

Responses to the reviewers' comments

Reviewer #1

We thank the reviewer for the comments. As suggested, we explained the significance of the research. The reviewer's comments are shown in italics below, followed by our response.

This study mainly focused on the changes of energy metabolism and serum opsonin activity during the perioperative period of ESD. The results showed that during the perioperative period of ESD, the resting energy expenditure and reactive oxygen species increased slightly. From the perspective of physical stress, ESD belongs to minimally invasive surgery. This article argues that ESD is a minimally invasive procedure from a special perspective. However, its scientific and clinical value is limited, and the research scheme is not perfect. in breif, in the process of ESD surgery, each patient's wound size, resection plan, and drug use before and after surgery are different, and simple measurement of REE and SOA cannot be effectively analyzed.

Reply: To our knowledge, no studies have been conducted to assess the degree of physical stress in patients during the perioperative period of ESD. In this study, we quantified and evaluated physical stress of ESD procedures using REE and SOA. Use of REE and SOA allow us to estimate the physical stress safely and easily. In the future, less-invasive surgeries will be developed. We believe that these methods could be a choice to study the physical stress of new techniques with lower invasiveness in many clinical fields.

Reviewer #2

We thank the reviewer for the comments. As suggested, we explained the significance of the research. The reviewer's comments are shown in italics below, followed by our response.

The authors experienced a mini review of assessment of physical stress during the perioperative period of endoscopic submucosal dissections. There is an important point to be addressed to the Authors' attention. Well, as a clinician, what is the clinical significance of assessment of physical stress during the perioperative period of ESD? Is there a specific impact on the complications or prognosis of different types of operations ?

Reply: Unfortunately, the prognosis and occurrence of complications in different types of operations could not be predicted from this study because severe complications were rare and no death was observed. However, assessing the physical stress and clarifying the associated factors have clinical significance as it helps identify patients who require additional care during perioperative management. Since these assessments are safe and easy, we believe that measurement of REE and SOA could be a choice to study the physical stress in many clinical fields.

Reviewer #3

We thank the reviewer for the comments. We have revised our manuscript according to the comments as described below. The reviewer's comments are shown in italics below, followed by our response

This is an interesting study which aimed to summarize the recent evidence on the assessment of physical stress during the perioperative period of ESD, focusing on changes in energy metabolism and serum opsonic activity (SOA). The authors concluded that the physical stress of ESD is less invasive than that of surgery. The authors compared the day of ESD, the next day of ESD and 4 days after ESD. Major comments: The authors demonstrated that: For gastric cancer, a significant increase in the PH and AUC of LgCL was observed on the day after ESD and 4 days after ESD. Both PH and AUC tended to decrease 4 days after ESD compared to those on the day after ESD. However, significant changes were not observed in the PH and AUC of LmCL during the perioperative period of ESD. The PH and AUC of LgCL were

significantly higher four days after ESD than on the ESD date for colorectal cancer. Significant differences were shown before ESD and after ESD. Why did the authors conclude that ESD is a less invasive procedure. (2) The comparison between ESD and surgery should be richer.

Reply: Neutrophils produce $O_2^{\cdot-}$, mediated by phagocytosis-activated NADPH oxidase, and the $O_2^{\cdot-}$ is then rapidly converted to H_2O_2 by superoxide dismutase. The azurophilic granules in neutrophils contain large amounts of myeloperoxidase, and their secretion during the degranulation process results in a reaction between H_2O_2 and Cl^- , producing $HClO$, a much stronger oxidant than its precursor H_2O_2 . These ROS produced by neutrophils have different levels of toxicity. LgCL reflects the production of $O_2^{\cdot-}$, while LmCL reflects the production of all ROS, including $HClO$. Therefore, it is generally considered that oxidative stress measured by LmCL is more toxic than that measured by LgCL. In this study, only SOA measured by LgCL was found to be increased during the perioperative period of ESD. On the other hand, in a previous study on patients undergoing gastrointestinal surgery with varying degrees of surgical stress, SOA measured by LmCL was found to be higher. The difference in SOA between ESD and surgery suggests that the degree of invasiveness of ESD is lower than that in surgery. We have added the description in the revised manuscript.

Minor comments: Reference 1: Should 32 be bold?

Reply: Thank you for pointing it out. We have corrected it.

EDITORIAL OFFICE'S COMMENTS

(1) Science editor:

We thank the editor for the comments. We have revised our manuscript according to the comments as described below. The reviewer's comments are shown in italics below, followed by our response.

This study mainly studied the changes of energy metabolism and serum opsonin activity during perioperative period of ESD. The manuscript does not meet the requirements of publication, its scientific and clinical value is limited, and the research scheme is not perfect. Self-Citation Count:7 The self-referencing rate should be less than 3%. It is unacceptable to have more than 3 references from the same journal. To resolve this issue and move forward in the peer-review/publication process, please revise your reference list accordingly.

Reply: To our knowledge, no studies have been conducted to assess the degree of physical stress in patients during perioperative period of ESD. In this study, we quantified and evaluated physical stress of ESD procedures using REE and SOA. Assessing the physical stress and clarifying the associated factors have clinical significance to help identify patients who require additional care during perioperative management. Furthermore, in the future, less-invasive surgeries will be developed. REE and SOA can be used to estimate the physical stress of such operations safely and easily. Therefore, we believe that REE and SOA could be a choice to study the physical stress of new less-invasive techniques in many clinical fields.

As for Self-Citation, we checked the email from BPG Editorial Office on October 14, 2021. It described, "(1) It is unacceptable to have more than 3 references from the same journal; (2) The self-referencing rate should be less than 10%. Authors are recommended to keep reasonable self-citations (i.e. those that are most closely related to the topic of the manuscript)." We have revised the manuscript according to its request. However, if the self-referencing rate less than 3% is better, we can revise the references again.

2) 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 Gastroenterology, 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 be sure to use Reference Citation Analysis (RCA) when revising the manuscript. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. For details on the RCA, please visit the following web site: <https://www.referencecitationanalysis.com/>. 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 lines and do not segment cell content.

Reply: We thank you for your comment. We have checked and revised our manuscript accordingly.