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Clinical practice guidelines for HCC between Korea, Europe, and United States

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Lecture : Guidelines for hepatocellular carcinoma (HCC) have been published globally among different countries. Unlike other cancers, there are discrepancies in treatment options for HCC according to characteristics of patients and availabilities of treatment options. In this session, for understanding the current treatment options among different countries, 3 guidelines for HCC around the world, including one guideline from Korea, another from Europe, and the last from the United States will be discussed. There are both similarities and differences in surveillance and treatment recommendations among guidelines due to variables of socioeconomic status in addition to acknowledgement of level of evidence.

Three guidelines for HCC around the world will be addressed, comprising 3 guidelines from Asia [the Korean Liver Cancer Study Group and the National Cancer Center (NCC) [1], one from Europe [the European Association for the Study of the Liver (EASL) [2], and the last from the United States [American Association for the Study of Liver Disease (AASLD) [3]. These current guidelines will be comparatively evaluated to systematically appraise these guidelines for HCC in this session.

Surveillance

Surveillance is the set of screening tests to detect early-stage cancer in a high-risk group such as chronic hepatitis B, chronic hepatitis, and cirrhosis in Korean guideline. The definition and description of the high-risk population varied according to the guidelines. The AASLD guideline recommends HCC screening and surveillance for the following high-risk groups defined by Asian male hepatitis B carriers over age 40, Asian female hepatitis B carriers over age 50, hepatitis B carriers with a family history of HCC, Africans and African Americans with hepatitis B, cirrhotic hepatitis B carriers, individuals with hepatitis C cirrhosis, individuals with stage 4 primary biliary cirrhosis, individuals with genetic hemochromatosis and cirrhosis, individuals with alpha 1-antitypsin deficiency and cirrhosis, individuals with cirrhosis from other etiologies.

Whereas most Asian guidelines recommend surveillance program based on combination of US and AFP, western guidelines don't recommend routine use of tumor biomarkers for early detection. The biomarkers tested (i.e. AFP, AFP-L3 and DCP) are regarded suboptimal in terms of cost-effectiveness for routine surveillance of early HCC in EASL and AASLD guidelines.

Diagnosis

Size-based diagnostic algorithms was recommended by Korean, EASL and AASLD guidelines by a nodule diameter of <1 cm, 1-2 cm and >2 cm. All the guidelines recommend four-phase multidetector computed tomography (MDCT) or contrast-enhanced dynamic MRI using extracellular contrast agents as the primary examination for the diagnosis of HCC as non-invasive methods. Although all the guideline highlights on imaging characteristics in common of arterial phase hypervascularity and venous or delayed phase wash-out, there are some disagreements among the guidelines. These include the use of tumor markers such as AFP, lesion size/growth, inclusion of sub-centimeter nodules, the number of required imaging modalities, and the use of contrast-enhanced ultrasonography (CEUS) and/or tissue-specific MRI contrast media.

Staging

Assessment of tumor stage is important for treatment option. Pre-treatment staging prior to liver transplantation includes abdominal dynamic CT or MRI, chest CT and bone scan. The Barcelona-Clinic Liver Cancer (BCLC) staging system is the most popular to guide treatment decision and has been endorsed by many guidelines

including AASLD, EASL-EORTC, and ESMO-ESDO. BCLC staging system includes prognostic factors related to tumor burden, hepatic functional reservoir, and patient's performance status, combined with treatment-dependent factors obtained from cohort studies and randomized clinical trials. Unlike other staging systems, this system links tumor stage with the treatment plan allowing an assessment of life expectancy related to specific HCC management. In contrast, the KLCSG-NCC have adopted the modified International Union for Cancer Control (UICC) staging system as a primary staging system for HCC which offers more advantages for assessing the prognosis of small HCC.

Treatment

Although BCLC has long been adopted as standard treatment algorithm or guiding plans for managing HCC, there are many disagreements among Asia-pacific experts. The concepts of BCLC, for surgical resection or other locoregional therapy, are considered too conservative. Asian guidelines including the KLCSG-NCC, the APASL, and JSH offers more treatment options such as surgical resection and TACE for more advance-staged tumors. Whereas BCLC staging system defines appropriate candidates for surgical resection as patients with a solitary tumor without the evidence of portal hypertension, KLCSG-NCC guideline is more generous in surgical resection as ≤ 3 intrahepatic tumors without macrovascular invasion if liver function is well preserved. The guidelines differ on appropriate candidates for surgery. For example, BCLC staging system defines appropriate candidates for a resection as patients with a solitary tumor without the evidence of portal hypertension. However, the KLCSG-NCC guideline widened the criteria for HCC resection as patients with ≤ 3 intrahepatic tumors without macrovascular invasion in well preserved liver function. There are many detailed discrepancy in selection of liver transplantation and down-staging between these guidelines.

Radiotherapy

Unlikely to other guidelines, KLCSG-NCC guideline characteristically recommends EBRT as an initial treatment option for intrahepatic HCC. EBRT can be considered for HCC patients ineligible for resection, LT, RFA, PEIT, or TACE; show incomplete response to TACE; with portal vein invasion when the dose-volume criteria are met; and to alleviate symptoms.

Conclusion

Current guidelines seems similar, but they show some discrepancies in surveillance and treatment options due to regional differences in disease and diversities omdiagnosis and staging systems. In contrast to other malignancies, the regional variances in tumor characteristics and resources unable us to have a universal guideline for HCC. Recommendations from the 3 groups (Asia, Europe, and USA) reflects geographic differences in the prevalence and available treatment such as organ availability for LT, economic status, and accessibility to chemotherpeutics. Therefore, It would be important to understand these differences in deciding appropriate treatment options when treating patients with HCC.

References

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