

## Review

# Hepatocellular Carcinoma: A Comprehensive Review

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## Abstract

Hepatocellular carcinoma (HCC) is the sixth most common malignancy globally and remains one of the leading causes of cancer-related mortality. Its incidence continues to rise worldwide, and it is currently the fastest-growing cancer by incidence in the United States. HCC most often arises in the context of chronic liver disease, particularly cirrhosis. While chronic viral hepatitis (hepatitis B and C) has traditionally been the primary etiologic factor, recent advances in antiviral therapies and prevention strategies have shifted the epidemiological landscape. Metabolic dysfunction-associated steatotic liver disease (MASLD) and alcohol-related liver disease are increasingly prominent risk factors, especially in Western populations. This shift underscores the need for targeted risk factor modification, improved early detection, and enhanced surveillance protocols. The management of HCC necessitates a multidisciplinary approach, incorporating locoregional therapies, surgical resection, liver transplantation, and systemic therapies for advanced-stage disease. Recent advances in systemic treatments, including immune checkpoint inhibitors and combination therapies, have transformed the therapeutic landscape. Despite these developments, significant challenges persist in optimizing treatment, identifying predictive biomarkers, and personalizing therapy. Ongoing research is focused on refining molecular classifications and advancing precision medicine strategies to improve outcomes. This review provides a comprehensive overview of the etiology, surveillance strategies, diagnostic approaches, molecular features, and current treatment modalities for HCC.

**Keywords:** HCC; hepatocellular carcinoma; liver cancer; cirrhosis; viral hepatitis; liver cancer etiology; liver cancer treatment



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## 1. Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver cancer, accounting for 75–85% of cases, followed by intrahepatic cholangiocarcinoma, which comprises 10–15% of [1] cases. HCC is the sixth most common cancer globally and the third leading cause of cancer-related mortality with a five-year survival rate of only 15% [1,2]. In the United States, the incidence of HCC has tripled since 1980, making it the fastest-growing tumor in the country. HCC-related mortality increased by 43% between 2000 and 2016 [3,4].

HCC primarily arises in the setting of chronic liver disease and cirrhosis, with only a small percentage of cases occurring in individuals without underlying liver pathology [5,6]. Approximately 80–90% of HCC patients have pre-existing cirrhosis, and the five-year cumulative risk of HCC development in cirrhotic patients ranges from 5%