Liver Stiffness, Platelets, and Spleen Size Is Reliable in Nondecompensated Cirrhotic Patients

Dear Sir:

We read with interest the recent article published in GASTROENTEROLOGY suggesting that a combination of liver stiffness (LS) evaluated by transient elastography (Fibroscan [FS]), platelet count (PC) and spleen diameter (SD; liver stiffness × spleen size/platelet [LSPS]) accurately identifies patients with clinically significant portal hypertension, among patients with compensated cirrhosis. The authors concluded that area under the receiver operating characteristic (AUROC) was 0.918, and in this cohort of patients, >80% of patients were accurately classified. Correlation between LS and hepatic venous pressure gradient (HVPG) has already shown to be poor among patients with chronic hepatitis C when HVPG was >10 or 12 mmHg. Moreover, in most of studies, FS alone was not found accurate in predicting the presence of large esophageal varices. Therefore, these results are very relevant; the combination of noninvasive factors like FS and factors directly influenced by portal hypertension such as spleen diameter and platelet count may be useful in predicting clinically significant portal hypertension and the presence of large esophageal varices.

The results are very interesting, because it is a major issue to identify patients with clinically significant portal hypertension, who are at risk to develop complications. In a study published in 2007, Ripoll et al have shown that patients with an HVPG of <10 mm Hg have a 90% probability of not developing clinical decompensation in a median follow-up of 4 years.

Another subset of patients would also benefit from noninvasive, rapid diagnosis of portal hypertension level, namely, bleeding cirrhotic patients. In this setting, patients displaying HVPG of >20 mm Hg are at high risk of death, and should benefit from early transjugular intrahepatic portosystemic shunt placement. However, HVPG measurement is only performed in expert centers, and is not easy in an emergency setting. Therefore, we aimed to assess whether LSPS would be accurate in predicting HVPG in decompensated patients with variceal bleeding. We conducted a prospective study in 52 consecutive patients with cirrhosis and variceal bleeding, and evaluated on the same day LS and HVPG, to assess whether LS could identify patients with an HVPG of >20 mm Hg. First, LS could be evaluated in 40 of 52 patients (76.9%). Unreliable results were mainly owing to the presence of ascites. Second, we established that correlation between LS and HVPG was poor (r² = 0.009). Most of patients had indeed a score of LS of 75 kPa during acute phase. Third, mean LSPS was 8.22 ± 4.37. The AUROC value of LSPS was 0.52 ± 0.16 in predicting HVPG >20 mm Hg.

Therefore, we conclude that the algorithm of Berzigotti et al is of major interest in compensated cirrhotic patients. However, it cannot be applied to patients with decompensated cirrhosis, especially during the acute phase of variceal bleeding.

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Conflicts of interests
The authors disclose no conflicts.

http://dx.doi.org/10.1053/j.gastro.2013.01.065

Noninvasive Predictors of Portal Hypertension

Dear Sir:

We read with interest the 2 recent, well-conducted studies on noninvasive predictors of portal hypertension (PHT), published in the January 2013 issue of GASTROENTEROLOGY. As discussed in the accompanying editorial, they represent important advances toward the key goal of a reliable, accurate, and readily available noninvasive method of detecting the presence of both esophageal varices (EVs) and clinically significant PHT in cirrhosis.

However, as with many studies on liver stiffness (LS) by elastography where either transient elastography (TE) or acoustic radiation force impulse imaging (ARFI; or other shear wave elastography) methods are used, they were both based on cohorts from tertiary centers predominately consisting of viral hepatitis patients and were subject to selection bias. In particular, the study by Berzigotti et al was not prospective; the 117 patients recruited into the “training set” over >4 years were retrospectively selected from those entered into 3 prospective trials of highly selected, well-compensated cirrhotics, more than half of whom had potentially resectable hepatocellular carcinoma.

There is increasing evidence for the superior applicability quality control of the ARFI technique in comparison
with TE in measuring LS, with fewer failed procedures and yet equivalent performance in accuracy.\(^4\) However, there is a need for data from studies reflecting patients in more “real-life” situations, with a wider range of both etiologies for cirrhosis and clinical manifestations.

Takuma et al\(^1\) demonstrated the high negative predictive value of spleen stiffness measurement (SSM) by ARFI in ruling out EVs, but overall predictive performance of SSM was less impressive. Thus, a large number of unnecessary endoscopies would be performed if this were the sole method employed for screening for EVs, because of the low positive predictive value (illustrated in Figure 2 in the article). Furthermore, the overall performance of this technique has not been well validated in both normal and disease populations, and may therefore be subject to higher intra- and interobserver variability and lower uptake than suggested by this study.

Castera and Garcia–Tsao\(^3\) discuss the relative performance of LS and SSM in both early and late PHT, and the fact that increased SSM may reflect the effects of increased portal inflow and hyperdynamic splanchnic circulation in the latter. However, this physiologic process may also be detected using standard Doppler ultrasonography by the measurement of increased portal vein diameter, reduced peak portal flow velocity or reversed flow, as well as the formation of collateral circulations.\(^5-7\)

Ultimately, an “ideal” noninvasive test for PHT needs to be well-validated with high overall predictive value for the detection of EVs, both at initial diagnosis of cirrhosis and also during subsequent surveillance. It must also be widely applicable, in terms of both available technology as well as individual operator expertise, and based on a single procedural session. These and other studies suggest that such a test will be ultrasound based, using a technique with which the majority of radiologists in secondary care would be comfortable. This is important because it may also be used at the primary/secondary care interface.

Given that only ARFI can be integrated into standard ultrasound machines, these requirements seem to rule out the use of both TE and SSM in such an ideal test. Thus, on the basis of current evidence, the predictive technique of first choice is likely to be based on a single ultrasound procedure incorporating ARFI software, and including the measurement of both LS as well as Doppler examination of the splenoportal system, with the addition of platelet count.

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**Conflicts of interests**  
The authors disclose no conflicts.

http://dx.doi.org/10.1053/j.gastro.2013.02.049

**Noninvasive Methods for Esophageal Varices Prediction in Cirrhotic Patients: Are We There Yet?**

Dear Sir:

This letter regards the interesting articles by Takuma et al\(^1\) and Berzigotti et al.\(^2\) The development of new, noninvasive methods to screen for esophageal varices (EV) in cirrhotics is important, because variceal bleeding is a dramatic complication of cirrhosis and it is recommended that patients be screened for EV by endoscopy,\(^3\) which implies a great burden to health systems and patients. The magnitude of the issue is evident in the editorial those articles deserved.\(^4\)

Until recently, the most promising noninvasive method for EV screening was the platelet count/spleen diameter ratio (PSR). Despite controversial conclusions concerning PSR in 2 recent systematic reviews,\(^5,6\) we agree with the authors of the articles to which this letter refers\(^1,2\) in that PSR is not ready to be used. This was also the conclusion of the systematic review by Chawla et al\(^6\) and was shown in a previous study we have published, evaluating the largest sample of all-cause cirrhosis completely independent of the center which first described PSR.\(^7\) Actually, our results for PSR were similar to those found by Takuma et al.\(^1\) Although we found a sensitivity of 77.5%, specificity of 45.5%, and accuracy of 68.9%,\(^7\) they published a sensitivity of 79.6%, a specificity of 61.1%, and an accuracy of 68.2%.\(^1\)

Analyzing the article by Takuma et al,\(^1\) spleen stiffness measured by acoustic radiation force impulse imaging (SS-ARFI), with a cutoff of 3.3 m/s for EV screening, had a sensitivity of 98.9% and a negative predictive value of 99.4%, but an accuracy of only 75%. The measurement was not possible in only 4.5% of patients. SS-ARFI was studied in a sample of 340 compensated and decompensated cirrhotics.\(^1\) The lack of histologic confirmation of cirrhosis in the majority of cases could be a problem, because some of patients without EV might not even have cirrhosis. Nevertheless, the major flaw of the study is that it does not have a validation set and, therefore, it is not possible to predict whether its results are reproducible in different populations. Another recent study evaluated SS, but it was measured by transient elastography (TE) and the analyzed sample was composed only by hepatitis C-related cirrhotics,\(^8\) so that the existence of both studies does not imply external validation of SS.