The Impact of Obesity and Metabolic Syndrome on Alcoholic Liver Disease

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KEYWORDS

• Obesity • Diabetes • Insulin resistance • Metabolic syndrome
• Alcoholic liver disease

KEY POINTS

- Obesity and metabolic syndrome are common in alcoholic liver disease (ALD) patients and increase the risk of liver-related mortality.
- Obesity is an independent risk factor for steatosis, acute alcoholic hepatitis, and cirrhosis in ALD.
- Obesity and alcohol synergistically enhance hepatic carcinogenesis.
- Diabetes is an independent risk factor for hepatic carcinogenesis in alcoholics and increases mortality in both cirrhosis and precirrhosis patients.

EPIDEMIOLOGY OF ALD

ALD is a major health burden in the United States. Approximately 18 million people abuse alcohol and 10 million people suffer from ALD.[1,2] ALD includes a spectrum of liver pathology from alcoholic fatty liver and alcoholic steatohepatitis (AH) to liver fibrosis and cirrhosis.[3] In the general population, the prevalence and mortality from ALD closely follows per capita ethanol consumption and increases as the per capita alcohol consumption increases.[4] ALD remains a major cause of liver failure and contributes to more than 20,000 deaths annually in the United States.[2]

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SPECTRUM OF ALD

Studies of the incidence and prevalence of different stages of ALD prior to the development of cirrhosis in the general population are difficult to conduct because patients with compensated liver disease usually do not seek medical attention.[5] Up to 90% of alcoholics have fatty liver, which usually resolves within 2 weeks if alcohol consumption is discontinued.[6] Although patients with pure alcoholic fatty liver are mostly asymptomatic, they have a 10% risk of progressing to cirrhosis and an 18% risk of cirrhosis or fibrosis over a median time period of 10.5 years. In those who drink more than 40 units of alcohol per week, the risk dramatically increases, with a 30% risk of cirrhosis and a 37% risk of cirrhosis or fibrosis[7,8]; 10% to 35% of all alcoholics have changes on liver biopsy consistent with alcoholic hepatitis.[8] The amount of alcohol intake that puts an individual at risk for alcoholic hepatitis is unknown, but a majority of patients have a history of heavy alcohol use (more than 100 g/d) for 2 or more decades.[9] Once alcoholic hepatitis has developed, the risk of cirrhosis is increased compared with simple steatosis. In one study, over a 5-year period, cirrhosis developed in 16% of patients with steatohepatitis and in 7% of patients with simple steatosis.[10] A subset of patients with ALD develops severe AH, which often presents acutely against a background of chronic liver disease and has a substantially worse short-term prognosis.[11] The progression to cirrhosis is a leading cause of morbidity and mortality in ALD.[2] Hepatic decompensation is common among patients with alcoholic cirrhosis. The risk of complications, including the development of ascites, variceal bleeding, or hepatic encephalopathy, is approximately 25% after 1 year and 50% after 5 years.[12] Once hepatic decompensation develops, the expected 5-year transplant-free survival rate is 60% for those who stop drinking alcohol and 30% for those who continue to drink alcohol.[13] Only 10% to 15% of alcoholics, however, develop cirrhosis. Although the amount and patterns of alcohol consumption are important, they do not fully account for the differences in cirrhosis incidence rates.[3] Several studies have been performed to investigate risk factors (gender, genetics, diet, type of alcohol, pattern of drinking, and hepatitis C virus infection) in the progression of ALD.[14] Given the rising prevalence of obesity and metabolic syndrome, this review focuses on current understanding of the potential impact of obesity and metabolic syndrome in the progression of ALD.

OBESITY ON THE PROGRESSION OF ALD

The World Health Organization and the National Center for Health Statistics define overweight as a body mass index (BMI) greater than 25 kg/m^2 and less than or equal to 29.9 kg/m^2 and obesity as a BMI greater than 30 kg/m^2.[15] Alcohol and obesity synergistically increase the risk of liver injury as measured by elevated serum alanine aminotransferase and aspartate aminotransferase levels.[16] A study of 1604 alcoholic patients revealed that overweight (as determined by BMI$\geq$25 kg/m^2 in women and $\geq$27 kg/m^2 in men) is a risk factor for the progression of alcoholic liver disease.[9] Being overweight for at least 10 years is independently correlated with the presence of steatosis, acute alcoholic hepatitis, and cirrhosis. These results show that the presence of excess weight for at least 10 years is a risk factor for progression of ALD.[9] Another study of asymptomatic alcoholic patients revealed that higher body weight is a risk factor for more severe histologic liver damage.[17]

Whether the exacerbation of ALD in overweight patients is a result of additive injury from nonalcoholic steatohepatitis (NASH), which is a hepatic manifestation of metabolic syndrome, or the metabolic derangement in obesity that exacerbates ethanol-induced liver injury remains a subject of further investigation. Ethanol feeding results