Japan’s Successful Model of Nationwide Hepatocellular Carcinoma Surveillance Highlighting the Urgent Need for Global Surveillance

Prof. M. Kudo
Editor Liver Cancer

Screening and surveillance for early detection of hepatocellular carcinoma (HCC) is currently being promoted in many clinical practice guidelines. These include guidelines issued by the American Association for the Study of Liver Diseases [1], the European Association for the Study of the Liver–the European Organization for Research and Treatment of Cancer (EASL–EORTC) [2], and the Asian Pacific Association for the Study of the Liver [3], as well as those established in Japan by the Japan Society of Hepatology [4, 5]. If HCC is detected at an early stage [e.g., Barcelona Clinic Liver Cancer (BCLC) classification stage 0 or A], curative treatments such as resection, ablation, or transplantation are indicated, with the aim of improving disease prognosis as well as minimizing overall medical costs. Moreover, the abovementioned three curative treatments are highly recommended in the EASL–EORTC guidelines because of substantial evidence supporting their value as therapeutic options. Furthermore, survival is improved if HCC is detected at a stage where these curative treatments are indicated.

However, nationwide surveillance for early detection of HCC has been established in Japan, and they have not yet been established in European, Asian, American, or African countries. In Japan, it has become common practice for not only tertiary referral centers, such as university hospitals, cancer centers, and main base hospitals, but also small hospitals and private practitioners to regularly conduct ultrasonography and tumor marker screening for the early detection of HCC in patients at high risk, such as those with cirrhosis and chronic hepatitis B or C. Physicians have lost a number of court cases because their high-risk patients who had been followed-up regularly with screening were diagnosed with HCC larger than 3 cm, for which curative treatments were not applicable. In part, because of such court cases, physicians who specialize in liver disease as well as general physicians nationwide are well aware that patients at high risk for HCC need to be screened regularly. Moreover, starting in the 1990s, the Japan Society of Hepatology designated a person in each of the 47 prefectures responsible for providing educational lectures several times a year to promote...
public awareness of the importance of early HCC detection by ultrasonography and tumor marker assessment. The Government actively engages in preventive measures against hepatitis and HCC, and offers free testing for hepatitis B and C virus at local public health centers and medical facilities nationwide to identify individuals at high risk. Furthermore, screening of individuals at high risk for HCC by ultrasonography and assessment of the tumor markers such as AFP, PIVKA-II, and AFP-L3 is covered by the national health insurance and the social insurance system.

As a result of these preventive measures, 62% HCC cases diagnosed in Japan are BCLC 0/A (early stage), 32% are BCLC B (intermediate stage), and only 6% are BCLC C/D (advanced/end stage). However, in Western countries, the figures are approximately 30% for BCLC A, 20% for BCLC B, 40% for BCLC C, and 10% for BCLC D (fig. 1). These figures indicate that HCC tends to be diagnosed after the onset of symptoms because of poor implementation of nationwide HCC surveillance in Western countries compared to Japan.

Another indicator of the effectiveness of nationwide surveillance is the 5-year survival rate of HCC patients. According to follow-up data from the Nationwide Registry implemented by the Liver Cancer Study Group of Japan, the nationwide 5-year survival rate of HCC patients in Japan was 43% for the last 5 years [6]. In contrast, the latest 5-year survival rate was 11–15% in the United States [7–10], suggesting that early detection of HCC is poorly practiced in this country despite the fact that it has the most advanced liver transplantation technology. However, many Asian countries have also not yet established nationwide surveillance systems, and even in Korea, which actively conducts screening of HCC high-risk patients at an institutional level. The latest nationwide 5-year survival rate in Korea was only 18.9% [11]. These findings clearly indicate that the prognoses of HCC patients could drastically improve by simply establishing a nationwide HCC surveillance system. Five-year survival rates are also influenced by lead time bias to a certain extent; nevertheless, there is no doubt that early detection of HCC, when curative treatment is indicated, will improve the prognoses of affected patients.

In conclusion, even though it is unquestionably important to continue developing new HCC treatment methods and remedies (e.g., extremely expensive molecularly-targeted drugs), from the Japanese experience, it is apparent that the most basic approach is lacking in the management of HCC in other countries. Japan’s well-implemented nationwide HCC surveillance system is a successful model of national surveillance for early detection of the disease. The system is economical and drastically improves the prognosis of HCC patients.
We believe that other countries, including developing countries as well as countries in Europe and the United States, should follow Japan’s lead and urgently establish their own nationwide surveillance systems.

Reference