Reviewer’s report

Title: Liver function changes after transarterial chemoembolization in US hepatocellular carcinoma patients: The LiverT study

Version: 0 Date: 31 Mar 2019

Reviewer: Roman Kloeckner

Reviewer's report:

The authors present an interesting study investigating the deterioration of liver function after TACE in a US-based "real-life" cohort of nearly 4000 patients. As liver function is one of the most important factors determining the prognosis of such patients and also has great impact on possible subsequent therapies in case of TACE failure, the topic is clinically relevant.

The authors conclude that around 40% of the patients presented with acute and around 25% with chronic liver function deterioration.

Overall, the LiverT study is well conducted and the data analysis seems to be sound. There are only several minor issues that should be addressed prior to publication:

1. General comments
   - One major issue is the choice of parameters indicating loss of liver function. Especially AST and ALT are not quite optimal to assess liver function (deterioration). As this issue cannot be changed retrospectively, I suggest to discuss this issue in the limitation section in depth.
   - What was the rationale for choosing the worst value available to assess the acute period and the last value available in the chronic period? Due to natural fluctuations this leads to a possible overestimation of liver function loss in the acute phase, especially when compared to the chronic phase.

2. Specific comments (minor)

   Introduction:
   - Overall, the introduction is well-written and comprehensible. However, the first paragraph could be shortened to make it more concise. I believe the readers of BMC Cancer know most of the information given here.

   Patients & Methods:
   - Adequately describes study methodology
   - P5 l10: As this has significant impact on prognosis please be more specific regarding portal vein thrombosis: Did you differentiate between bland portal vein thrombosis (PVT) and portal vein tumor thrombosis (PVTT)? Please clarify.
   - P7 l 32 Why was the threshold for INR different in TACE and TARE? How is the longer observation period post-TARE connected with that?
Results:
- Overall, results are concisely presented
- Good readability due to subheadings
- P8 l 39-46: "Importantly, levels of AST and ALT were almost completely restored to baseline values in the chronic period,…": This is not really surprising as neither AST nor ALT are really good indicators for liver function but more for the extent of (acute) liver injury.

Discussion
- Overall, adequate discussion including several important issues and discussing the most relevant papers.
- Good structure and readability, comprehensible summary at the beginning.
- Limitations:
- Please discuss the fact that you did not provide detailed data on the selectivity of TACE (which you correctly mention at the beginning of the discussion) as there is evidence that a more selective approach leads to less liver damage.
- Although it is adequately discussed in the limitations section, the bias towards sicker patients remains a significant drawback. In most centers the treatment interval is 6-8 weeks and the exclusion of all patients receiving a second TACE within the first 3 months generates a selection bias. This could be one of the major reasons why the proportion of patients suffering from relevant deterioration was higher in your study compared to others.

Tables:
- Table 1: As stand-alone it is hard to understand the second part of table 1. Please consider splitting the table (into primary analysis using the respective parameters and sensitivity analysis) or explain more detailed in the table legend.
- Table 3 could be shortened by moving the respective patient numbers into a separate column between "Laboratory Parameter" and "Baseline (value closest to index TACE)" This would save one line per each parameter and improve readability.

Language:
- Overall, the manuscript is well written and comprehensible. The text is well structured using subheadings. Overall length is appropriate.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

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No competing interests

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