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PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 87252

Title: ANY ROLE FOR TRANSARTERIAL RADIOEMBOLIZATION (TARE) IN UNRESECTABLE INTRAHEPATIC CHOLANGIOCARCINOMA (iCCA) IN THE ERA OF ADVANCED SYSTEMIC THERAPIES?

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06144658

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2023-08-01

Reviewer chosen by: Geng-Long Liu (Quit 2023)

Reviewer accepted review: 2023-09-02 02:40

Reviewer performed review: 2023-09-05 07:26

Review time: 3 Days and 4 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input checked="" type="checkbox"/> Grade D: No novelty



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Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input checked="" type="checkbox"/> Grade D: No creativity or innovation
Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" 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 type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" 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

This manuscript lacks innovation

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05723533

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Professor, Doctor, Surgeon, Surgical Oncologist

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2023-08-01

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-09-08 08:53

Reviewer performed review: 2023-09-09 11:00

Review time: 1 Day and 2 Hours

Scientific quality	<input checked="" 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 type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty

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

SPECIFIC COMMENTS TO AUTHORS

It is a high quality mini-review. Authors reviewed more than 30 published papers and concluded that TARE may have a role in the treatment of iCCA, either as a standalone treatment or in combination with systemic chemotherapy. However, I have some comments. 1. "Epidemiology, clinical characteristics and treatment of CCA" should be condensed as it is a mini-review. The repetitious details need not be given here. 2. "TARE as a therapeutic strategy in hepatocellular carcinoma (HCC)" should be an essential part, which is helpful for readers to get a better understanding of TARE. As the knowledge of foreshadowing, this part needn't to be long, just be concise and to the point. 3. The first column in Table 1 &2 should be written with reference number (in brackets). 4. The latest papers should be cited (10.1016/j.jvir.2023.07.028, 10.1016/j.jvir.2023.05.026). The α -particle-emitting transarterial radioembolization (α TARE) should be generically mentioned (10.1186/s41181-023-00205-3).

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05106340

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2023-08-01

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-09-25 07:04

Reviewer performed review: 2023-09-29 08:55

Review time: 4 Days and 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
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty

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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

The manuscript offers a comprehensive overview of the epidemiology, clinical manifestations, and therapeutic approaches for intrahepatic cholangiocarcinoma (iCCA). Specifically, the manuscript delineates the technology of transhepatic arterial radioembolization (TARE), both as a standalone modality and in conjunction with systemic chemotherapy, CT-HDRBT, among other treatments. Furthermore, the work delves into the therapeutic strategy of TARE in managing unresectable iCCA, highlighting its efficacy, safety, and the variables contributing to prognostic determinations. The article's clinical implications are evident, with a commendably coherent structure and succinct prose. However, there are several points that warrant further elaboration and clarification: 1. While the manuscript provides an introduction to the TARE technology, there's a noticeable dearth of specific insights into its nuanced application in iCCA. The authors are encouraged to delve deeper into the operational

complexities of TARE, tailored specifically for iCCA scenarios, such as lobar or segmental perfusion? 2.It's widely recognized that iCCA is frequently associated with lymph node metastasis, an occurrence that is even more pronounced in advanced-stage patients. Given that TARE is primarily designed to address intrahepatic lesions, the authors should clarify their stance on concurrent management strategies. Specifically, how would one approach the treatment of patients presenting with both intrahepatic lesions and lymph node metastasis? 3.The manuscript does not shed light on the optimal radiation dosing guidelines for iCCA patients undergoing TARE. This omission is significant and should be rectified. 4.An essential aspect that requires elaboration is the identification of specific clinical attributes of iCCA that make patients viable candidates for TARE. The authors should contemplate incorporating this information into the manuscript. 5.A finer point, yet of potential clinical significance, is the selection of embolic agents and their infusion methodologies tailored for TARE in the context of iCCA. It would be beneficial if the authors could shed light on this aspect. 6.The information provided in Table 1 concerning the Median OS and radiologic response in iCCA treated with TARE is valuable. However, to provide a more robust understanding, the table should be expanded to encompass the number of cases, inclusion criteria, and operational techniques from various studies. Moreover, a nuanced analysis discussing the potential reasons behind the observed OS variations across studies would add depth to the research. In closing, while the manuscript is robust in its current form, addressing the aforementioned areas of concern will undeniably enhance its depth, comprehensiveness, and overall clinical relevance.