
a series of fact sheets written
by experts in the field of liver
disease

Disease Progression: Steatosis

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STEATOSIS, ALSO KNOWN AS FATTY INFILTRATES in the liver or Fatty Liver, is a condition characterized by the accumulation of fat in the liver, and it is commonly seen in people infected with the hepatitis C virus (HCV). It is estimated that about 55% (range: 34.8 to 81.2%) of HCV positive individuals have steatosis, which is two to three times the prevalence seen in the general population. Studies have found that the combination of hepatitis C and steatosis increases the risk of HCV disease progression, reduces the likelihood of responding to HCV treatment, and may contribute to the development of liver cancer (hepatocellular carcinoma, or HCC).

Metabolic Factors

The exact mechanism by which HCV increases the risk of steatosis in the liver is not well-understood. Contributing factors that have been found to increase the incidence of steatosis in the general population include:

- Type II diabetes (diabetes mellitus) – a disease in which the body does not produce or effectively use insulin

- Hyperlipidemia – elevation of lipids (fats) in the bloodstream. These include cholesterol, cholesterol esters (compounds), phospholipids, and triglycerides
- Heavy alcohol consumption
- High body mass index – the body mass index (BMI) formula assesses body weight relative to height

Most experts believe that there is an additional viral factor that increases the likelihood of HCV patients developing steatosis, but exactly what this is remains unclear

Genotype 3

It is clear that there is a direct viral mechanism involved in the development of steatosis in people infected with HCV genotype 3, even though this mechanism has not yet been determined. It has been found that about 74% of people with HCV Genotype 3 have some degree of steatosis compared to 47.9% of people with HCV genotype non-3. Furthermore, the severity of steatosis is also higher in those with HCV genotype 3 compared to people with HCV non-genotype 3 (29.6% vs. 5.5%). Interestingly, patients with genotype 3 who achieve a sustained virological response (SVR, continued undetectable HCV viral load six months after the completion of therapy) to HCV treatment have a marked decrease and sometimes a complete resolution of steatosis, regardless of any additional co-factors. This clearly indicates that there is a relationship between steatosis development and genotype 3 HCV. This is in stark contrast to patients with HCV genotypes other than 3, who show little or no improvement in the level of steatosis even after achieving an SVR.

Non-3 Genotypes

In patients with HCV genotypes other than 3, co-factors such as high BMI, heavy alcohol intake, elevated blood lipids, glucose intolerance, and diabetes greatly promote the development of steatosis. Other genotypes do not have as clear an association with steatosis as genotype 3. However, since more patients with non-3 genotypes develop steatosis than patients without HCV, experts

believe that there is a synergy between steatosis, HCV of any genotype, and the other co-factors listed above.

HCV Disease Progression

Steatosis appears to increase the rate of HCV disease progression. Recent studies have shown that higher grades of steatosis correlates with higher grades of fibrosis, and with more rapid development of fibrosis and cirrhosis.

Liver Cancer

It has been documented that steatosis is an independent risk factor for the development of liver cancer. Steatosis, cirrhosis, and increasing age are reported as independent and significant risk factors for liver cancer.

Treatment Response

Steatosis appears to reduce the likelihood of obtaining a sustained virological response from HCV medications – at least in people with HCV genotype non-3. The impact of steatosis on SVR in HCV genotype 3 is less clear. In some retrospective studies, patients without steatosis were more likely to achieve SVR. However, this information is difficult to tease out because the co-factors associated with steatosis (obesity, metabolic syndrome, etc.) also lower treatment response rates. However, Thierry Poynard and colleagues conducted a retrospective analysis of the effect of steatosis on treatment response and found that SVR rates (*Hepatology* 2003; 38: 75-85) were decreased by 18-32% in patients with steatosis compared to patients without steatosis, after adjusting for other co-factors that affect treatment such as genotype, fibrosis score, and viral load level.

Treatment for Steatosis

Unfortunately, there are no medications at this time to treat steatosis. However, there are strategies to help reduce steatosis in people with hepatitis C and to lessen the impact of steatosis on HCV disease progression and treatment outcome. A recent study found that HCV patients who participated in a diet and exercise

program for three months lowered their grade of steatosis and, remarkably, their fibrosis score. It appears that diet, exercise, and maintaining a healthy weight are important strategies to help reduce and possibly eliminate steatosis. This appears to be the case for all genotypes, even genotype 3.

It is clear that steatosis plays an important role in HCV disease progression and treatment outcome. If you are concerned about steatosis, talk to your medical provider about a diet and exercise program that will help to reduce steatosis and the negative impact it has on hepatitis C progression. This is an important piece of information for medical providers and patients to know about for the management of hepatitis C. In addition to their direct effect on steatosis, incorporating exercise and a healthy diet, along with other important lifestyle changes, such as reducing or eliminating alcohol and avoiding substances that harm the liver, can improve the health of the liver and general body health, which will ultimately lead to a stronger immune system to help fight hepatitis C.

For more information about hepatitis C, hepatitis B and HCV coinfections, please visit www.hcvadvocate.org.

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