



Editorial

Transarterial chemoembolization as adjuvant treatment after surgery: The cure of huge hepatocellular carcinoma?

Andrea Chierici^a, Andrew Ofosu^b, Ivan Cincione^c, Rodolfo Sacco^d, Christian Cotsoglou^a, Antonio Facciorusso^{d,*}

^a General Surgery Department, ASST-Vimercate, Vimercate 20871, Italy

^b Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Stanford, CA 94305, United States

^c Department of Clinical and Experimental Medicine, University of Foggia, Foggia 71122, Italy

^d Department of Surgical and Medical Sciences, Gastroenterology Unit, University of Foggia, Viale Pinto, 1, Foggia 71122, Italy

Hepatocellular carcinoma (HCC) represents the sixth common cancer and the second leading cause of cancer-related death. Its incidence is higher in Eastern countries. HCC is frequently detected at advanced stage of disease, and therefore, the mortality is high [1].

Huge HCC has always been considered one of the most challenge issues for both hepatologists and surgeons. Although in the past it was considered above any potential treatments, in the last two decades we have been facing an impressive growth in literature concerning novel therapeutic strategies due to the development of surgical and non-surgical approaches. Huge HCC is not just a larger liver tumor, but it can somehow be considered as a more aggressive subtype of HCC for its intrinsic pathologic features. In fact, it is frequently accompanied by other negative prognostic factors such as vascular invasion, portal vein thrombosis, absence of tumor capsule and multifocality [2,3]. Surgical approach, liver resection or liver transplantation, still represents the gold standard for HCC treatment when feasible; unfortunately, huge HCC is not eligible for liver transplantation based on the currently available inclusion criteria: Milan [4] and Up-to-Seven criteria [5]. Moreover, its wide extension often demands major (and sometimes non-anatomical) liver resections that expose the patient to a high risk of intraoperative and postoperative threatening complications such as major bleeding and post-hepatectomy liver failure (PHLF), increased by several prognostic factors such as the underlying liver chronic disease and cirrhosis [6]. In these situations, R1 or R2 resections are not rare. A recent meta-analysis [7] conducted on 13 studies comparing liver resection for non-huge and huge HCC and including minor and major resections for both groups demonstrated no significant differences in surgery-related morbidity and mortality. On the other hand, huge HCC is related to worse 1-year, 3-year and 5-year recurrence-free survival (RFS) and overall survival (OS).

Many other treatments such as transcatheter arterial chemoembolization (TACE), stereotactic body radiotherapy (SBRT), and ra-

diofrequency or microwave ablation (RF/MWA) have been introduced to manage HCC avoiding liver resection. However, TACE alone is not found to be superior to surgery [8] in huge HCC and ablative treatments are effective in treating small and early-stage cancers while their local control rate decreases with larger and more advanced-stage tumors [9].

In the last few years, the need of a multimodality approach for liver cancer to improve the treatment outcomes has become increasingly prominent. This philosophy, in the field of huge HCC, has been particularly focused on the association between TACE and liver resection. A Chinese multicenter propensity matching analysis [10] evaluated the effects of preoperative TACE demonstrating no increase in perioperative morbidity and mortality and longer OS and RFS. As reported in the article by Wang et al. [11], postoperative adjuvant TACE is proven to be effective in improving OS and RFS in low- and intermediate-stage HCC but there is no evidence in literature related to huge HCC.

Wang et al. added an important piece of the puzzle to the treatment of HCC and highlighted the importance of multimodality to achieve the best possible results in term of disease recurrence and OS [11]. They conducted a propensity matching analysis on two cohorts of patients ($n = 138$) who received or did not receive postoperative TACE after R0 liver resection for huge HCC. They demonstrated that postoperative TACE represents an effective treatment that can destroy residual tumor cells after liver resection, significantly increasing the 1-, 3-, 5- and 7-year RFS and OS and reducing early recurrence (< 2 years). Using a propensity matching analysis and focusing only on huge HCC, the authors reduced the possible inclusion bias producing strong evidences on the benefits of postoperative TACE.

Multimodality represents the way forward to achieve the best possible treatment for patients with advanced HCC [12,13]. Randomized-controlled trials evaluating the association between TACE and surgery and studies comparing the benefits of radiotherapy with surgery and other non-surgical strategies are required to explore further effective treatments in hepato-oncology.

* Corresponding author.

E-mail address: antonio.facciorusso@virgilio.it (A. Facciorusso).

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Andrea Chierici: Conceptualization, Data curation, Writing - original draft, Writing - review & editing. **Andrew Ofosu:** Writing - original draft, Writing - review & editing. **Ivan Cincione:** Writing - review & editing. **Rodolfo Sacco:** Writing - review & editing. **Christian Cotsoglou:** Writing - review & editing. **Antonio Facciorusso:** Writing - original draft, Writing - review & editing.

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