

Point-by-point responses to reviewers

We sincerely thank the editor for giving us an opportunity to resubmit our manuscript and the reviewers for their valuable suggestions, which have greatly improved our manuscript.

We have provided point-by-point responses to the reviewers' comments.

Reviewer 1:

The experimental and control groups are systematically set up in detail, the research ethics are impeccable, and there is a separate category for statistical analysis. The limitations of the study are also well summarized at the end.

Response:

I truly appreciate your favorable comments.

Reviewer 2:

1. Is the borderline value of 33% defined for over- and under-excision of lesions convincing? Is it because exceeding this threshold will affect the prognosis of patients and make them prone to metastasis or recurrence?

Response:

Thank you for your thoughtful comments. As you recognize, lesions that are candidates for endoscopic submucosal dissection (ESD) are early cancers or adenomas. Therefore, the size discrepancy does not directly affect oncological prognosis. However, the lesion size is effective in the technical difficulty of ESD. Therefore, accurate estimation of the lesion size is important for a safe and secure procedure. The figure of 33% is subjectively determined in this study because referable previous papers are lacking, and this point should be a limitation. However, we consider that this threshold will be acceptable for discriminating the correct/incorrect scaling because three-fourths of the lesions are allocated to the correct scaling group by defining it as -33% to +33% of discrepancies. According to your suggestion, we have added the following sentence to the Discussion section as one of the limitations: "Fourth, the threshold of discrepancies (33%) was subjectively determined in this study because referable previous papers were lacking".

2. Similarly, is the definition of expert ill-considered and is 100 cases of ESD experience too little? Could experts be categorized into more groups based on years of endoscopic experience rather than a dichotomous classification such as whether they are experts or not.

Response:

We appreciate this practical comment. Categorizing the experience by the number of ESDs is based on the hypothesis that endoscopists who have extensive experience of ESD may be able to predict the lesion size more accurately because they also have extensive experience of directly measuring the lesion by pinning down the specimen. In defining an expert, we referred to a previous study*, which showed that the level of skill stabilizes after approximately 100 cases of ESD experience. As you suggest, it might be informative to categorize experts into more groups based on years of endoscopic experience, but we were also concerned about a negative effect by decreasing each number in groups. Indeed, we analyzed incorrect scaling by allocating the lesions into three groups based on years of endoscopic experience (novice: 5 years or less, moderate: 6 to 10 years, experienced: more than 10 years), and found no significant difference among the three groups ($p = .352$). This result has also been shown in previous studies, in which years of endoscopic experience were not effective for endoscopic polyp size estimation.^{9,12}

Based on your comments, we have added the following paper as a reference¹³.

*Jeon HH, Lee HS, Youn YH, Park JJ, Park H. Learning curve analysis of colorectal endoscopic submucosal dissection (ESD) for laterally spreading tumors by endoscopists experienced in gastric ESD. *Surg Endosc.* 2016;30:2422-2430.

3. In Table 4, the p-value of “Experience in Endoscopist-related factor” is greater than 0.05, is it still necessary to include in the next multifactorial analysis?

Response:

Thank you for your comment. We are aware that the selection of factors for multivariate analysis is debatable. We decided to include ESD experience in the multivariate analysis considering clinical relevance, because it tended to influence the underscaling ($p = 0.056$). As a result, the factor was clearly significant in the multivariate analysis. This was probably because the experts encountered lesions that were difficult to measure more frequently than the nonexperts, e.g., lesions with $>1/3$ circumference and ≥ 40 mm diameter ($p = 0.006$ and $p = 0.001$, respectively). In this situation, the univariate analysis might underestimate the effect of ESD experience on accurate scaling.

4. Is the inclusion of only 16 lesions in the “Overscaling group” in Table 6. too few?

Response:

Thank you for this important comment. As you mentioned, the number of the overscaling group was small compared to the underscaling group. Previous studies have indicated that small polyps are likely to be overestimated.^{9,10} In this study, the lesions were relatively large because this study included lesions removed by ESD. Therefore, we consider that the lesions in this study were less likely to be overscaled.

According to your suggestion, we have added the following sentence: “The small number of lesions in the overscaling group may be due to the nature of the lesions included in this study. Previous studies have indicated that small polyps are likely to be overestimated.^{9,10} In this study, the lesions were relatively large because this study included lesions removed by ESD. Therefore, we consider that the lesions in this study were less likely to be overscaled”.

We also changed the abstract as per your instructions and reduced references from 20 to 14 as only two references are allowed from the same journal.

Round 2

Specific Comments to Authors: Thank the authors for sharing their research and drawing our attention to the tumor size discrepancy between endoscopic and pathological evaluations in colorectal ESD. Two reviewers have already given their opinions. Regarding the reply submitted by the authors, contacting the previous reviewer for reevaluation may be better and necessary. From my point of view, I have some suggestions as follows: 1. The authors mentioned, "However, the lesion size is effective in the technical difficulty of ESD. Therefore, accurate estimation of the lesion size is important for a safe and secure procedure" in answering Reviewer 2. But in fact, the more critical impact factor is the depth of the lesion rather than just the size of the lesion. Such a response can easily cause unnecessary misunderstanding for the reader. In addition, the lesion size is no longer the biggest obstacle for a true ESD specialist. Therefore, it may also be an obvious flaw in the study design. 2. The author's definition of experts as those with 100 ESD cases is inappropriate, especially in Japan, a country with a wealth of ESD cases and experience, so I agree with reviewer 2. As for the literature published in 2016 cited by the authors as a reference for the definition of expert, I'm afraid I have to disagree with it. This paper was published 8 years ago, and its research data is much older, which does not represent the definition of an ESD expert that should be published in the research published in 2024 and will seriously affect the results of this paper. It is hoped that the above suggestions will be helpful to the author's subsequent research and papers.

Point-by-point responses to the reviewer

We sincerely thank the editor for giving us an opportunity to resubmit our manuscript and the reviewers for their valuable suggestions, which have greatly improved our manuscript. We have provided point-by-point responses to the reviewers' comments. Reviewer #1: The authors responded well to every point of concern. Although accurate size estimation may not be necessary for experienced endoscopists (The size does not matter for ESD), this study pointed out the discrepancy in polyp size estimation between endoscopy and pathology (pinned specimen). This is the truth that endoscopists know, so they report the polyp size by measurement on pinned specimens. For real-time accurate endoscopic measurement, AI technology may help us soon. Response: We sincerely appreciate your insightful comments. We also expect the development of AI technology for accurate diagnosis, including lesion size, in the near future. Reviewer #2: 1. The authors mentioned, "However, the lesion size is effective in the technical difficulty of ESD. Therefore, accurate estimation of the lesion size is important for a safe and secure procedure" in answering Reviewer 2. But in fact, the more critical impact factor is the depth of the lesion rather than just the size of the lesion. Such a response can easily cause unnecessary misunderstanding

for the reader. In addition, the lesion size is no longer the biggest obstacle for a true ESD specialist. Therefore, it may also be an obvious flaw in the study design. Response: Thank you for your thoughtful comments. Secure en bloc resection is essential for an accurate histological diagnosis, including the depth of the lesion. To obtain secure en bloc resection, preoperative assessment of the technical difficulty should be important. As you point out, the lesion size may not be a great obstacle for a true ESD specialist. However, such a specialist is not always available at every institution. In this situation, lesion size is still a relevant factor for assessing the technical difficulty of ESD, as recent studies have reported.⁶ We have replaced Reference 6 with a more recent study. The sentence in the Introduction section has also been revised accordingly to reflect the changes in the new reference. New reference 6: Zhu M, Xu Y, Yu L, et al. Endoscopic submucosal dissection for colorectal laterally spreading tumors: Clinical outcomes and predictors of technical difficulty. *J Dig Dis* 2022;23:228-236. [DOI: 10.1111/1751-2980.13091] 2. The author's definition of experts as those with 100 ESD cases is inappropriate, especially in Japan, a country with a wealth of ESD cases and experience, so I agree with reviewer 2. As for the literature published in 2016 cited by the authors as a reference for the definition of expert, I'm afraid I have to disagree with it. This paper was published 8 years ago, and its research data is much older, which does not represent the definition of an ESD expert that should be published in the research published in 2024 and will seriously affect the results of this paper. It is hoped that the above suggestions will be helpful to the author's subsequent research and papers. Response: We appreciate this practical comment. Categorizing the experience by the number of ESDs is based on the hypothesis that endoscopists who have extensive experience of ESD may be able to predict the lesion size more accurately because they also have extensive experience of directly measuring the lesion by pinning down the specimen. More precisely, it is necessary to separate endoscopists who have measured more cases from those who have less experience. Therefore, since the expressions "expert" and "non-expert" are not appropriate, we have classified them into two categories: "experienced" and "less-experienced". Regarding the number of ESD experiences, a recent study has divided the number of ESD experiences into two groups of less than 100 cases for predicting technical difficulties.⁶ In this study, we used 100 cases as the cutoff value, not for defining "expert", but for the influence of experience in measuring lesion size. We have amended the corresponding parts of the manuscript. Unfortunately, we failed to search for references corresponding to "experience" in this study; therefore, we eliminated reference 13. New reference 6 Zhu M, Xu Y, Yu L, et al Endoscopic submucosal dissection for colorectal laterally spreading tumors: Clinical outcomes and predictors of technical difficulty. *J Dig Dis* 2022;23:228-236. [DOI: 10.1111/1751-2980.13091]