Trends in Hepatocellular Carcinoma among Hepatitis C Patients Achieving Sustained Virological Response Following Direct-Acting Antivirals Treatment

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Hepatitis C continues to be a major worldwide health concern necessitating intervention due to one of its complications, Hepatocellular Carcinoma (HCC).[1] Data from the World Health Organization (WHO) in 2022 estimates that over 50 million persons are chronically infected with the hepatitis C virus, with an annual incidence of roughly 1 million new infections.[2] The introduction of Direct-Acting Antivirals (DAAs) has transformed the treatment approach for hepatitis C from a previously difficult-to-cure disease to a curable infection.[3] Prior to the discovery of the DAAs, interferon therapy was the primary treatment for hepatitis C, despite its relatively low efficacy and more severe adverse effects.[4]

Chronic Hepatitis C Virus (HCV) infections treated with DAAs have achieved Sustained Virological Response (SVR). SVR is a sign that the Hepatitis C treatment has successfully eliminated the virus from the patient's body, as demonstrated by blood tests that indicate undetectable HCV levels 12 weeks after the treatment has been completed. DAAs medication generally lasts for 12 weeks in patients with non-cirrhotic chronic HCV infection or 24 weeks in those with liver cirrhosis. The success rate of SVR with DAAs reaches over 90% in the majority of cases, suggesting a little likelihood of HCV infection recurrence post-SVR achievement.[5,6]

The annual incidence of HCC ranges from 1% to 8% with a history of HCV infection.[7] Furthermore, the occurrence of HCC is markedly reduced in the SVR group (5.1 per 1,000 person-years) in contrast to the non-SVR group (15.0 per 1,000 person-years). Risk factors linked to the occurrence of HCC encompass age, gender, diabetes mellitus, alcohol use, and co-infection with Hepatitis B virus or HIV.[8,9] Older age, the presence of cirrhosis, and diabetes mellitus are risk factors for the occurrence of HCC in the SVR group treated with DAAs.[10,11]

A meta-analysis study in 2024 reported that the risk of HCC is lower in SVR treated by DAAs than those in non-responders. The incidence of HCC in post-SVR is three times higher in patients with cirrhosis than in those without. However, there is no significant difference between the DAAs and interferon groups regarding the occurrence of HCC post-SVR.[12] Patients receiving interferon and ribavirin therapy frequently encounter exacerbated side effects and prolonged treatment periods, which may negatively impact their quality of life and increase the possible long-term risk of HCC.[13]

Long-term monitoring for patients who have achieved SVR is crucial for the early detection of HCC, which is essential for improving survival rates. Early identification of HCC enhances the probability of effective treatment by interventions like resection or liver transplantation, resulting in five-year survival rates above 50%. Moreover, consistent monitoring facilitates the detection of potential complications, allowing for timely prevention or subsequent intervention.[14] Consequently, long-term surveillance must be an essential component of treating patients who have attained SVR.[15,16]

In conclusion, the primary risk factors for the occurrence of HCC in Hepatitis C patients who have achieved SVR after DAAs therapy are advanced age, liver cirrhosis, and diabetes mellitus. Timely DAA intervention is especially crucial for those with cirrhosis. Despite the remarkable efficacy of DAAs in eradicating the Hepatitis C virus, the risk of HCC remains present. Pre-treatment liver state, viral genotype, and liver fibrosis status are significant predictors of HCC development. Ongoing surveillance is essential in the management of Hepatitis C patients who have attained sustained SVR. HCC screening is advised every 6 months, contingent upon individual

risk factors to allow for the early detection of HCC, which is vital for improving treatment outcomes and managing complications effectively.

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