Use of FibroScan for Noninvasive Assessments Of Liver Disease

Introduction
The prevalence of chronic liver diseases continues to rise worldwide. The obesity epidemic has led to significant rates of non-alcoholic fatty liver disease (NAFLD), affecting approximately 27% to 34% of individuals in the United States; furthermore, 6 million are expected to have progressed to non-alcoholic steatohepatitis (NASH), and roughly 600,000 have developed NASH-related cirrhosis.1 Moreover, between 3 and 4 million individuals in the United States have chronic hepatitis C virus (HCV) infections and many of these individuals are unaware of their serostatus.2 In August 2012, the Centers for Disease Control and Prevention recommended that all baby boomers, a high-risk population of individuals born between 1946 and 1964, undergo HCV testing at least once in their lifetime.3 In June 2013, the US Preventive Services Task Force made a similar recommendation.4 As a result, the number of individuals diagnosed with HCV has increased considerably.5,6

For patients with chronic liver disease, the early identification of liver fibrosis is critical, particularly for those with cirrhosis who are more likely to develop hepatocellular carcinoma (HCC).5,6 Clinical guidelines recommend that cirrhotic patients undergo an ultrasound liver examination every 6 months.7 Of concern, the annual incidence of HCC between 2001 and 2010 rose from 2.7 to 7.7 cases per 100,000 population, causing 5.5 deaths per 100,000 population,8 and the physician should be seated on a stool, not standing.

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FibroScan: A Novel, Noninvasive Technique
FibroScan is a noninvasive test that assesses liver stiffness by employing vibration-controlled transient elastography (VCTE®) to emit a shear wave through the liver and measure its velocity via ultrasound.8 Although this technology was approved for marketing in the United States in April 2013, it has been available in Europe since 2003, in China since 2008, and in Japan since 2011. It is easy to administer at the point of care, takes only 5 to 7 minutes to conduct, and results are available within 10 minutes. FibroScan is not painful, does not require sedation, and evaluates 100 times more liver volume than biopsy.9,10

During the procedure, clinicians induce a 50-Hz shear wave into the liver from a small mechanical actuator on the end of an ultrasound probe during patient expiration. The technology measures the velocity of the shear wave passing through the liver, in meters per second, and then converts the measurement into a liver stiffness value, which is expressed in kilopascals (kPa).8 Higher kPa values indicate more extensive fibrosis. Results are offered following 10 or more successful measurements and a median interquartile range/median ratio less than 0.30.8 FibroScan can be used as a stand-alone tool or as an adjunct to liver biopsy, and it is particularly useful for identifying patients who have very advanced liver disease or cirrhosis.9 FibroScan is often the first test clinicians order when a patient presents with liver disease.

FibroScan comes with 2 different probes: M and XL. The XL probe, which is indicated for use in obese patients, employs a 2.5-MHz ultrasonic transducer for improved vibration amplitude and measurement depth for accurate measurements in this patient population; the M probe is intended for use in the general population.11 Clinicians need to be aware of a few subtleties when conducting the test: Patients should be instructed not to consume any food or liquid 2 hours before testing; measurements may be taken anytime during a patient’s respiratory cycle; and the physician should be seated on a stool, not standing.

Because FibroScan has not yet received a current procedural terminology (CPT) code, some clinicians are batching the tests, putting their billing in a holding pattern. For patients paying out of pocket, the test costs approximately $131 (North Shore LIJ Health System charges $375), which is much cheaper than biopsies that may cost $2,255 or more once all clinician fees are factored in.12

In early 2014, FibroScan was included in joint HCV management guidelines from the Infectious Diseases Society of America and the American Association for the Study of Liver Diseases as a point-of-care option for measuring liver stiffness in order to distinguish the presence of cirrhosis.13 Doctors are also using it in patients with other types of liver disease, including NASH, alcoholic fatty liver disease, hepatitis B virus (HBV) infection, and cholestatic liver disease.14

Clinical Data on FibroScan
The most thorough clinical testing of FibroScan has been conducted in patients with chronic HCV. In a prospective multicenter study of 327 patients with chronic HCV, investigators compared results from FibroScan and liver biopsy. FibroScan results were well correlated with fibrosis stage (Kendall correlation coefficient, 0.55; P<0.0001).13 The investigators generated cutoff values with a high degree of accuracy for more
serious Metavir fibrosis stages: 8.8 kPa for stage F2 or greater, 9.6 kPa for stage F3 or greater, and 14.6 kPa for stage F4 (Table 1).\(^\text{15}\)

Another study involved 109 patients with chronic HCV who underwent a FibroScan test within 6 months of liver biopsy at the National Institutes of Health from 2006 to 2011. With a cutoff value of 13.1 kPa, there was a negative predictive value of 1.0 for the diagnosis of cirrhosis.\(^\text{16}\) The specificity of 0.89 resulted in a positive predictive value of 0.58, but 7 of 10 patients with increased liver stiffness consistent with cirrhosis had a noncirrhotic biopsy result.\(^\text{16}\) This cohort, however, had other clinical and radiologic features of cirrhosis, which suggests that liver biopsy had understaged the disease.\(^\text{16}\)

Other researchers have identified the optimal cutoff value for cirrhosis in patients with HCV as 12 kPa.\(^\text{17}\)

FibroScan has shown similar utility for patients with HIV/HCV coinfection. One investigation compared the diagnostic accuracy of FibroScan with 4 other noninvasive serum markers for predicting fibrosis among 100 patients with HIV/HCV coinfection: APRI, Forns Index, FIB-4, and HGM2.\(^\text{18}\)

FibroScan was more accurate for the diagnosis of advanced fibrosis (≥F3) and cirrhosis, resulting in significantly higher area under the receiver-operating characteristic curves compared with FIB-4 (0.92 vs 0.69; \(P=0.06\)), APRI (0.93 vs 0.77; \(P=0.007\)), HGM2 (0.92 vs 0.80; \(P=0.03\)), and the Forns Index (0.92 vs 0.75; \(P=0.002\)).\(^\text{18}\)

Additionally, prospective studies have demonstrated that VCTE is reliable for the evaluation of fibrosis or cirrhosis in patients with HBV, with cutoff values similar to those observed for HCV.\(^\text{14,15}\) Research also supports the use of FibroScan for assessing liver fibrosis in patients with cholestatic liver disease and alcoholic liver disease, with precision comparable to that observed in patients with viral hepatitis.\(^\text{20,21}\)

At Beth Israel Deaconess Medical Center in Boston, clinicians have been using liver stiffness values between 12 and 15 kPa to indicate a high probability of cirrhosis and a value greater than 15 kPa as a diagnosis of definite cirrhosis.\(^\text{16}\) Table 2 provides cutoff values for stiffness staging across several chronic liver diseases.\(^\text{14,15,16,21}\) A diagnostic algorithm for the assessment of liver fibrosis is provided in the Figure.

**Conclusion**

FibroScan has been used extensively as a point-of-contact test in liver clinics throughout Europe. Guidelines from the National Institute for Health and Care Excellence, the European Association for the Study of the Liver, and the Asian Pacific Association for the Study of the Liver recommend using FibroScan technology for the initial evaluation of liver diseases.\(^\text{15}\) The procedure has been validated in more than 760 peer-reviewed publications and has been administered to over 100,000 patients. The primary benefit of this procedure is the exclusion or inclusion of advanced fibrosis and cirrhosis, but FibroScan can also be used for serial testing to assess disease progression or treatment response; additionally, it can serve as an adjunct to liver biopsy as well as clinical, radiologic, and serum marker testing.

**References**


Disclosures: Dr. Bernstein reported that he has received grant support from AbbVie, Bristol-Myers Squibb, Gilead, Merck, and Vertex. He has also served as a consultant for AbbVie, Gilead, and Merck.