Noninvasive Assessment of Fibrosis Regression in Hepatitis C Virus Sustained Virologic Responders

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Abstract: The emergence of direct-acting antiviral (DAA) therapies and noninvasive measures of liver fibrosis has streamlined the management of patients with chronic hepatitis C virus (HCV) infection. DAA therapy is associated with a significantly higher rate of sustained virologic response (SVR) compared to interferon-based therapies. Concomitantly, validated noninvasive measures of fibrosis allow evaluation of patients for therapy without an invasive liver biopsy. Noninvasive measures of fibrosis can be classified as serologic tests or imaging modalities. Several serologic tests have shown robust reliability and clinical applicability. Similarly, imaging modalities such as vibration-controlled transient elastography and magnetic resonance elastography can be used to assess liver stiffness and correlate with fibrosis. Combinations of serologic and imaging tests further improve accuracy compared to an individual modality. The availability of noninvasive fibrosis measures coupled with high SVR rates has shifted the paradigm in the management of HCV infection in the DAA era. Although these noninvasive tests are valuable in evaluating hepatic fibrosis prior to HCV therapy, use of these measures in monitoring fibrosis regression after HCV eradication is currently limited. Furthermore, for patients with pretreatment cirrhosis, the association between fibrosis regression after successful therapy and the risk of hepatocellular carcinoma (HCC) over time is unclear. There are no guidelines on long-term fibrosis monitoring and HCC surveillance after SVR is achieved. This article summarizes the current data on the applications of noninvasive methods to measure hepatic fibrosis and portal hypertension in HCV. In addition, a road map is provided for monitoring patients with advanced fibrosis after HCV eradication.

The management of hepatitis C virus (HCV) infection has undergone tremendous changes over the past several decades. A positive impact has been made by the advent of direct-acting antiviral (DAA) agents, which have a success rate of over 90% in achieving sustained virologic response (SVR), or virologic cure, including in patients with decompensated cirrhosis. The availability...
of noninvasive techniques to measure hepatic fibrosis enables the identification of patients who are at high risk of disease complications without subjecting them to invasive diagnostic modalities such as liver biopsy. The combination of these 2 scientific advances has produced a more streamlined approach to managing patients with chronic HCV infection.

There is evidence that patients who achieve SVR after therapy have a reduced risk of liver-related complications, such as liver failure and hepatocellular carcinoma (HCC).6 This is likely attributed to the regression of fibrosis after HCV eradication.7 However, patients who have pretreatment cirrhosis or advanced fibrosis remain at a higher risk of complications even after achieving SVR.6,7 Other comorbidities, such as obesity, nonalcoholic steatohepatitis (NASH), diabetes mellitus, and alcohol abuse, may also contribute to liver-related complications.6-10

In this era of highly effective DAA agents leading to tremendous cure rates, identifying and monitoring patients who remain at a high complication risk after achieving SVR continues to be a critical issue. Several validated methods for noninvasive measurement of liver fibrosis can be used in the management of HCV infection. The utility of these noninvasive modalities in detecting fibrosis regression and predicting complication risk after achieving SVR, however, is not well defined. To address this gap in knowledge, this article summarizes data on the current available noninvasive modalities and discusses their applications in the management of individuals after successful HCV treatment.

**Noninvasive Serologic Tests for Fibrosis**

Several noninvasive serologic markers have been developed to determine the degree of liver fibrosis. The test characteristics and cutoff values of these serologic markers are illustrated in Tables 1 and 2, respectively. The Aspartate Aminotransferase (AST)-to-Platelet Ratio Index (APRI) score, which was originally proposed in 2003 by Wai and colleagues,11 is a validated measure. In one study, the baseline APRI score predicted HCC development in noncirrhotic patients who achieved SVR (mean, 3.2±2.58 IU/L; \( P = .04 \)).8 The Fibrosis-4 (FIB-4) index is another validated noninvasive serologic measure of fibrosis.12 In a recent study of 113 patients, the APRI score and the FIB-4 index correlated the stage of fibrosis with liver biopsies 5 years after achieving SVR.13 These scores were able to reliably determine moderate to advanced fibrosis (Metavir score F2-F4) and advanced fibrosis (F3-F4) on liver biopsy (area under receiver operating characteristic [AUROC] of >0.8 and accuracy of >70%) in posttreatment patients with normalization of serum aminotransferase levels and absence of hepatic inflammation.13

Several other noninvasive serologic markers have not yet been studied in patients who have achieved SVR but have nonetheless proven to be reliable markers of fibrosis. For example, the FibroTest (BioPredictive) is a patented formula consisting of 5 different biomarkers and 2 clinical variables, and provides a numerical value between 0 and 1.14,15 FibroTest can be used to characterize the severity of liver disease, ranging from mild disease to cirrhosis, in HCV patients.15 Similarly, FibroMeter (BioLiveScale) is another patented formula, which actually performed better in detecting significant fibrosis and cirrhosis compared to the APRI score or FibroTest.16,17 HepaScore (Quest Diagnostics) has also been validated in several studies18-23 and has proven to be slightly better for the detection of cirrhosis compared to the APRI score and FibroTest.17,24

**Noninvasive Nonserologic Modalities for Fibrosis**

The advent of liver stiffness measurement (LSM) has led to the development of sophisticated methods for
noninvasively detecting fibrosis. Technologies such as vibration-controlled transient elastography (VCTE) or magnetic resonance elastography (MRE) have revolutionized the monitoring of patients with liver disease in a clinical setting. These technologies provide reliable ways to measure fibrosis without a liver biopsy. A comparison of these modalities and serologic tests is shown in Table 2.

Vibration-Controlled Transient Elastography
VCTE, often referred to as FibroScan (Echosens), has made its way into the clinical setting of many different centers throughout the United States and other countries. It is approved for use by the US Food and Drug Administration and now serves as the standard of care in many health centers. VCTE outperforms serologic tests for the diagnosis of cirrhosis; in addition, it has a short procedure time, provides immediate results, and is easily operated at the bedside. VCTE uses an ultrasound probe that measures the shear velocity propagating through the liver and expresses it as a volume, which is directly related to the LSM. The units are measured in kilopascals (kPa) and range from 2.6 kPa to 75.0 kPa, with a normal value being approximately 5.0 kPa.

In 2005, Ziol and colleagues investigated VCTE in a prospective study of 327 patients with HCV infection. The study found VCTE to be very reliable for detecting severe fibrosis and cirrhosis. This noninvasive technique was further validated in several other subsequent studies and is now the most widely used noninvasive measure of fibrosis. The cutoff value for limited fibrosis (≥F2) is 7.1 kPa (sensitivity, 67%; specificity, 89%; negative predictive value [NPV], 48%; positive predictive value [PPV], 95%), whereas the cutoff value for cirrhosis (F4) is 12.5 kPa (sensitivity, 87%; specificity, 91%; NPV, 95%; PPV, 77%). A low score on VCTE most likely rules out cirrhosis, but an elevated score must be interpreted in the clinical context.

The limitations of VCTE include the presence of increased necroinflammatory activity and edema within the liver, manifested as aminotransferase elevations. These pathologic changes can falsely elevate the score and overestimate the degree of fibrosis. Other factors that can lead to inaccuracy include recent consumption of a meal, obesity, waist circumference, thoracic fold thickness, ascites, hepatic congestion, extrahepatic cholestasis, and the distance between the skin and liver capsule. However, despite these limitations, VCTE is still a useful tool that allows for a more streamlined approach to monitoring fibrosis in patients during the management of HCV and other liver diseases. VCTE also allows for a simpler way to monitor patients after HCV eradication who have baseline pretreatment advanced fibrosis or cirrhosis.

### Table 2. Comparison of Noninvasive Tests for Detecting HCV Fibrosis

<table>
<thead>
<tr>
<th>Noninvasive Test</th>
<th>Stage of Fibrosis</th>
<th>Cutoff</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
<th>PPV</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>APRI score</td>
<td>F3-F4</td>
<td>1.0</td>
<td>61%</td>
<td>64%</td>
<td>81%</td>
<td>40%</td>
<td>Lin et al²⁴⁴</td>
</tr>
<tr>
<td></td>
<td>F4</td>
<td>1.0</td>
<td>76%</td>
<td>72%</td>
<td>69%</td>
<td>55%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.0</td>
<td>46%</td>
<td>91%</td>
<td>63%</td>
<td>82%</td>
<td></td>
</tr>
<tr>
<td>FIB-4 index</td>
<td>F3-F4</td>
<td>&lt;1.45</td>
<td>74.3%</td>
<td>80.1%</td>
<td>94.7%</td>
<td>NA</td>
<td>Vallet-Pichard et al²⁵⁵</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;3.25</td>
<td>37.6%</td>
<td>98.2%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FibroTest</td>
<td>F3-F4</td>
<td>0.52</td>
<td>80%</td>
<td>82%</td>
<td>94%</td>
<td>55%</td>
<td>Leroy et al²⁶⁴</td>
</tr>
<tr>
<td></td>
<td>F4</td>
<td>0.63</td>
<td>74%</td>
<td>82%</td>
<td>96%</td>
<td>53%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.72</td>
<td>90%</td>
<td>85%</td>
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<td>60%</td>
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<td></td>
<td></td>
<td>0.78</td>
<td>96%</td>
<td>78%</td>
<td>99%</td>
<td>42%</td>
<td></td>
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<tr>
<td>HepaScore</td>
<td>F3-F4</td>
<td>0.47</td>
<td>79%</td>
<td>85%</td>
<td>95%</td>
<td>53%</td>
<td>Leroy et al²⁶⁴</td>
</tr>
<tr>
<td></td>
<td>F4</td>
<td>0.64</td>
<td>78%</td>
<td>82%</td>
<td>97%</td>
<td>34%</td>
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<td></td>
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<td>0.72</td>
<td>90%</td>
<td>85%</td>
<td>97%</td>
<td>60%</td>
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<td></td>
<td></td>
<td>0.78</td>
<td>96%</td>
<td>78%</td>
<td>99%</td>
<td>42%</td>
<td></td>
</tr>
<tr>
<td>VCTE</td>
<td>≥F2</td>
<td>7.1</td>
<td>67%</td>
<td>89%</td>
<td>48%</td>
<td>95%</td>
<td>Castéra et al²³²</td>
</tr>
<tr>
<td></td>
<td>≥F3</td>
<td>9.5</td>
<td>73%</td>
<td>91%</td>
<td>81%</td>
<td>87%</td>
<td></td>
</tr>
<tr>
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<td>F4</td>
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<td>4.11</td>
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<td>85%</td>
<td>NA</td>
<td>NA</td>
<td>Singh et al²⁵²</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.71</td>
<td>91%</td>
<td>81%</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

*APRI, AST-to-Platelet Ratio Index; AST, aspartate aminotransferase; FIB-4, Fibrosis-4; HCV, hepatitis C virus; MRE, magnetic resonance elastography; NA, not available; NPV, negative predictive value; PPV, positive predictive value; VCTE, vibration-controlled transient elastography.*

*Disease-specific cutoffs are still not available for this test.*


**Magnetic Resonance Elastography**

MRE is emerging as an accurate method for cross-sectional and longitudinal evaluation of fibrosis, and has been validated in numerous randomized clinical trials. This method utilizes a conventional magnetic resonance imaging machine but applies shear wave frequency of 40 to 60 Hz with a device that delivers mechanical vibrations during the scanning process. The main advantages are the inclusion of the entire liver in the assessment of fibrosis and the detection of concerning incidental liver lesions (such as HCC), as well as the method’s accuracy and reliability in patients with obesity or ascites. A recent cross-sectional study of 104 patients with biopsy-proven nonalcoholic fatty liver disease (NAFLD) examined the performance of MRE vs VCTE. When compared to liver biopsy, MRE had an AUROC for detection of any fibrosis (stage 1 or more) of 0.82, compared to 0.67 with VCTE. In another study, MRE was compared to several clinical prediction tools (AST/alanine aminotransferase ratio, APRI score, BARD score, FIB-4 index, NAFLD fibrosis score, Bonacini cirrhosis discriminant score, Lok index, and NASH Clinical Research Network model) for the diagnosis of advanced fibrosis (determined on liver biopsy as stage 3-4), and was shown to have greater accuracy. (The AUROC of 2-dimensional MRE was 0.96). The limitations of MRE include cost, availability, and the need for advanced radiographic imaging capabilities at a specialized imaging center. MRE’s use is also limited in patients with iron overload disorders, claustraphobia, or pregnancy. Specific MRE fibrosis cutoffs are well studied in patients with NAFLD and NASH, but less established in patients with viral hepatitis. A recent meta-analysis devised a cutoff for each stage of fibrosis in 697 patients with chronic liver diseases across 12 studies, with diagnosis of any fibrosis starting at 3.45 kPa with 73% sensitivity and 79% specificity, and cirrhosis at 4.71 kPa with 91% sensitivity and 81% specificity.

**Application of Noninvasive Technology for Fibrosis**

**Prediction of Fibrosis**

A streamlined approach for noninvasive prediction of fibrosis in the clinical setting is important. VCTE is a commonly used, noninvasive method of fibrosis measurement. It has revolutionized the diagnostic algorithm in liver disease. Its largest impact has been on patients with HCV infection, as their level of fibrosis influences treatment strategy. However, VCTE still has disadvantages and limited accuracy in detecting moderate fibrosis. The combining of individual tests is gaining in popularity and is commonly done in a clinical practice scenario in order to better predict fibrosis and avoid liver biopsy. In a study of 180 HCV-infected patients, Leroy and colleagues evaluated 6 different noninvasive scores and found that the combination of the APRI score and FibroTest could rule out significant fibrosis with a NPV of 94.1% for concordant results below the lower cutoff values (APRI score <0.5 and FibroTest <0.22). The PPV for significant fibrosis and severe fibrosis was 96.7% and 92.2%, respectively, for discordant results above the upper cutoff (APRI score >2 and FibroTest >0.59). Another study evaluated the combination of the APRI score with FibroTest in 2035 HCV-infected patients, and identified cirrhosis with 92% accuracy and reduced the need for liver biopsy in 81.5% of patients. Hence, liver fibrosis can be reliably predicted noninvasively by simple blood tests without advanced techniques such as VCTE or MRE. The combination of VCTE with FibroTest had 95.7% accuracy in detecting cirrhosis and reduced the need for liver biopsy in 78.8% of patients. In a study of 1785 patients with HCV using a combination of VCTE with FibroMeter, Boursier and colleagues were able to accurately classify fibrosis and obviate the need for liver biopsy in 86.7% of patients. Noninvasive strategies for measuring fibrosis will continue to evolve as the accuracies of individual and combination tests improve. Studies evaluating combination test strategies after HCV eradication are lacking.

A newer way to noninvasively measure fibrosis uses shear wave technology. LSM using shear wave elastography (SWE) reported higher stiffness among treatment-naive patients compared to those who had achieved SVR. In this study, the shear wave propagation velocity was 1.23±0.14 m/s in the healthy control group (n=58), 1.56±0.32 m/s in the group that achieved SVR (n=51), and 1.69±0.31 m/s in the treatment-naive group (n=85). Significant differences were observed between the control group and the group that achieved SVR and between the group that achieved SVR and the treatment-naive group. However, the results for SWE are still preliminary and early for clinical application.

**Prediction of Portal Hypertension**

Portal hypertension can result in liver-related complications and has important prognostic implications. Clinically significant portal hypertension (CSPH) is associated with the development of esophageal varices, ascites, hepatoportal syndrome, spontaneous bacterial peritonitis, and hepatic encephalopathy. It is recommended that patients with CSPH should undergo endoscopic surveillance for esophageal varices. Monitoring portal hypertension once diagnosed is important, as its progression or improvement determines disease prognosis. Measuring the hepatic venous pressure gradient (HVPG) is the standard method for detecting the severity of portal hypertension or improvement. However, the HVPG is invasive and not widely available. Other noninvasive methods such as transient elastography (FibroScan) have been developed to estimate the HVPG. Recent studies have shown that FibroScan can accurately predict the presence and severity of CSPH.

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hypertension, but is invasive and costly. Accurate non-invasive methods for measuring portal hypertension are desirable.

Several noninvasive strategies to measure portal hypertension have been explored. Biochemical and morphologic tests—including platelet count/spleen diameter ratio, a biochemical combination test (AST, albumin, and international normalized ratio), and a combination of the Lok index with the Forns index—have a role in the assessment of portal hypertension; however, they do not estimate the degree of portal hypertension.51-54 These tools may be used as first-line tests in the evaluation of portal hypertension, but do not replace the need for upper endoscopy.53-56 Doppler ultrasonography can be useful for identifying features of portal hypertension (eg, collateral vessels, splenomegaly), but cannot be used alone to determine prognosis.

LSM by transient elastography has correlated with HVPG measurements in detecting CSPH in a number of reports.57,58 In one study, the AUROC for detecting CSPH by transient elastography was 0.945 (95% CI, 0.904-0.987).57 Transient elastography accurately predicted CSPH in 92% of patients using a cutoff value of 21.0 kPa.57 The results were encouraging, but LSM did not identify 100% of the cases detected by HVPG. Measurement of spleen stiffness using transient elastography has also been evaluated and was found to correlate with HVPG portal measurements.59,60 However, reports on this method show conflicting results.61,62

Combination tests can be used to increase the accuracy of portal pressure determination. For example, the portal hypertension risk score, which combines LSM, sex, and spleen diameter/platelet count ratio, had yielded an AUROC of 0.935 for identifying CSPH compared to LSM or LSM–spleen diameter to platelet ratio score.63 The recent Baveno VI Consensus states that upper endoscopy can safely be avoided in patients who have a LSM of less than 20.0 kPa on FibroScan and a platelet count of more than 150,000.69 These criteria have been partially validated but require larger clinical trials before routine implementation is possible.

Reversing the Natural History of Hepatitis C Virus

Improved understanding of the HCV genome has led to the development of novel therapeutic targets. Treatment of HCV has evolved from unsatisfactory interferon- and ribavirin-based therapies with only 54% to 56% cure rates and numerous side effects64,65 to highly effective and well-tolerated DAA therapies with cure rates of more than 90%.66,67 These new oral treatment regimens have led to the reduction of HCV-related complications and have reversed the natural history of HCV in a significantly higher proportion of patients compared to interferon-based therapy.

Regression of Fibrosis

Patients at the highest risk of liver-related complications and HCC after HCV eradication are those with advanced fibrosis and cirrhosis.8 In a systematic review and meta-analysis of 33,000 HCV-infected patients treated with interferon with or without ribavirin, the risk of developing HCC at 5 years after achieving SVR was 2.9% in the general cohort, 5.3% in those with cirrhosis, and 0.9% among those with HCV/HIV coinfection.6 Five-year mortality was 1.98% in the general cohort, 4.9% among cirrhotic patients, and 1.49% in patients with HCV/HIV coinfection.6 In a long-term follow-up study of 642 patients in Taiwan treated with interferon-based therapy, the 5-year risk of HCC in cirrhotic patients was 22.6% compared to 3.2% in those without cirrhosis.8

The correlation of fibrosis regression and HCC risk after HCV eradication remains controversial, as it requires long-term follow-up studies. There is evidence that reversal of cirrhosis after SVR is associated with an absence of liver-related complications,68 but fibrosis regression after achieving SVR is variable.7 In fact, progression of fibrosis has been noted in some cases.7 In a study of 97 patients with SVR at a mean of 5.8 years after treatment, the stage of liver fibrosis measured by biopsy had regressed in 44 patients (45%), progressed in 6 patients (6%), and remained stable in 47 patients (48%).7 The incidence of HCC was noted to be significantly higher in patients with progressive fibrosis, compared to those with regression or stability of fibrosis after achieving SVR (33% vs 4% at 5 years; P<.001).7 The regression of fibrosis appears to be a slow process. In one study, the mean regression of fibrosis after a median of 3.7 years was -0.28±0.03 units/year.69 The noninvasive modalities discussed are valuable tools to study hepatic fibrosis in long-term studies following successful HCV eradication, especially in the era of DAA therapy.

Regression of Portal Hypertension

There are emerging data showing the improvement of portal hypertension after achieving SVR in HCV patients. In one study, there was a significant reduction in the follow-up HVPG measurements across all baseline HVPG measures in patients who achieved SVR with interferon-free regimens: 6 to 9 mm Hg (baseline, 7.37±0.28 mm Hg vs follow-up, 5.11±0.38 mm Hg; P<.001), 10 to 15 mm Hg (baseline, 12.2±0.4 mm Hg vs follow-up, 8.91±0.62 mm Hg; P<.001), and at least 16 mm Hg (baseline, 19.4±0.73 mm Hg vs follow-up, 17.1±1.21 mm Hg; P<.001).
Patients with Child-Pugh class B cirrhosis were less likely to have a decrease in HVPG (hazard ratio, 0.103; 95% CI, 0.02-0.514; \(P=0.018\)) compared to patients with Child-Pugh class A cirrhosis, indicating less portal pressure reduction in those with more advanced liver disease. LSM in combination with serologic markers is an ideal modality to further evaluate the relationship between SVR and improvement of portal hypertension and clinical outcomes.

**Comorbid Conditions That Affect Fibrosis Regression in Sustained Virologic Response**

The evaluation and treatment of other comorbid conditions in the context of HCV management is important. NASH has been associated with more severe fibrosis on liver biopsy in patients with HCV infection. It is possible that NAFLD may cause progression of liver fibrosis in patients who have achieved SVR. Further data are needed for confirmation. An elevated \(\gamma\)-glutamyltransferase level, which is a surrogate marker for fatty liver, insulin resistance, and oxidative stress, was associated with the development of HCC in noncirrhotic patients. Similarly, type 2 diabetes mellitus was associated with HCC occurrence in noncirrhotic patients after achieving SVR. Excess body mass index and recurrent alcoholism have also been observed to be associated with worsening liver disease and liver-related outcomes. Lastly, a consideration of a heterozygous state (particularly MZ phenotype) for \(\alpha\)-1 antitrypsin deficiency should be made in patients with progressive fibrosis despite achieving SVR. These data underline the importance of a comprehensive approach to

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**Figure.** A proposed algorithm for monitoring patients who have achieved SVR after HCV treatment.

\(a\)Concomitant liver disease includes, but is not limited to, nonalcoholic fatty liver disease, alcoholic liver disease, and autoimmune liver disease.

\(b\)Consider use of serologic markers (eg, AST-to-Platelet Ratio Index, Fibrosis-4 index) if VCTE and MRE are not available.

AST, aspartate aminotransferase; EGD, esophagogastroduodenoscopy; HCV, hepatitis C virus; MRE, magnetic resonance elastography; PCP, primary care physician; SVR, sustained virologic response; VCTE, vibration-controlled transient elastography.
management of liver disease even after achieving SVR for HCV infection.

Discussion

The management of HCV infection has dramatically changed. The advent of DAA agents has led to cure rates of more than 90% in patients who are infected with the virus. These high cure rates, along with the development of several reliable noninvasive measures of fibrosis, have provided clinicians the ability to identify and prioritize a higher number of patients for therapy. The focus of HCV management is undergoing a paradigm shift as the number of HCV-infected patients achieving SVR increases. Achieving SVR is associated with a lower risk of liver-related complications, such as liver failure and HCC. However, patients with advanced hepatic fibrosis and comorbid conditions continue to be at high risk of disease complications and require continued monitoring after successful therapy.

The European Association for the Study of the Liver recommends indefinite screening for HCC in patients who have achieved SVR and have advanced fibrosis or cirrhosis. Subjecting patients to liver biopsy after HCV eradication is not warranted. Despite the availability of a number of different noninvasive modalities, a truly validated surveillance approach in patients who have achieved SVR has not yet been determined. After HCV eradication, the degree of fibrosis regression varies, and liver-related complications remain in some patients despite having achieved SVR. Based on the current evidence and experience, we propose an algorithm for patient management after successful HCV therapy (Figure). Primary care physicians could follow patients with mild hepatic fibrosis who have no other liver-related comorbidities. Patients with advanced fibrosis or cirrhosis should continue to be monitored by liver specialists regularly with abdominal imaging every 6 months for HCC surveillance, annual noninvasive fibrosis measurement, and upper endoscopy every 2 to 3 years for variceal screening. In addition, patients with moderate fibrosis or other liver-related comorbidities should undergo noninvasive fibrosis evaluation annually after successful HCV therapy. If the fibrosis regresses, their management should focus on treating the underlying liver disease. If patients develop advanced fibrosis or cirrhosis, then they should undergo routine HCC and variceal surveillance. VCTE or MRE is preferred for monitoring fibrosis. Noninvasive serologic markers, however, can be used if VCTE or MRE is unavailable. Given the limited guideline on the long-term care of patients who have achieved HCV eradication with effective antiviral therapy, a cautious approach should be maintained by the treating clinician when managing these patients.

Summary

The advent of DAA therapy has dramatically increased the rate of HCV eradication even for patients with significant liver disease. Patients with advanced fibrosis or cirrhosis, however, continue to be at increased risk of liver-related complications and should be monitored regularly after achieving SVR. Management after successful therapy among those with moderate fibrosis remains unclear, and a cautious approach is necessary. The availability of validated noninvasive measures of fibrosis has obviated the need for liver biopsy for the majority of patients with chronic HCV infection prior to therapy. These noninvasive modalities are attractive tools for long-term monitoring of hepatic fibrosis after successful HCV therapy, in particular for patients who remain at risk for liver complications. Ongoing research and long-term follow-up studies are essential to determine the prognosis and management strategies of patients with chronic HCV infection after achieving treatment-induced viral eradication.

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