

Response to Reviewers' Comments:

Reviewer: 2

Comments to the Author:

1. Authors concluded that the SB knife allows safe and effective ESD of early esophageal neoplasms. How safe and effective is the SB knife? This is a single arm study.

Response: *We thank the reviewer for this comment. We agree that this is a single-arm study; however, it has the strength of accurate data on adverse events and the availability of long-term data on local and distant recurrence. We believe that no perforation occurred in our study population because of the innovative design of the SB knife, which allows for better control and safer dissection. We agree that as this study is a single-arm study, there is a need to conduct randomized studies to compare new devices. We have added this information to the conclusion, as follows:*

(DISCUSSION; Page 12)

*In conclusion, ESD procedures using the SB knife are feasible, safe, and effective for treating early esophageal neoplasms, yielding favorable short- and long-term outcomes. No perforation occurred in our study population, attesting to the innovative design of the SB knife, which allows better control for safer dissection. The availability of this tool may promote widespread adoption of ESD to treat early-stage cancers of the esophagus. **There is need to conduct RCT studies to compare this new innovative device with established devices.***

2. How about difference of any parameters between two hospitals?

Response: *Thank you for your comment. I am sorry for the confusion. The name of our hospital is “Kure Medical Center and Chugoku Cancer Center” (<http://www.kure-nh.go.jp/english.html>), and it is a single hospital.*

3. Do use of SB knife affect survival analysis and long-term outcome compared other devices?

Response: *Thank you for your comment. The survival rate of patients treated with an SB knife is similar to that of patients treated with other devices. I have added this in the Discussion, with 3 references:*

(DISCUSSION; Page 10).

Before

Furthermore, none of the patients experienced local recurrences or metastases long-term, and overall survival rates were highly favorable.

After

Furthermore, no patient experienced local recurrences or metastases in the long term, and the overall survival rates were highly favorable and **similar to those for other devices**^[8,28,29].

4. Why did authors include adenocarcinoma in this study? I recommend to analyze efficacy and safety for patients with SCC alone.

Response: Thank you for your comment. We agree with you and have excluded cases of adenocarcinoma. Finally, a total of 96 SENs in 70 patients qualified for analysis. We have re-analyzed the data and now show the short- and long-term outcomes and survival rates (results are included in the revised manuscript, revised Figures 1 and 5, and Tables 1 and 2). According to the new analysis, the difference in the survival rates between curative and non-curative resections were smaller than before. Therefore, we have revised the sentences below;

(RESULT, survival analysis; page 10)

Before

However, the difference in survival between curative and non-curative resections by ESD was not statistically significant, ~~likely because so few resections were non-curative.~~

After

However, the difference in survival between curative and non-curative resections by ESD was not statistically significant.

(DISCUSSION; page 11)

Before

In analyzing longer-term patient outcomes, 3- and 5-year survival rates tended to be poorer if resections were non-curative (78.7% and 39.4%, respectively) rather than curative (85.2% and 75.1%, respectively), ~~and the differences fell short of statistical significance.~~

After

On analyzing longer-term patient outcomes, 3- and 5-year survival rates tended to be **slightly, but not significantly**, poorer if the resections were non-curative (**74% and 49%**, respectively) rather than curative (**85% and 75%**, respectively).

We hope that these revisions are now acceptable.

5. Please show sample power.

Response: Thank you for your comment. First, we have excluded cases of adenocarcinoma and re-analyzed the data. According to the new analysis, the difference in the survival rates between curative and non-curative resection were smaller than before; therefore, we have deleted the sentence on few non-curative cases, as follows:

(RESULT, survival analysis; page 10)

Before

However, the difference in survival between curative and non-curative resections by ESD was not statistically significant, likely because so few resections were non-curative.

After

However, the difference in survival between curative and non-curative resections by ESD was not statistically significant.

Moreover, no sample size calculation was performed a priori, as the study was based on a convenience sample of all consecutive cases during the period of data collection. As this was a practice study, with no between-group comparisons, we do not feel that a post-hoc power calculation would be useful. The precision of the outcome estimates can be inferred from the reported 95% confidence intervals. As explanations on the log-rank test and P value were missing previously, we have added this information to the statistics section, as follows:

(MATERIAL AND METHODS, statistical analysis; page 8)

A log-rank test was used to evaluate the significance of differences between curves, and a P value of less than 5% was considered significant.

We hope that these revisions are acceptable.