Hepatic Arterial Infusion Chemotherapy versus Trans-arterial Chemoembolization in Unresectable Hepatocellular Carcinoma: A Systematic Review and Meta-Analysis

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Introduction: Trans-arterial chemoembolization (TACE) has been one of the standard options for patients with unresectable hepatocellular carcinoma (HCC). Recent studies have shown that liver arterial infusion chemotherapy (HAIC) has favorable outcomes in these patients, but its use has been limited due to the need for technical expertise. In this systematic review and meta-analysis, we compared the efficacy and safety of HAIC vs. TACE for unresectable HCC.

Methods: We performed a comprehensive literature search of PubMed, Embase, and Cochrane databases through January 12, 2022, for all peer-reviewed studies that compared the outcomes of HAIC vs. TACE in patients with large, unresectable HCC. Our primary outcomes were the objective response rate (ORR), disease control rate (DCR), and progressive disease (PD). The secondary outcomes were overall survival (OS), progression-free survival (PFS), and grade ≥3 adverse events (AEs). Pooled risk ratio (RR) and hazard ratio (HR) with the corresponding 95% confidence intervals (CIs) were obtained by the Mantel-Haenszel method within a random-effect model. Heterogeneity was assessed using the Higgins I2 index.

Results: Six studies (one randomized controlled trial [RCT], two non-randomized trials, and three retrospective cohort studies) were eligible for final analysis. A total of 899 patients were included for the final evaluation. HAIC was associated with significantly higher ORR (RR 2.70, 95% CI 2.06-3.55, P<0.001, I2=10.1%) and DCR (RR 1.42, 95% CI 1.19-1.70, P<0.001, I2=54.5%) and substantially reduced PD (RR 0.55, 95% CI 0.40-0.75, P<0.001, I2=56.6%) compared to TACE. The median OS was significantly longer in the HAIC group, ranging from 11.4 to 23.1 months vs. TACE, ranging from 4 to 16.1 months (HR 0.49, 95% CI 0.28-0.85, P=0.01 I2=84.7%). The median PFS was significantly longer in the HAIC group, ranging from 5.5 to 9.6 months, vs. TACE, ranging from 1.5 to 5.4 months (HR 0.45, 95% CI 0.26-0.79, P=0.001, I2=84.6%). Notably, the incidence of grade≥3 AEs was lower in the HAIC group than in TACE (RR 0.61, 95% CI 0.47-0.80, P<0.001, I2=16.4%).

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Conclusion: Compared to TACE, HAIC significantly improved ORR, DCR, and OS in unresectable HCC with a significantly better safety profile. However, our meta-analysis is hampered by the limited number of studies. Future large-scale multicenter RCTs are warranted to further evaluate the outcomes of HAIC vs. TACE in the management of unresectable HCC.

