

June, 14 2021

Dear Editor-in-Chief

Re: Submission of a Revised manuscript to the WORLD JOURNAL OF GASTROINTESTINAL ENDOSCOPY

Thank you very much for giving us the opportunity to revise our *invited review* (manuscript number: 05548650)

We would be grateful for the consideration of our revised manuscript “*Indications and outcomes of endoscopic resection for non-pedunculated colorectal lesions: A narrative review*” (by Endrit Shahini et al.) for publication in the *World Journal of Gastrointestinal Endoscopy*.

The authors have read and complied with author guidelines, and they all have seen and approved this manuscript for publication. None of the authors had a conflict of interest to disclose concerning this manuscript.

We are grateful to the Editors for their precious contributions and comments. We have revised our manuscript accordingly for grammar, style, structure and we hope that you will now find it suitable for publication in the *World Journal of Gastrointestinal Endoscopy*. In case of final acceptance, we agree to make this manuscript open-access.

The changes in the manuscript are identified in track change mode. Below you can find a point-by-point reply to the reviewers. We used red to denote revised or inserted text.

Thank you for your precious time.

We are looking forward to receiving your decision in due time.

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Reply to Editors:

- 1. Reviewer #1: Dear authors: this is a very complete review about a hot topic in endoscopy. However, I find the structure of the manuscript a bit confusing, there is a lot of information about endoscopic resection but a more focused approach should be preferable.**

Thanks to the reviewer for his comments. Our narrative review aimed to perform a comprehensive and in-depth analysis of the current endoscopic scenario describing all the best diagnostic strategies for predicting malignancy based on the morphologic features of colorectal non-pedunculated lesions according to current endoscopic technology. We have reordered accordingly the subheadings of those paper sections that contributed to create a little confusion, as per your suggestion.

- 2. Reviewer #2: This narrative review aims to describe the best diagnostic strategies for predicting malignancy based on the morphologic features of colorectal non-pedunculated lesions according to current endoscopic technology, to choose wisely among EMR and ESD procedures. The study is well conducted and the authors' conclusions rely on appropriate references. I appreciate the authors' efforts for this review, and I have some comments described hereafter: Point 1: All acronyms should be explained the first time they appear in the text, such as "EMR", "ESD". Point 2: Too many subheadings at the same level are not logical. For example, with respect to EMR/ESD, you can use a headings first, and then subheadings for detailed classification. Point 3: The lack of figures or tables directly indicates the differences between various endoscopes. In addition, why is Table 2 the format of the picture? Point 4: The content is complete, but the conclusion is too simple. The core question concerns the SMIC assessment system and the choice of ESD or EMR, please clarify.**

Thanks to the reviewer for his comments and suggestions. Point 1: we have explained accordingly the mentioned acronyms (page 4). Point 2: we provided to remove many of the mentioned subheadings as per your suggestion. Point 3: we decided to insert only two tables and the second one summarizing all current meta-analyses to lessen the heterogeneity of the available studies. Point 4: to strengthen our neat conclusive message we have added the sentence *"Admittedly, the prevailing unsolved challenge concerns the requirement for a secure SMIC estimation method, proper to stratify the chance of the post-*

procedural necessity for surgery following ESD, and proficient in determining the at-risk subgroups of patients in whom ESD could obtain the most fitting approach” (page 17).

- 3. Reviewer #3: This study analyzed all meta-analyses comparing EMR versus ESD outcomes for colorectal sessile or non-polypoid lesions of any size, preoperatively estimated as non-invasive. The research topics are interesting, but there may be some defects. 1. Why only summarize all the meta-analyses? Some studies may not be included in the meta-analyses. 2. This study lists a lot of data, especially in Table 1, but the source is not indicated, which reduces the credibility. It is suggested to add references. 3. This study describe the best diagnostic strategies for predicting malignancy based on the morphologic features of colorectal non-pedunculated lesions according to current endoscopic technology, to choose wisely among endoscopic mucosal resection (EMR) and ESD procedures. The conclusion of this study is common, and there is no significant difference compared with previous published studies.**

1. Appreciations to the reviewer for his comments and suggestions. We summarized all the prevailing meta-analyses considering these types of studies follow stringent standards for the selection of the most appropriate studies through our purpose to determine which of the endoscopic techniques amongst EMR and ESD can be the most effective and harmless for removing non-pedunculated colorectal lesions. Moreover, we also analyzed all the most relevant studies about EMR and ESD procedures, even those non included by the same meta-analyses.

2. As suggested, we inserted in Table 1 (page 32) the precise references from which we extrapolated the mentioned percentages related to sensitivity, specificity, PPV, and NPV concerning the morphological pattern, Kudo pit pattern, NICE, and JNET classifications.

3. We have endeavored to offer as comprehensively as possible the professional reader (and not) an overview of the contemporary endoscopic scenario concerning this last topic by discussing the most meaningful works about diverse updated articles. Regrettably, there are still deeper dilemmas than certainties due to the heterogeneity of the published studies and profoundly distinctive expert competencies of Eastern and Western actualities.