Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) is one of the most frequently occurring malignancies in Asia. The incidence exceeds 30 cases/100,000 population/year in the east Asian region,[1,2] which dwarfs the incidence in the western world (e.g. 3–5 cases/100,000 population/year in the USA).[2,3] The high incidence of HCC in Asia is thought to be attributable to a high prevalence of hepatitis B virus infection and cirrhosis throughout most of this region, except in Japan, where chronic hepatitis C infection is believed to be the main causative factor, as is the case in western countries.[4]

Owing to the high incidence of HCC and the asymptomatic nature of early-stage disease, most Asian countries have adopted screening programmes for patients considered to be at risk of developing HCC.[1] Active surveillance programmes in Asia promote diagnosis of early-stage disease and, therefore, a greater proportion of patients undergo surgical resection in Asia than in the West. Despite improving detection rates, these programmes have only benefited a small fraction of the high-risk population as most HCC patients in Asian countries still present with symptomatic advanced disease. Post-resection survival rates remain disappointing with 5-year survival of only 30–60%.[5] It has been suggested that these low survival rates are linked to the aetiological factors behind HCC in Asian countries. However, it may be more likely that the more aggressive use of resection in patients with larger tumours, multiple nodules and tumours with vascular invasion has a greater influence on this poor prognosis. Indeed, when compared using uniform clinical and pathological criteria, 5-year post-resection survival rates appear to be similar for eastern and western countries.[6] In recent years, post-resection outcomes have improved in conjunction with improvements in surgical techniques and patient selection,[7] but further improvement depends on the advent of new treatment strategies, especially effective adjuvant therapy. Liver transplantation offers the best chance of cure for patients with early HCC associated with cirrhosis, but its application is severely limited by the shortage of deceased liver graft donors in Asian countries. Compared with the West, live donor liver transplantation is used more often in the East for treatment of HCC, but its overall impact on survival of HCC patients is small.

The prognosis for patients with unresectable HCC in Asia remains poor.[8] Radiofrequency ablation and transarterial chemoembolisation (TACE) can improve survival in some patients with small tumours and well-preserved liver function;[9,10] Nevertheless, new treatment approaches are urgently needed for patients with more advanced disease, especially given that conventional chemotherapy has not been shown to offer survival benefit in HCC patients. However, emerging evidence has suggested that molecularly targeted therapy offers great promise in the treatment of HCC. Data from the recent Sorafenib HCC Assessment Randomised Protocol (SHARP) trial reported that sorafenib 400mg twice daily can offer a 44% improvement in overall survival (OS) versus placebo in Western patients with advanced HCC (hazard ratio 0.69, 95% confidence interval: 0.55–0.88; p=0.00058).[11] More recently, a similar study requested by Asian health authorities found that treatment with sorafenib significantly increased OS versus placebo in Asia-Pacific patients with advanced disease (hazard ratio 0.68, 95% confidence interval: 0.50 – 0.93; p=0.014).[12]

These data confirm the potential for targeted agents in the treatment of HCC, and indicate that further study of sorafenib in other settings in HCC is warranted. Ongoing studies investigate sorafenib in post-TACE in Japanese and Korean patients, sorafenib as adjuvant to surgery/RFA treatment, and sorafenib as an addition to local regional therapies.

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