

ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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Utilization of FibroScan Testing in Hepatitis C Virus Management



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G&H How can FibroScan be used to stratify patients with hepatitis C virus infection for treatment with direct-acting antiviral agents?

SH FibroScan (Echosens and Sandhill Scientific), also known as vibration-controlled transient elastography, is a noninvasive test that assesses stiffness in the liver, which has been shown to correlate with fibrosis. Several studies have explored this correlation, most recently a study by Afdhal and colleagues, which was published online ahead of print in *Clinical Gastroenterology and Hepatology*. The authors found that it was possible to accurately assess whether a patient had stage 3 or greater fibrosis (advanced fibrosis) if the FibroScan score was above 9.6 kPa. The American Association for the Study of Liver Diseases (AASLD) practice guidelines for the management of hepatitis C virus (HCV) infection state that patients with stage 3 or greater fibrosis are an important group to treat because they have the most urgent need for treatment. FibroScan can be used to stratify patients in terms of the urgency of their need for treatment because it can accurately detect patients with advanced fibrosis.

G&H How does this process compare with the traditional stratification of patients with HCV infection?

SH Until the advent of noninvasive tests, such as FibroScan, we relied on percutaneous liver biopsy to help us determine the severity of a patient's underlying liver disease and to decide whether the patient should be treated aggressively, which was particularly important in

the days of interferon management. At that time, treatment carried a significant number of side effects, so if a patient had mild liver disease, he or she sometimes chose to wait for better treatment options (ie, ones with fewer side effects).

Now, better therapeutic options have finally arrived in the form of direct-acting antiviral (DAA) agents, which have minimal side effects, and therefore our reasons for performing liver biopsies have shifted somewhat. We now use liver biopsy in the setting of HCV infection to help determine whether a patient has cirrhosis, as this impacts the potential length of treatment with DAA agents. This is where FibroScan has stepped in; there have been many studies showing that this tool is a good test for determining whether a patient has advanced disease, which gives clinicians the opportunity to avoid putting that patient through a liver biopsy. As previously mentioned, advanced liver disease is generally signified by a FibroScan score above 9.6 kPa, as the AASLD practice guidelines suggest using this cutoff for determining which patients should be treated.

However, it could also be argued that a higher cutoff should be used. In fact, in the aforementioned study by Afdhal and colleagues, 12.8 kPa was the cutoff for cirrhosis. In addition, 12.8 kPa is the cutoff used in the DAA agent package inserts for separating patients with cirrhosis from those without cirrhosis.

G&H Is liver biopsy still needed in patients with HCV infection?

SH I rarely perform liver biopsy in the setting of HCV infection alone, which is a dramatic change from the past.

The only time that I still use liver biopsy is in situations in which FibroScan is less accurate—for example, if the patient just ate (we typically like to have at least a 3-hour fast prior to performing the procedure), if there is a significant amount of steatosis or inflammation in the liver, or if the patient has ascites, cholestasis, jaundice, or congestive heart failure. A surrogate marker of significant inflammation in the liver is a high alanine aminotransferase level (>100 U/L in some studies). If the patient has ascites, it is obvious that the liver is cirrhotic, so there is no sense in using FibroScan anyway.

G&H How can the measurement of liver stiffness be used to determine the length of HCV treatment?

SH With the DAA regimens from Gilead, Janssen, and AbbVie that are currently approved by the US Food and Drug Administration, certain criteria are required to help determine the appropriate length of therapy (8-24 weeks). These criteria include prior treatment experience, the presence or absence of cirrhosis, HCV genotype, and viral load. FibroScan can help in this setting; if a patient has a liver stiffness measurement above 12.8 kPa, then the liver is considered to be cirrhotic, which is important information to know when one is trying to determine which regimen to use and how long treatment should last.

G&H What implications does this information have for insurance reimbursement?

SH FibroScan scores can be used to validate advanced fibrosis/cirrhosis for insurance companies, health care plans, or medical centers that require a significant amount of fibrosis before approving or allowing the start of HCV treatment. As discussed earlier, FibroScan is very accurate at detecting advanced fibrosis in the setting of chronic HCV infection. Many studies, including the aforementioned one by Afdhal and colleagues, have shown that a cutoff of 9.6 kPa identifies patients with advanced fibrosis. A score higher than 9.6 kPa is generally sufficient to gain insurance approval.

G&H Can FibroScan be used in combination with liver fibrosis biomarkers?

SH Yes. Several studies have examined FibroScan in combination with various biomarker panels. FibroTest (known as FibroSure [LabCorp] in the United States), a panel that includes γ -glutamyl transferase, total bilirubin, haptoglobin, α -2-macroglobulin, and apolipoprotein A1 as well as the clinical markers of age and gender, has been shown to enhance sensitivity for detecting cirrhosis when

used in combination with FibroScan, according to a study by Poynard and colleagues.

Several other biomarker panels can be combined with FibroScan to increase diagnostic accuracy, albeit at an additional cost. FibroMeter, a proprietary biomarker panel offered by Echosens (the manufacturer of FibroScan), has also been studied in combination with FibroScan and was shown to increase the diagnostic accuracy of the device in a study by Boursier and colleagues.

G&H Are there any other advantages, or any disadvantages, of FibroScan?

SH FibroScan is a noninvasive test performed by a machine that is relatively small (~5 feet tall, approximately 12 inches wide, and only 4 or 5 inches thick). This means that it can easily fit in the corner of an examination room, be pulled out quickly, and within 10 minutes be used to assess a patient's liver stiffness and, thus, his or her probability of having advanced disease. In addition, this test shortens the time interval for the initiation of treatment because it is not necessary to wait for a liver biopsy.

One disadvantage is that the clinician is not necessarily able to detect any degree of fibrosis; the clinician is just ruling out advanced disease. In addition, it is not possible to identify other, coexisting liver diseases with this test.

G&H Is this test associated with a significant learning curve?

SH Yes. I would say that approximately 100 procedures are needed before a clinician can truly begin to understand the nuances of the machine—for example, to know when to use the M probe vs when to use the XL probe and to understand what the numbers really mean. However, I believe that once a clinician becomes familiarized with the test, it is quick and easy to use.

G&H How expensive is it?

SH My understanding is that FibroScan currently costs approximately \$120,000 to \$140,000. However, there are now current procedural terminology codes for it, so clinicians may be reimbursed for the procedure, by both Medicare and Medicaid, as well as private pay insurance.

G&H Should FibroScan be used only in specialized centers?

SH To my knowledge, fewer than 200 of these machines are currently in the United States, although this number is increasing steadily, and there are many machines throughout Europe. Right now, it is probably more likely

that FibroScan is being used in specialized centers, but I would encourage any clinicians who are aggressively treating HCV infection to consider the use of this noninvasive test in their clinical practice.

G&H Are there any unmet needs in research in this area?

SH There is a huge unmet need in the area of non-alcoholic fatty liver disease (NAFLD), which is the most common liver abnormality that gastroenterologists and hepatologists encounter today in the United States, and for that matter probably around the world. FibroScan needs refinement to become more accurate at detecting the advanced stages of fibrosis in a patient with NAFLD, so this area is important moving forward and needs to be looked at closely. More studies are needed, as we do not currently have any published data in the United States on the use of this test in NAFLD.

Dr Harrison serves on the advisory boards of Nimbus Discovery, NGM Biopharmaceuticals, FibroGen, and the Chronic Liver Disease Foundation.

Disclaimer

The opinions in this manuscript do not constitute endorsement by San Antonio Military Medical Center, the US Army Medical Department, the US Army Office of the Surgeon General, the Department of the Army, the Department of Defense, or the US Government of the information contained therein.

Suggested Reading

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