Manuscript 79954. Point-to-point response to reviewers

Dear Editors,

Thank you for your assessment of our article "How to avoid overtreatment of benign colorectal lesions: rationale for an evidence-based management", and for allowing us to resubmit it after revision.
We have addressed all comments and suggestions by the Reviewers, and have revised our manuscript accordingly. We believe these modifications have significantly improved the quality of our paper.
Please, see our point-to-point replies below. We hope you will find our responses and revised paper acceptable for publication in the World Journal of Gastroenterology. Thank you for your time in reviewing our submission.

Rewiewers´comments to the author:

Reviewer #1:

1. The author described the results of surgery vs endoscopic resection from Western studies. If any, suggestion of differences between data for surgery vs endoscopic resection from Eastern and Western would be helpful

   There are not so many Eastern studies comparing endoscopic resection to surgery, and they are focused more on ESD. But we agree with the reviewers that talking more about ESD in our review is necessary. We have added a comment on these studies on page 5, first paragraph.

   "Some observational studies performed in Eastern countries and focused on ESD confirm that the latter has a shorter hospital length stay, an inferior 30-day readmission rate, and a lower complication rate"

2. Recently, various virtual EMR education programs have been introduced. It would be better to be discussed briefly that these program affect EMR procedure improvement.

   This is a good point. We have introduced a comment on endoscopic therapy educational programs in page 11 "The expert endoscopist" section when the ESGE curriculum was mentioned. We have reworded the whole paragraph.

   "The implementation of structured learning tools or courses could help to evaluate who may be competent in endoscopic resection techniques. In vivo and virtual tools have been described for EMR and ESD [49, 50], and a formal curriculum for ESD has been developed by the ESGE [51]. However, there is not a similar curriculum for EMR training, which has essentially been limited to that obtained during residency and has repeatedly proven to be insufficient [52]."

3. In addition resection techniques, recent studies regarding techniques to decrease recurrence rate of complex polyps would be better to be discussed briefly

   This is a nice suggestion. We have added a comment on the same section "The expert endoscopist" when describing those techniques that an endoscopist devoted to complex resections should know.

   Strategies to decrease the recurrence rate, like margin ablation, margin marking, or hybrid argon plasma coagulation [54-56] should be mastered as well.

4. Minor points P.5, line 5, DSE is replaced with ESD. The author should give full name for all abbreviations in the main text. P.6, line 7, What does ESR mean?

   We have fixed the typos.

Reviewer #2:

1. Most of the evidence that will be reviewed here focus on endoscopic mucosal resection (EMR) , however, endoscopic submucosal dissection (ESD) is also widely used in the treatment of benign colorectal diseases, and this evidence can be appropriately added.

   This is a good point. We have briefly added some comments on ESD when appropriate:

   In the "why should endoscopic resection and not surgery be the therapy of choice for the treatment of benign colonic lesions?", on page 5, the first paragraph.
   "Some observational studies performed in Eastern countries and focused on ESD confirm that the latter has a shorter hospital length stay, an inferior 30-day readmission rate, and a lower complication rate"

   In the "The expert endoscopist section" when commenting on the number of cases needed to achieve proficiency:

   "Regarding ESD, there is also a high variability in the reported number of cases needed to achieve proficiency ranging from 20 to 250 cases[48]. To maintain proficiency, the ESGE curriculum recommends performing at least 25 cases per year"

   In the "The reference endoscopy unit" section a comment has been added in the last paragraph:

   Regarding ESD, the American Society of Gastrointestinal Endoscopy recommends setting up an "ESD cart" with the necessary equipment for the procedure and the management of adverse events. The presence of experienced nurses and technicians is also addressed [48].

2. A new mode of endoscopic therapy - patients are admitted to surgery, and endoscopic therapy is completed under general anesthesia of tracheal intubation with the help of surgeons in the operating room. If there is bleeding or perforation beyond the control of endoscopy during the operation, or the lesion cannot be completely removed, convert to laparoscopy or laparotomy. Whether the relevant research of this new mode of endoscopic therapy needs to be included in the review, please reevaluate.

   This is an interesting comment that we have discussed in our lab thoroughly. We agree that this is a relatively new area for research, with increasing implementation in practice. However, we think that it is slightly out of the scope of this opinion review. Other reviewers have suggested shortening the manuscript a little bit, so we have chosen not to include a specific reference to this topic. It may well be a topic for a future review.

Reviewer #3:

1. I think the manuscript could be improved by adding recent literature showing the improvement of EMR technology through different margin ablation approaches and how they reduce recurrence rates, achieve (in expert hands) high success rates while guarding low procedure times and low complication rates. This even more strengthens the point of using EMR over surgery but makes referral to expert centers using this technology more mandatory

This is a good point, also suggested by another reviewer (Reviewer #1, point 3). We have added the recommended references (see comment above).

2. The last third of the manuscript is a bit long and should be shortened a bit

We have tried to shorten some paragraphs in the "what lesions should be referred to and to whom?" section. For instance, the previous paragraph replicated some data from table 3, so we have reworded this paragraph:

The BSG suggests other objective features that anticipate a complex resection, grouped into three areas: increased risk of malignancy evidenced by optical diagnosis, increased risk of incomplete resection, and increased risk of adverse effects (table 3). Notably, the experience of the endoscopist is included as a criterium for defining a complex polyp because of an increased risk of adverse events [42].

We´d like to thank the reviewers for the time and effort they have put in our manuscript.

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