EDITORIAL

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Potential prognostic factors for solitary hepatocellular carcinoma ≤ 5 cm after transarterial chemoembolization

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Hepatocellular carcinoma (HCC) is one of the most prevalent cancer-related deaths [1]. HCC occurs most often in the setting of underlying chronic liver diseases including advanced fibrosis or cirrhosis, usually related to chronic hepatitis B virus (HBV) infection or hepatitis C virus infection. Nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, and prolonged alcohol use are also significant risk factors for HCC [2].

Despite the widespread implementation of surveillance programs for at-risk populations, curative treatments such as hepatic resection, liver transplantation, and radiofrequency ablation (RFA) cannot be applied in most patients with HCC. Hepatic resection is the standard treatment modality for patients with resectable HCC and normal liver function, but it is considered extremely challenging in cirrhotic patients. Liver transplantation is the best curative treatment option since it treats both HCC and underlying liver diseases; however, this treatment is limited by the availability of a suitable donor. RFA is an alternative potentially curative treatment for relatively early-stage HCC, but its efficacy depends on the tumor size, morphology, and location.

Transarterial chemoembolization (TACE) is a well-established therapy for HCC, and the current guidelines recommend TACE as a first-line non-curative treatment for intermediate- or advanced-stage HCC for palliative care or downstaging/bridging purposes [2-4]. Randomized controlled trials and meta-analyses have demonstrated the superiority of TACE over best supportive care for intermediate-stage HCC [3,4]. However, it is a palliative treatment and thus is not recommended as a curative option for HCC. Nevertheless, TACE covers a broad spectrum of treatment indications based on clinical judgment, including both intermediate- and early-stage HCC. In addition, several clinical studies have evaluated patients with solitary HCC undergoing TACE. TACE involves the intra-arterial infusion of a cytotoxic drug, such as doxorubicin or cisplatin, that is emulsified in the oil-based radio-opaque agent lipiodol. This is followed by embolization of the blood vessel using gelatin sponge particles or microspheres, resulting in a strong and sustained cytotoxic effect combined with ischemia [5]. Therefore, the presence of a significant arterioportal shunt secondary to large-sized HCC may interfere with TACE, because anticancer drugs and iodized oils easily pass through the shunt. Moreover, more daughter nodules or satellite le-

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sions go undetected in large-sized HCCs, rendering it difficult to achieve a complete response (CR) with TACE [6]. Indeed, single nodularity and tumor size (≤ 5 cm) are predictive factors for a CR after TACE, but little is known about the efficacy of TACE for solitary HCC ≤ 5 cm.

In the latest issue of the *Korean Journal of Internal Medicine*, Baek et al. [7] reported the clinical outcomes of 175 patients with solitary HCC ≤ 5 cm treated with TACE, as an initial treatment, and evaluated the predictive factors for a CR, recurrence after a CR, and overall survival (OS). The results demonstrated that a tumor size < 3 cm was significantly predictive of a CR. The correlation between HCC size and a CR has been reported in several previous studies. Golfieri et al. [8] reported that approximately 70% of patients with HCC ≤ 5 cm achieved a radiologic CR after a single session of TACE, compared with only 25% of patients with HCC > 5 cm. Terzi et al. [9] showed that among the factors evaluated, only the tumor diameter, specifically a tumor size ≤ 3 cm, was significantly predictive of a radiologic CR, particularly in patients with solitary HCC. Baek et al. [7] similarly showed that HCC size (≤ 3 cm) was significantly related to the tumor response after TACE. However, in contrast to the positive correlation between HCC size and CR rate reported previously, Baek et al. [7] reported a statistically insignificant association between tumor diameter and recurrence rate, suggesting that predictors of a CR are not directly linked to predictors of HCC recurrence.

Baek et al. [7] also revealed that HBV infection is another predictive factor for tumor response. Although there has been no report of the influence of HBV infection on achieving a CR after TACE, those authors suggested that microcirculation of hepatic arterial blood flow differs in HCC caused by HBV infection compared with other causes of HCC, and that it may afford an effective super-selective approach in TACE. Antiviral therapies can diminish the risk of reactivation, preventing the deterioration of liver function after TACE; therefore, a favorable CR rate after TACE might be associated with prolonged antiviral treatment with oral nucleos[t]ide analogs rather than with HBV infection *per se*. Baek et al. [7] also showed that age > 65 years was inversely related to HCC recurrence after CR and suggested that patients aged > 65 years might have less aggressive tumors and less active tumor neo-angiogenesis compared with younger patients.

Finally, Baek et al. [7] demonstrated that Child-Pugh class A and CR were independent prognostic factors for OS, suggesting that TACE should be considered as a treatment option for patients with single HCC ≤ 5 cm who are ineligible for surgery and/or RFA. In addition, favorable treatment outcomes might be obtained from selected patients, such as those with well-preserved liver function and/or with an initial radiologic CR after TACE, considering the favorable safety profile of TACE.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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