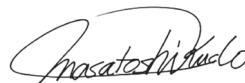


Editorial

Locoregional Therapy for Hepatocellular Carcinoma

Prof. M. Kudo



Editor *Liver Cancer*



Transplantation, resection, and ablation are recommended for the treatment of very early (single <2 cm diameter) and early (single or <3 nodules <3 cm diameter) stage hepatocellular carcinomas (HCCs) as determined using the Barcelona Clinic Liver Cancer (BCLC) staging system [1]. In addition, transarterial chemoembolization (TACE) is recommended for intermediate-stage multinodular HCCs, systemic therapy with sorafenib for advanced-stage HCCs, and best supportive care for end-stage HCCs, respectively. In this issue, we review current locoregional therapeutic modalities including local ablation, TACE and arterial infusion chemotherapy.

Although radiofrequency ablation (RFA) [2, 3] is the best current method for ablation, many differences exist between the techniques used in Japan and those used in other countries such as the United States and in Europe. In Japan, computed tomography is used to assess the outcome of RFA immediately after the procedure, and the technique is repeated until a sufficient ablative margin is obtained, which has been found to produce nearly a 100% tumor necrosis rate. In other words, the RFA is repeated to achieve a complete response (CR) in most cases, and this is markedly different from the RFA treatment performed in the United States and Europe, in which the outcome is usually assessed at one month after a single ablation. Consequently, necrosis rates of HCC following RFA are different between Japan and the other aforementioned countries, which is described in detail in the review articles by Drs. Kang and Rhim [4].

Furthermore, TACE, which is the representative regional therapy, has conventionally been performed by first infusing doxorubicin or epirubicin suspended in Lipiodol, followed by embolization with a gelatin sponge (conventional Lipiodol-TACE). Conversely, in the United States and Europe, drug-eluting beads TACE (DEB-TACE) with microspheres (DC beads) is frequently performed as the standard method. In addition, radioembolization with yttrium-90 for internal irradiation has also been performed proactively in recent years.

We are proud of TACE, which was first developed in Japan and that has evolved markedly over the years, because the complete cure of HCC is now possible with the use of superselective or subsegmental TACE. However, conventional TACE is often ineffective, or it may even adversely affect hepatic functional reserve when used in patients with huge and/

or multinodular HCCs that are commonly observed in Western countries. Instead of conventional TACE, DEB-TACE may be indicated for huge HCCs or bilateral multinodular HCCs that are observed worldwide. Although DC beads treatment was recently approved in Japan, it is thought that superselective Lip-TACE will continue to be the curative treatment for patients with a few or small HCCs. In contrast, DEB-TACE is often performed in patients with large multinodular HCCs, or those who are refractory to conventional TACE. The advantages of using DEB-TACE include no significant decline in hepatic functional reserve and a sustained release of anticancer drugs. More details are described in the review article by Tsurusaki and Murakami [5].

Although not listed as a recommendation in the BCLC staging system, Japanese physicians have been proactively performing hepatic arterial infusion chemotherapy (HAIC), in which an infusion reservoir is implanted in the body, in patients with bilateral multinodular HCCs or HCCs with vascular invasion [6, 7]. Because HAIC has not been investigated prospectively, the retrospective data currently lacks sufficient clinical evidence. Despite this, the response rate of Japanese patients treated with HAIC is high, ranging from 40–50%, with 10% of patients achieving a CR. Based on our experience, it is clear that the survival rate is high among complete and partial responders. In this regard, it is no longer ethical in Japan to perform a comparative clinical study using a non-treatment group. HAIC is safe even in patients with a tumor invading the main branch of the hepatic portal vein (Vp4), or in patients with Child–Pugh stage B liver disease, who do not qualify to receive sorafenib therapy, which often results in the drastic disappearance of tumor-related vascular invasion. Consequently, HAIC is performed proactively in daily clinical practice in Japan [8]. In fact, the treatment algorithm in the Japan Society of Hepatology consensus-based clinical practice guidelines for the management of HCC published by the Liver Cancer Study Group of Japan recommends HAIC for patients with good hepatic functional reserve and vascular invasion or those with a contraindication to TACE [7, 9]. This is one of the big differences in the treatment approach for HCC between Japan and Western countries. Furthermore, with a recent report about the extremely good outcome of arterial infusion chemotherapy with concurrent radiotherapy [10], HAIC is expected to be adopted widely around the world in the future.

References

- 1 Bruix J, Sherman M, American Association for the Study of Liver Diseases: Management of hepatocellular carcinoma: an update. *Hepatology* 2011;53:1020–1022.
- 2 Lin SM: Local ablation for hepatocellular carcinoma in Taiwan. *Liver Cancer* 2013;2:73–83.
- 3 Teng W, Liu KW, Lin CC, Jeng WJ, Chen WT, Sheen IS, Lin CY, Lin SM: Insufficient ablative margin determined by early computed tomography may predict the recurrence of hepatocellular carcinoma after radiofrequency ablation. *Liver Cancer* 2015;4:26–38.
- 4 Kang TW, Rhim H: Recent advances in tumor ablation for hepatocellular carcinoma. *Liver Cancer* 2015; (in press).
- 5 Tsurusaki M, Murakami T: Surgical and locoregional therapy of HCC: TACE. *Liver Cancer* 2015; (in press).
- 6 Kudo M: Clinical practice guidelines for hepatocellular carcinoma differ between Japan, United states, and Europe. *Liver Cancer* 2015;4:85–95.
- 7 Kudo M, Izumi N, Kokudo N, Matsui O, Sakamoto M, Nakashima O, Kojiro M, Makuuchi M, HCC Expert Panel of Japan Society of Hepatology: Management of hepatocellular carcinoma in Japan: Consensus-Based Clinical Practice Guidelines proposed by the Japan Society of Hepatology (JSH) 2010 updated version. *Dig Dis* 2011;29:339–364.
- 8 Obi S: Current status of hepatic arterial infusion chemotherapy. *Liver Cancer* 2015; (in press).
- 9 Kudo M, Matsui O, Izumi N, Iijima H, Kadoya M, Imai Y, Okusaka T, Miyayama S, Tsuchiya K, Ueshima K, Hiraoka A, Ikeda M, Ogasawara S, Yamashita T, Minami T, Yamakado K, Liver Cancer Study Group of Japan: JSH consensus-based clinical practice guideline for the management of hepatocellular carcinoma: 2014 update by the liver cancer study group of Japan. *Liver Cancer* 2014;3:458–468.
- 10 Lee DS, Seong J: Radiotherapeutic options for hepatocellular carcinoma with portal vein tumor thrombosis. *Liver Cancer* 2014;3:18–30.