anti-HBC, anti-hepatitis B virus core antibody; GGT, glutamyl transpeptidase; ROC, the receiver operating characteristic curve.

This model only used serum markers, mainly consists of routine clinical laboratory tests, is easy to obtain, and it is suitable for most medical institutions. In addition, our team group also analyzed the serum of patients with liver fibrosis of CHB by metabolomics, proteomics and functional mechanism studies, and selected non-invasive biomarkers with specific diagnostic value, actively explored the role of these biomarkers in ALT<2ULN, so as to provide the basis for early antiviral therapy in this part of patients. Our team group will later include a large number of multicenter clinical cases of CHB for research, and establish non-invasive model for early antiviral therapy, so as to reduce the need for clinical liver biopsy.

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