

Hepatitis C

Fibrosis Improves with Interferon Treatment

Successful treatment with interferon-based therapy can eradicate hepatitis C virus (HCV) and halt liver disease progression, but less is known about whether it improves existing fibrosis. As reported in the February 2009 *Journal of Viral Hepatitis*, J. Vergniol and colleagues used noninvasive blood biomarkers (FibroTest) and transient elastometry (FibroScan) to evaluate changes in liver fibrosis among 416 French hepatitis C patients enrolled between May 2003 and March 2006, of whom 112 started antiviral treatment. Liver fibrosis was staged using FibroTest and FibroScan at study entry, then every year in untreated individuals and at the end of treatment and six months later in treated pa-

tients. These noninvasive measures are not as accurate as liver biopsy, but patients may be more willing to undergo repeated procedures to assess changes over time.

The treated group had significantly higher FibroTest and FibroScan scores than untreated patients both at baseline and at the end of treatment. At the end of post-treatment follow-up, however, scores were similar, indicating improvement in the treated group. Interestingly, FibroTest and FibroScan scores fell in all treated patients, regardless of virological response. In conclusion, the researchers stated, "whatever the virological response, treatment for HCV infection is associated with an improvement of FibroScan and FibroTest values."

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Long-Term Outcomes

Sustained virological response to hepatitis C treatment is defined as continued undetectable HCV viral load six months after completion of therapy; less is known, however, about longer-term outcomes beyond this point. As reported in the March 2009 *Hepatology*, S.L.

George and colleagues from St. Louis University followed 150 chronic hepatitis C patients who achieved SVR after interferon-based therapy for five years. Participants with evidence of stage 2 or greater fibrosis on their pretreatment biopsy were offered a follow-up biopsy after four years. Within this group, 49 received the subsequent biopsy and had their paired pretreatment and follow-up biopsies blindly rescored.

After four years of follow-up, most participants showed evidence of improved liver disease: 40 (82%) had decreased fibrosis scores and 45 (92%) had decreased inflammation scores. A subgroup of 10 patients (20%) had normal or nearly normal liver histology on the follow-up biopsy. None of the participants had conclusive evidence of HCV relapse. However, two patients who had cirrhosis prior to treatment developed hepatocellular carcinoma (HCC) and one died, despite achiev-

ing sustained response. "In a cohort of 150 patients with SVR followed for five years, the majority of patients had good outcomes," the researchers concluded. "A minority of patients had normal or nearly normal liver tissue on long-term follow-up biopsy," they continued, but people with pretreatment cirrhosis "are at a low but real risk of HCC after SVR."

HCC Despite Sustained Response

Though uncommon, people without liver cirrhosis prior to treatment who achieve sustained response can still develop HCC; to date, more such cases have been reported in Japan than in North America or Europe. As described in the February 2009 *European Journal of Gastroenterology and Hepatology*, J.L. Sewell and colleagues identified five patients with hepatitis C seen in the University of California at San Francisco hepatology practice who developed HCC despite not having cirrhosis on their pretreatment liver biopsy and achieving SVR after treatment. At the time of HCC diagnosis, two patients were still non-cirrhotic, one had clearly progressed to cirrhosis, and two did not have repeat histology results.

"Physicians often base

screening and treatment decisions on an initial liver biopsy performed years earlier," the researchers noted. "As fibrosis may advance, and because SVR and lack of cirrhosis do not fully protect against HCC, future study should further evaluate the risk of HCC among hepatitis C patients after sustained virologic response."

In a related report published in the January 7, 2009 *Cases Journal*, T. Mashitani and colleagues described a patient who developed HCC more than a decade after successful antiviral therapy. This 73-year-old Japanese man was diagnosed with chronic hepatitis C in 1992 after being referred due to "liver dysfunction" (the authors did not specifically state whether he had cirrhosis). After treatment with conventional interferon monotherapy, the man achieved SVR, his liver function normalized, and his histological findings improved. He received HCC screening until 2000, when he dropped out of follow-up. In 2006—13 years after achieving SVR—the man returned with abdominal pain and was found to have multiple large liver tumors, confirmed by biopsy to be HCC. However, he still had undetectable HCV RNA and had only mild fibrosis in non-

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cancerous liver tissue. "Our report highlights the need for careful follow-up for more than 10 years even if patients with chronic hepatitis C achieve SVR to interferon therapy," the clinicians concluded.

Treatment for HCV/ HBV Coinfection

Due to overlapping transmission routes, people may become chronically infected with both HCV and hepatitis B virus (HBV), especially in areas where either virus is endemic. As reported in the February 2009 *Gastroenterology*, C.J. Liu and colleagues evaluated interferon-based therapy for hepatitis C in HCV/HBV coinfecting patients in Taiwan. The study included 321 participants with active HCV infection, 161 of whom were also hepatitis B surface antigen (HBsAg) positive. Patients with HCV genotype 1 were treated with 180 mcg/week pegylated interferon alfa-2a (Pegasys) plus 1,000-1,200 mg/day ribavirin for 48 weeks, while those with genotype 2 or 3 received the same pegylated interferon dose plus 800 mg/day ribavirin for 24 weeks.

Participants with HCV/HBV coinfection and those with HCV alone had similar—and high—SVR

rates: 72.2% vs. 77.3%, respectively, for genotype 1, and 82.8% vs. 84.0%, respectively, for genotypes 2/3.

"Combination therapy with peginterferon alfa-2a and ribavirin is equally effective in patients with HCV monoinfection and in those with dual chronic HCV/HBV infection," the researchers concluded.

Since HCV and HBV appear to inhibit each others' replication, suppressing one virus can lead to worsening of the other. Here, 36.3% of the 77 coinfecting patients who had undetectable HBV viral load prior to hepatitis C treatment developed detectable HBV DNA after therapy, although this was not accompanied by significant clinical symptoms. On the other hand, pegylated interferon (without ribavirin) is also used to treat hepatitis B, and 11.2% of the dually infected patients experienced HBsAg clearance after hepatitis C therapy.

Mortality in HIV/HCV Coinfecting Patients

Since the advent of effective antiretroviral therapy for HIV, liver disease has become a major cause of death for HIV/HCV coinfecting individuals. Several studies indicate that coinfecting patients experience faster liver

disease progression than those with HCV alone, but those with well-preserved immune function may fare nearly as well. In a study published in the February 2009 *HIV Medicine*, L.H. Omland and investigators from two large Danish HIV cohort studies compared rates of death in 483 HIV/HCV coinfecting patients and 1,932 HCV monoinfecting individuals matched for age, sex, and year of hepatitis C diagnosis.

Overall, HIV/HCV coinfection was associated with a significantly increased rate of death, with five-year survival probabilities of 74% for the coinfecting patients versus 87% for those with HCV alone. However, having HIV was not associated with increased mortality among coinfecting individuals who maintained a CD4 T-cell count above 300. "HIV infection has a substantial impact on mortality among HCV-infected individuals," the authors concluded, but this was "mainly because of HIV-induced immunodeficiency." These findings imply that HIV/HCV coinfecting individuals should receive timely antiretroviral treatment to raise or prevent a decline in CD4 cells.

