Dear Sir:

We have read with interest the recent review by Befeler et al\(^1\) on the subject of liver transplantation for hepatocellular carcinoma. They have presented an overview of the current knowledge of this neoplasm. We wish to disagree with one of their opinions regarding the need for liver biopsy in the diagnosis of HCC. Diagnosis of HCC can be made radiologically or on biopsy. Biopsy is invasive and carries small but well-defined risks that imaging does not have. Whether one or both of these techniques should be used depends on the sensitivity and specificity of the tests, and these parameters vary with the size of the lesion and the presence or absence of cirrhosis. Whether a biopsy is required and if so, when it is required, remains controversial. There are very few studies addressing this issue, so any conclusions that can be drawn from the existing literature have to be culled from research studies that were designed for other purposes. This issue was considered at the EASL Monothematic Conference on HCC that was published in 2001.\(^2\) This meeting recommended that lesions larger than 2 cm did not require biopsy if the lesions were shown to be hypervascular on 2 dynamic radiological studies in the setting of a cirrhotic liver. In a noncirrhotic liver, where the pre-test probability of HCC is much lower, biopsy is recommended. Biopsy was recommended for smaller lesions (1–2 cm) and follow-up for even smaller lesions. Befeler et al take issue with the recommendation for lesions larger than 2 cm, on the basis of a retrospective study that they have performed, and instead suggest that biopsies should be performed for all such lesions. These data have also been presented at the AASLD Single Topic Research. Conference on HCC held in 2003, and at the AASLD Annual Meeting in 2004.\(^3\)

However, the data presented by Befeler et al were derived from a population that included noncirrhotic patients, and patients with lesions smaller than 2 cm, ie, from a population that was less homogenous than the population for which the EASL criteria were established. The 2 populations are therefore not comparable, and the recommendations by Befeler et al apply only to their population, and not to the larger population of HCC lesions > 2 cm in cirrhotic livers. Furthermore, the study referred to by Befeler lacked scientific rigor. Whether an HCC met EASL criteria or not was determined from a review of the radiological reports, not a review of the actual images. Since there was no standardization of terminology by the reporting radiologists the category to which each tumor was assigned has to be viewed with caution. It is not clear from the brief report that there were 2 imaging studies in each case. There was no mention of blinding, so that observer bias cannot be excluded. Second, the population, as already discussed, was not homogenous. The range of tumor sizes was not reported in the article, although it has been reported elsewhere. The proportion of patients with cirrhosis is also not reported. These are important omissions, since it makes it impossible for the reader to assess whether Befeler et al are referring to the same population as the EASL report. It is extremely important to ensure homogeneity of the population referred to when discussing the diagnosis of HCC, because different rules apply at different tumor sizes. The Befeler cohort was not homogenous by size criteria, nor by presence of cirrhosis.

The issue of specificity of the radiological appearances of HCC have been addressed by Bolondi et al.\(^4\) In their study, which was specifically designed to address the accuracy of the EASL recommendations, all lesions larger than 2 cm that met the EASL criteria were HCC, confirming the validity of the EASL criteria.\(^2\)

Thus, we think that the description of the retrospective study in the article is misleading, and we re-emphasize the importance of applying the EASL criteria to the appropriate population.

Today, the recommendation would likely be different, since the recommendation would include a consideration of the phenomenon of “washout,” a feature that enhances the radiological diagnostic accuracy. Nonetheless, we still consider the EASL criteria to be accurate and don’t believe that the Befeler study negates the recommendations.

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