

June 21, 2015



Dear Editor,

I would like to thank the reviewers for their insight and comments. I have addressed each of their points below, and all changes made to the main document are highlighted in yellow.

Thank you very much for taking the time to review my article, and I hope that the changes made based on the comments/suggestions are satisfactory for publication in your journal.

Please find enclosed the edited manuscript in Word format (file name: 18028-review.doc).

Title: Portal vein embolization effect on colorectal cancer liver metastasis progression: lessons learned

Author: Eman Al-Sharif, Eve Simoneau, Mazen Hassanain

Name of Journal: *World Journal of clinical oncology*

ESPS Manuscript NO: 18028

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated per editor's suggestions

2 Revision has been made according to the suggestions of the reviewers

Reviewer #1:

1. English needs to be improved by professional writers. English language was revised and improved by native English speakers.

2. As a review, it will benefit from figures and tables, which make the technique more clear, and show its definition, procedures, efficiency, adverse effects, and challenges in corresponding report.

One figures was added to provide a general overview of clinical settings in which portal vein embolization may be used. Additionally, we added to this mini-review article a table summarizing the results of several studies describing the effect of PVE on tumor progression.

Reviewer #2:

1- Much of the paper deals with the increase of size of the lesions following PVE, but the authors should also discuss the potential clinical impact of such increase. Does the published data indicate that the increase result frequently in subsequent unresectability?

Several studies reported that some patients were deemed unresectable after PVE due to tumor progression or inadequate liver hypertrophy. We mentioned in this article that PVE affects patient overall survival because of its complications that include intrahepatic and extrahepatic tumor progression (references #19, 24 were added)

1- End of page 6, the author should add the p value regarding their previous study: "The study showed a positive TGR (+0.07 cm³/day) in the PVE group compared to a negative TGR (-0.06 cm³/day) in the control (no PVE) group"

P value was added to the text ($P < 0.001$)

2- Beginning of page 7. "This greatly influences clinicians' MANAGEMENT because it reduces the benefit gained from chemotherapy." I don't think that this statement is supported by the data, as the benefit of chemotherapy would be either to enable resection by downstaging (and the results presented does not show that PVE diminish that) or to provide long-term benefit by reducing recurrence (and PVE certainly enhance that by allowing for resection). I would recommend to modify this sentence.

The sentence was deleted

3- Second paragraph of page 8 " The next issue to be addressed is how can we abort the response of tumor progression post-PVE once it has been triggered? " From an oncological perspective, the terminology of "response of tumor progression" is misleading, I would suppress terms "the reponse of"

The phrase (response of) was removed

4- Regarding radioembolization, it was in fact proposed as an alternative to PVE rather than an addition to PVE. This may be modified.

The sentence was modified. We explained that radioembolization post-PVE might help in decreasing the risk of tumor progression since it decreases blood flow to the liver. Currently, data supporting the use of radioembolization as an adjunct treatment to PVE is still lacking.

In addition, we clarified that chemoembolization post-PVE significantly decreases the rate of tumor progression after PVE.

5- "In the light of current knowledge provided by those reports, researchers can carry out clinical trials to prove efficacy of these protective modalities in this category of patients." I'm unsure whether such trial would be feasible...

The sentence was removed

6- The ref n°14 and 15 are in russian and norwegian; for an international audience, I would suggest to delete them

These two references were deleted as recommended

3 Two reference was added (#19 and 24)

4 Audio core tip was created

Thank you again for publishing our manuscript in the *World Journal of Clinical Oncology*.

Sincerely yours,



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