Peer Review File

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Review comments

Reviewer A

Comment 1: Under chromoendoscopy, the authors should include a short discussion on the evidence of dye based chromoendoscopy and virtual chromoendoscopy for at-risk patients such as those with polyposis syndromes or those with long standing colitis.
Reply 1: To address this, we have written more about chromoendoscopy in patients with colonic inflammatory bowel disease. We feel that polyposis syndromes may be a bit beyond the scope of our review.

Comment 2: For completeness, the authors should mention other virtual chromoendoscopy techniques such as i-SCAN and flexible spectral imaging color enhancement (FICE) or discuss their utility in clinical practice.
Reply 2: Thank you for this feedback. We have written new sections on i-SCAN and FICE underneath the newly inserted heading, “Image Enhanced Endoscopy”.

Reviewer B

Comment 1: Dear authors, I read your paper with interest. Paper goes over techniques used for polyp characterization comprehensively. I would recommend authors to add a paragraph in the regarding current standard of practice and future perspectives regarding techniques for polyp characterization and its implications.
Reply 1: Thank you for your valuable feedback. We have elected to make multiple edits by embedding comments about standard of care throughout the text and added a conclusion paragraph about future perspectives about polyp characterization and its implications.

Reviewer C

Comment 1: Good review of current status.
Reply 1: Our team sincerely appreciates your time and consideration.

Reviewer D

Comment 1: P5, line 130
Finally, Types VI 130 and VN are considered neoplastic/cancerous (16). Accordingly, the indications for endoscopic resection include Types II, IIIs, IIIL, and IV.
⇒This statement is not true.
Mild irregularity in VI and small regionality in advanced VI are eligible for resection.
REF) Matsuda T, Fujii T, Saito Y, et al. Efficacy of the invasive/non-invasive pattern by magnifying chromoendoscopy to estimate the depth of invasion of early colorectal neoplasms.

Am J Gastroenterol. 2008 Nov;103(11):2700-6.P5, line 147
Reply 1: We have amended the statement on eligibility of resection, as you suggested, and cited the paper by Matsuda et al.

Comment 2: In Japan, an 80 X magnifying endoscope ((GIF-H260), Olympus Medical Systems Corp., Tokyo, Japan) is available and suitable for discerning Kudo's pit pattern.
⇒GIF is a gastroscopy. For colonoscopy, CS 290Z or recently CS 1200Z is used.
Reply 2: Thank you for bringing this to our attention. We have stricken from the manuscript text the mention of that specific gastroscope model (GIF-H260) and its magnification. Instead, we have replaced that line with a more general statement for accuracy.

Reviewer E

Comment 1:
Dear authors, we greatly appreciate the time and expertise applied in creating this manuscript. The full series of articles is focused on endoscopic resection of neoplastic lesions of the gastrointestinal tract.
This review should teach how colon polyp morphology and mucosal pattern interpretation guides endoscopic management. For example, a hyperplastic polyp may be diminutive, Paris Is, Kudo II, NICE/JNET type I. These classification systems may be utilized by an endoscopist to decide appropriate management (i.e., you may decide not to resect a diminutive rectal hyperplastic polyp).
Very pertinent to the review is how the classification systems guide resection. A 3.5 cm rectal Paris Is-IIa, Kudo IV-VI, and JNET2B --- would warrant ESD rather than EMR not just to ensure negative margins and complete resection, but also because of a higher likelihood of harboring early invasive cancer. (Large, Paris Is-IIa polyps in the left colon "i.e., a dominant nodule within a lateral spreading tumor [LST]" have an increased risk of early invasive cancer). Burgess NG, Hourigan LF, Zanati SA, Brown GJ, Singh R, Williams SJ, et al. Risk Stratification for Covert Invasive Cancer Among Patients Referred for Colonic Endoscopic Mucosal Resection: A Large Multicenter Cohort. Gastroenterology. 2017;153(3):732-42 e1.
Reply 1: Thank you. We have taken your comments into account and also cited the suggested resource from Burgess et al.

Comment 2:
Because the presence of Kudo VI was noted within the polyp which was otherwise predominantly Kudo IV, ESD is recommended over EMR.
There is the opportunity to educate the reader on how these classification systems are complementary and a "language" that may guide when to leave a lesion alone (hyperplastic polyp), when, and how to resect (en-bloc via ESD versus piecemeal via EMR), and when to refer to surgery (deep invasive cancer---JNET3, Kudo Vn, Paris III). It would be helpful to explain that the role of ESD is not just en-bloc resection to decrease the possibility of endoscopic recurrence, but also to provide histopathologic information about early cancers, if present within the polyp that otherwise would not be available by piecemeal resection (negative deep margins, presence of lymphovascular invasion, depth of submucosal invasion, etc). These details predict the possibility of lymph node metastases and residual cancer within the colon.

Reply 2: Guided by your comments, we have incorporated literature about the concepts you have mentioned and further specified the role of ESD in the manuscript.

Comment 3:
I agree with the reviewers' comments on acknowledging that NBI (Olympus) is a form of imaging and including literature to support the performance of i-scan (Pentax) and FICE (Fujinon).
Reply 3: Thank you for this feedback. We have written two new sections on i-SCAN and FICE.

Comment 4: It would also be very helpful to describe how chromoendoscopy, particularly methylene blue and indigo carmine may be used to define polyps. The section on crystal violet may be shortened or removed, as the review is from a US perspective and crystal violet is unavailable here. Would focus more on indigo carmine and methylene blue.
Reply 4: In response to this comment, we have removed most of the text on crystal violet. We have added content to elaborate on indigo carmine and methylene blue instead.

Comment 5:
While the sections on EUS, CT colonography, and MRI were interesting and much effort was placed into these sections, please remove this information from the manuscript as they do not guide morphology and mucosal patterns.
Reply 5: The sections on EUS, CT, and MRI have been removed as requested.

Comment 6:
The section on AI may be included, but writing may briefly describe the current state of AI as CADe (computer assisted detection) to help improve adenoma detection rate. The focus of the review is on morphology and mucosal pattern, and how they guide endoscopic management. In this regard, computer assisted diagnosis (CADx) may be helpful in predicting the presence of invasive cancer within a polyp and guiding whether and how a lesion may be endoscopically managed (EMR vs ESD), and when it should be referred to colectomy (deep invasive cancer). The current status of CADx and colon polyps may be nice to write about if AI is to be included in the review.
Reply 6: We have fleshed out the section on artificial intelligence to discuss its application to colon polyps, including more about CADx.

Comment 7:
Would advise spending less time expanding upon the history of various modalities beyond a sentence or two. For example, the section on white light endoscopy may not be necessary beyond stating when high-definition endoscopes were introduced, and how this ushered in the era improved polyp detection, pit pattern interpretation (which previously relied upon imaging magnification) and polyp morphology—and how these classification systems evolved together with the development of endoscopic resection techniques.
Reply 7: In response to this comment, we have condensed the white light endoscopy section and trimmed out various details on the history of modalities in the manuscript.