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Dr. Lian-Sheng Ma
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World Journal of Gastrointestinal Oncology

RE: Manuscript NO. 77042, Observational Study, entitled "The role of gender and primary tumor site on psychological distress, quality of life, and coping of patients with advanced cancer of the digestive tract"

Subject: Point-by-point response to the comments of the reviewers and the editorial office.

In accordance with the reviewers' suggestions and concerns regarding the manuscript entitled " The role of gender and primary tumor site on psychological distress, quality of life, and coping of patients with advanced cancer of the digestive tract ", please find the new version enclosed.

On behalf of all the co-authors, I would like to thank the editor and the reviewers for their thoughtful and insightful comments on our work, which we have very thoughtfully taken into consideration in preparing the revised version of the manuscript as detailed in the following point-by-point reply.

We hope that we have addressed the issues raised by the reviewers to their satisfaction and that you now find the manuscript suitable for publication in your journal.

Thank you very much for your consideration.

Respectfully,

Dr Vilma Pacheco-Barcia MD, MSc, PhD

REVIEWER #1:

1.) The article confirms data from other populational studies and provide useful information for oncologists. However the numbers of patients with digestive cancers others than colorectal are two small to allow a significant conclusion.

Our study includes patients with digestive tumors included consecutively according to whether they were seen for the first time in medical oncology consultations. The number of cancers by location reflects the incidence of these neoplasms in clinical practice. This translates into a good representation of patients with colorectal (101), pancreatic (56), and gastric (23) cancer while there are few cases of esophageal (9), biliary tract (7), liver (5) and anus (2) cancers.

Therefore, we agree that one of the limitations of our study is the under-representation of some non-colorectal gastrointestinal tract malignances subtypes that may not be reflected in the overall estimates. When we initially drafted the article, we took this into account and included it in the limitations section of the manuscript.

The series by Czerw et al., BMC Palliative Care 2020 (reference 56 of the manuscript), includes a similar sample size to ours with 46 patients with pancreatic cancer, 93 with gastric cancer but did not include other more infrequent tumor sites such as esophagus, bile duct and anus, which in turn reduces the representation of non-colorectal digestive cancer.

REVIEWER #2:

1.) Yes, the title reflects the main subject/hypothesis of the manuscript 2 Abstract: Yes, the abstract summarize the work described in the manuscript 3 Key words: Yes, the key words reflect the focus of the manuscript 4 Background: The background is well written and organized. It adequately describe the background, present status and significance of the study 5 Methods: The methods are described in adequate detail that is easy to follow and replicate 6 Results: Authors have achieved their stated objects. The study contributes by adding knowledge on gender differences in psychological distress among patient with and without colorectal cancer 7 Discussion: The discussion is concise and clear. It appropriately and adequately highlights the main aspects of the manuscript 8 Illustrations and tables: The tables and Figures are of good quality. They don't require any modifications 9 Biostatistics: Yes. The manuscript met the requirements of biostatistics 10 Units: Yes, the manuscript meet the requirements of use of SI units 11 References: The authors have cited relevant and latest references 12 Quality of manuscript organization and presentation: The manuscript IS well, concisely and coherently organized and presented. The style, language and grammar are accurate and appropriate 13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories using STROBE statement 14 Ethics statements: The manuscript met the requirements of ethics

We would like to thank Reviewer # 2 for re-reading the manuscript, and for considering it to be an interesting scientific contribution.

REVIEWER #3:

1.) This paper is unique, and indeed, we GI researchers generally focus on prognosis (how long the cancer patients could live), but we do not pay enough attention on how well they live (distress and anxiety). This paper has a nice take-home message as "The degree of disease acceptance in gastrointestinal malignancies may be gender dependent", and is useful to GI surgeons and gastroenterologists. Therefore, I think it could be accepted by WJG, and be attractive to the readers.

We would like to start by thanking reviewer #3 for his positive assessment of our work and even more so for highlighting the importance of paying attention to other patient outcomes beyond survival. This is especially relevant in gastrointestinal malignancies when analyzing biopsychosocial variables according to the sex and gender of the patients.

Given the increasing evidence of sexual dimorphism in cancer, and the differences in biology between cancers arising in women and men, European Society of Medical Oncology (ESMO) decided to address this topic and organized a first workshop "Gender Medicine and Oncology" in 2018. Following the success of this workshop, the ESMO Gender Medicine Task Force was created in 2019. The missions of this task force are to raise awareness of the presence of potential sex differences in biology and treatment outcomes of non-sex-related cancers and the impact of gender on access, quality of life and long-term consequences of tumor therapy.

This real-world data (RWD) analysis using the Spanish NEOetic_SEOM cancer registry database aims, in line with the ESMO Gender Medicine Task Force missions, to expand knowledge on how sex and gender influence patients with colorectal and non-colorectal malignancies, as well as the impact on psychological distress, quality of life, and coping with cancer, to expose areas where there is room for improvement to avoid healthcare disparities.

REVIEWER #4:

1.) Thank you for inviting me to evaluate the observational study titled "The role of gender and primary tumor site on psychological distress, quality of life, and coping of patients with advanced cancer of the digestive tract". It is an interesting study , which was a real-world data (RWD) analysis using the Spanish NEOetic_SEOM cancer registry database aims to evaluate psychological distress, quality of life, and coping strategies in patients with advanced

colorectal cancer compared to non-colorectal cancer based on gender. And they concluded that women and patients with non-colorectal gastrointestinal tract malignancies have more physical symptoms and somatization and women suffer more psychological distress. This analysis suggests the desirability of considering stratification and analysis by sex and site of the primary tumor in studies of digestive malignancies to identify differences and individualize communication with the patient to achieve a suitable approach to their psychological and physical situation. So, the information in this study is helpful to clinical communities. The paper is well arranged and the logic is clear, and. The cited literature is comprehensive. The provided figure and tables are well composed and understandable. The quality of language of the manuscript is acceptable for me. So, I recommend to you that this manuscript may be accepted. There is advice for author: 1) The aim of the study is to analyze whether there are differences between colorectal and non-colorectal digestive cancer, so, the title seems to need to be revised to more accurately describe the content of the article.

Aware of the value your critical reading lends to our text, we would like to begin by thanking the Reviewer#4 for having evaluated the text and for considering that it may be of scientific interest. Please find below our response to the comments made.

In accordance with the reviewer's suggestion, we have modified the title to make it clear that a colorectal cancer series is compared to a non-colorectal digestive cancer series:

Title: The role of gender on psychological distress, quality of life, and coping of patients with advanced colorectal and non-colorectal cancer

2.) "Conclusions. The degree of disease acceptance in gastrointestinal malignancies may be gender dependent. Future interventions should specifically address gender and tumor site differences in individuals with advanced digestive cancer." The description here is inaccurate. According to this article, at least, the acceptance of patients with gastrointestinal malignancies is related to gender and primary tumor location.

We have reviewed the abstract and changed the conclusions following the recommendations of the reviewer: "Conclusions. The degree of disease acceptance in gastrointestinal malignancies may depend on gender and location of the primary digestive neoplasm."

SCIENCE EDITOR:

1.) In this retrospective, transversal, multicenter study, the authors investigated an interesting, meaningful, but rarely studied topic: how gender and primary tumor site affect the psychological distress and life quality of GI tumor patients. This topic is no doubt of significance in clinics. The topic of this study fits the criterion of this journal. The writing is good. The design of the research is sound. The conclusion can not only benefit patients in clinical practice, but also attract the readers.

We agree with the science editor, it is an important topic that benefits both patients and clinicians.

COMPANY EDITOR IN CHIEF:

1.) 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 Oncology, 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. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lined and do not segment cell content. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper).

If the picture is “original”, the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright The Author(s) 2022.

We are grateful to the Company Editor in Chief for his review and we will provide the decomposable figures as well as edit the tables as recommended by the Editor.

May 14, 2022. Madrid, Spain.