LETTER TO THE EDITOR

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A comment on 'A morpho-molecular prognostic model for hepatocellular carcinoma'

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Sir,

We read with great interest the recent study by Srivastava *et al* (2012) regarding a new staging model for hepatocellular carcinoma (HCC). In this study, the authors constructed a new risk model for the prognostic evaluation of HCC. In the final system, CD31, p53, AFP, CD44, tumour size and vascular invasion were included for risk score calculation. Patients were dichotomised into high- and low-score groups using the cut-off point, 3.240, which was found to be the median final score in the study population. Srivastava *et al* (2012) demonstrated significantly decreased overall survival in the high-score group and validated these results in another cohort.

We would like to discuss a couple of points about the patient characteristics and risk factors included in the study. First, we feel that there is not enough description of the study population regarding the status of the underlying liver disease, which is also an independent predictor of survival in patients with HCC. The authors did not specify pertinent parameters to assess liver disease, such as the Child–Pugh score, or the incidence of cirrhosis, on the basis of imaging or pathological criteria.

Second, although CD44 overexpression is a cancer stem cell marker (Zhu *et al*, 2010) and was found to be a poor prognostic factor in HCC, it was not found to be significantly overexpressed in tumour tissue compared with in adjacent non-tumour hepatic tissue in this study.

Increased expression of CD44, which was considered in this study to be a cancer stem cell marker, was also observed in inflammation and mediates tumorigenesis (Heldin *et al*, 2008). In animal models, CD44 knockdown was shown to decrease inflammation in the liver (Kimura *et al*, 2008). Therefore, CD44 expression in non-tumour hepatic may indicate an underlying ongoing inflammation in liver. Thus, in this study, the poor prognostic value of overexpressed CD44 may partially reflect the severity of the underlying liver disease rather than being a marker of tumour cell stemness.

In conclusion, although this morpho-molecular prognostic model for HCC promisingly identified HCC patients with different risk factors, the absence of parameters pertinent to the underlying liver function will make it challenging to interpret the study results. Moreover, the role of CD44 in this staging model should be also clarified.

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