EDITORIAL

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Selecting the Right Tool for the Right Job: Which Response Criteria Better Predicts Survival of Patients Treated with Transarterial Radioembolization?

Bo Hyun Kim

Division of Gastroenterology, Department of Internal Medicine, Center for Liver and Pancreatobiliary Cancer, National Cancer Center, Goyang, Korea

See "The Modified Response Evaluation Criteria in Solid Tumors (RECIST) Yield a More Accurate Prognoses Than the RECIST 1.1 in Hepatocellular Carcinoma Treated with Transarterial Radioembolization" by Jae Seung Lee, et al. on page 765, Vol. 14, No. 6, 2020

Improving survival is the main goal of all anticancer therapy, but estimating overall survival is not easy because it necessitates a relatively long follow-up period. Furthermore, the impact of a certain therapy on overall survival is diluted by subsequent treatments for progression. Thus, evaluation of tumor response is a surrogate indicator to identify which patients are most likely to benefit from, and survive longer after receiving, anticancer therapy. Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 is considered the standard for response evaluation in most solid cancers.

Hepatocellular carcinoma (HCC) is a hypervascular tumor, and although normal liver parenchyma receives a dual blood supply from the hepatic artery and portal vein, HCC is mostly supplied by the hepatic artery, enabling transarterial therapy via this vessel. Transarterial chemoembolization (TACE) combines regional chemotherapy and embolization of the feeding artery, which results in necrosis of the embolized area. The goal of TACE is to directly induce tumor necrosis; however, it does not always lead to tumor shrinkage, especially in the short-term.

The World Health Organization (WHO) criteria and RECIST criteria were designed to evaluate the response to cytotoxic chemotherapy. The original RECIST criteria evaluated only the reduction in tumor size and did not take into consideration the presence of necrosis. In 2010, the modified RECIST criteria were developed for HCC. These criteria introduced the concept of tumor viability, thereby accounting for tumor necrosis. The European Association for the Study of the Liver (EASL) criteria also assess viable tumor bidimensionally.

Viable tumor size-based criteria (modified RECIST and EASL criteria) have demonstrated good correlation with overall survival in patients receiving TACE.[1] For conventional or drug-eluting bead TACE, the EASL and modified RECIST criteria correlated better with overall survival than did RECIST 1.1 criteria.[2,3] Clinical guidelines have recommended using modified RECIST criteria to assess response to locoregional therapy in HCC.[1,4] However, these criteria have not been thoroughly investigated for transarterial radioembolization (TARE), a newer method of transarterial therapy.

In this issue of *Gut and Liver*, Lee *et al*.[5] compared the RECIST 1.1 and modified RECIST criteria to predict overall survival in patients with HCC receiving TARE. The modified RECIST criteria successfully predicted better overall survival, whereas the RECIST 1.1 criteria failed to demonstrate any correlation with survival outcomes. Responders who had a complete response or partial response according to modified RECIST criteria at 1 month or 3 months after TARE exhibited significantly better survival than non-responders.[5] The best response, defined as the most favorable response during the first 6 months after TARE, also predicted longer survival when using modified RECIST criteria.

Successful radioembolization will eventually induce tumor shrinkage; therefore, whole tumor size-based criteria (WHO and RECIST 1.1 criteria) would ultimately be helpful for predicting survival outcome.[6] However, these criteria can take up to 4 to 6 months to capture tumor response since tumor shrinkage occurs slowly following TARE.[7] Moreover, treatment-related intratu-

Correspondence to: Bo Hyun Kim
Division of Gastroenterology, Department of Internal Medicine, Center for Liver and Pancreatobiliary Cancer, National Cancer Center, 323 Ilsan-ro Ilsandong-gu, Goyang 10408, Korea
Tel: +82-31-920-1758, Fax: +82-31-920-2798, E-mail: bohkim@ncc.re.kr
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moral hemorrhage, peritumoral edema, and necrosis can induce a paradoxical increase in tumor size, which may confound accurate response evaluation.[6] By contrast, viable tumor size-based criteria can identify responders earlier (at 2 to 3 months following TARE) and better discriminate individuals with longer survival.[7,8] Adopting whole tumor size-based criteria instead of viable tumor size-based criteria may have contributed to failure to demonstrate a correlation between tumor response and overall survival in large phase III clinical trials of TARE.[9,10]

One limitation of viable tumor size-based criteria is that they may overestimate tumor response because hyperattenuating lipiodol deposition during conventional TACE may mask viable portions of tumor. However, TARE uses a radioactive isotope instead of an emulsion of chemotherapeutic agent and lipiodol. Another limitation of viable tumor size–based criteria is intra- and interobserver variability. Although both intra- and interobserver variability have been reported as acceptable for HCC treated with TARE, this variability necessitates caution when interpreting treatment response.[11] Furthermore, viable tumor size-based criteria require an optimized and consistent imaging protocol to obtain high-quality enhancement images. Inappropriate arterial phase imaging can hamper accurate evaluation of enhancing lesions.

As with other transarterial therapies, it is apparent that the modified RECIST criteria outperform RECIST 1.1 criteria for predicting patients most likely to benefit from TARE. However, optimization of image quality and reproducibility are necessary to overcome potential limitations.

CONFLICTS OF INTEREST

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

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ORCID

Bo Hyun Kim https://orcid.org/0000-0001-8355-3126

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