Clinical Practice in Intermediate Hepatocellular Carcinoma in the Real World

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Hepatocellular carcinoma (HCC) is the second most common type of cancer and the second leading cause of cancer-related death worldwide. According to international guidelines, staging HCC is critical for determining the appropriate treatment strategy. Stage B HCC, also known as intermediate stage or Barcelona Clinic Liver Cancer (BCLC) stage B HCC, is characterized by the presence of multiple tumorous lesions confined to the liver.[1–3]

Intermediate stage HCC is the most prevalent stage of the disease and affects the greatest number of patients. Trans-arterial chemoembolization (TACE) is the most frequently used therapeutic approach in these patients, but there is a significant disconnect between clinical practice and guidelines. Numerous therapeutic strategies, including radio-embolization followed by radical resection, have been reported for such patients. Most contraindications to TACE stem from the patients' impaired liver function and progression of pre-existing liver disease. HCC is primarily associated with viral hepatitis, most commonly HBV or HCV infections, in eastern and Asian countries.[4,5]

It is mainly caused by alcoholic liver disease in western countries. Cirrhosis's etiology has been shown to affect patients with HCC's prognosis. HBV is responsible for 54.4 % of all diagnosed cases of HCC worldwide. Around 55% of HCV-infected patients were alcoholics, according to the report.[6,7]

A study of Hasan et al (2022) using HCC patients database from 2013 to 2016 in Cipto Mangunkusumo Hospital and Dharmais Cancer Hospital include the patients with intermediate-stage HCC. A total of 456 patients were diagnosed with HCC, but only 151 (33.1%) patients with intermediate-stage HCC were included. Fifty-four patients (35.7%) were treated with TACE as first-line treatment. Overall median survival was 617 days (1.7 years).[8]

A Metanalysis to compare effectiveness of different transarterial embolization therapies alone or in combination with local ablative or adjuvant systemic treatments for unresectable hepatocellular carcinoma showed the median survival period with best supportive treatment alone was 13.9 months (95% CI: 11.0–17.7), but increased to 18.1 months (95% CI: 15.6–21.6) with TACE, 20.6 months (95% CI: 14.5–29.4) with DEB-TACE, and 20.8 months (95% CI: 16.2–27.1) with bland TAE. Adjuvant systemic agents did not improve survival significantly when compared to transarterial therapies. In the case of TARE, the median survival increased to 24.3 months (95% CI: 16.8–35.3). When conventional TACE was combined with external radiotherapy (30.1 months; 95% CI: 24.6–37.3) or percutaneous liver tumor ablation (33.3 months; 95% CI: 26.4–42.5), projected median survival exceeded 30 months.[9]

According to current BCLC staging, intermediate stage HCC is characterized by a heterogeneous patient population with varying tumor burdens. While significant advances have been made in advanced stage HCC, TACE remains the standard of care for the intermediate group and is considered palliative. Other treatments ranging from curative (resection, LT, ablation) to those used in advanced disease (systemic agents) have all demonstrated promise in subgroups of patients, making it difficult to make broad recommendations across the stage. To optimize patient outcomes in this group, additional research is needed to determine when and how to use these treatments, as well as how to best subclassify the intermediate stage.

REFERENCES

1. Levi Sandri GB, Ettorre GM, Aldrighetti L, Cillo U, Dalla Valle R, Guglielmi A, et al. Laparoscopic liver resection of hepatocellular carcinoma located in unfavorable segments: a propensity score-matched analysis from the I Go MILS (Italian Group of Minimally Invasive Liver Surgery) Registry. Surg Endosc 2019;33:1451–8.
2. Golfieri R, Bargellini I, Spreafico C, Trevisani F. Patients with Barcelona Clinic Liver Cancer Stages B and C hepatocellular carcinoma: time for a subclassification. Liver Cancer 2019;8:78–91.
3. Galle PR, Tovoli F, Foerster F, Wörns MA, Cucchetti A,

Bolondi L. The treatment of intermediate stage tumours beyond TACE: From surgery to systemic therapy. J Hepatol 2017;67:173–83.
4. Guo W, He X, Li Z, Li Y. Combination of transarterial chemoembolization (TACE) and radiofrequency ablation (RFA) vs. surgical resection (SR) on survival outcome of early hepatocellular carcinoma: a meta-analysis. Hepatogastroenterology 2015;62139:710–4.
5. Iezzi R, Cesario V, Siciliani L, Campanale M, de Gaetano AM, Siciliano M, et al. Single-step multimodal locoregional treatment for unresectable hepatocellular carcinoma: balloon-occluded percutaneous radiofrequency thermal ablation (BO-RFA) plus transcatheter arterial chemoembolization (TACE). Radiol Med 2013;118:555–69.
6. Budny A, Kozłowski P, Kamińska M, Jankiewicz M, Kolak A, Budny B, et al. [Epidemiology and risk factors of hepatocellular carcinoma]. Pol Merkur Lekarski 2017;43:133–9.
7. Ghouri YA, Mian I, Rowe JH. Review of hepatocellular carcinoma: epidemiology, etiology, and carcinogenesis. J Carcinog 2017;16:1.
8. Hasan I, Loho IM, Lesmana CR, Gani RA, Siregar L, Waspodo AS, et al. Treatment for Intermediate-stage Hepatocellular Carcinoma: Current Practice and Outcome in Real World Study. Indones J Gastroenterol Hepatol Dig Endosc 2022;23:24-8.
9. Katsanos K, Kitrou P, Spiliopoulos S, Maroulis I, Petsas T, Karnabatidis D. Comparative effectiveness of different transarterial embolization therapies alone or in combination with local ablative or adjuvant systemic treatments for unresectable hepatocellular carcinoma: A network meta-analysis of randomized controlled trials. PLoS One 2017;12:e0184597.