

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 76626

Title: Identification of predictive factors for post-transarterial chemoembolization (TACE) liver failure in hepatocellular carcinoma patients: A retrospective study

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02539765

Position: Peer Reviewer

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: India

Author's Country/Territory: China

Manuscript submission date: 2022-03-23

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-24 16:42

Reviewer performed review: 2022-04-02 03:35

Review time: 8 Days and 10 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
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SPECIFIC COMMENTS TO AUTHORS

In the treatment of HCC patients, post-TACE liver failure is a major concern. The authors' conclusion in a retrospective analysis that microsphere plus gelatin embolization is a risk factor for the development of post-TACE liver failure in HCC patients is a relevant finding. I have only few comments about this paper. As already highlighted by the authors, there is no uniform/standard definition of post-TACE liver failure, making it difficult to interpret the results compare them with other studies. The inclusion of "increase in ascites" in the definition brings subjectivity, which needs to be addressed in the discussion. Over 90% of HCC patients in both groups were cirrhotic. Were there any differences in the severity of cirrhosis (e.g., CTP/MELD scores) between the two groups?

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02526287

Position: Editorial Board

Academic degree: MD

Professional title: Medical Assistant

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2022-03-23

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-04-05 09:05

Reviewer performed review: 2022-04-15 16:07

Review time: 10 Days and 7 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input checked="" type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

We read with interest the paper entitled “ Identification of predictive factors for post-transarterial chemoembolization (TACE) liver failure in hepatocellular carcinoma patients: a case-control study” by Min Yuan et al. it is a retrospective case-control study carried out on 199 HCC patients undergoing TACE, 70 of whom developed post-TACE liver failure. The authors retrospectively analyzed data from these patients and concluded that microsphere plus gelatin embolization and main tumor size > 5 cm were risk factors for post-TACE liver failure while previous history of HCC resection could protect from this complication. Although the authors addressed an interesting issue in the field of HCC treatment, the paper has several drawbacks that limit its scientific impact Study design is retrospective According to standard statistical definition the present study cannot be defined as a case-control study. This is a retrospective observational study carried out on an unselected cohort of patients undergoing TACE with or without post TACE liver failure. As stated in materials and methods, microspheres and gelatin sponge particles were administered only to patients with HCC > 5 cm. Thus, these two variables are redundant and should not be included together in univariate and multivariate analysis since they identify the same patient. The two groups of patients are very inhomogeneous as to the treatment received in association with TACE and this make difficult to compare them as to the end point of post-TACE liver failure According to the above-mentioned statistical drawbacks, this study is not reliable to build up a predicting risk model. Moreover, every predicting model should be internally and externally validated in ad hoc different cohorts beside the original training cohort before being proposed for clinical employment. Looking at



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the ROC diagrams the accuracy performance of this predicting risk model is quite low ((never exceeding the value of 0.6) According to international guidelines, vascular invasion is a well-known contraindication for TACE and some patients with vascular invasion were included in the study. According to BCLC algorithm patients with extrahepatic metastases are not suitable for TACE. To better understand the results, patients should be staged in keeping with BCLC staging system. The authors should specify how many patients belonged to intermediate and how many belonged to advanced stage. In table 1 Child-Pugh score should be reported (as % of patients belonging to A,B,C class, and mean value) Language and style deserve a mother-tongue deep revision

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05231749

Position: Peer Reviewer

Academic degree: PhD

Professional title: Doctor

Reviewer's Country/Territory: France

Author's Country/Territory: China

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Reviewer chosen by: AI Technique

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Reviewer performed review: 2022-04-18 11:20

Review time: 9 Days and 4 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

This is an interesting and well-written real-life study that highlights the relevance of the technique and the importance of patient selection regarding transarterial chemoembolization (TACE) as a treatment for hepatocellular carcinoma (HCC). The message is clearly expressed; a double embolization technique to treat large size HCC tumors (> 50 mm) is prone to severe complications. Large size HCCs (> 50 mm) not suitable for surgery are difficult tumors to treat, as they are frequently associated with tumor microinvasion, which results in TACE failure. Improving the chemoembolization technique is a solution, but this study clearly shows the limits of the technique. This is the main interest of the current strategies which consist in combining treatments (Kudo et al, TACTICS trial. Gut. 2019), or proposing a systemic treatment in first intention (Reig et al, « BCLC strategy for prognosis prediction and treatment recommendation », J Hepatol 2022), with chemoembolization secondarily, to treat the residuals. We have moved from "palliative" chemoembolization aimed at slowing tumor progression to "curative" chemoembolization aimed at achieving complete tumor necrosis, with radiological response correlated to survival (Gillmore R et al, EASL and mRECIST responses are independent prognostic factors for survival in hepatocellular cancer patients treated with transarterial embolization. J Hepatol. 2011). In this context, patient selection with non-surgical hepatocellular carcinoma using an up-to-seven criteria model (as highlighted by the authors through reference #3 Giannini et al AJG 2016) or a score (HAP score : Kadalayil et al, Ann Oncol 2013), are methods to avoid this post chemoembolization toxicity. As the authors remind us in the discussion, the criteria associated with overtotoxicity are well identified and should be taken into account for the



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treatment strategy. In this study, a majority of patients had cirrhosis; non-tumor portal thrombosis was reported in nearly 20% of patients, and there were also patients with pre-treatment ascites (table 1). The abstract is pertinent, the introduction correctly states the problem. The embolization method (procedure) is well explained, the presentation of the results is clear. The descriptive study is associated with a multivariate analysis, which supports the results. Finally, the authors propose a nomogram as an aid to decision making. The discussion is well conducted; no alternative solution is envisaged to treat these large size lesions (> 50 mm), but this is not the purpose of the article. It is necessary to check whether the presentation of the references corresponds to that requested by the journal (PMDI to be cited)

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Manuscript NO: 76626

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02526287

Position: Editorial Board

Academic degree: MD

Professional title: Medical Assistant

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2022-03-23

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2022-06-13 07:03

Reviewer performed review: 2022-06-13 07:40

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

All the issues raised by the reviewer have been successfully addressed