

Peer Review File

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Reviewer Comments

I find the results and the conclusion to be very interesting. However, I think the readability and the presentation of the paper could use a bit of work. I have some comments listed below.

Response: Thank you for reading my paper and for your appreciation.

Introduction: Short and to the point.

Methods:

- Preoperative staging: Please clarify whether all of the criteria for hepatic lesion were fulfilled for this classification (rim enhancement, T2 hyperintensity ...) or if one or two were sufficient.

Response:

- Firstly, I would like to thank you for reviewing my manuscript and for your expert ideas and suggestions. I appreciate your valuable comments. Criteria for hepatic lesions included all of the factors mentioned ie. rim enhancement, T2 hyperintensity and diffusion restriction.
- **After revision:** The statement, “Hepatic lesions were classified as definitive metastases if they showed all of the following, rim enhancement in the arterial phase, a defect in the hepatobiliary phase, T2 hyperintensity, and diffusion restriction” was added in the methods section

- MRI: If T2-weighting and DWI were part of the classification, a brief summary of these sequences should be included, (ex. b-values).

Response

- Thank you for your comment. I have added statements giving a brief summary of T2-weighting and DWI in the methods section.
- **After revision:** The statement, “Magnetic resonance images were obtained using 3.0-T whole-body magnetic resonance systems (Philips HealthCare) with a 32-channel (3.0 T) phased-array coil as the receiver. Imaging used the dynamic contrast enhancement and conventional sequencing, including the dual-echo in- and opposed- phase spoiled gradient echo T1-weighted method; fat-saturated respiratory-triggered T2-weighted method; and fat-saturated heavily T2-weighted and diffusion-weighted method (with b-factors of 0, 50, 500, and 800 s/mm²). Un-enhanced and contrast-enhanced (arterial, portal venous, 3-min delay, and hepatobiliary phases) transverse images were obtained using a T1-weighted 3-dimensional gradient recalled echo sequence (T1 high-resolution isotropic volume examination, Philips HealthCare). Coronal images were also obtained for the hepatobiliary phase. Before imaging, intravenous gadoxetic acid was administered via the antecubital vein using a power injector at a rate of 1 mL/s for a dose of 0.025 mmol/kg of body weight, followed by a 20-mL saline flush” was added in the methods section.

- Statistics: Continuous data eligible for a t-test should be tested for normality, and then alternatively be analysed with a non-parametric test if non-normally distributed. Consider using Mann-Whitney U-test which is also incorporated in SPSS. If this has been done, please inform on this in the text.

Response:

- Thank you for your excellent suggestion. I have used the Mann-Whitney U test for all continuous variables as the data was not normally distributed. I

have added this in the methodology as well as made changes in the results and tables as appropriate.

- **After revision:** The statement, “Continuous data were compared using Mann-Whitney U test.” Was added in the methods section.

Results:

- There are a lot of different groups reported here. Perhaps the readability of the study would be enhanced by focusing on what the primary goal of the paper is. For instance, I cannot deduce from the text whether patients with GE-MRI more often received adjuvant chemo or not.

Response:

- Thank you for your comment. I have added several more statements in the results to help increase readability of the paper. The patients with GE-MRI more often received adjuvant chemotherapy.
- **After revision:** The following changes have been made in the results section. The statements, “The division of patients based on if they received adjuvant or neoadjuvant chemotherapy is shown in figure 1.

The patients with GE-MRI more often received adjuvant chemotherapy.

However, even though the number of nodules detected were significantly greater, the use of GE-MRI did not affect the recurrence-free survival of the patients.” Were added in the results section.

Patients who received neoadjuvant chemotherapy showed no difference in recurrence-free survival or overall survival irrespective of whether a preoperative CECT or GE-MRI was performed.

Discussion:

- On line two there is a reference without reference number.

Response:

- Thank you for bringing this to my notice. I have added the reference in line 2.
- **After revision:** Kang et al.(5) showed that GE-MRI detected metastases in 90 patients who showed no lesions on CT, which caused the surgical plan to be altered in 3% of patients.

- I miss some discussion of why what we consider better diagnostics is not transferred into better survival. If there is more treatment in the GE-MRI group, in the form of adjuvant treatment or surgery, could the negative result be an indicator of the increased treatment resulting in higher morbidity?

Response:

- This is an excellent observation. I should have addressed this earlier. Only patients who received adjuvant chemotherapy were included in the final analysis. Though a larger number of patients who underwent a GE-MRI received adjuvant chemotherapy, studies have previously shown reduced recurrences of both liver metastasis as well as colorectal cancer after adjuvant chemotherapy. Even though GE-MRI detected more nodules as compared to CECT and had a higher sensitivity for detecting malignant nodules, the size of the nodules were probably insignificant to cause any reduction in recurrence as well as survival. In addition there probably could have been a number of false positives as well All patients with additional nodules detected were not treated, some were followed up which could lead to a delay in diagnosis thus not affecting the final recurrence and overall survival rates.
- **After revision:** The statement, “Although GE-MRI had a higher sensitivity for detecting nodules as compared to CECT, the recurrence rate postoperatively was not affected. This could be attributed to the fact that the size of the nodules being detected was not significant enough to cause a survival

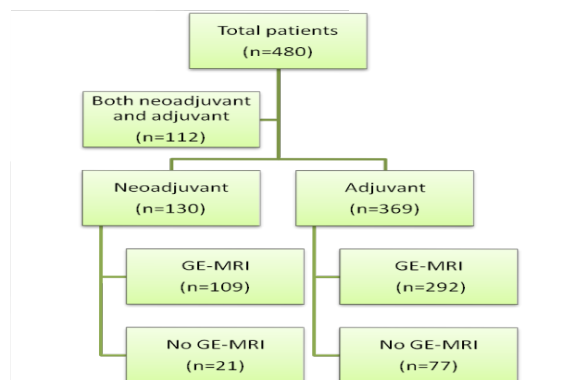
difference, besides some of the nodules identified on GE-MRI could be false positive. In addition, all of the detected nodules were not treated immediately, with some being under surveillance on follow-up.” was added in the discussion.

Figures and tables:

- The images are extremely sparsely described and not easy to understand. Please work more on the presentation and explanation of the images.
- o Figure 1: The figure indicates that there are two different groups of 480 patients. Also, the overlap between the adjuvant chemotherapy and adjuvant chemotherapy should be indicated so that the numbers add up. The last column has different information for the adjuvant and the neoadjuvant group. This makes the figure more confusing than informative. Please make the figure consistent regarding the information.

Response:

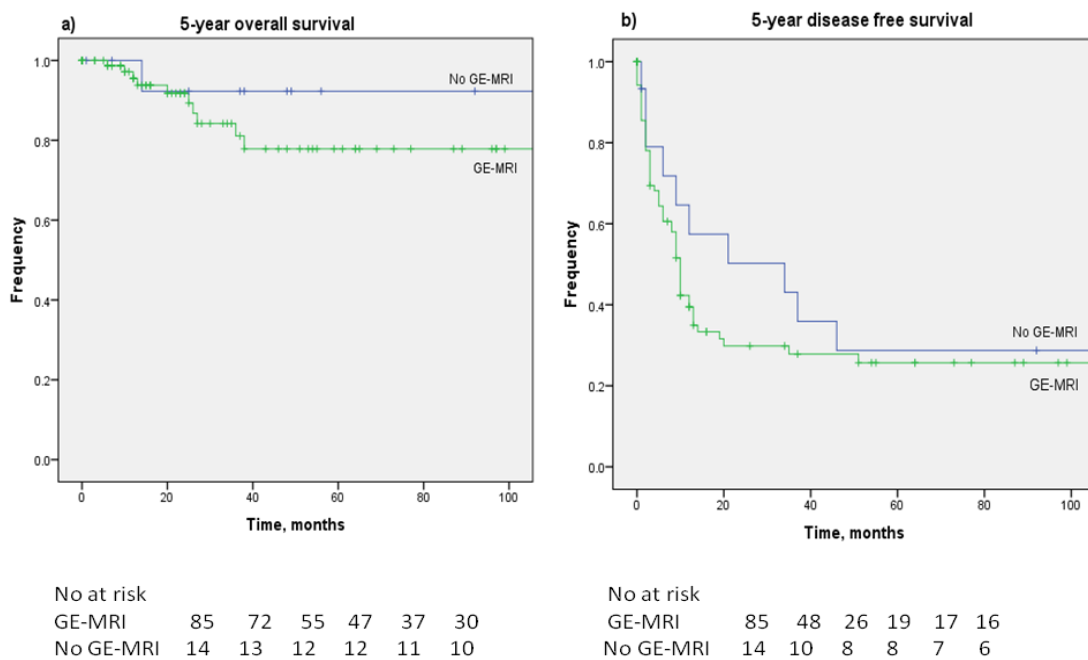
- Thank you for your comment. I have edited the figure in order to make it understandable. Both columns of adjuvant as well as neoadjuvant chemotherapy convey similar information.
- **After revision:** Figure 1



o Figure 2: It is not clearly indicated which group is which. Consider using some other program than SPSS for Kaplan-Meier plots. At least the legend should be more informative. The x-axis should state that this measure is in months. P-values could also be added to the figure or figure text. Some journals requests the number of patients in each group for different time points to be included in every Kaplan-Meier plot, this makes it much easier for the reader to determine the validity of the analysis.

Response:

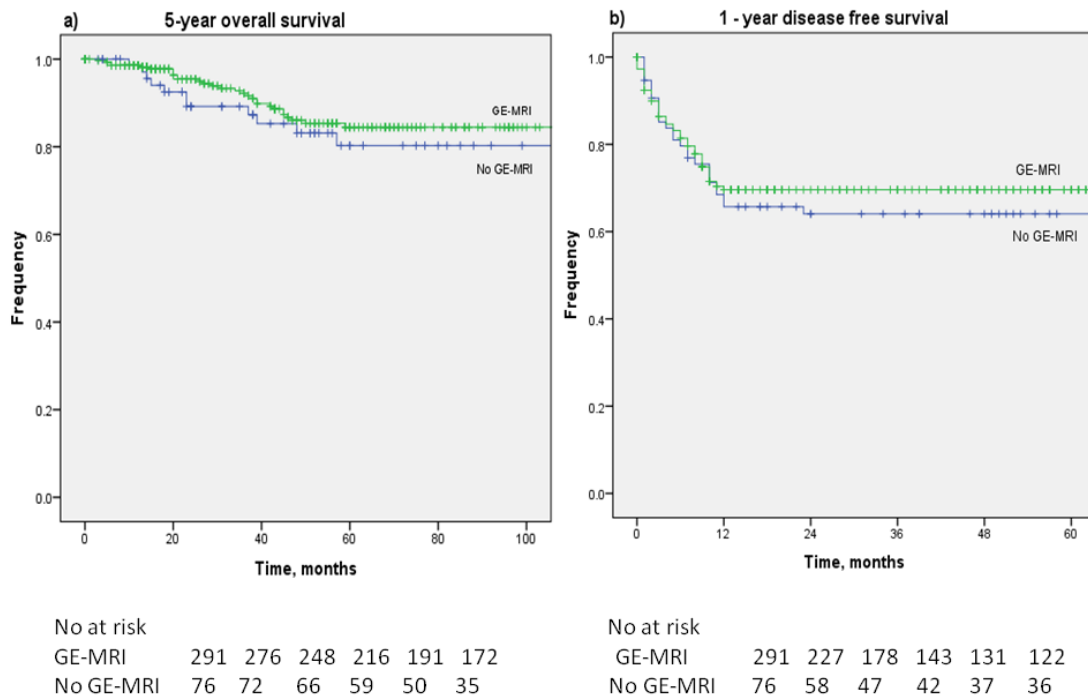
- Thank you for your comment. I have made the changes in figure 2.
- After revision: Figure 2



o Figure 3: Same as for figure 2.

Response:

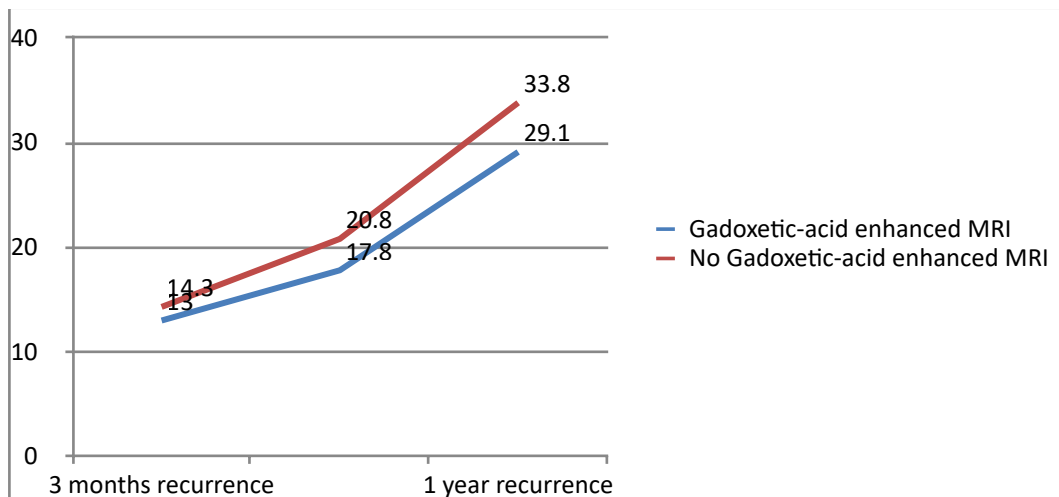
- Thank you for your comment. I have made the changes in Figure 3
- After revision: Figure 3



o Figure 4: The abbreviation EOB should be written out in the figure text. The line plot itself should have markers, indicating that this is only three measurement points. The figure and the figure text should explain more clearly what type of recurrence this is, and which patients are included in this measure.

Response:

- Thank you for your comment. I have changed the abbreviations in the figure as well as added data labels into the figure. The figure legend has been edited to better explain the figure
- **After revision:** Figure 4- Cumulative recurrence over 1 year in patients who received adjuvant chemotherapy



- Tables should also have more information regarding the total number of patients in each group and what the percentages are calculated from.
 - o Table 1 should state the number of patients in each column. If I understand correctly that there are only four patients in the No GE-MRI group, I'm not sure whether there is any meaning to doing the statistics on these groups. One or two patients more in this group could completely change the picture.

Response

- Thank you for your comment. I agree the numbers in the groups are very small and this has been included as a limiting factor in the study but nevertheless studying the characteristics of patients in both these groups are important.
- **After revision:** Table 1 has been changed to supplementary table 1

- o Table 2: This table is very difficult to understand. The number of patients with recurrence or no recurrence should be indicated, and how the percentages are calculated should be explained.

Response

- Thank you for your comment. The number of patients with no recurrence and recurrence has been indicated
 - **After revision:** Table 2 changed to table 1. Recurrence n=15, no recurrence n=7
- o Table 3, also here there should be more information about what the denominator for the different groups are.

Response

- Thank you for your comment. I have added the denominator in table 3. Table 3 has been changed to table 2
- **After revision:** Table 3 has been changed to table 2.