

Dear Editors of "World Journal of Gastrointestinal Oncology",

We are sending you the revised manuscript entitled "**EXPRESSION PROFILES OF GASTRIC CANCER MOLECULAR SUBTYPES IN REMNANT TUMORS**" (Manuscript NO.: 61932, Retrospective Study).

The manuscript was revised according to the reviewers' comments and responses to each question are provided below. Text modifications are highlighted in red.

We are glad for the opportunity to send the revised manuscript to this renowned journal.

Thank you in advance for your time.

Respectfully,

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Response to the Reviewer(s)' Comments

REVIEWER #1:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: A well written retrospective study looking at molecular expression between primary gastric cancer and remnant gastric cancer occurring a minimum of 5 years after original resection in the case of resection for malignancy and any time after resection for benign disease. A few questions

1. Do the authors have access to the original specimens in the case of the 4 cases of previous resection for cancer. If so were these specimens also studied remembering that even paraffin slides can be tested. If so were there any differences in the molecular expressions

Unfortunately, we do not have a paraffin tissue sample of the tumor from the first surgery of these patients. We only had access to the anatomopathological report. So we don't know if in these cases the characteristics of the new primary tumor are similar to the previous gastric cancer

2. There is always the argument that the original development of gastric cancer is associated with a field defect and their incidence of cancer in remnant may be higher. If the 4 gastric cancer specimens are excluded does that change the significance of the results or alter any of the studies.

Previous gastric resection is a risk factor for the development of RGC, whether the first gastrectomy for benign (peptic ulcer) or malignant conditions. As the objective of the study was to evaluate the expression profile in remnant tumors - regardless of the first resection -

we believe that the inclusion of these 4 patients with the first surgery for adenocarcinoma does not change the results found in the study. A larger number of cases with a previous gastrectomy due to adenocarcinoma would be necessary to suggest any change in the expression profile compared to patients with resection for benign ulcers.

Furthermore, to avoid this interpretation bias, cases with the previous GC are considered as RGC only those with an interval between the first and the second surgery greater than 5 years, so that the tumor in the remaining stomach is not regarded as disease recurrence

3. Six of the recurrent cases were COJ cancers (Siewert 3). Did these 6 cases have any difference in their expressions remembering potential different etiologies for COJ adenocarcinoma including possibility of HPV.

No particularity was found concerning the six GC Siewert III. Of these, 1 was classified as EBV subtype and the other five as CIN (all with normal p53 expression).

Regarding HPV, there was no morphological change to suggest research for the virus. The incidence of HPV-related cancer is not common in gastric cancer. Considering viral infection, gastric cancer is more related to EBV infection. Regarding the oral route, HPV is more related to oropharyngeal tumors.

4. Did the authors identify any Siewert 2 or 1 recurrent cancers in this study who may have been excluded.”

Patients with Siewert I and II tumors were not included in the study, as these patients are submitted to esophagectomy at our Institution. Only Siewert III that performed completion gastrectomy was included. This criterion was added in the methods section of the manuscript.

EDITORIAL OFFICE’S COMMENTS

SCIENCE EDITOR:

1. Scientific quality: The manuscript describes a retrospective study of the expression profiles of gastric cancer molecular subtypes in remnant tumors. The topic is within the scope of the WJGO.

(1) Classification: Grade A;

(2) Summary of the Peer-Review Report: The authors reported a well written retrospective study looking at molecular expression between primary gastric cancer and remnant gastric cancer occurring a minimum of 5 years after original resection in the case of resection for malignancy and any time after resection for benign disease. However, some questions raised by the reviewer should be answered; and

(3) Format: There are 2 tables and 3 figures. A total of 41 references are cited, including 13 references published in the last 3 years. There are 9 self-citations, which are related to this study.

2. Language evaluation:

Classification: Grade A. A language editing certificate issued by AJE was provided.

3. Academic norms and rules: The authors provided the Biostatistics Review Certificate, and the Institutional Review Board Approval Form. The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement, and written informed consent signed by the patients. No academic misconduct was found in the Bing search.

We provided the Copyright License Agreement and Conflict-of-Interest Disclosure Form with the Final manuscript. The informed consent statement was waived by the local Ethics Committee because of the retrospective nature of the study.

4. Supplementary comments: This is an invited manuscript. The study was supported by 1 grant. The topic has not previously been published in the WJGO.

5. Issues raised:

(1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

As requested, we have included the approval term for the research grant obtained by FAPESP.

(2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

The original editable figures in power point and tables were added in the review of the manuscript.

(3) The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text; and

The topic "Article Highlights" was previously included in the manuscript submitted shortly after the conclusion of the article. The item is highlighted in red in the new submission.

(4) Authors should always cite references that are relevant to their study. Please check and remove any references that not relevant to this study. Authors should not cite their own unrelated published articles. Please check and remove any references not relevant to this study. The authors self-referencing number should be no more than 3.

As requested, references were withdrawn. Only 3 were maintained.