PERSPECTIVE

Incision revision

Antiviral medication is leading surgeons to re-evaluate how they treat hepatitis-induced liver cancer, writes **Myron Schwartz**.

Hepatocellular carcinoma (HCC), a form of cancer that begins in the liver, is the second-most-common cause of cancer-related death around the world. HCC is nearly always the result of an underlying chronic liver disease, usually viral hepatitis, and the choice and outcome of treatment depend on both the extent of the tumour and the overall condition of the liver. When cancer is confined to just part of the liver and the function of the organ remains normal, removing the diseased area (a procedure called resection) is the preferred treatment and can be curative. But if the organ has been damaged too badly by underlying disease, the only option might be to remove the entire liver and replace it with a donated one — a liver transplant. This procedure can be life saving, but not only does it carry a high risk for the patient, there are also too few donated organs to meet the demand.

However, thanks to recent advances in the treatments for viral hepatitis, HCC is not always an immediate threat. These treatments, combined with the development of better ways to diagnose and treat liver tumours at early stages, are changing the way that surgeons approach liver cancer: an increasing number of people can avoid liver transplants, and some with small tumours can be cured without any surgery at all.

Worldwide, the most common disease underlying HCC is infection with hepatitis B virus (HBV). Since the introduction of effective antiviral treatment for HBV in 1998, the survival rates of people with HBV-related liver cancer have dramatically improved. Treating the underlying HBV infection not only stabilizes or even improves liver function, thereby enabling people to better tolerate surgery, it also reduces the incidence of new HCC after successful resection by 70% or more.

In Western countries, however, the predominant disease underlying HCC is hepatitis C virus (HCV). In contrast to HBV, HCV has proven difficult to treat, particularly in people with HCC who have extensively scarred livers because the available HCV treatments have been both toxic and only marginally effective. At the Mount Sinai Medical Center in New York City, the five-year survival rate after both resection and transplantation for HCV-related HCC has been 10–15% worse than for HBV-related HCC, primarily owing to cancer recurrence after resection and progressive damage to the new liver as a result of HCV recurrence.

HOPE FOR HEPATITIS C

The good news is that with the approval last year of a new antiviral medicine called sofosbuvir, HCV infection has suddenly become easy to cure. This landmark development has important implications not just for HCV but also for treating and even preventing liver cancer.

HCC emerges only late in the course of HCV infection, after years of inflammation and constant regeneration have led to a substantial build-up of scar tissue (fibrosis) and a constellation of molecular changes that culminate in cancer. The old, toxic HCV treatment rarely cured people, but when it did, it reduced the risk of developing HCC by a factor of 5 to 6; sofosbuvir, if started before the development of cirrhosis, could potentially reduce that risk to almost zero. However, curing HCV does not eliminate other risk factors for HCC, such as alcohol abuse, obesity and diabetes, all of which are common among people with HCV in the United States. These factors, together with male gender, older age, and the extent of fibrosis, can contribute to ongoing risk of HCC after HCV clearances.

The advent of effective HCV treatment will almost certainly improve the results of surgery in people with HCV-related HCC. The success rates for liver transplants are highly likely to reach the level seen in people on antiviral therapy with HBV-related HCC, who have a five-year survival rate of 75–80%. For resection, predicting the degree of improvement is more difficult. Both recurrence of the original HCC and development of new HCC within the liver have been more common after resection in people with HCV than in those with HBV, and eliminating the virus can only reduce recurrence. In people with HCV-associated HCC who are good candidates for either transplant or resection, there is little difference in success rates between the two approaches. In fact, when survival is calculated from the time that people are put on the transplant waiting list instead of from the time the transplant is performed, survival after resection is often superior to that for transplant: people can die or become ineligible for transplant during the often-prolonged waiting time for a matched donor to become available.

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Donor livers are a scarce resource. When deciding how to best use them, we must consider the benefit of a transplant relative to the alternatives. For people with HCC who have borderline liver function, a strategy of initial non-surgical HCC treatment to forestall tumour progression and a 12-week course of antiviral therapy might improve the condition of their livers and thereby render them more suitable for resection. Historically, 76% of people with HBV-related HCC treated surgically at our centre have undergone resection compared with only 40% with HCV-related HCC; with use of sofosbuvir, the latter figure is likely to rise and results should improve.

As more people become eligible for potentially curative liver-cancer treatments, it is now a public-health imperative to promote screening and surveillance programmes aimed at identifying HCC at an early stage, when it is amenable to curative therapy.

Beyond helping patients who already have HCC, however, the most important effect of the new HCV drugs will be preventing liver cancer from occurring in the first place. Clearing HCV infection before people develop significant fibrosis effectively eliminates their risk of HCV-related HCC. The challenge now will be identifying the people who are already infected; in the United States, a recent government mandate for HCV screening is an important step in the right direction. We must mount a campaign to raise public awareness about this potentially devastating illness, which can now be simply diagnosed and cured. ■

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