Editorial

eISSN 2005-8330
https://doi.org/10.3348/kjr.2022.0510
Korean J Radiol 2023;24(1):6-9

Korean Journal of Radiology
KJR

2022 Korean Liver Cancer Association-National Cancer Center Korea Practice Guidelines for Transarterial Therapy of Hepatocellular Carcinoma: What's New?

In Joon Lee[1], Ho Jong Chun[2], Jin Wook Chung[3]

[1]Department of Radiology, National Cancer Center, Goyang, Korea; [2]Department of Radiology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea; [3]Department of Radiology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea

Take-home points

- Conventional transarterial chemoembolization (cTACE): the three recommendations concerning cTACE in the revised version are the same as those in the previous version because there are no new issues warranting significant changes to the existing recommendations.
- Drug-eluting bead TACE (DEB-TACE): the quality of evidence for DEB-TACE as an alternative to cTACE has been upgraded from B to A, except for small (< 3 cm) tumors.
- Transarterial radioembolization (TARE): although there is no change in the quality of evidence for TARE as an alternative treatment for cTACE, the overall wording has changed positively with the description of the advantages of TARE over cTACE, that is, a better quality of life and lower occurrence of postembolization syndrome. Additionally, TARE is only considered when the remnant liver function after the procedure is expected to be sufficient because of the risk of hepatic decompensation.

Received: July 24, 2022 **Accepted:** September 13, 2022
Corresponding author: In Joon Lee, MD, PhD, Department of Radiology, National Cancer Center, 323 Ilsan-ro, Ilsandong-gu, Goyang 10408, Korea.
• E-mail: 2injoon@gmail.com

Transarterial therapies include conventional transarterial chemoembolization (cTACE), drug-eluting bead TACE (DEB-TACE), and transarterial radioembolization (TARE). The 2022 Korean Liver Cancer Association (KLCA)-National Cancer Center (NCC) Korea Practice Guidelines for hepatocellular carcinoma (HCC) include five recommendations for transarterial therapies, reflecting up-to-date research results and real-world Korean practice since the release of the 2018 version [1]. A summary of the key updates for each treatment is as follows.

cTACE

The three recommendations concerning cTACE in the 2022 version [1] are the same as those in the 2018 version because there are no new issues warranting significant changes to the existing recommendations.

DEB-TACE as an Alternative Treatment to cTACE

Compared with cTACE, DEB-TACE has better pharmacokinetics, less post-procedural pain, and a shorter duration of hospitalization by a day; most importantly, it has demonstrated similar therapeutic outcomes and adverse events in randomized controlled trials [2-4]. The European Association for the Study of the Liver (EASL) guidelines state that either of the two treatments can be utilized, and the choice is left to the clinician [5]. In Korea, compared with Western countries, TACE with superselective or ultraselective techniques is popularly used for small HCCs. Retrospective studies from Western countries have reported

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a two-fold higher incidence of biliary damage after DEB-TACE compared with cTACE [6]. Therefore, the efficacy and safety of DEB-TACE in real-world Korean practice must be defined. A prospective multicenter registry study demonstrated that the tumor response to DEB-TACE was lower in < 2-cm tumors than in 2–5-cm tumors [7,8]. A retrospective study demonstrated that DEB-TACE had a significantly lower tumor response than did cTACE in < 3-cm tumors [9]. When the tumor was > 3 cm, there was no difference in local tumor control. The incidence and severity of biliary injury after cTACE and DEB-TACE were not different when DEB-TACE was performed in the same superselective fashion as cTACE. Therefore, in the 2022 revised version, the quality of evidence for DEB-TACE as an alternative treatment to cTACE has been upgraded from B to A, except for small (< 3 cm) tumors.

Recommendation

Compared with cTACE, DEB-TACE has similar clinical outcomes in ≥ 3 cm HCCs; therefore, it can be considered as an alternative treatment to cTACE (high evidence, weak recommendation).

TARE as an Alternative Treatment to cTACE

To date, no well-designed randomized trials have compared TARE with cTACE. In small randomized trials and retrospective cohort series on conventional standard dosimetry, compared with cTACE, TARE has shown a better quality of life, less frequent postembolization syndrome, and a similar overall survival. However, recent studies have reported that a relatively higher radiation dose for TARE yielded improved therapeutic outcomes [10,11]. Specifically, the radiation subsegmentectomy technique for personalized dosimetry safely delivered an ablative dose to the tumor with an excellent local tumor response [12]. In a prospective single-arm study of small (< 3 cm) solitary HCC, all patients had an initial objective response, and 90% of them had a sustained complete response [13].

Although the current research outcomes of personalized dosimetry suggest potential improved therapeutic benefits of TARE over cTACE, further well-designed clinical trials are needed. In addition, TARE has a significantly higher cost than do cTACE or DEB-TACE and it is not widely available in Korea. Therefore, it is difficult to strongly recommend TARE as an alternative treatment for HCC in general, and it is important to select appropriate patients for TARE with a multidisciplinary team. To maximize the advantages of TARE, older patients, patients with poor performance status or severe comorbidities, or patients with large tumors would be good candidates. However, hepatotoxicity caused by TARE, which is known as radioembolization-induced liver disease, can be a significant problem. In some patients, delayed hepatic decompensation may occur 6 months after TARE [14]. In screening patients for TARE, the remnant liver function after the procedure should be carefully evaluated by considering the baseline hepatic functional reserve, territory of irradiation, and dose. TARE should be performed as selectively as possible and planned only when the remnant liver function after the procedure is expected to be sufficient.

Recommendation

Compared with cTACE, TARE results in a better quality of life and lower occurrence of postembolization syndrome; therefore, it can be considered an alternative treatment to cTACE when the remnant liver function is expected to be sufficient after the TARE treatment (moderate evidence, weak recommendation).

TACE and TARE as First-Line Treatments

As do other international practice guidelines for HCC, the 2022 KLCA-NCC guidelines regard TACE as the best option for multinodular HCCs, especially when the tumors are three or more in number or > 5 cm.

Although curative treatments are strongly recommended for early stage HCCs and new systemic agents have been introduced for advanced-stage HCC, cTACE remains either the best or an alternative option for every mUICC stage in the updated guidelines regarding the first-line treatments for patients with HCC (in the conditions of Child–Pugh class A, no portal hypertension, and the ECOG performance status scale 0–1) [1].

Curative treatment modalities have the best outcomes in early stage HCC. However, in clinical settings, this is not feasible in several situations; [15] in cases of suspected multiplicity, comorbidities, difficult imaging guidance for local ablation, or patient preference, TACE can be an alternative curative option, which is called treatment stage migration. According to real-world data from Korea, the overall survival of patients after cTACE for early stage HCC was similar to those of surgical resection and local ablation therapy, although local recurrence was more frequent and

 https://doi.org/10.3348/kjr.2022.0510

repeated treatments were more commonly required [16-18].

For advanced-stage HCC, recent phase III randomized controlled trials have revealed the survival advantage of new first-line systemic therapies (atezolizumab + bevacizumab and durvalumab + tremelimumab) over sorafenib. With advances in systemic therapies, there is a growing need for systemic therapies as a first-line treatment for advanced-stage HCC, including diffuse or disseminated multinodular HCC without vascular invasion [5].

However, advanced HCC has a diverse spectrum, with a variable distribution (localized or diffuse) or extents of parenchymal tumor and vascular invasion [19]. Localized disease with limited vascular invasion is advantageous for locoregional therapies. A Korean single-center phase II randomized controlled trial showed that the combination of cTACE with external beam radiotherapy was superior to sorafenib in terms of overall survival [20]. Therefore, in the 2022 update of the KLCA-NCC guidelines, cTACE combined with external beam radiotherapy or cTACE alone are regarded as a few of the best options alongside first-line systemic therapy for advanced HCC with vascular invasion. To define the best option for advanced HCC, it is necessary to compare new first-line systemic therapies with locoregional therapy alone or in combination, considering the diverse disease spectrum.

In the 2022 update of the KLCA-NCC guidelines, TARE was suggested as an alternative option for localized diseases such as a single tumor, multiple tumors involving a localized area of the liver, and branch portal vein invasion (Vp1–2). For these localized conditions, TARE can be performed selectively at tumor-feeding arteries, maximizing the antitumor effect by the local deliver of a high radiation dose. The risk of post-TARE decompensation can also be minimized by preserving the normal liver parenchyma as much as possible.

Key words

HCC; KLCA-NCC; Guideline; Recommendation; Embolization; Radioembolization; Drug-eluting bead

Availability of Data and Material

Data sharing does not apply to this article as no datasets were generated or analyzed during the current study.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

ORCID iDs

In Joon Lee
https://orcid.org/0000-0002-5779-5153
Ho Jong Chun
https://orcid.org/0000-0003-4512-6152
Jin Wook Chung
https://orcid.org/0000-0002-1090-6872

Funding Statement

None

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