Screening for Hepatocellular Carcinoma in Patients with Hepatitis C Virus Infection

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Clinical Inquiries provides answers to questions submitted by practicing family physicians to the Family Physicians Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (http://www.cebm.net/?o=1025).

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Clinical Question
Is measurement of serum α-fetoprotein (AFP) levels better than imaging when screening symptomatic patients with hepatitis C virus (HCV) infection for hepatocellular carcinoma?

Evidence-Based Answer
There is no evidence that it is beneficial to screen for hepatocellular carcinoma in symptomatic patients with HCV. (Strength of Recommendation [SOR]: C, based on a systematic review and case series studies.) Neither serum AFP measurement nor imaging is an ideal screening test. Patients can be screened for hepatocellular carcinoma using AFP measurement or ultrasonography; these tests have similar sensitivity and specificity. Computed tomography and magnetic resonance imaging offer increased screening sensitivity, but may be limited by cost and availability. (SOR: C, based on retrospective case series.) Combined testing with AFP measurement and ultrasonography improves sensitivity but decreases specificity.

Evidence Summary
A systematic review of five studies (two prospective cohort and three case-control studies; n = 1,734) showed that a serum AFP level greater than 20 ng per mL (20 µg per L) has a sensitivity of 41 to 65 percent, a specificity of 80 to 94 percent, a positive likelihood ratio of 3.1 to 6.8, and a negative likelihood ratio of 0.4 to 0.6 when used to screen for hepatocellular carcinoma in patients with HCV. At least 239 patients (14 percent) included in this meta-analysis were HCV-negative, and many were already cirrhotic, which limits extrapolation of results to the asymptomatic population.

No prospective data are available to directly compare the effectiveness of AFP measurement and imaging in identifying hepatocellular carcinoma in symptomatic patients with HCV. Case-control and case series reports of patients with end-stage liver disease who were transplant candidates showed that the sensitivity of serum AFP measurement in detecting hepatocellular carcinoma ranged from 20 percent (using the highest threshold) to 65 percent (using the lowest; Table 1). In these studies, the diagnostic standard was pathologic examination of the liver. Ultrasonography had similar sensitivity (43 to 59 percent) but better specificity in patients with end-stage cirrhosis. Tumor detection rates were 53 to 91 percent for computed tomography, and 78 percent for magnetic resonance imaging.

A prospective cohort control study of 18,816 patients (9,373 participants in the screening group and 9,443 participants in the control group) with hepatitis B or other chronic hepatitis evaluated the utility of combining serum AFP measurement with ultrasonography to detect primary liver cancer. Serum AFP measurement alone (using a threshold of greater than 20 ng per mL) had a sensitivity of 69 percent (95% confidence interval [CI], 54 to 80 percent) and a specificity of 95 percent (95% CI, 94.7 to 95.3 percent) to detect liver cancer. Ultrasonography alone was more sensitive (84 percent; 95% CI, 73 to 93 percent) and specific (97 percent; 95% CI, 96.9 to 97.3 percent) than AFP measurement. Combining AFP measurement with ultrasonography improved sensitivity to 92 percent (95% CI, 80 to 97 percent), but decreased specificity to 93.5 percent (95% CI, 92 to 93 percent). The study’s usefulness for

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evaluating for hepatocellular carcinoma in patients with HCV was limited because of the lack of study details.

**Recommendations from Others**

The American Association for the Study of Liver Diseases recommends ultrasonography for patients with HCV and cirrhosis every six to 12 months, and recommends AFP measurement only when ultrasonography is not available. Based on fair-quality evidence, the National Cancer Institute found that screening would not decrease mortality from hepatocellular carcinoma, and could result in rare but serious adverse effects from diagnostic testing.

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**REFERENCES**


