

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 49198

Title: Long-term outcomes of hepatocellular carcinoma that underwent chemoembolization for bridging or downstaging

Reviewer's code: 00761439

Reviewer's country: Greece

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-06-03 08:40

Reviewer performed review: 2019-06-03 18:28

Review time: 9 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is an interesting and well written paper regrading long-term outcomes of patients with hepatocellular carcinoma (HCC) who underwent liver transplantation (LT) after DEB-TACE for downstaging (those outside Milan criteria, n=64) versus bridging (those

within Milan criteria, n=136). The authors found no difference between downstaging and bridging: 5-year post-transplant overall survival was 73.5% in downstaging and 72.3% bridging groups ($p=0.31$), and recurrence-free survival was 62.1% in downstaging and 74.8% bridging groups ($p=0.93$). evaluated 200 patients (However, there are several issues which should be addressed by the authors 1) How the authors decided to create and evaluate group 4 pts. In addition, the number of patients in this group was too small for final conclusions 2) Can the authors clarify the terms “coagulopathy” and thrombocytopenia”? 3) AUC should be provided regarding the discriminative ability of max HCC diameter 4) Page 6: “...Post-transplantation recurrence occurred more frequently in the downstaging group 25% (5/20) than in the bridging group 5.81% (5/86) ($p=0.020$); however, these events did not significantly affect recurrence-free survival ($p=0.874$).” However, in the same page: “...Kaplan-Meier’s 1, 3, and 5-year post-transplant recurrence-free survival probability were 95%, 82.8%, 62.1% in the downstaging group, and 80.2%, 76.5%, 74.8% in the bridging group ($P=0.935$)..” . Why the p values were different? 5) Did the authors provide the drop out rates in each group? 6) The authors should provide the median values for variables without normal distribution. For example, AFP in Table 3? 7) Was AFP an exclusion criterion for LT or TACE? 8) An update in Refs is needed (e.g. Sinha J, et al. Hepatology. 2019)

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 49198

Title: Long-term outcomes of hepatocellular carcinoma that underwent chemoembolization for bridging or downstaging

Reviewer's code: 00051373

Reviewer's country: Taiwan

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-06-03 15:10

Reviewer performed review: 2019-06-04 15:34

Review time: 1 Day

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input checked="" type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

It is a very interesting topic to explore the DC bead TAE for down staging before liver transplantation and well manuscript written.



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7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 49198

Title: Long-term outcomes of hepatocellular carcinoma that underwent chemoembolization for bridging or downstaging

Reviewer's code: 00053950

Reviewer's country: Finland

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-06-06 06:31

Reviewer performed review: 2019-06-30 19:19

Review time: 24 Days and 12 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
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			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors present a study of 200 HCC patients treated with TACE before liver transplantation. The patients are divided in two groups depending on the intention of the treatment, bridging or downstaging. Both methods are widely adopted in the liver

transplant surgery but not thoroughly studied reflecting the importance of the study. Remarks: 1. The title is long-term outcome of HCC. However, the follow-up was only 3 years in the mean and as we well know HCC often recurs after this time period in LT patients. 2. The abstract summarizes adequately the work, but the conclusion is rather simplified and should be presented better in details. 3. Methods. Patients in the bridging group are within the Milan criteria and in the downstaging group there were patients even with the total tumor diameter beyond 8cm. Both groups were treated with TACE preLT and only patients within Milan criteria after TACE were transplanted. This fact should be clearly pointed out in the paper and in the abstract. 4. Results. The major finding of the study was that LT after downstaging of HCC to Milan criteria would give the same results as TACE in patient within Milan from the beginning. Could it be concluded that TACE is not needed for patients within Milan criteria? 5. How are the tumor status in the explanted livers taken in account? 6. The number of dropouts was high, 1/3 also in the MC-group. Why is that as they were treated with TACE? 7. There were about 7% Child C patients in the both groups. It is quite expected that such patients end readily up to dropouts? 8. Table 2. The level of AFP was as high as 22000 in some patient. Was AFP used as a criterion for treatment response? 9. Table 2. The highest amount of nodules was 9 and the maximal tumor diameter 17cm in the downstaging group. Was it realistic to get these patients to the Milan criteria? 10. Table 4. Quite many patients died in 30 days after LT even in the bridging group. Was any of these related to the TACE. The two columns right in the table seem to be unnecessary. 11. Table 7. It should be stated that patients with Child C or with AFP >1000 were not transplanted? P-values? 12. The discussion is clear and the shortages of the study have been noted.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 49198

Title: Long-term outcomes of hepatocellular carcinoma that underwent chemoembolization for bridging or downstaging

Reviewer's code: 00181520

Reviewer's country: Egypt

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-06-03 11:43

Reviewer performed review: 2019-06-30 21:11

Review time: 27 Days and 9 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Thank you for submitting this interesting study. I have a few minor comments: Page 3 line 8 : Could you please rephrase this sentence to clarify what you mean to say ? "It was identified a subgroup never before described, Group 4" Page 4 "DEB-TACE

protocol was previously described". This gives the impression that it was described in your manuscript above. Could you please clarify that it was previously described "in the literature" or by "Cavalcante et al and Nasser et al " or "by other investigators"? Page 5 "Eligibility". Could you please write "Eligibility for transplantation" ? Page 6 "Receiver operating characteristic curve analysis revealed that patients with maximal tumor diameter up to 7.05 cm are more likely ...". Please write "were" instead of "are". Page 9 line 4" Please replace " suchlike " with "just like" Page 9 last line "We recognize that the subgroup analysis is strongly limited by the low number of patients included in each subgroup." Try to complete this paragraph with "But " or "Nevertheless" and say the strengths of your study. I am surprised you performed DEB TACE for CTP score till 15. Didn't they decompensate further ? In table 2 please correct "trombocytopenia" to read "thrombocytopenia" Table 3: Please remove the column of "Total"

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