

Dear Editors of "World Journal of Gastrointestinal Surgery",

We are sending you the revised manuscript entitled "**Remnant gastric cancer: an ordinary primary adenocarcinoma or a tumor with its own pattern?**" (Manuscript NO.: 60663, 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,

Marcus F. Kodama P. Ramos, MD, Ph.D.

Department of Gastroenterology

Cancer Institute, University of Sao Paulo Medical School

Avenida Doutor Arnaldo, 251. Sao Paulo, SP. Brazil.

Zipcode: 01246-000

Response to the Reviewer(s)' Comments

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors: Thank you for the privilege of reviewing your work. In this manuscript, the authors reported the remnant GC had similar clinicopathological characteristics and prognosis to primary PGC. This manuscript is well written. While interesting, the manuscript has number of small shortcomings.

1. In method section. I cannot understand “prospective medical database”

The selection of patients for the study was carried out through a prospectively maintained database, where all data of gastric cancer patients undergoing surgical treatment at the institution are documented. This sentence was better clarified in the revised manuscript.

2. This study had some significant difference in clinical and surgical characteristics. I think you should use the inverse probability of treatment weighting as a statistical analysis.

Multivariate logistic regression and propensity score matching (PSM) are employed to adjust the potential bias of covariates (i.e., the potential confounders) on the outcome. Inverse probability of treatment weighting (IPTW) is based on the propensity score (PS) to create a synthetic sample in which the distribution of measured baseline covariates is independent of treatment assignment. PSM and IPTW are mostly used to mimic the conditions of a randomized clinical trial (RCT), so the probability that a patient receives a particular treatment is the same for all participants despite its age, sex, staging (etc.). Both RCT and PSM/IPTW allow one to estimate marginal treatment effects. The marginal treatment effect is interpreted as the average treatment effect on the population: how the treatment changes the number of outcomes observed in the population? When using logistic regression, the conditional

treatment effect is estimated. It is the change in the odds of the outcome for an individual when exposed to treatment compared to receive no treatment, conditional on that individual's potential confounders/covariates. Thus, the conditional effect is interpreted at the individual level. The PSM/IPTW has the advantage to estimate the effect of treatment on the outcome only after an acceptable balance in measured baseline covariates has been achieved. However, when using logistic regression, the analysis starts from the outcome.

The aforementioned suggests that researchers need to carefully distinguish between marginal and conditional treatment effects. In part, study design and the planned analysis should consider which treatment effect is more meaningful in that context. Thus, if the objective of an observational study is to answer the same question as an RCT, the marginal effect may be of greater interest and PSM/IPTW used. In our study we did not intend to mimic an RCT design. The "treatment" in our study was "RGC". There was no option to be assigned to PGC or RGC group. Further, as we seek to evaluate the treatment at the individual level and the outcome was already known we thought that logistic regression was more suitable for our analysis.

3. The author described the strong point of this study was conducted single institution. But, this may be the limitation of this report.

The reason why we consider the "single-center study" as a high point refers to the fact that all patients were evaluated, treated, and followed in the same way - which guarantees homogeneity in the evaluated population.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Comments for WJGS 03873177 The article entitled "Remnant gastric cancer: an ordinary primary adenocarcinoma or a tumor with its own pattern?" write

by Marcus Fernando Kodama Pertille Ramos et al, want to evaluate the clinicopathological characteristics and prognosis of RGC after previous gastrectomy for benign disease compared to patients with primary proximal gastric cancer (PGC) undergoing total gastrectomy (TG) for primary cancer. Despite the concepts might be interesting there are some points which need clarification. Minor points

1. Clarify precise international indications to perform minimal invasive surgery and traditional open surgery.

Minimally invasive approach is usually decided discreetly in each institution based on the expertise of the staff members that participate in this type of surgery. In our study, the option for open or laparoscopic surgery was decided in a multidisciplinary meeting, with the surgeon responsible for the case. This information was added to the method section of the manuscript.

2. Authors should specify that their data are preliminary and that the confirmation by a larger number of cases is mandatory.

The limitations of the study concerning external validation in a larger cohort of patients were added to the discussion of the revised manuscript.

3. The authors should clarify the specific sites of remnant gastric cancer

The description of the tumor location in the gastric remnant was previously presented in Table 1 of the manuscript.

4. The authors should modify Introduction, very short and Discussion, very long

As suggested, the introduction and discussion were revised, and some information present in the discussion was included in the introduction section; and some topics in the discussion were synthesized and/or removed

EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor: 1 Scientific quality: The manuscript describes a retrospective study of the remnant gastric cancer. The topic is within the scope of the WJGS. (1) Classification: Grade B and Grade C; (2) Summary of the Peer-Review Report: In this manuscript, the authors reported the remnant GC had similar clinicopathological characteristics and prognosis to primary PGC. This manuscript is well written. The questions raised by the reviewers should be answered; and (3) Format: There are 3 tables and 2 figures. A total of 38 references are cited, including 12 references published in the last 3 years. There are 2 self-citations. 2 Language evaluation: Classification: Grade A and Grade B. A language editing certificate issued by a native English speaker was provided. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the Institutional Review Board Approval Form. Written informed consent was waived. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJGS. 5 Issues raised: (41) The "Author Contributions" section is missing. Please provide the author contributions; (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; (3) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text. 6 Re-Review: Required. 7 Recommendation: Conditional acceptance.

(2) Editorial office director: I have checked the comments written by the science editor. The authors have written the "Author Contributions" section.

(3) Company editor-in-chief: I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastrointestinal Surgery, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

The original figures, tables, and "Article Highlights" section, were added in the review of the manuscript. We also provided the Copyright License Agreement and Conflict-of-Interest Disclosure Form with the Final manuscript.