Reviewer 1:

The authors present the largest cohort to date of patients with HCC > 10cm diameter undergoing resection for cure and compares with patients from the same cohort who underwent TACE at the same group of 7 hospitals. 426 resected patients with tumors > 10 cm were compared to 361 similar patients treated with TACE. The resection group had superior overall and disease free survival at 1,3 and 5 years and lower 30 and 90 day mortality. The major challenge with this most important part of the paper is that the groups were not randomly selected for the different treatments but the authors have not clearly outlined why resection vs TACE was selected for particular patient groups, although they give enough data to clearly show that the groups were not the same. TACE patients were older, more advanced in staging by both AJCC and BCLC, and had poorer biochemistry. While they applied the IPTW to correct for differences in liver function and other discrepant characteristics, they should address the significant weakness of comparing apples and oranges. In the end, they demonstrate that surgical resection is preferable if it can be accomplished, but have not given much insight into which patients they would consider for resection. Of interest, they document that resection was superior even in BCLC stage B patients. They also suggest a new category of stage T1 to recognize that the outcomes in these very large tumors are poorer. The other two analyses look at outcomes with resection of tumors < 10 cm vs > 10 cm and present a substantial number of outcomes that are very much as would be expected: smaller tumors had lower operative mortality, and better 5 year overall and disease free survival. The last analysis looks at outcomes in the recent era as compared to an earlier cohort and again no real surprises as they demonstrate lower mortality and better outcomes in recent years.

Answer:

Thanks for the reviewer's precious suggestions. We have addressed the significant weakness of comparing resection vs. TACE and outlined the selection criteria for resection in the revised manuscript, as follows.

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"**Disscussion**

…. Despite remarkable findings, the current study still has several limitations. As mentioned above, since the most appropriate treatment modality for huge HCC has not been established, the management disposition (i.e., surgery or TACE for L-HCC) was based on the discretion of individual physician in the current study. As a result, the background demographics and biochemical profiles were heterogeneous between

the surgical and TACE group. This heterogeneity was a significant weakness and rendered the statistics biased….."

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"**Discussion**

…. As a result, with acceptable performance status and liver functional reserve (i.e., ECOG 0-1, Child-Pugh A, ICG-15 < 10%, absence of Vp4 invasion, and future liver remnant >30%), we suggest liver resection should be performed for single huge HCC larger than 10cm or huge HCC with limited daughter nodules confined in the same lobe."

Editorial Office's Comment

5 Issues raised: (1) The "Author Contributions" section is missing. Please provide the author contributions; (2) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s); (3) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (4) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout; (5) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text; and (6) The scientific quality can't meet the requirement of WJG 6 Recommendation: Transferring to the World Journal of Hepatology.

Answer:

Thanks for the editor's comments. The manuscript has been amended according to the suggestions.

(1) Authors' contributions

CWL designed the study, conducted the research, and drafted the manuscript. MCY, CCW, and WCL performed the operations, formulate the concept, supervised the study, and revised the manuscript. HIT and FCK confirmed the statistics, interpreted the data, and revised the manuscript. CWC and YCH collected the data and analyzed the results. HYC coordinated the entire study, performed the statistics, and approved the manuscript. All authors read and approved the final manuscript.

(2) The funding agency copy of the approval document was uploaded.

(3) The original figures arranged in PowerPoint document were uploaded.

(4) The reference list was revised to provide the PubMed numbers, DOI citation numbers, and all authors of the references.

(5) **Article Highlights**

Research background

The treatment of hepatocellular carcinoma (HCC) larger than 10cm remains challenging. The Chang Gung Research Database (CGRD) contains all medical records of the Chang Gung Memorial Foundation (CGMF) and has become one of the largest clinical databases worldwide. By utilizing the data from CGRD, we attempted to analyze the outcome of HCC larger than 10cm.

Research motivation

Owing to advancement in surgical technique and perioperative care, the surgical risks associated with liver resection are decreasing in the recent decades. However, the surgical outcome regarding HCC larger than 10cm has not been updated.

Research objectives

We aimed to consolidate the role of surgical resection for HCC larger than 10cm. The survival outcomes between surgery and transarterial chemoembolization (TACE) were also compared.

Research methods

Eligible HCC patients were identified from the CGRD, and two models were adopted: the surgical outcome between HCC ≥ 10 cm (L-HCC) and HCC < 10cm (S-HCC) (model 1); the survival of L-HCC after either liver resection or TACE (model 2). To eliminate the potential confounding bias originating from heterogeneous baseline features and disproportionate case numbers, inverse-probability of treatment weighting (IPTW) between different groups was adopted.

Research results

Although worse than the S-HCC, the surgical and long-term oncological outcome of L-HCC had improved in the recent decades. Moreover, surgery could provide a better survival outcome for L-HCC than TACE.

Research conclusions

With acceptable performance status and liver functional reserve, we suggest liver resection should be conducted for HCC larger than 10cm. Due to its inferior survival, T1 stage should be further sub-divided to precisely predict patient outcome.

Research perspectives

The current study demonstrated the inferior survival of L-HCC. The necessity of adjuvant therapy following liver resection for L-HCC should thus be determined by further randomized controlled trials.