To the Editor:

We would like to point out an omission in the AASLD Practice Guidelines on Chronic Hepatitis B published in the February 2007 issue of Hepatology. In the section discussing the counseling and prevention of hepatitis B on pages 508-509 and in the accompanying table (Table 3), when discussing infants born to hepatitis B virus (HBV)-infected mothers, the authors neglected to discuss the issue of breast-feeding. This is certainly worth mentioning because some mothers feel breast-feeding to be an integral part of the care they provide to their infants, and mothers prohibited from breast-feeding may feel some sense of inadequacy. As you know, breast-feeding is not prohibited in HBV-infected mothers, as proven by several studies, some of which are listed here. Furthermore, because infants should routinely receive HBV immune globulin and HBV vaccine, they are almost universally protected against postpartum maternal HBV transmission.

We think an additional 1-2 sentences should be included in the guidelines to address this issue.

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References

Reply:

We agree with Dr. Jhaveri and Dr. Murray that available data show that there is no evidence of hepatitis B transmission from infected mothers to infants who are breast-fed and that breast-feeding should not be prohibited, particularly for infants who receive appropriate prophylaxis with hepatitis B immune globulin and hepatitis B vaccine. Because of space constraints, it was not possible for the guidelines to include all aspects of hepatitis B management. We appreciate Dr. Jhaveri and Dr. Murray for bringing this to our readers’ attention.

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Potential conflict of interest: Nothing to report.

External Validation of FibroIndex

To the Editor:

We read with interest the Koda et al. report on the description of a new panel of biomarkers for predicting significant fibrosis in patients with chronic hepatitis C (CHC) called FibroIndex. This panel was derived from the platelet count, AST, and gamma globulin measurements. They built and validated their model on a cohort of 360 CHC patients (AUCs), sensitivities, specificities, and positive and negative predictive values. The Hanley-McNeil test was used to compare AUCs; χ2 or Fisher exact test were used to compare proportions. Serum samples were taken on the day of biopsy, for determination of biochemical markers to assess FibroIndex, APRI, Forns index, and Fibrotest. Biochemical marker analysis was performed in accredited laboratories following the guidelines recommended for Fibrotest assessment by the authors of the initial publication.

We studied the diagnostic accuracy of the FibroIndex and compared it to APRI, Forns index, and Fibrotest in a cohort of 125 CHC patients prospectively enrolled in Fibroscore, a French national multicenter study. Of the 125, 85 (68%) were men, and mean age was 47 ± 9 years. Signed informed consent was obtained from all patients before their inclusion. Liver biopsy and biochemical markers were done the same day. Liver biopsy was performed in each center and analyzed by the resident pathologist. For all patients, ultrasound examination was performed before liver biopsy. Information relating to the patient demographic data, risk factors, virological status, clinical examinations, biological data (platelets, prothrombin time ratio, serum albumin level) was prospectively recorded in each center on the day of biopsy. All data were anonymously recorded in the database. Diagnostic accuracies were measured using area under ROC curves (AUCs), sensitivities, specificities, and positive and negative predictive values. The Hanley-McNeil test was used to compare AUCs; χ2 or Fisher exact test were used to compare proportions. Serum samples were taken on the day of biopsy, for determination of biochemical markers to assess FibroIndex, APRI, Forns index, and Fibrotest. Biochemical marker analysis was performed in accredited laboratories following the guidelines recommended for Fibrotest assessment by the authors of the initial publication.

In the hospital-based cohort, gamma glutamyl transpeptidase and total bilirubin levels were measured using a Hitachi 917 Analyzer and Roche Diagnostics reagents (both from Mannheim, Germany). Alpha2-macroglobulin, apolipoprotein A1, and haptoglobin were measured using a Modular analyzer (BNII, Dade Behring; Marburg, Germany). Platelets were measured with a Beckman Coulter LH 750 hematology analyzer. Biochemical assays were performed on fresh serum, decanted, and stored for 72 hours maximum at 2°C/8°C while...
than in those with scores of F0 or F1, this parameter cannot be
serum gamma globulin was higher in patients with scores of F2 or F3
only the 2 former can be assessed with precision. Despite the fact that
the FibroIndex (AST, platelet count, and serum gamma globulin),
observed in the diagnostic accuracy. Among the 3 variables included in
ported.
APRI and Forns index are similar to the corresponding results re-
was done by the formula: (% of the area under the pic)
semiquantitative assessment of serum gamma globulin. Calculation
a particular protein preparation. Electrophoresis provided only a
visualized as well as separated, permitting a researcher to estimate
serum gamma globulin with expected fluctuations. In our study, the
distribution of our cohort is comparable to the one of the validation set
of Koda et al.
The AUC results are presented in Table 1. For significant fibrosis, the
AUC in our study is higher than those in Halfon’s study.

Table 1. AUC Results

<table>
<thead>
<tr>
<th>Test</th>
<th>F01 vs. F34</th>
<th>F01 vs. F34</th>
<th>F01 vs. F23</th>
<th>F01 vs. F23</th>
<th>F012 vs. F3</th>
</tr>
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<tbody>
<tr>
<td></td>
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<td>Koda et al.</td>
<td>FibroIndex</td>
<td>Koda et al.</td>
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<tr>
<td></td>
<td>AUC(95% CI)</td>
<td>AUC(95% CI)</td>
<td>AUC(95% CI)</td>
<td>AUC(95% CI)</td>
<td>AUC(95% CI)</td>
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<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>FibroIndex</td>
<td>0.76</td>
<td>0.86</td>
<td>0.72</td>
<td>0.85</td>
<td>0.72</td>
</tr>
<tr>
<td></td>
<td>(0.68-0.83)</td>
<td>(0.81-0.92)</td>
<td>(0.64-0.80)</td>
<td>(0.79-0.91)</td>
<td>(0.63-0.80)</td>
</tr>
<tr>
<td>FT</td>
<td>0.78</td>
<td>0.80</td>
<td>0.72</td>
<td>0.87</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>(0.70-0.85)</td>
<td></td>
<td>(0.64-0.82)</td>
<td></td>
<td>(0.63-0.81)</td>
</tr>
<tr>
<td>APRI</td>
<td>0.81</td>
<td>0.82</td>
<td>0.78</td>
<td>0.81</td>
<td>0.77</td>
</tr>
<tr>
<td></td>
<td>(0.73-0.82)</td>
<td>(0.76-0.89)</td>
<td>(0.69-0.85)</td>
<td>(0.74-0.88)</td>
<td>(0.68-0.84)</td>
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<tr>
<td>Forns</td>
<td>0.80</td>
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<td>0.76</td>
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<tr>
<td></td>
<td>(0.72-0.86)</td>
<td>(0.77-0.90)</td>
<td>(0.70-0.85)</td>
<td>(0.77-0.89)</td>
<td>(0.67-0.84)</td>
</tr>
</tbody>
</table>

References


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Potential conflict of interest: Nothing to report.

Reply:

We are delighted that Halfon et al. provided external validation for FibroIndex. They proposed a problem in gamma globulin for the discrepancy between our study and their data. The importance of serum gamma globulin in chronic hepatitis C has already been reported by several investigators. Imbert-Bismut et al. reported that serum gamma globulin was higher in patients with F2 or F3 than in those with F0 or F1. Our other study series also revealed that serum gamma globulin values were quantitatively correlated with staging scores. Therefore, it leaves no doubt that serum gamma globulin reflects the hepatic fibrosis in chronic hepatitis C.

Next, they point out that the measurement method of gamma globulin is not always reliable. We also emphasized the importance of the accuracy control of each parameter in the index comprising laboratory tests. In fact, we have described in the text that each parameter is under strict quality control. In our study, gamma globulin was measured using a single and dedicated analyzer with minimal interlaboratory variability (coefficient of variation at least <6%) as well as aspartate aminotransferase (AST) and platelet count. Although Halfon et al. do not show their quality control of gamma globulin measurement, this discrepancy may indicate the importance of the standardization and the strict quality control of each parameter. Indeed, AUROCs of APRI and Forns index conducted by AST and platelet in our study are higher than those in Halfon’s study.

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Potential conflict of interest: Nothing to report.