



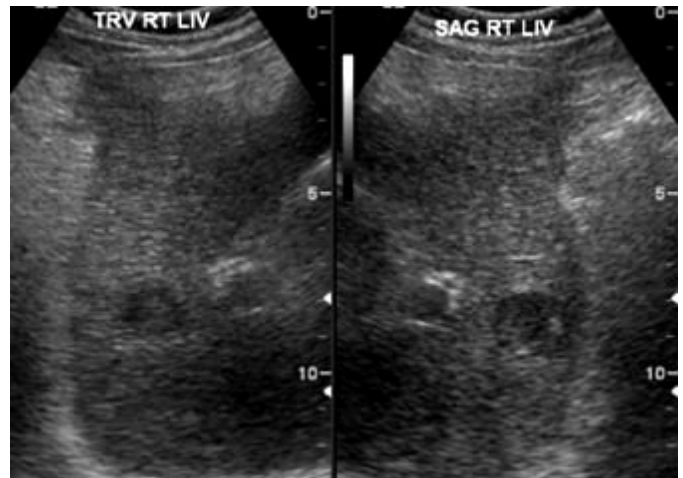
Screening for Hepatocellular Cancer in Cirrhotic Patients

- Patients with cirrhosis have an annual risk of 1-6% of developing hepatocellular cancer (HCC);
- Liver transplantation is an effective treatment and, therefore, it is justifiable to screen patients at high risk for developing HCC every 6-12 months;
- Ultrasound imaging and monitoring blood concentrations of alpha-fetoprotein are recommended for screening;
- If ultrasound images detect a lesion, or if the liver echotexture is heterogeneous because of severe cirrhosis, MRI is recommended for further evaluation

The incidence of hepatocellular carcinoma (HCC) has increased dramatically in the United States within recent decades and it is now the fourth leading cause of cancer-related deaths worldwide. The increase has been driven mainly by the epidemic of hepatitis C infection - persons with HCV cirrhosis have about a 20% lifetime risk of developing HCC. However, all etiologies of cirrhosis increase the risk and patients with cirrhosis have an annual risk of 1-6% of developing HCC. Non-alcoholic steatohepatitis, which is associated with type II diabetes and obesity, also appears to be associated with an increased risk for developing HCC. However, about 90% of all cases are found in patients who are cirrhotic and, in the USA, HCC is most commonly found in men aged 45-65.

If HCC is detected early, when there is a single tumor less than 5 cm or no more than three tumors less than 3 cm and the disease is intrahepatic, it can be treated successfully with liver transplantation. The survival rate after transplantation approaches that for patients who undergo transplants for reasons other than cancer. Alternatively, patients can be treated by surgical resection with partial hepatectomy or by ablation *in situ* (see *Percutaneous Radiofrequency Ablation of Tumors in the Liver and Kidney*, [Radiology Rounds, September 2004](#)). However, if the diseased liver is not completely removed, the patient is at high risk for developing another tumor.

Unfortunately, many patients with HCC are not diagnosed until the disease is advanced and not treatable, when the median survival time after diagnosis is 6-20 months. Therefore, there is considerable interest in screening high-risk patients for HCC in order to detect early stage disease that is



Transverse and sagittal ultrasound images show an HCC in a cirrhotic liver.

amenable to treatment. However, at this time there is no good evidence to show that early detection increases long-term survival. In addition, it is not clear how to optimally screen at risk patients for HCC based on current evidence.

Screening Methods

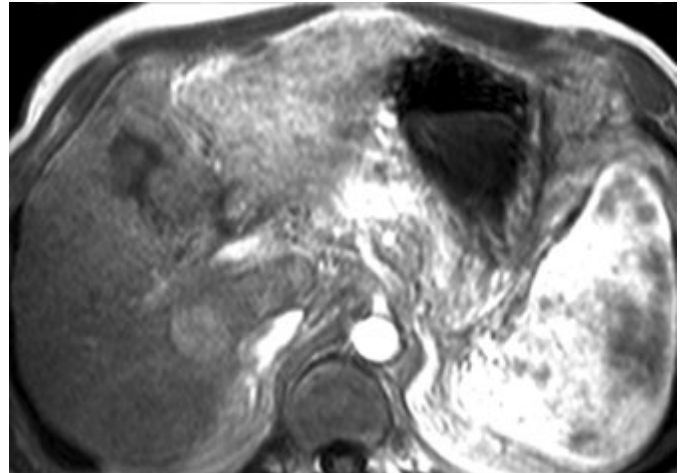
Screening for HCC is most commonly conducted every 6-12 months in patients at risk by measuring of blood alpha-fetoprotein (AFP) concentrations and ultrasonography. The sensitivity and specificity of AFP screening varies with the level of AFP selected and the risk of HCC in the population selected. Overall, neither the sensitivity nor the specificity is high and the positive predictive value varies from 9-50%.

Reports of the sensitivity of ultrasound have varied widely, ranging from 20-58%. Many of the higher estimates of sensitivity have come from Asia, where patients are slimmer than those in the USA. Since the quality of ultrasound images is degraded at greater depths of tissue, the sensitivity of ultrasound in overweight patients is relatively poor. In addition, the difficulty in detecting HCC lesions in

ultrasound images of livers that have gross abnormalities due to cirrhosis decreases sensitivity. In studies in which explanted severely cirrhotic livers were examined after liver transplantation, the sensitivity has been reported to be as low as 20% for 2-3 cm lesions and 13% for 1-2 cm lesions. Nevertheless, the specificity for detecting HCC with ultrasound is high (92-96%) and the sensitivity improves with lesion size.

| Biomarkers of HCC | | | |
|---------------------------------------|-------------|-------------|---------------------------|
| | Sensitivity | Specificity | Positive Predictive Value |
| alpha-fetoprotein >20 ng/ml | 39-65% | 76-94% | 9-50% |
| Ultrasound | 20-58% | 92-96% | 69-78% |
| CT | 54-85% | 66-96% | 67-87% |
| MRI | 55-88% | 57-86% | 88-91% |

Note: The values for the imaging biomarkers are those for per lesion sensitivity and specificity



In same patient, Gadolinium contrast MR image shows transient enhancement of the tumor during the arterial phase.

Detecting HCC with MRI and CT

Both MRI and CT can detect HCC with a higher sensitivity than ultrasound but these imaging methods also detect other focal abnormalities and about 10% of findings are false negatives. In both cases dynamic imaging using a contrast agent is necessary to detect the tumors, which are highly vascularized with an arterial, as opposed to portal, blood supply. The tumors are, therefore detected as a transient enhancement as the contrast agent passes through the arterial blood vessels. The sensitivity of MRI appears to be somewhat higher than CT but neither technique has high sensitivity for detecting lesions <1 cm. However, it has been shown that about 50% of lesions that are <1.5 cm do not develop into HCC and are not apparent on images acquired at follow-up after 12 months.

Scheduling

Ultrasound screening of patients at high risk of developing HCC is performed at Mass General West Imaging in Waltham, Mass General Imaging in Chelsea, or in the Yawkey Center on the main MGH campus. Appointments can be scheduled by calling 4-XRAY (617-724-9729) or through the web-based Radiology Order Entry system, <http://mghroe/>.

Recommendations

Although there is insufficient evidence to clearly demonstrate that screening for HCC is beneficial for patients, the existence of an effective curative treatment (liver transplantation) justifies screening cirrhotic patients who are at increased risk. Ultrasound is the least sensitive of the imaging modalities for the detection of HCC but, due to constraints of cost and resource availability, neither MRI nor CT is suitable as a routine screening method. Therefore, ultrasound imaging should be the initial screening method, together with monitoring blood concentration of alpha-fetoprotein. If the ultrasound examination shows a normal liver, additional imaging is unlikely to find HCC. However, if the ultrasound images are abnormal, either because the liver has a heterogeneous appearance due to cirrhosis or because a lesion is detected by ultrasound, contrast-enhanced MRI or CT is recommended for further evaluation of the patient.

Further Information

For further questions, please call [Peter Hahn, M.D.](#), Associate Radiologist, Abdominal Imaging and Intervention Division, at 617-726-8396.

We would like to thank [Raymond Chung, M.D.](#), MGH Gastrointestinal Unit, for his advice and assistance in the preparation of this article.

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