Drug-Eluting Beads Versus Conventional TACE

Where do we stand in the transcatheter treatment of patients with hepatocellular carcinoma?

BY RICCARDO LENCIONI, MD

Transcatheter arterial chemoembolization (TACE) is the current standard of care for patients with large or multinodular hepatocellular carcinoma (HCC). A cumulative meta-analysis of all published randomized controlled trials (RCTs) indicates that patient survival is significantly improved by this therapy. In addition, TACE is widely used to treat recurrent HCC after previous curative resection or percutaneous ablation. Nevertheless, the long-term outcomes of patients managed with conventional TACE regimens—based on the administration of an emulsion of lipiodol/Ethiodol (Guerbet, Villepinte, France) with doxorubicin or cisplatin and an embolic agent—remain unsatisfactory. In RCTs, a sustained response lasting > 3 to 6 months was observed in only 27% to 35% of cases, and in nonresponders, no survival benefit was identified in comparison to the best supportive care. Among patients in whom initial response is achieved, the 3-year cumulative rate of intrahepatic recurrence reached 65%, with recurrent tumors showing a significantly shorter median doubling time. Overall, the 3-year survival rate of TACE-treated patients did not exceed 26% to 29%, even in the RCTs that have shown a survival benefit.

The ideal TACE scheme should allow maximum and sustained concentration of the chemotherapeutic drug within the tumor with minimal systemic exposure combined with calibrated tumor vessel obstruction. Recently introduced embolic microspheres have the ability to actively sequester doxorubicin hydrochloride from a solution and release it in a controlled and sustained fashion. They have been shown to substantially diminish the amount of chemotherapy that reaches the systemic circulation compared with lipiodol-based regimens, thus significantly increasing the local concentration of the drug and the antitumoral efficacy.

Recent RCT Data

In a multicenter RCT including 201 European patients (PRECISION V), the use of DC Bead resulted in a marked and statistically significant reduction in liver toxicity and drug-related adverse events compared with conventional TACE.

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in the residual surviving cancerous tissue and induces expression and subsequent angiogenesis. Moreover, TACE increased vascular endothelial growth factor production.

**FUTURE PROSPECTS**

Tumor recurrence after TACE is characterized by increased vascular endothelial growth factor production and subsequent angiogenesis. Moreover, TACE increases vascular endothelial growth factor expression in the residual surviving cancerous tissue and induces expression of other proangiogenic factors, such as hypoxia-inducible factor 1 alpha. Based on these findings, the combination of TACE and agents with antiangiogenic properties would appear to be a rational approach. The first large studies in which an interventional locoregional treatment is evaluated in combination with a systemically active molecular-targeted drug are currently ongoing. In particular, a large RCT, the SPACE (Sorafenib or Placebo in Combination With TACE) study, is aimed at comparing DC Bead TACE plus placebo versus DC Bead TACE plus sorafenib, a multitargeted inhibitor with antiangiogenic and antiproliferative properties. The results of these investigations are eagerly awaited because they have the potential to further increase the impact of transcatheter treatment with drug-eluting beads on patient survival.

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