

Alcoholic Liver Disease High Risk or Low Risk for Developing Hepatocellular Carcinoma?

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KEYWORDS

- Alcoholic liver disease Hepatocellular carcinoma risk Cirrhosis Hepatitis B
- Hepatitis C Diabetes Obesity

KEY POINTS

- Although the evidence has been conflicting, it seems that the linkage between alcoholic liver disease (ALD)-associated compensated cirrhosis and hepatocellular carcinoma (HCC) is best characterized as medium-high risk.
- Alcohol interacts with other causes of liver disease, including hepatitis B and C, and conditions, such as diabetes and obesity, to increase the risk for developing HCC, either synergistically or additively.
- HCC risk in patients with ALD-associated cirrhosis increases with age and with quantity and duration of alcohol consumption and is pronounced in women.

INTRODUCTION

In the United States, alcoholic liver disease (ALD) is the second leading cause of liver transplantation and cirrhosis behind chronic infection with hepatitis C virus (HCV).^{1–3} Globally, alcohol accounts for 50% of all deaths due to cirrhosis.⁴ The clinical spectrum of ALD includes steatosis, sclerosing hyaline necrosis, acute on chronic liver failure, alcoholic hepatitis, cirrhosis, and hepatocellular carcinoma (HCC). Although the prevalence of ALD-associated cirrhosis (defined here as cirrhosis that develops exclusively as the result of alcohol intake, with no other contributing factors) is high globally,

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the incidence of HCC associated with alcoholic cirrhosis is lower than the incidence associated with cirrhosis of other etiologies, including chronic HCV, chronic hepatitis B virus (HBV), and hereditary hemochromatosis.⁵ To better understand the relationship between ALD and the development of HCC, several studies have investigated alcohol as the primary cause and as a cofactor for carcinogenesis along with other etiologies of liver disease, such as viral hepatitis, hemochromatosis, and fatty liver disease. Additionally, studies have shown that host factors such as gender, genetics, and ethnicity may influence disease progression. This review critically assesses the literature to evaluate the risk posed by alcohol as a primary cause of and as a cofactor for the development of HCC.

AS A PRIMARY CAUSE: THE RISK OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH ALCOHOLIC LIVER DISEASE-ASSOCIATED CIRRHOSIS

There have been conflicting findings on the level of HCC risk in patients with compensated ALD-associated cirrhosis. Seven studies evaluating HCC risk in patients with cirrhosis associated exclusively with alcohol consumption (with no evidence of ongoing viral hepatitis infection) have suggested that the 10-year cumulative incidence may range from 6.8-28.7%.⁶⁻¹² In some of these studies, patients with ALD-associated cirrhosis were evaluated alongside patients with chronic hepatitis B (CHB)- and chronic hepatitis C (CHC)-associated cirrhosis.^{6,9,11,12} (Tables 1 and 2).

Study	Country	Total Patients (n)	Follow-up (y)	Age (v)	Male/ Female	Hepatocellular Carcinoma Cumulative Incidence
Toshikuni et al, ⁶ 2009	Japan	227	3.5 ^b	59 ^b	67/8	Annual: 0.6% 3-y: 1.3% 5-y: 6.8% 7-y: 6.8% 10-y: 6.8%
Jepsen et al, ⁷ 2012	Demark	8482	4.1 ^b	54.4 ^b	5655/2827	5-y: 1.0%
Ioannou et al, ¹¹ 2007	USA	2126	3.6 ^a	NA	2062/64	0.6/100 Patient-year
Uetake et al, ⁸ 2003	Japan	91	5.9 ^b	50.1 ^b	91/0	3-y: 2.4% 5-y: 6.4% 7-y: 18.9% 10-y: 28.7%
N'Kontchou et al, ⁹ 2006	France	771	4.1ª	59.7ª	336/142	5-y: 16%
Mancebo et al, ¹⁰ 2013	Spain	450	3.5 ^b	53.9ª	369/81	Annual: 2.6% 5-y: 13.2% 10-y: 23.2%
Lin et al, ¹² 2013	Taiwan	966	5.2 ^a	49.3 ^b	165/37	Annual: 1.9% 3-y: 4.8% 5-y: 8.9% 10-y: 21.4%

^a Mean.

^b Median.

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