

HCC IN FOCUS

Current Developments in the Management of Hepatocellular Carcinoma

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Elastography and the Risk of Hepatocellular Carcinoma



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G&H How can elastography be performed?

JT The most common way to perform elastography, or measurement of the stiffness of a liver, is by using an ultrasound-based platform. The vast majority of ultrasound-based liver elastography is performed in the office either by the provider or a trained designee. Ultrasound-based elastography can also be performed in the radiology suite with an ultrasound machine if the appropriate technology has been loaded onto the machine.

Three platforms have been used: vibration-controlled transient elastography (FibroScan, Echosens), which is the most common; shearwave elastography (Aixplorer, Supersonic Imagine/Sandhill Scientific); and acoustic radiation force impulse elastography (Siemens).

The other method of performing elastography involves magnetic resonance imaging. This technique is more time-consuming and uses more expensive technology that is harder to access because patients need to use a magnetic resonance imaging scanner as opposed to an ultrasound-based platform, which may be available during a routine visit to their doctor's office.

G&H Which patients are appropriate candidates for elastography?

JT Currently, hepatitis C virus–infected patients eligible for treatment require elastography to determine the extent of their hepatic fibrosis. This information affects their treatment protocol in terms of the medication selected and the duration of the therapy. Patients

who have more extensive fibrosis will typically require longer treatment courses. In addition, hepatitis C virus–infected patients and their providers need to know how much fibrosis they have because even patients cured of their hepatitis C virus infection have an ongoing risk for hepatocellular carcinoma if they have cirrhosis; thus, these patients need to be followed and screened for

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hepatocellular carcinoma. If a patient's liver heals and the extent of fibrosis resolves to the point of no or insufficient fibrosis, screening for hepatocellular carcinoma would no longer be warranted.

The other group of patients who need elastography consists of individuals with fatty liver disease. It has become increasingly important to determine the extent of fibrosis in these patients because there are several clinical drug trials being conducted, and fibrosis staging information is needed in order to participate in these trials.

G&H Is elastography contraindicated or less reliable in any subgroups of these patients?

JT In my experience, the patients who are most poorly suited for elastography are those who are extremely obese, those who have large amounts of abdominal fat (which may include some patients with fatty liver disease), and those who have small rib spaces. With ultrasound elastography, there may be indeterminate or unclear results simply because patients are so obese that the ultrasound is not able to adequately probe their liver and return reliable results. However, this technique is not contraindicated in these patients.

G&H Is there a significant learning curve associated with performing elastography?

JT Elastography can be performed by physicians, but, like any ultrasound-based technology, it is more commonly performed by nonphysicians such as medical assistants or licensed vocational nurses. These individuals should undergo appropriate training (usually approximately 100 cases), but the elastography images should still be reviewed by a physician.

G&H What are the most significant risk factors for hepatocellular carcinoma?

JT The most significant risk factor is the presence of cirrhosis or advanced fibrosis in the liver, and the second most significant risk factor is untreated underlying liver disease, such as active viral hepatitis or hemochromatosis. Other important risk factors are family history of liver disease, advancing age, and male sex.

G&H What is the current understanding of the relationship between elastography and the risk of hepatocellular carcinoma?

JT A 2013 meta-analysis by Singh and colleagues looked at 9 studies (214 cases of hepatocellular carcinoma; all patients in the studies had viral hepatitis), and found that patients who had a higher degree of liver stiffness had a higher risk of hepatocellular carcinoma. Overall, there was an 11% increase in hepatocellular carcinoma risk for each kilopascal increase in liver stiffness measurement (using transient elastography). In cirrhotic patients, each kilopascal increase in liver stiffness measurement raised the risk of hepatocellular carcinoma by 4%.

These findings are important and have actionable implications, meaning that patients who have more advanced fibrosis should be screened more carefully for hepatocellular carcinoma. This is particularly important

in hepatitis C virus–infected patients who may have stage 3 fibrosis and may have an incremental risk of hepatocellular carcinoma greater than patients without fibrosis but less than those with cirrhosis. Patients who have higher degrees of fibrosis still have a cancer risk and need to be

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continually screened for hepatocellular carcinoma. Thus, elastography is helpful in determining the amount of fibrosis in a patient, which is the most important risk factor of hepatocellular carcinoma, as previously mentioned.

G&H Is elastography alone sufficient to determine the risk of hepatocellular carcinoma?

JT Liver stiffness is an additive risk factor among the several risk factors previously mentioned, which should all be looked at together. For example, sex is a risk factor (men have a higher risk of hepatocellular carcinoma than women), but women who have risk factors such as advanced fibrosis still require screening for hepatocellular carcinoma. Elastography can identify the extent of fibrosis and is a useful tool in screening and diagnosing patients, but it may not be completely accurate, and it is not the only tool that should be used to determine a patient's risk for hepatocellular carcinoma. Elastography results should be used in context with other clinical findings, such as blood tests, other imaging, examination findings, and the patient's symptoms. An isolated abnormal elastography result (eg, a high kilopascal value) does not necessarily indicate cirrhosis. A single elastography result in a single patient viewed without considering other clinical parameters can yield results that are inaccurate. Elastography has variation. Even if the same patient is examined sequentially, results can vary by as much as 1.5 kilopascals.

G&H Which other tests or biomarkers should be used in combination with elastography to determine the risk of hepatocellular carcinoma?

JT In 2013, Feier and colleagues performed a case-matching study to examine elastography data and common biomarkers for the detection of hepatocellular carcinoma in patients with hepatitis C virus–related liver cirrhosis. Multivariate analysis showed that higher values of liver stiffness, alanine aminotransferase, α -fetoprotein, and interquartile range of liver stiffness measurements were independently associated with the presence of hepatocellular carcinoma (odds ratios of 8.27, 1.01, 1.04, and 1.16, respectively). The researchers concluded that combining these 4 measures into a regression model may allow hepatocellular carcinoma to be predicted noninvasively and with good accuracy.

However, it should be noted that the role of α -fetoprotein in hepatocellular carcinoma has been debated. It is easily obtainable because it is a blood draw, it can be measured frequently, and the results can be easily interpreted (the higher the level, the greater the risk of hepatocellular carcinoma); however, this test is not particularly sensitive or specific when used by itself.

The recommended screening tool is cross-sectional or ultrasound-based imaging of the liver performed every 6 months, which is the protocol recommended for a new patient with cirrhosis. As previously mentioned, elastography can be used to identify patients at risk of hepatocellular carcinoma and can be helpful in the management of those patients in terms of how vigorously to follow them based upon their underlying risk. For example, if a patient moves from a high kilopascal value to a low value (eg, from 10 to 7 kilopascals), the patient can be discharged from the clinic because there is insufficient fibrosis to warrant ongoing screening. Elastography can be performed

in several minutes on a yearly basis, if needed, to follow these patients.

G&H What further research is needed in terms of hepatocellular carcinoma risk and elastography?

JT Further research is needed to determine whether elastography can be used to adjudicate benign from malignant liver lesions, including patients treated with chemoembolization, as well as whether elastography can improve risk stratification of patients with early or intermediate fibrosis for long-term risk of hepatocellular carcinoma.

Dr Trotter has no relevant conflicts of interest to disclose.

Suggested Reading

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