

Dear editor and reviewers,

Thank you for your kind advice on my manuscript. I have revised the manuscript according to your comments. The changes are highlighted in red with underlines in the main document. Answers to the comments are as detailed below.

1)Comment: It is possible that small sample size affect the validity of the experimental results.

Answer: The sample size was calculated to assess the efficacy of CO<sub>2</sub> insufflation for reduction of ME immediately after ESD. This sample size worked out well and we could demonstrate the reduction of postprocedural ME using CO<sub>2</sub> insufflation. Clinical effects such as VAS scores of pain and distention were the secondary outcome measurements. We did not design this study to show the alleviation of pain and distention or clinical courses. In addition, some randomized trials in ERCP have reported that CO<sub>2</sub> insufflation was not effective in reducing procedure related pain, the same as in this trial.

2) Comment: the study did not show if small sample size affect the validity of the experimental results.

Answer: The answer is the same as answer 1.

3) Figure 1,2 and 3 are monochrome images originally.

I look forward to hearing from you as to its acceptability.

Sincerely,

Yuki Maeda