The increase of incidences of Hepatocellular Carcinoma (HCC) will continue in the next decades. The therapies about hepatitis C infection has been questioned as a risk factor. Some authors emphasized that sustained virologic response (SVR) with interferon-based therapy reduced the risk of developing HCC. In contrast, some publications that suggest an increasing risk of HCC in patients treated with Direct-Acting Antivirals (DAA). Whether these therapies are associated with an increased risk of HCC remains to be studied and continued long-term observational studies will be needed. The goal in HCV care needs to go beyond merely achieving an SVR.

**Key words.** Liver. Cancer. Drugs. Hepatitis.
due to drug-related causes and death from liver cancer. On the other hand, in a multicenter cohort study, the researchers observed the low risk for all cause-mortality in patients with chronic hepatitis C who achieved SVR with interferon-based treatment. The risk was almost 4-fold lower compared without SVR. In Canada, Janjua, et al. reported on a provincial British Columbia database of 8147 patient treated with interferon-based therapy and found that SVR was associated with a lower risk of HCC (subdistribution HR = 0.20, 95% CI: 0.13-0.3). They emphasized that SVR with interferon-based therapy reduced the risk but that a significant risk of HCC still remained.

Nowadays with the introduction of direct-acting antiviral (DAA) for the treatment of HCV the viral eradication in most if not all patients who undergo treatment. The question arise if those patients treated with the DAA have a lower risk to develop HCC than those patients treated with pegylated interferon and ribavirin. Interesting there are some publications that to suggest an increasing risk for HCC in patients treated with DAA. But other publications did not support this finding.

From a treatment perspective, it appears that HCC itself diminishes the likelihood of virus eradication. In Prenner’s study published recently, the aim of that study was to assess the efficacy of all oral-DAA regimens in HCV + cirrhotic patients who have or had HCC compared to those without HCC. The investigators studied 421 patients HCV with cirrhosis of whom 33% had active, or a history of, HCC. The most frequent genotype was type 1 (86%) and 60% had been previously been treated for HCV. The results of this study showed that the presence of active HCC tumor at the time of HCV treatment initiation was associated with treatment failure using all-oral DAA regimen (p = 0.04) but that successfully treated HCC was associated with a high likelihood of achieving SVR.

In addition, some studies report surprisingly high rates of recurrence HCC in patients treated successfully with DAA regimens after their tumors had been treated, presumably successfully, by various therapies other than liver transplant. This suggests that DAA associated SVR does not protect against HCC recurrence post HCC treatment. For example Conti, et al. confirmed in patients previously treated for HCC that there is still a high risk of tumor recurrence, despite successful DAA treatment. They analyzed 344 patients’ cirrhotic patients, 285 without HCC and 59 with previous HCC with follow up for 24 weeks. The development of recurrent HCC was found in 17 patients of 59 (with previous HCC) compared to 9 of 285 without. Advanced cirrhosis represented a predictor of recurrent HCC.

At the same time Reig, et al. observed HCC in patients with a complete response after HCC treatment by resection, ablation, or chemoembolization and after antiviral therapy using DAAs. The patients who achieved a SVR had an unexpectedly high rate of HCC recurrence (28%).

If the previously mentioned projections are accurate, we can expect increases in the complications of cirrhosis in the future. Therefore the long-term non-virologic effects of antiviral treatment must continue to be evaluated. Some authors hypothesize that the type of therapeutic option employed to treat the HCC may condition its reappearance and this may influence the apparent oncologic DAA failure (i.e. HCC recurrence). Although the early studies reporting HCC post-DAA may be due to unforesen selection or ascertainment bias, never-the-less, they are hypothesis-generating and underscore the fact that patients with cirrhosis who have achieved a SVR still need regular surveillance for HCC.

In conclusion, the risk for developing HCC remains, even though SVR has been achieved and these patients should undergo HCC monitoring for the long term. Whether DAAs themselves are associated with an increased risk of HCC remains to be studied and continued long-term observational studies will be needed.

The goal in HCV care needs to go beyond merely achieving an SVR. We should identify in all patients the risk factors for complications, comorbidity’s and we have to know the hepatic damage at the time patients achieve SVR and in this way we can determine the frequency of the medical visits. In this regard, we agree with Jacobson, et al., who have published a clinical practice update proposing a modulation of surveillance or management of gastroesophageal varices, modification of the use or dosing of medications metabolized by the liver, guidance regarding alcohol consumption, and assessment of patient candidacy for major surgeries.

REFERENCES


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