FPIN's Clinical Inquiries

Screening for Hepatocellular Carcinoma in Patients with Hepatitis C Virus Infection

KELLY BOSSENBROEK FEDORIW, MD, *University of North Carolina School of Medicine, Chapel Hill, North Carolina*
KATHERINE RICKETT, MSLS, MSEd, *East Carolina University, Greenville, North Carolina*

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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.[1] 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*).[1-5] 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.[2-5] Tumor detection rates were 53 to 91 percent for computed tomography, and 78 percent for magnetic resonance imaging.[2-4]

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.[6] 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

Table 1. AFP Measurement vs. Imaging for Detecting Hepatocellular Carcinoma in Liver Transplant Candidates with HCV

Study type	*Number of patients*	*Cause of carcinoma*	*Test*	*Sensitivity (%)*	*Specificity (%)*
Systematic review (2 prospective cohort, 3 case-control)[1]	1,734 (239 were not HCV-positive)	NS	AFP > 20 ng per mL (20 µg per L)	41 to 65	80 to 94
Retrospective (blinded) case-control[2]	106 (19 with hepatocellular carcinoma)	Mixed (58 percent HCV)	AFP > 20 ng per mL	58	91
			AFP > 50 ng per mL (50 µg per L)	47	96
			Ultrasonography	58	94
			Computed tomography	53	94
Retrospective case series[3]	166 (27 with hepatocellular carcinoma)	Mixed (63 percent HCV)	AFP > 20 ng per mL	63	87
			AFP > 200 ng per mL (200 µg per L)	27	100
			Ultrasonography	59	93
			Computed tomography	91	96
Retrospective case series[4]	239 (all with hepatocellular carcinoma)	Mixed (55 percent HCV)	AFP > 50 ng per mL	31	96
			AFP > 200 ng per mL	20	>99
	199		Ultrasonography	58	NA
	164		Computed tomography	69	NA
	197		Magnetic resonance imaging	78	NA
Retrospective case series[5]	200 (28 with hepatocellular carcinoma)	NS	Ultrasonography	43	95

AFP = α-fetoprotein; HCV = hepatitis C virus; NA = not available; NS = not specified.

Information from references 1 through 5.

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.[7] 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.[8]

Address correspondence to Kelly Bossenbroek Fedoriw, MD, at kbossen@email.unc.edu. Reprints are not available from the authors.

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