Letter to the Editor

JOURNAL OF HEPATOLOGY

Individualized prediction of hepatocellular carcinoma occurrence in a large cohort of patients with cirrhosis

To the Editor;

We read with interest the article from Sharma and collaborators.[1] The authors proposed a score based on four variables (age, sex, etiology of cirrhosis, and platelet count) to predict the risk of hepatocellular carcinoma (HCC) in a cohort of 2,079 patients with cirrhosis validated in an external cohort. Points were assigned to each independent predictor of HCC according to its hazard ratio (HR) to create the Toronto HCC Risk Index (THRI). This score stratifies patients into three equally spaced categories to obtain low (<120), medium (120–240) and high (>240) risk thresholds. As interest in the individualized prediction of the risk of HCC in patients with cirrhosis is increasing,[2–4] we took the opportunity to evaluate the usefulness of such a model to predict HCC occurrence in another large cohort of patients with cirrhosis.[5] We evaluated the risk of HCC among 752 patients with cirrhosis and divided them into three etiologies of liver disease: alcoholic liver disease (ALD) (n = 529), chronic hepatitis C virus (HCV) infection (n = 145), and non-alcoholic fatty liver disease (NAFLD) (n = 78). During follow-up, 85 patients (11%) developed HCC. Three variables were independently associated with a risk of HCC: age (HR 1.03; 95% CI 1.00–1.06; $p = 0.03$); male gender (HR 2.41; 95% CI 1.39–4.15; $p = 0.002$), and etiology of cirrhosis (HR 0.39 for ALD; 95% CI 0.20–0.76; $p = 0.005$). Platelet count used as a continuous variable did not reach statistical significance (HR 1.00; 95% CI 0.99–1.00; $p = 0.08$). We categorized age using three cut-offs (<45, 45–60, >60 years) and we included platelet count using four cut-offs (<80, 80–139, 140–200, and >200 Giga/mm^3), as did Sharma and collaborators. We considered four groups of liver disease (HCV with sustained virological response [SVR+], HCV without SVR [SVR−], ALD, and NAFLD). We built two models. In the first model, points were attributed to each factor according to its HR in the multivariate model (Fig. 1A). In the second model, we used the same variable weights as the THRI model. We stratified the population into three groups according to risk of HCC at 10 years. In the first model, risks of HCC were 9.1% (95% CI 1.4–16.8), 15.7% (7.6–23.8), and 29.1% (19.7–38.5) in the low (<71 points) medium (71–115), and high (>115) risk groups, respectively (p <0.001; Fig. 1B). In the second model, the corresponding risks were 0%, 14.6% (8.5–20.7), and 28.4% (18.8–38.0) in the low (<120 points) medium (120–240), and high (>240) risk groups, respectively (p <0.001; Fig. 1C).

Thus, we have confirmed that an individualized model is useful for prediction of HCC occurrence in patients with cirrhosis. However, the weight of each factor differed according to the population of patients. These models point out the importance of considering the different etiologies of liver disease when evaluating the risk of HCC in patients with cirrhosis. In contrast to Sharma and collaborators, however, we believe that ALD and NAFLD patients should be considered separately as the risk of

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Variables	HR	95% HR CI	*p* value	Risk score
Age				
<45	1			0
45-60	1.15	0.38-3.45	0.8	6
>60	2.22	0.74-6.66	0.2	49
Etiology				
ALD	1			0
HCV SVR$^+$	1.88	0.51-6.89	0.3	35
NAFLD	2.17	1.04-4.50	0.04	47
HCV SVR$^-$	2.73	1.41-5.28	0.003	69
Gender				
Female	1			0
Male	2.60	1.37-4.93	0.004	64
Platelets				
>200	1			0
140-200	1.10	0.47-2.57	0.8	4
80-139	1.60	0.76-3.35	0.2	24
<80	3.50	1.32-9.28	0.01	100
Total				0-282

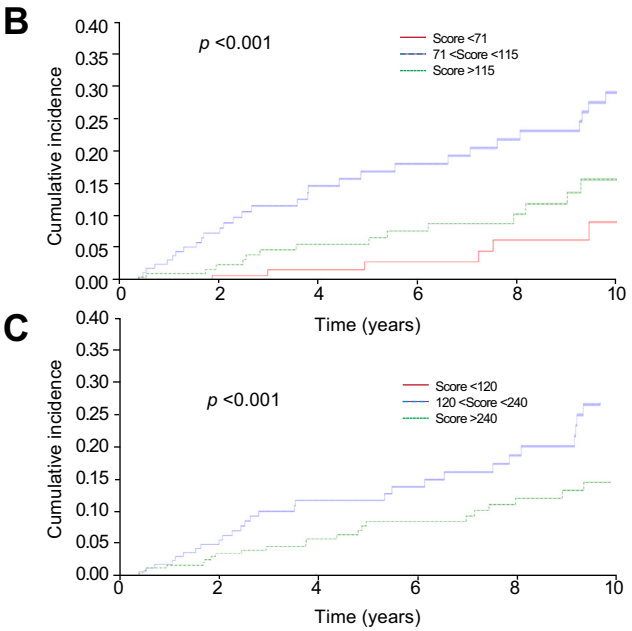

Fig. 1. Predictive scores for HCC. (A) Components of the predictive score with points attributed to each factor according to its HR in our multivariate model. (B) Incidence of HCC according to the predictive score: model derived from our multivariate model. (C) Incidence of HCC according to the Toronto HCC Risk Index: model built with the same variable weights as in the Sharma et al. study. ALD, alcoholic liver disease; CI, confidence interval; HCC, hepatocellular carcinoma; HCV, chronic hepatitis C virus; HR, hazard ratio; NAFLD, non-alcoholic fatty liver disease; SVR, sustained virologic response.

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HCC differs between them, although a clear distinction between these two etiologies is sometimes not easy to identify (see supplementary material for our definitions).

Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

Please refer to the accompanying ICMJE disclosure forms for further details.

Acknowledgement

We acknowledge the contribution of Sandy Field, Ph.D., for her assistance concerning English-language editing.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jhep.2018.06.007.

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