

# HCC IN FOCUS

Current Developments in the Management of Hepatocellular Carcinoma

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## Surveillance for Hepatocellular Carcinoma



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### G&H What are the current guidelines for hepatocellular carcinoma surveillance?

**CF** There are several sets of guidelines. According to guidelines from the American Association for the Study of Liver Disease (AASLD) and the European Association for the Study of the Liver, an ultrasound should be performed every 6 months in patients who are at elevated risk for hepatocellular carcinoma (HCC). These include patients with cirrhosis, certain patients with hepatitis B virus infection (including those with a family history and those who also have cirrhosis), patients who are of African descent, Asian men older than 40 years, and Asian women older than 50 years. The Asian Pacific Association for the Study of the Liver, the National Comprehensive Cancer Network, and the US Department of Veterans Affairs endorse the use of alpha-fetoprotein (AFP) in addition to ultrasound for surveillance. Other groups, such as the Japan Society of Hepatology, recommend testing for AFP, Lens culinaris agglutinin-reactive AFP (AFP-L3), and des-gamma-carboxy prothrombin (DCP) in addition to ultrasound every 6 months.

### G&H How sensitive is ultrasound for HCC surveillance?

**CF** The sensitivity of ultrasound depends on who is performing the procedure and who is being surveilled. Many of the studies looking at the sensitivity of ultrasound for HCC were performed in Asia, which means that the procedures were used predominantly in patients who have hepatitis B virus infection, often in combination with a

low body mass index (BMI), and who do not necessarily have cirrhosis. If a patient has cirrhosis, the liver is often very nodular, which decreases the sensitivity of ultrasound owing to the difficulty of detecting nodules in such a setting. The sensitivity of ultrasound also decreases if a person has a high BMI and a thick abdominal wall.

In addition, ultrasound technicians in specialty centers who have been specifically trained to use ultrasound for HCC screening can perform ultrasound with high sensitivity, particularly compared with technicians at low-volume community centers. These technicians may not have specialized training to scan through the liver carefully or may not have the time to do so. The experience of the technician is very important. The sensitivity of ultrasound can vary from 30% to 90% depending upon the patient and the performing technician.

### G&H Does the quality of the ultrasound need to be defined?

**CF** Yes. Unfortunately, clinicians do not usually receive a report telling them how good an ultrasound is. I know that when I receive reports from patients who have undergone ultrasounds elsewhere, I do not know whether these ultrasounds are of good or poor quality. Therefore, I do not know how much I can trust the ultrasounds. It would be very helpful if the quality of an ultrasound were defined on the accompanying radiology report so that clinicians could know whether the ultrasound could be trusted. It also would be helpful if clinicians knew whether the technician performing the ultrasound has been trained specifically for nodule detection in a cirrhotic liver. Several

centers are starting to train their ultrasound technicians to report the quality of their ultrasounds; however, most centers are still not doing this.

### G&H What are the advantages and disadvantages of using ultrasound for HCC surveillance?

**CF** The advantages are that ultrasound is inexpensive and fairly easy to perform. The provider does not have to worry about contrast or renal function, which makes the procedure relatively cost-effective in these patients.

The main disadvantage of ultrasound is its sensitivity. As discussed earlier, the sensitivity can vary greatly, and it is difficult to know the sensitivity of a particular ultrasound in a specific patient.

### G&H Should there be a BMI limit for ultrasound?

**CF** This issue has been discussed in many forums. It is well known that the higher the BMI, the worse the quality of the ultrasound. The problem with making a specific cutoff is that different patients carry their weight differently. Ultrasound quality actually depends less on BMI than on abdominal wall thickness, which is what affects the penetration of the beam. For example, some patients have a very high BMI yet carry their weight very low or in areas other than the abdominal wall; therefore, it might still be reasonable to perform an ultrasound in these patients.

The other issue that can affect the quality of ultrasound in patients with a high BMI is whether or not the liver has steatosis, and this can vary greatly among patients. Therefore, simply making a BMI cutoff would potentially prevent some patients from using ultrasound even though it could be sensitive enough in them. It would be helpful if guidelines existed to better predict in which patients the quality of ultrasound would likely be poor, and then recommend what to do.

### G&H Do biomarkers currently have a role in HCC surveillance?

**CF** At this point, the biomarkers AFP, AFP-L3, and DCP should be used for surveillance only in conjunction with imaging; using the biomarkers on their own is inadequate. If a clinician cannot obtain surveillance imaging for any reason, then the biomarkers could be used on their own because they are better than nothing. Currently, these biomarkers are not included in the AASLD guidelines for HCC surveillance, but are included in other guidelines as detailed earlier. AFP had been included but was taken out of the guidelines because of concerns regarding sensitivity and specificity, resulting in difficulty of interpretation.

However, I still find that these biomarkers are quite helpful in terms of risk prediction for patients and determining whether a more sensitive imaging test is needed in a particular patient. Nevertheless, there needs to be more research, specifically in terms of how to use the biomarkers. I think that one of the most helpful uses of biomarkers is looking at the change of AFP over time, which has been shown to have very good sensitivity for HCC. As AFP increases, the likelihood of HCC is increased, and an increase of AFP should trigger a more sensitive imaging test such as computed tomography (CT) or magnetic resonance imaging (MRI).

In addition, there are models that include various biomarkers, such as the GALAD (gender, age, AFP-L3, AFP, and DCP) and BALAD (bilirubin, albumin, AFP-L3, AFP, and DCP) models. Scores of these models predict the HCC risk and prognosis of a particular patient. This information provides a risk projection to determine whether ultrasound alone is enough or whether a more sensitive imaging test is needed.

### G&H What are the advantages and disadvantages of the existing biomarkers?

**CF** The advantages are that they are easy to obtain (only a simple blood test is needed), they are not very expensive, and they provide more information than just using an imaging test.

One disadvantage is that we do not have much data on biomarkers thus far, so interpretation can be confusing if there is an unexpected finding. Interpretation also can be difficult for people who do not use biomarkers often, as the sensitivity and specificity of the biomarkers depend on the patient, the disease state, the presence of active virus, and other factors.

The lack of data, specifically involving US patients, is a large part of the reason that biomarkers are not yet recommended in the AASLD guidelines. Much of the data that are currently available on biomarkers have come from Japan, and there are some concerns regarding whether those findings are generalizable to the US population.

### G&H When should surveillance be changed to MRI or CT?

**CF** Owing to concerns regarding recurrent radiation exposure, I do not use CT as my main surveillance tool. I reserve this for the rare cases in which MRI or ultrasound cannot be used for some reason.

Usually, I order an ultrasound and then talk to the technician to find out the quality. If the quality of the ultrasound was very poor (eg, the ultrasound involved a very obese patient with abdominal thickness and/or a very nodular liver), I often switch to MRI in that patient. In

addition, I predominantly use MRI to perform surveillance on patients who are on the liver transplant waiting list. These patients often have issues that make the quality of ultrasound very poor (eg, cirrhosis, decompensation with ascites, and bowel gas from lactulose use). Failure to detect HCC in a patient on the liver transplant waiting list can have a significant impact on the patient's overall care.

#### **G&H** How cost-effective is HCC surveillance?

**CF** Some physicians and publications have suggested that surveillance for HCC is not cost-effective and that it does not save lives. This is incorrect. HCC surveillance with ultrasound is very effective in terms of cost per life saved. If HCC can be found early, it may be curable. Surveillance is indicated and worth doing in patients who are at risk for HCC. Unfortunately, the rate of surveillance in some communities is currently very poor—as low as only 20% to 30% of the people at risk for HCC.

However, it should be noted that HCC surveillance with CT or MRI is not cost-effective for the general

population. One of the focuses of research in HCC right now is finding a more cost-effective way to use single-phase MRI for surveillance. This would be very helpful; if researchers could figure out a way to make MRI cheaper, I think the improved sensitivity of MRI would be worth it.

*Dr Frenette has served as a consultant for Wako Diagnostics.*

#### **Suggested Reading**

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