Review Article

Alcohol Use in Patients with Chronic Liver Disease

Daniel Fuster, M.D., Ph.D., and Jeffrey H. Samet, M.D., M.P.H.

Globally, alcohol consumption is the seventh leading risk factor for both death and the burden of disease and injury. Alcohol use accounts for 6.8% of age-standardized deaths in men and 2.2% in women, with a disproportionate effect on young people. The overall costs associated with alcohol use represent more than 1% of the gross national product in high- and middle-income countries, with the costs of social harm (e.g., violence and road accidents) being far greater than health costs alone. In short, except for tobacco, alcohol accounts for a higher burden of disease than any other drug. In this review, we discuss the effects of alcohol use on various forms of liver disease, as well as the assessment and treatment of alcohol use in patients with chronic liver disease.

Alcoholic Liver Disease

Alcohol use is a major cause of preventable liver disease worldwide, and alcoholic liver disease is the main alcohol-related chronic medical illness. Globally, per capita alcohol consumption is strongly correlated with the rate of death due to liver cirrhosis. Alcohol-related and viral hepatitis–related liver disease are not mutually exclusive; nevertheless, it is plausible that with the advent of direct-acting antiviral agents for chronic hepatitis C virus (HCV), alcohol will again become the most prominent driver of liver disease worldwide. Alcoholic liver disease is the leading cause of liver transplantation in Europe and the second-leading cause of liver transplantation in the United States, after HCV-related liver disease.

Alcoholic liver disease encompasses several histopathologic changes, from simple steatosis to alcoholic steatohepatitis, progressive liver fibrosis (which usually starts in the perivenular area of the hepatic lobule), cirrhosis, and liver cancer. Rather than being distinct stages of the disease, these features can coexist in the same person. Once steatohepatitis is established, liver damage is not totally reversible with abstinence from alcohol, but abstinence can ameliorate portal hypertension. Acute alcoholic hepatitis is a severe complication that can occur at any point in the course of alcoholic liver disease and is associated with liver failure and with short-term mortality as high as 40%.

Patients with alcoholic liver disease, as opposed to those with other forms of liver disease, often have at least a 20-year history of regular consumption of alcohol above the threshold of 20 g of pure alcohol per day for women and 30 g for men. In most persons who consistently drink more than 60 g per day (i.e., approximately four standard drinks, with a standard drink [i.e., 12 oz of beer, 5 oz of wine, or 1.5 oz of 80-proof liquor] containing approximately 14 g of alcohol) for as little as 2 years, liver steatosis will develop, which is reversible with cessation of alcohol intake. Although cirrhosis will not develop in all patients who consume alcohol above those thresholds, higher levels of consumption are associ-
Alcohol intake promotes accumulation of acetaldehyde and other reactive oxygen moieties in the liver, a process associated with oxidative stress, impaired hepatocyte metabolism, and cell death. Alcohol consumption also promotes the growth of intestinal gram-negative bacteria and increases intestinal permeability, consequences that raise the levels of lipopolysaccharide, also known as endotoxin, in the peripheral blood. An excess amount of lipopolysaccharide reaching the liver can activate Kupffer cells, thus generating free radicals and inflammatory cytokines that lead to the initiation of necroinflammation and fibrotic changes in the liver. Endotoxin also activates quiescent hepatic stellate cells, which are the main fibrogenic cell type of the injured liver, thereby stimulating the secretion of proinflammatory cytokines and the initiation and progression of liver fibrosis. The pathogenic changes involved in alcohol-related liver disease are depicted in Figure 1.

**Effect of Alcohol Use**

The effect of alcohol use in patients with liver disease is multidimensional. Figure 2 summarizes the effects of alcohol consumption on the four most prevalent forms of liver disease, which are also outlined below.

**HCV-Related Liver Disease**

Counterintuitively, adults with HCV infection tend to consume greater amounts of ethanol than other adults. Adults with HCV infection are more than twice as likely as those without HCV infection to regularly consume more than one alcoholic drink per day (35% vs. 14%) and almost 8 times as likely to regularly consume more than three drinks per day (19% vs. 2%).

Alcohol use is associated with more persistent HCV infection and more extensive liver damage than no alcohol use, because of interactions between alcohol use and HCV that affect immune responses, cytotoxicity, and oxidative stress. In addition, alcohol use may have an effect on HCV viral replication in certain subgroups of patients. No safe level of alcohol consumption has been determined for patients with HCV, and even those who drink moderate amounts of alcohol can have progressive liver fibrosis. A meta-analysis showed that the relative risk of progression to liver cirrhosis or de-
compensated liver disease was 2.3 times as high among patients with HCV who drank alcohol as the risk among abstainers.29

HCV infection in patients with alcohol-use disorder is associated with poorer outcomes, such as longer hospital stays and higher in-hospital mortality, than in patients with alcohol-use disorder who do not have HCV infection.30 This association may be partially explained by group differences in coexisting conditions or behaviors associated with poorer survival; however, even in studies that have accounted for those factors, HCV infection in patients with alcohol-use disorder is associated with elevated overall and liver-related mortality.31 Among patients with alcohol-use disorder who are admitted to the hospital for detoxification, mortality is higher if the patients have HCV infection than if they do not, especially in younger patients and patients who also have human immunodeficiency virus (HIV) infection.32

In the era of interferon-based antiviral therapy for HCV infection, alcohol consumption was associated with lower odds of a sustained virologic response, mainly owing to lower adherence to the medication.27 In the era of direct-acting antiviral agents, alcohol use is still a major contributor to decompensated cirrhosis in HCV-infected patients,33,34 but it does not appear to mitigate achievement of sustained virologic suppression.7 Abstinence from alcohol is not required for treatment, and its ongoing use should not be a contraindication for treatment; nevertheless, it seems prudent to recommend that patients stop...
the use of alcohol if they plan to undergo antiviral therapy for HCV infection.

**HEPATITIS B VIRUS–RELATED LIVER DISEASE**
Alcohol use increases hepatitis B virus (HBV) replication in mice, increases HBV surface antigen levels in humans, and delays the clearance of HBV.\(^3\)\(^5\) Alcohol use is associated with an increased risk of progression of liver fibrosis and of the occurrence of hepatocellular carcinoma in patients with HBV-related cirrhosis.\(^3\)\(^6\) Correspondingly, the presence of HBV infection is associated with the development of hepatocellular carcinoma and liver-related death in patients with alcoholic liver disease.\(^3\)\(^7\) Even though one cross-sectional study involving patients with chronic HBV infection showed that the prevalence of advanced fibrosis in those who reported drinking 1 to 20 g of alcohol per day was similar to the prevalence in those who abstained,\(^3\)\(^8\) alcohol consumption should be kept to a minimum in patients with HBV infection.\(^3\)\(^9\)

**NONALCOHOLIC FATTY LIVER DISEASE**
Nonalcoholic fatty liver disease is a consequence mainly of obesity and the metabolic syndrome. In the Global North, nonalcoholic fatty liver disease is one of the leading causes of liver transplantation because of the high prevalence of these clinical conditions.\(^4\)\(^0\) The likelihood of abnormal liver-function test results\(^4\)\(^1\) and hepatic steatosis\(^4\)\(^2\) in obese patients who are also heavy drinkers is significantly greater than the likelihood in heavy drinkers who are not obese. Some, but not all, observational studies have reported beneficial effects on cardiovascular outcomes of low or moderate alcohol consumption in patients with nonalcoholic fatty liver disease.\(^4\)\(^3\) Currently, there are no guidelines on how to counsel patients with nonalcoholic fatty liver disease about alcohol use, but abstinence should be the goal, since heavy alcohol intake, or even low or moderate alcohol consumption in those with the metabolic syndrome,\(^4\)\(^4\) is associated with increased fibrosis progression.\(^4\)\(^3\)

**HEREDITARY HEMOCROMATOSIS**
Alcohol consumption is associated with increased iron overload and faster progression to liver cirrhosis in patients with hereditary hemochromatosis. This condition is characterized by increased absorption of iron, which generates reactive oxygen species and causes peroxidation of cell membranes, cell damage, and liver injury.\(^4\)\(^5\) Alcohol has an additive effect on liver damage; in one study, which was controlled for age, 61% of patients with hemochromatosis who drank more than 60 g per day had severe fibrosis or cirrhosis as compared with 7% of those who drank lower amounts.\(^4\)\(^6\)

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**Figure 2. Effects of Alcohol Use on Various Forms of Chronic Liver Disease.**

<table>
<thead>
<tr>
<th>Alcohol Use</th>
<th>Hepatitis C Virus Infection</th>
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<tbody>
<tr>
<td></td>
<td>Increased infection exposure and persistence</td>
</tr>
<tr>
<td></td>
<td>More extensive liver damage</td>
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<td></td>
<td>Faster progression of liver fibrosis</td>
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<td>Higher mortality</td>
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<tr>
<th>Nonalcoholic Fatty Liver Disease</th>
<th>Hepatitis B Virus Infection</th>
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<tbody>
<tr>
<td>Greater prevalence of steatosis and abnormal liver test</td>
<td>Increased risk of hepatocellular carcinoma</td>
</tr>
<tr>
<td>Increased fibrosis progression</td>
<td>Increased risk of hepatocellular carcinoma</td>
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<table>
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<tr>
<th>Hereditary Hemochromatosis</th>
<th>Hepatitis C Virus Infection</th>
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</thead>
<tbody>
<tr>
<td>Increased iron overload</td>
<td>Increased fibrosis progression</td>
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Alcohol use is one of the most common triggers of acute decompensation in persons with chronic liver disease, which is known as acute-on-chronic liver failure and is associated with organ failure and short-term mortality. Nevertheless, acute-on-chronic liver failure precipitated by alcohol has a better prognosis than liver failure precipitated by infections or upper gastrointestinal bleeding. Information about the effect of alcohol consumption on less prevalent forms of liver disease (e.g., Wilson’s disease and autoimmune and cryptogenic liver disease) is scarce, but the use of alcohol, which is a hepatotoxin in patients with another cause of chronic liver disease, seems unwise. In addition, alcohol can be an underrecognized factor in the exacerbation of these forms of liver disease.

Assessment of alcohol use is appropriate for any person with liver disease, given the elevated risks of alcohol-related hepatotoxicity. The Alcohol Use Disorders Identification Test (AUDIT) is a validated tool for identifying alcohol-use disorder in patients. It is recommended by both American and European guidelines, but it can be difficult to use in a clinical setting because of its length, unless it is administered before the clinical visit. A shorter version exists (AUDIT-C), which is another option. Also, the National Institute on Alcohol Abuse and Alcoholism single-question screening tool has been validated for the screening of unhealthful alcohol use (i.e., the spectrum from risky use to alcohol-use disorder) in the primary care setting. The question is, “How many times in the past year have you had X or more drinks in a day?,” where X is five for men and four for women, and a response of one or more times is considered positive and merits further assessment.

In fact, there is no known safe threshold of alcohol consumption for patients with chronic liver disease, especially those with HCV infection, obesity, or the metabolic syndrome. If a threshold exists, it is probably very low, and even alcohol use that does not reach the risky range can be detrimental. Abstinence from alcohol intake improves clinical outcomes in patients with chronic liver disease and is associated with survival benefits even after the development of cirrhosis. Therefore, complete abstinence is the clinical goal for patients with alcohol-use disorder and liver disease, especially those in whom liver cirrhosis has already developed.

### Treatment of the Alcohol Withdrawal Syndrome

Patients with alcohol-use disorder are at risk for the alcohol withdrawal syndrome after discontinuation of or decrease in frequent heavy alcohol consumption. The cornerstone of treatment for the alcohol withdrawal syndrome is the use of benzodiazepines (Table 1). Long-acting benzodiazepines (e.g., diazepam and chlordiazepoxide) protect against seizures and delirium, but short- and intermediate-acting benzodiaz-

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Use in Patients with Liver Disease</th>
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</thead>
<tbody>
<tr>
<td>Diazepam</td>
<td>10–20 mg orally every 1–2 hr as needed until symptoms are minimal*</td>
<td>Yes, but avoid use in patients with poor synthetic function, decompensated cirrhosis, or both</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>50 mg orally every 1–2 hr as needed until symptoms are minimal*</td>
<td>Yes, but avoid use in patients with poor synthetic function, decompensated cirrhosis, or both</td>
</tr>
<tr>
<td>Lorazepam†</td>
<td>2 mg orally every 1–2 hr as needed until symptoms are minimal*</td>
<td>Yes</td>
</tr>
<tr>
<td>Oxazepam†</td>
<td>30 mg orally every 1–2 hr as needed until symptoms are minimal*</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* An initial dose regardless of symptoms can be considered in high-risk patients (i.e., those with prior seizures or multiple alcohol detoxifications). † When the patient’s symptoms are minimal, consider a taper to avoid benzodiazepine withdrawal.
Benzodiazepines (e.g., lorazepam and oxazepam), which presumably have efficacy similar to long-acting benzodiazepines, are safer for patients with poor synthetic liver function, because the drugs are associated with a reduced risk of toxic effects due to medication accumulation resulting from slow hepatic catabolism. Lorazepam metabolites are eliminated by the kidney rather than the liver, which makes the drug particularly useful in patients with chronic liver disease. As a second-line therapy, phenobarbital can be used for the treatment of withdrawal, but it is not recommended in patients with liver disease. For uncomplicated withdrawal, carbamazepine and oxcarbazepine can help mitigate symptoms, but the evidence for their use is of lower quality than that for benzodiazepines.

Given that benzodiazepines may precipitate and worsen hepatic encephalopathy, other drugs such as baclofen, clonidine (which can in turn ameliorate tachycardia and hypertension in association with the alcohol withdrawal syndrome), gabapentin, and topiramate have been proposed as alternatives in patients with alcoholic liver disease, but the quality of the data supporting their use is still poor. Alcohol use for therapeutic purposes does not have an empirical basis in the treatment of the alcohol withdrawal syndrome.

**Prevention of Relapse and Promotion of Abstinence**

**Nonpharmacologic Therapies**

In patients with liver disease, brief intervention and motivational interviewing (which involves nonconfrontational counseling by the clinician to encourage choices that are consistent with the patient’s long-term goals) can be used to reduce alcohol use that does not qualify as alcohol-use disorder. Also, feedback around abnormal liver-test results has been associated with decreased alcohol use in patients who are at risk for chronic liver disease.

A recent systematic review advocated the use of cognitive behavioral therapy and motivational enhancement therapy as effective psychosocial interventions that can be implemented in combination with pharmacotherapy and comprehensive medical care. Data supporting the use of contingency management — or more intensive forms of treatment provision, such as chronic care management or collaborative care — are still inconclusive. In addition, the paucity of data concerning the combination of pharmacologic and nonpharmacologic treatment for alcohol-use disorder in patients with chronic liver disease limits evidence-based recommendations from extending beyond those for patients without liver disease. Several nonpharmacologic strategies for relapse prevention can be implemented in primary care. These include establishing a supportive patient–physician relationship; scheduling regular follow-up visits; mobilizing family support; suggesting involvement in 12-step programs; developing a plan to recognize, cope with, and manage early relapse; facilitating positive lifestyle changes; and treating coexisting conditions that can trigger relapse.

**Pharmacologic Therapies**

Three medications (naltrexone, disulfiram, and acamprosate) have been approved by the Food and Drug Administration for the treatment of alcohol-use disorder (Table 2), and a newer drug (nalmefene) has been approved in many European countries for the reduction of alcohol consumption. However, few clinical trials examine the effectiveness of these drugs against alcohol-use disorder in patients with advanced liver disease, and most of the recommendations are based on research that involved patients without overt liver disease. In general, patients with minor or mild forms of liver disease can be treated with any of the approved medications, but caution should be exercised with the administration of disulfiram and naltrexone in patients who have cirrhosis, especially if it is decompensated or if the patient has features suggestive of synthetic dysfunction.

Disulfiram inhibits acetaldehyde dehydrogenase action, thus provoking what is known as the acetaldehyde syndrome (facial flushing, nausea, vomiting, tachycardia, and hypotension) when disulfiram is consumed with alcohol. Disulfiram has been approved for promoting abstinence since the 1950s, given its potential as a deterrent for alcohol consumption. Open-label studies have shown promising results, but evidence of its efficacy has been mixed in clinical trials. A meta-analysis that reviewed randomized clinical trials published up to 2011 showed...
that only 6 of 11 trials showed a significant effect of disulfiram on abstinence.65 Disulfiram treatment is more efficacious in patients who are committed to maintaining abstinence and when it is provided in a monitored fashion, since treatment failure has been attributed to patients’ decision to stop the medication so that alcohol use can be restarted.64 Treatment should be given for at least 3 months, and it is not uncommon to maintain treatment for a year or more Table 2.54 The use of disulfiram is contraindicated in patients with liver cirrhosis, especially in those with synthetic dysfunction, given that liver failure leading to death or liver transplantation has been reported.66 Liver toxicity has also occurred in patients with no previous liver problems, so monitoring of liver enzymes during treatment is highly recommended.67

Naltrexone is a mu-opioid and kappa-opioid receptor antagonist that reduces alcohol-related dopamine release in the nucleus accumbens and reduces the reward sensation, thus making patients less motivated to drink.68 There is mixed evidence around markers that predict a favorable response to naltrexone treatment, such as male sex, a positive family history of alcoholism, high levels of craving, and a polymorphism of the opioid receptor gene OPRM1.69 In clinical trials, naltrexone use is associated with lower rates of relapse of alcohol consumption as compared with placebo and a higher percentage of days of abstinence.70 Treatment for at least 4 months is indicated, with monthly follow-up for up to a year.71 Hepatotoxicity is rare with the use of naltrexone at the recommended doses, but elevated liver enzyme levels are not uncommon.71 Naltrexone use is formally contraindicated in patients with acute hepatitis or liver failure and should be used with caution in patients with active liver disease (i.e., patients who present with liver enzyme levels that are greater than the upper limit of the normal range), since high doses of the drug (≥100 mg daily) can lead to liver enzyme levels of more than five times the upper limit of the normal range and the margin of separation between the apparently safe dose and the dose causing hepatic injury appears to be small.63,72 Because of the risk of injection-site hematomas, naltrexone injections should not be given to patients with advanced chronic liver disease who have a low platelet count or prolonged prothrombin time. In addition, the use of naltrexone for

### Table 2. Summary of Pharmacologic Treatment Recommendations for Patients with Alcohol-Use Disorder and Liver Disease.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>FDA-Approved for Treatment of Alcohol-Use Disorder*</th>
<th>Use in Patients with Liver Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naltrexone</td>
<td>50 mg orally once a day or 380 mg intramuscularly monthly for ≥4 mo</td>
<td>Yes</td>
<td>Yes, but use with caution in patients with acute hepatitis and decompensated cirrhosis</td>
</tr>
<tr>
<td>Disulfiram</td>
<td>250–500 mg once a day for ≥3 mo</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Acamprosate</td>
<td>666 mg three times a day†</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Baclofen</td>
<td>10 mg three times a day; ≥80 mg once a day</td>
<td>No</td>
<td>Yes‡</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>900–1800 mg once a day</td>
<td>No</td>
<td>Data are limited§</td>
</tr>
<tr>
<td>Ondansetron</td>
<td>1–16 μg per kg of body weight twice a day</td>
<td>No</td>
<td>Data are limited¶</td>
</tr>
<tr>
<td>Topiramate</td>
<td>300 mg once a day</td>
<td>No</td>
<td>Data are limited</td>
</tr>
<tr>
<td>Varenicline</td>
<td>2 mg once a day</td>
<td>No</td>
<td>Data are limited</td>
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</table>

* FDA denotes Food and Drug Administration. † In patients who weigh less than 60 kg, the recommended dose of acamprosate is 333 mg four times a day (two 333-mg pills with breakfast, one with lunch, and one with dinner). ‡ Studies of the efficacy of baclofen have had mixed results. § Gabapentin can be addictive. ¶ Liver toxicity has been reported with the use of ondansetron. † The side effects of topiramate may mimic the symptoms of hepatic encephalopathy.
alcohol-use disorder is contraindicated in patients with concomitant opioid-use disorder who are receiving treatment with such mu-opioid agonists as methadone or buprenorphine.

Acamprosate is believed to act as an N-methylD-aspartate receptor antagonist and a modulator of γ-aminobutyric acid (GABA) type A receptor and to reduce symptoms of protracted abstinence. Results in clinical trials have been mixed,
but meta-analytical data show that acamprosate reduces alcohol intake in mild-to-moderate forms of alcohol-use disorder\(^4\) and can be safely used in patients receiving opioid treatment.\(^75\) Acamprosate has no hepatic metabolism. It could be considered safe, but it has not formally been tested in patients with advanced forms of liver disease.\(^63\) Its dose should be adjusted in patients with chronic kidney disease, and its use is contraindicated when creatinine clearance is less than 30 ml per minute.\(^54\) In addition, long-term administration of acamprosate could increase the risk of encephalopathy because of the drug’s antagonism of the glutamate receptor.\(^63\)

Nalmefene is a mu-opioid and delta-opioid receptor antagonist and a kappa-opioid receptor partial agonist that has been approved in Europe for the reduction of heavy drinking.\(^62\) Nalmefene has a longer half-life than naltrexone, and there is no evidence of hepatotoxicity associated with nalmefene,\(^63\) but questions have been raised about its overall efficacy.\(^76\) The following two cautions are noteworthy with respect to its use in persons with liver disease: there is an absence of data involving patients with advanced liver disease, and abstinence — and not just the reduction of alcohol consumption, which is nalmefene’s intended use — is the preferred treatment goal for patients with liver disease.\(^8\)

Baclofen is a selective GABA type B receptor antagonist used to control spasticity.\(^4,54\) There is no evidence of an association between baclofen use and liver toxicity, and the drug has been formally tested in patients with clinically significant liver disease, including patients with HCV, in both clinical trials and open-label studies, with mixed results.\(^63,77-79\) Even though it has not been formally approved for the treatment of alcohol-use disorder by regulatory agencies, its off-label use is common in France.\(^4\)

Four other treatments that have been tested in patients with alcohol-use disorder include gabapentin, ondansetron, topiramate, and varenicline.\(^54,80\) Gabapentin can be addictive in some patients, but in clinical trials its use is associated with abstinence, fewer days of heavy drinking, and fewer relapse-related symptoms (e.g., insomnia, dysphoria, and craving).\(^31\) Given their minimal to nonexistent hepatic metabolism, ondansetron and topiramate could be safely used in patients with alcoholic liver disease.\(^63\) However, topiramate should be used with caution in patients with hepatic encephalopathy, since its side effects of memory loss and concentration problems may confound a patient’s clinical course and treatment. Cases of liver toxicity have been reported with the use of ondansetron; however, this relationship with ondansetron is not clearly determined.\(^63\) Limited evidence suggests that varenicline may be effective in reducing alcohol craving and of overall alcohol consumption, but it has not been tested in patients with active liver disease.\(^82\) So far, evidence is not strong enough to support widespread use of these four drugs in patients with alcoholic liver disease.\(^54\) Treatment details are given in Table 2. Except for the known interaction between alcohol and disulfiram, there are no relevant interactions between alcohol and the drugs used for the treatment of alcohol-use disorder.

### Table 2

<table>
<thead>
<tr>
<th>Alcohol Use and Liver Transplantation</th>
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<td>The allocation of organs to patients with alcoholic liver disease currently involves consideration of urgency and usefulness. Patients with alcoholic liver disease who are candidates for liver transplantation are often stigmatized and not referred for evaluation, since some physicians consider alcoholic liver disease a self-inflicted disease. It is notable, however, that graft survival rates in patients with alcoholic liver disease are similar to those in patients with other causes of end-stage liver disease.(^83) Most guidelines promote the 6-month alcohol-abstinence rule as a prerequisite for receipt of a liver transplant, not only to establish the likelihood of long-term abstinence after liver transplantation but also to permit some patients to recover from decompensated liver disease through the decrease of portal hypertension, thus obviating the need for liver transplantation.(^5) However,</td>
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empirical data regarding this approach are mixed. Only a return to heavy drinking after transplantation is associated with poor outcomes, and this pattern of drinking is reported in only 20% of patients. A case–control study showed that rapid liver transplantation would improve survival among patients with severe alcoholic hepatitis who did not have a response to medical therapy. In the study, recidivism in alcohol use was less than 15%. These data could be informative in consideration of the development of an alternative approach for persons with alcohol-use disorder and liver failure, which has been explored recently by other groups, with promising results. Alcohol use is common among patients with liver disease and is associated with poor outcomes. Advanced liver disease can complicate the pharmacologic treatment of alcohol-use disorder and alcohol withdrawal syndrome. Medications approved for alcohol-use disorder are prescribed to a minority of patients, yet they could be used by patients with chronic liver disease. Abstinence from alcohol should be encouraged in patients with chronic liver disease. Liver transplantation could be considered for patients who abstain from alcohol and present with progressive liver failure. It would be wise to expand alcohol-use disorder treatment in everyday clinical practice to include treatment in patients with advanced liver disease.

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## CONCLUSIONS AND FURTHER DIRECTIONS

Alcohol use is common among patients with liver disease and is associated with poor outcomes. Advanced liver disease can complicate the pharmacologic treatment of alcohol-use disorder and alcohol withdrawal syndrome. Medications approved for alcohol-use disorder are prescribed to a minority of patients, yet they could be used by patients with chronic liver disease. Abstinence from alcohol should be encouraged in patients with chronic liver disease. Liver transplantation could be considered for patients who abstain from alcohol and present with progressive liver failure. It would be wise to expand alcohol-use disorder treatment in everyday clinical practice to include treatment in patients with advanced liver disease.

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