Prevention of Hepatocellular Carcinoma in Japan and a New Challenge for the Japan Society of Hepatology

JMAJ 53(1): 47–48, 2010

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Our society started as the Japanese branch of the International Association for the Study of Liver in 1959, and the Japan Society of Hepatology was founded in 1965. The number of society members is currently 10,600. The aims of our activities are to provide information on hepatology to society members, promote research on hepatology, and contribute to the advancement of science in Japan.

To achieve these aims, our society holds annual meetings in spring-summer and in autumn, and a western or eastern branch meeting in autumn. We publish a monthly Japanese journal, "Kanzo," and a monthly international journal, "Hepatology Research." Many manuscripts on liver and liver diseases are submitted to Hepatology Research from all over the world, and the journal's 2008 impact factor is 1.562. We encourage research by young researchers by presenting several research awards to selected researchers every year. We also hold meetings for the general public in various parts of Japan to educate people about liver diseases, especially viral hepatitis and hepatocellular carcinoma. Our society founded the Specialty Board of Hepatology in 1988, and the number of hepatologists with a Diploma in Hepatology is currently 4,084. To receive the Diploma in Hepatology, candidates must have been trained according to the curriculum established by the board for five or more years in an authorized hospital and have passed the written examination. More than 500 trainees take the written examination every year.

Current major topics in hepatology in Japan are viral hepatitis and hepatocellular carcinoma. Hepatocellular carcinoma is one of the leading causes of cancer death in Japan, accounting for approximately 34,000 deaths per year in a population of 120 million. Approximately 70% of these cases are associated with hepatitis C virus infection and 15% are associated with hepatitis B virus infection. The frequencies of HBV infection and hepatitis C virus infection in Japan are estimated to be approximately 1% and 1.5%, respectively. However, due to implementation of a nationwide program for the prevention of mother to baby transmission of the hepatitis B virus via anti-hepatitis B immunoglobulin and a vaccine launched in 1986, the hepatitis B virus carrier rate amongst young people aged under 20 years in Japan is now less than 0.1%. Screening of blood products for hepatitis C virus began in 1989, and due to this measure and the use of disposable medical supplies, new cases of hepatitis C virus infection are now very rare in Japan.

We are also actively treating patients infected with the hepatitis C virus with pegylated interferon and ribavirin, but the current sustained virological response rate is insufficient. Due to the existence of many more hepatitis C virus- and hepatitis B virus-infected patients who have a high possibility of developing hepatocellular carcinoma, the Japanese Government announced a 7-year strategy for hepatitis research in 2008 to increase the efficacy of the treatment of patients infected with the hepatitis C virus or hepatitis B virus. This program was further strengthened in 2009 through the establishment of a law that supports patients with hepatitis and promotes research on hepatitis.

Although we are effectively preventing hepatocellular carcinoma, we also need to effectively treat patients who have developed hepatocellu-

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lar carcinoma. To detect hepatocellular carcinoma as early as possible, we examine patients with chronic viral hepatitis by determining tumor markers (AFP and PIVKA-II) every three months and by imaging modalities (ultrasonography, contrast-enhanced computed tomography, or contrast-enhanced magnetic resonance imaging) once every six months. We examine patients with liver cirrhosis by determining tumor markers every three months and by imaging modalities once every three to four months. The costs are covered by the national health insurance system in Japan.

There are three curative treatment modalities for hepatocellular carcinoma: resection, radiofrequency ablation therapy, and liver transplantation. However, liver transplantation for hepatocellular carcinoma is limited because of the very low availability of cadaver organs in Japan. Thus we have to choose either resection or radiofrequency ablation therapy for hepatocellular carcinoma as a curative treatment when indicated. Both resection and radiofrequency ablation therapy have been reported to give a good survival time. A controlled randomized trial supported by our society is currently being under-taken to compare the effectiveness of resection and radiofrequency ablation therapy for hepatocellular carcinoma. The recurrence of hepatocellular carcinoma after curative treatment is another important problem. Several trials are being undertaken in Japan to prevent the recurrence of hepatocellular carcinoma after curative treatment.

The increase in the number of obese people is becoming an important health problem in Japan. Obesity is associated with various life-style related diseases and is the main cause of non-alcoholic fatty liver diseases and non-alcoholic steatohepatitis. The number of patients with non-alcoholic fatty liver diseases is estimated to be approximately 10 million, and that of patients with non-alcoholic steatohepatitis is 0.8 to 1 million. NASH is known to lead to liver cirrhosis and eventually hepatocellular carcinoma.

Since the number of obese people in Japan is increasing, the incidence of non-alcoholic fatty liver diseases and non-alcoholic steatohepatitis will definitely increase steadily and become an immense problem amongst liver diseases. We believe that we must promote research on non-alcoholic fatty liver diseases and non-alcoholic steatohepatitis to prevent the spread of obesity-associated liver diseases.