Spleen size for the prediction of clinical outcome in patients with primary sclerosing cholangitis

Dear Sir,

We read with interest the work of van der Meer *et al*[1] who propose a risk score for patients with chronic Hepatitis C. The authors demonstrate that the assessment of readily available and objective parameters can stratify patients according to the risk of disease progression. Patients with primary sclerosing cholangitis (PSC) usually develop progressive liver fibrosis and end-stage liver disease within 10–20 years.[2] Simple and non-invasive means for disease stratification and prediction of prognosis are urgently needed. Indeed, the International PSC Study Group recently declared the research on surrogate end-point markers as a high-priority task,[3] since several clinical studies investigating novel treatment strategies will be initiated in near future. Transient elastography has recently been shown to predict disease progression in PSC.[4] However, transient elastography is not widely available and harbours technical challenges especially in obese patients. Additionally, liver stiffness may be influenced by liver inflammation, prandial status and biliary obstruction,[5–7] which is of concern in patients with PSC. We therefore assessed spleen length (SL) as a simple and readily available means to predict the outcome of patients with PSC. The study was approved by the local review boards.

A total of 126 patients with the diagnosis of PSC who were seen at the University Medical Center Hamburg-Eppendorf, Germany, and who received an ultrasound-based measurement of SL between 2006 and 2014 were included in the study. Median follow-up was 43 months. Liver transplantation, death and hepatic

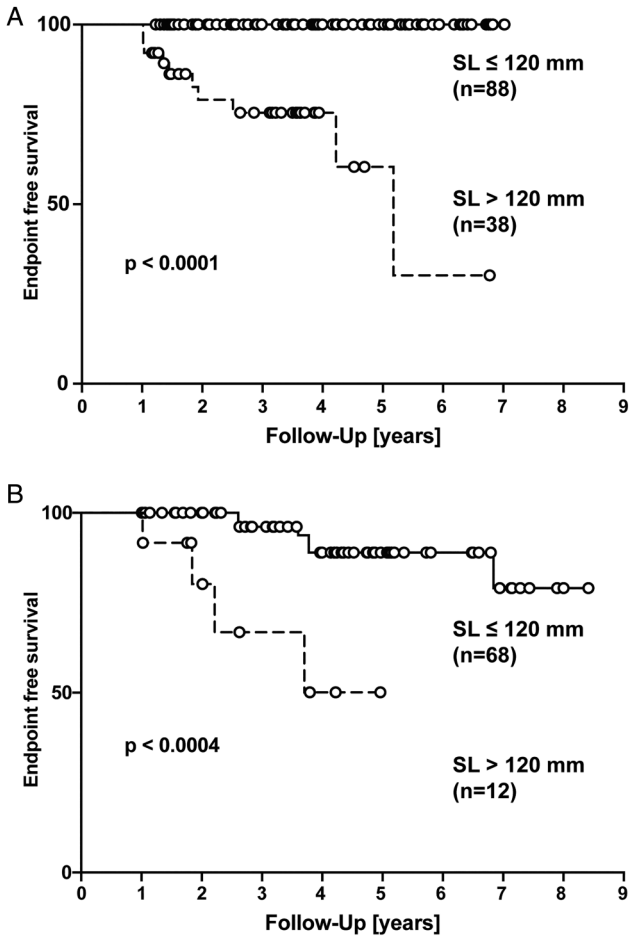

Figure 1 Kaplan–Meier estimates according to a spleen length cut-off of 120 mm. (A) Hamburg cohort is shown, n=126 primary sclerosing cholangitis (PSC) patients, with spleen size determined by ultrasound (log-rank test, p<0.0001). (B) Paris cohort is shown, n=80 patients, with spleen size determined by MRI (log-rank test, p<0.0004).

decompensation were defined as end points related to fibrosis progression. Hepatobiliary malignancy, such as cholangiocarcinoma or gallbladder cancer, was not included as end points since these are not associated with fibrosis stage. For a cut-off of 120 mm, SL was strongly associated with patient outcome, and the median survival of patients with SL over 120 mm was only 5.2 years (figure 1A).

In an independent cohort of 80 patients with PSC from the University Hospital St Antoine, Paris, France, with very similar patient characteristics (data not shown), SL measurement based on MRI imaging confirmed the association with the clinical prognosis (figure 1B). Sixty patients (Hamburg) had received a liver biopsy within 6 months (median 1 month) of the ultrasound examination. The area under the receiver operating characteristic curve for the diagnosis of liver cirrhosis was 0.85 (95% CI 0.72 to 0.98, table 1).

Table 1 Performance of spleen length (SL) measurement for the diagnosis of cirrhosis (F4) in primary sclerosing cholangitis (PSC) for different cut-off values

AUROC (95% CI)	Cut-off (mm)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
Length of spleen						
0.850 (0.717 to 0.982)	111	93 (81 to 100)	57 (41 to 70)	41 (25 to 58)	96 (89 to 100)	65 (53 to 77)
	121	73 (51 to 96)	73 (60 to 86)	48 (27 to 68)	89 (79 to 99)	73 (62 to 84)
	136	67 (43 to 91)	96 (90 to 100)	83 (62 to 100)	90 (81 to 98)	88 (80 to 96)

We conclude that the non-invasive and widely available baseline measurement of SL by ultrasound or MRI can be used to stratify patients with PSC according to the risk of disease progression. SL is highly associated with cirrhosis in patients with PSC. AUROC, area under the receiver operating characteristic; NPV, negative predictive value; PPV, positive predictive value.

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REFERENCES

1 van der Meer AJ, Hansen BE, Fattovich G, *et al*. Reliable prediction of clinical outcome in patients with chronic HCV infection and compensated advanced hepatic fibrosis: a validated model using objective and readily available clinical parameters. *Gut* 2015;64:322–31.
2 European Association for the Study of the Liver. EASL Clinical Practice Guidelines: management of cholestatic liver diseases. *J Hepatol* 2009;51:237–67.
3 Ponsioen CY, Chapman RW, Chazouillères O, *et al*. Surrogate endpoints for clinical trials in primary sclerosing cholangitis; review and results from an International PSC Study Group consensus process.

Hepatology Published Online First: 29 Sep 2015. doi:10.1002/hep.28256
4 Corpechot C, Gaouar F, Naggar El A, *et al* Baseline values and changes in liver stiffness measured by transient elastography are associated with severity of fibrosis and outcomes of patients with primary sclerosing cholangitis. *Gastroenterology* 2014;146:970–9; quize15-6.
5 Castera L, Pinzani M. Biopsy and non-invasive methods for the diagnosis of liver fibrosis: does it take two to tango? *Gut* 2010;59:861–6.
6 Tapper EB, Cohen EB, Patel K, *et al*. Levels of alanine aminotransferase confound use of transient elastography to diagnose fibrosis in patients with chronic hepatitis C virus infection. *Clin Gastroenterol Hepatol* 2012;10:932–937.e1.
7 Ehlken H, Lohse AW, Schramm C. Transient elastography in primary sclerosing cholangitis-the value as a prognostic factor and limitations. *Gastroenterology* 2014;147:542–3.

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Notes