

Dear Editor-in-chief and reviewers:

Thank you for your kind comments. We have revised our manuscript by following all the suggestions and comments made by the reviewers. The following are our point-by-point responses to each comment or question.

Responses to Reviewer: 03474228

Major:

1. Please give information on the rejection rate for inclusion of the trial.

Response: There were three patients rejected. We added this to the flowchart and to the Results section. The rejection rate for inclusion in the trial was 1.3% (3/229).

2. The authors randomized the eligible patients when their polyps were detected. How many patients who had no diminutive polyps were excluded before randomization?

Response: There were 18 patients (7.9%: 18/229) who had no diminutive polyps and were therefore excluded before randomization. We added this to the flowchart and to the Results section.

3. Please add above information (1. & 2.) to the flow chart.

Response: We have added the above information (1. & 2.) to the flow chart on page 19.

4. Authors conducted only “per-protocol” analysis for the data interpretation. Usually in the RCT, both “intention-to-treat” and “per-protocol” analysis are performed and “intention-to-treat” analysis should be put much value on for the primary outcome measure. Please conduct the ITT analysis in consideration of the polyp retrieval failure cases, EMR-converted cases, and resected non-neoplastic polyps. If you were not able to gain the endoscopic/pathological data for the failure cases, you could treat these lesions as lesions whose cut margins were positive in ITT analysis (worst case scenario analysis). Please consult the statistician before conducting this analysis. (If you consider the ITT analysis was not appropriate for this trial, please mention the reason in the discussion section.)

Response: We excluded the non-neoplastic polyps from ITT analysis because pathological evaluation of these polyps could not originally be performed.

In our modified ITT analysis, we considered polyps converted to EMR and polyp retrieval failure as incomplete en-bloc resection and pathological resection.

The target of modified ITT analysis was 157 polyps in CSP and 138 polyps in HFB.

The results of this modified ITT analysis were that the en-bloc resection rate was significantly higher with CSP than with HFB (87.9% [138/157] vs. 76.0% [105/138], $p < .0001$).

The complete resection rate was significantly higher with CSP than with HFB (70.1% [110/157] vs. 44.2% [61/138], $p < .0001$).

There was no significant difference between the original data and modified ITT analysis.

This data has been added to the revised manuscript on pages 10-11.

Minor:

1. Please provide 95% confidence interval for all the outcome measures.

Response: We added the 95% confidence intervals to Tables 3 and 4 for all the outcome measures on page 24 and 25 in our manuscript.

HFB seems to be unpopular in the West now, which might reduce the generalization of this RCT. Please explain the today's position/situation of HFB in the treatment of diminutive colorectal polyps in the West in the limitation section.

Response: Hot forceps biopsy (HFB) can be used to remove diminutive polyps; it has been widely used in Japan because it is comparatively easy to use when this study started.

As you commented, HFB seems to be unpopular in the West now as it has disadvantages associated with electrocautery, such as perforation and delayed bleeding.

This comment has been added to the revised manuscript on pages 13 in the limitation section.

Responses to reviewer 03262874:

1. Why choose hot biopsy forceps and not cold biopsy forceps to compare with cold snare as cold biopsy forceps is more widely used and not hot biopsy forceps due to known risk of thermal injury.

Response: When this study was planned, hot forceps biopsy (HFB) was a common

method used to remove diminutive polyps; it has been widely used in Japan because it is comparatively easy to use.

As you mentioned, although the HFB approach has disadvantages associated with electrocautery, such as perforation and delayed bleeding, it is advantageous in that possible adenomatous remnants are fulgurated and the blood vessels are coagulated. We described the disadvantages on page 6.

To our knowledge, CSP and HFB have not been directly compared. Therefore, the present study aimed to compare the efficacy and safety of CSP and HFB for removing colorectal polyps measuring 3–5 mm.

2. Please let us the amount of time that it took for complete polyp resection of each colonoscopy by these two different techniques and let us know the P values for the two techniques. This is important as currently forceps biopsy (cold/hot) polypectomy is preferred for cold snare of diminutive polyps due to added time.

Response: In this study, we did not assess the amount of time required using each of the two techniques for complete polyp resection in each colonoscopy because we expect that the time for polypectomy did not differ between cold forceps polypectomy as almost same technique of HFB and cold snare polypectomy in a previous study (Parks SK et al *Gastrointest Endosc.* 2016 Mar; 83(3):527-32). We did not compare the two procedures. These comments has been added to the revised manuscript on page 13.

In summary, we believe that incorporating all the suggestions and comments of both reviewers significantly improved the theoretical and methodological quality of our paper. We would like to thank the editors and reviewers for their valuable comments about our present study and for having allowed us to revise and improve our manuscript. We hope that this manuscript is now suitable for publication in the *World Journal of Gastroenterology*.