December 25, 2016

To the Editorial Board and the reviewers of the World Journal of Gastroenterology

We thank you for the opportunity to resend the revised manuscript.

We accepted all comments and revised the manuscript accordingly.

We would like to thank you, the editors and the reviewers: the review process has significantly improved the quality of our manuscript.

All the authors have agreed to the contents of the manuscript in its submitted form. Our work has not been submitted elsewhere in whole or in parts.

For language revision, we acknowledge Dr. Eitan Amir and Dr. Daliah Galinsky-Tsoref. Dr. Eitan Amir is a senior oncologist in the Princess Margaret Cancer Centre and an Assistant Professor in the Department of Medicine at the University of Toronto. Dr. Amir is well known for his over 200 peer-reviewed publications as well numerous published abstracts and book chapters. We also acknowledge Dr. Daliah Galinsky -Tsoref is a senior physician in our Institute, who was born and raised in England.

We hope that we responded to the reviewers' comments adequately and that after we made these changes, you will find our manuscript suitable for publication in your journal.

Please find below our response to each of the comments made by the reviewers and the action taken.

A point by point response to the reviewers' comments and the action taken:

Reviewer 1 (reviewer no. 2438889):

1. "A glossary is needed to keep track of all the abbreviations.".
   Thank you for this comment. We added a glossary in the end of the manuscript, page 29.

2. "The smoking history is less prevalent in the elderly. Could you speculate why?".
   Smoking prevalence was indeed significantly different between the groups, with 24.6% octogenarians having history of smoking or being current smokers, compare to 44.3% in the control group. It is not clear to us whether this represent a true difference in smoking prevalence. Other possible explanations might be underreporting of distant past smoking in octogenarians, or less meticulous medical history evaluation in the older population. According to the health ministry in Israel, people older than 65 smoke less compared to the younger population (http://www.health.gov.il/publicationsfiles/smoking_2015.pdf). This might be consistent with our finding; however, the health ministry does not include data regarding former smokers.

3. " Is overall suvival equivalent to DFS ?."
   Overall survival (OS) is defined as time between diagnosis to death of any cause. Disease free survival (DFS) is the time between status of no evidence of disease to local or distant recurrence or death from any cause. DFS is evaluated for patients with non-metastatic disease. The definition of OS and DFS is elaborate in the comments, terminology section (page 13, paragraph 2, line 13-17).

4. " In results and tumor characteristics you mention the well differentiated histology but this is not in table 2."

   Thank you for this comment. Well differentiated is equivalent to grade 1. Grade 2 and grade 3 are equivalent to moderately and poorly differentiated, respectively. We clarified this issue in the results, tumor characteristics section (page 7, paragraph 4, line 25) and in Table 2 (page 24).

5. " In figure 1 and 2 the legend is missing."

   Done. Legends were added (page 28).

Reviewer 2 (reviewer no. 3674667):

1. " CRC entity should be discussed in more detailed way in order to clarify this entity for readers that are not familiar with CRC (e.g. prevalence, tumor characteristic etc.)."

   Thank you for this important comment. We further elaborated the entity of CRC in the introduction section (page 5, paragraph 1, lines 2-8)

2. " It should be explained why octogenarians received less CRC treatment and why the treatment was less aggressive."

   We agree with this comment. Similar to other studies, we found older patients were less likely to receive treatment. As treatment approach is different between patients with metastatic disease to patients with non- metastatic disease we analysis the data according to these subgroups and found similar findings in both subgroups. Moreover, as treatment decision is affected by the patients' performance status (PS), we also compared the differences in treatment approach only in patients with good PS (ECOG PS 0-1).

Indeed, even octogenarians with good PS received less treatment compared to the control group. As older patients are considered to be more frail and are more likely to have other comorbidities, concern from treatment related complications might be one reason for avoidance of treatment in this population. For patients with non-metastatic disease the purpose of treatment is to prevent late recurrence, which most commonly occurs at the first years after diagnosis. As the life expectancy of octogenarians is shorter than the younger population, the importance of preventive treatment in the old population is not always clear due to competing risk of death from other causes. There are no randomized controlled trials which address this important issue. We believe the under-treatment of Octogenarians is one of the significant findings of our study. Nonetheless, this was an observational study and the reason for avoidance could not be retrieved as it is usually a decision comprise of multiple factors. We elaborate in the discussion section the differences in treatment approach our study cohort. (page 11, paragraph 4, line 1, page 12, paragraph 1, line 1).

Sincerely,

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