

December 2020

Varut Lohsiriwat and Shu-You Peng

Editors-in-Chief

World Journal of Gastrointestinal Surgery

Dear Editor:

We wish to resubmit our manuscript for publication in *World Journal of Gastrointestinal Surgery* after incorporating the revisions suggested by the reviewers.

The title has been revised to “Assistant skill in gastric endoscopic submucosal dissection using a Clutch Cutter.”

The manuscript ID is 59902 and the invited manuscript ID is 0487607.

We wish to thank you and the reviewers for your careful review of our manuscript. The manuscript has benefited immensely from these insightful suggestions. We hope that this revised version of the manuscript is now suitable for publication in the *World Journal of Gastrointestinal Surgery*.

The manuscript has been rechecked and the necessary changes, which are indicated in yellow, have been made in accordance with your and the reviewers’ suggestions. We have also provided point-by-point responses to all the comments.

Thank you again for your efforts in reviewing our manuscript. We look forward to hearing from you.

Sincerely yours,

Mitsuru Esaki

Division of Gastroenterology and Hepatology, Department of Medicine, Nihon University School of Medicine

1-6, Kanda-Surugadai, Chiyoda-ku, 101-8309, Tokyo, Japan

Department of Gastroenterology and Metabolism, Graduate School of Medicine Sciences,

Phone: +81-3-3293-7111-

Fax: +81-3-3293-7111

Email: esaki_saiseikai@yahoo.co.jp

Response to Reviewer #1

Reviewer's comments

1. Why use a Clutch Cutter instead of other knives, such as IT knife, Flush knife. Can other studies obtain similar conclusions?

Thank you very much for your valuable comments. A Clutch Cutter is characterized as a unique scissor-type ESD device that requires the assistant to rotate the device at an appropriate position and grasp the target tissue. Therefore, it is much more complicated than other knives, such as an IT knife and a flush knife, in ESD procedures. Hence, the technical skills of the assistant, as well as those of the operator, might have an impact on the treatment outcomes in ESD when using a Clutch Cutter. Thus, we conducted this study using *an ex vivo* porcine animal model to determine whether or, if any, how assistant skills are associated with treatment outcomes in ESD using a Clutch Cutter. We did not assess whether assistant skills contributed to the treatment outcomes of ESD using an IT knife and flush knife, and, if any, whether there was a difference in the extent of the assistant skills' contribution between the usage of Clutch Cutter and other knives. The results of this study could be applied exclusively to ESD with scissor-type knives. This limitation has been added to the Discussion section of the revised manuscript.

Revised Manuscript (page9, lines 186-193)

ESD-C is characterized as a unique procedure using a scissor-type knife, which is different from ESD with other knives. The ESD-C procedure requires the technical skills of the assistant to rotate the device at an appropriate position and grasp the target tissue (Figure1). These are not required for ESD using other knives such as needle-type and insulated-tip knives. Thus, it is considered that the skills of the assistant, as well as those of the operator, might have an impact on the treatment outcomes of ESD-C [17, 18].

Revised Manuscript (page18, page 399-403)

Fourth, the manipulation by the assistant in ESD-C was different from that in ESD with other-types of knives such as needle-type and insulated-tip knives. It is unclear whether the results of this study could be applied to ESD with other-types of knives. Further studies using other-types of knives are required in the future.

2. In Figure3, what is the difference between supervisor and assistant? In fact, only one assistant is needed for endoscopic submucosal dissection.

Thank you very much for your valuable comments. The assistant participated in the manipulation

of the ESD devices such as Clutch Cutter and injection needle, while the supervisor simply guided the operators on how to proceed with the ESD procedure when required. The objective of this study was to determine whether or, if any, how assistant skills (i.e., experts vs. trainees) are associated with treatment outcomes in ESD using a Clutch Cutter. The trainee operators were selected in this study considering the sensitivity of detection. In the ESD-C-E group, the expert assistant not only manipulated the Clutch Cutter but also guided the ESD procedure when required. On a level playing field with the ESD-C-E group, one expert was positioned beside the operator (separate from the trainee assistant) to guide the ESD procedure in the ESD-C-NE group. This allowed us to determine a pure difference in technical skills in assisting with ESD-C procedures. Following your suggestion, in order to make it clearer, we have made the following revision to the manuscript:

Revised Manuscript (page12, line252-256)

All 16 trainees performed two ESD-C procedures each. As a result, 32 ESD-C procedures were performed in total. One ESD-C was performed with an expert assistant who also guided the ESD procedure when required (ESD-C-E), and the other was performed with a non-expert assistant (ESD-C-NE). On a level playing field with the ESD-C-E group, one expert was positioned beside the operator (separate from the trainee assistant) to guide the ESD procedure in the ESD-C-NE group.

Response to Reviewer #2

Reviewer's comments

1. This was an *ex vivo* experimental study, and the number of cases was significantly small, and the lesions were only limited in the middle or lower third of the Stomach

Response: Thank you very much for your valuable comments.

As you pointed out, this was a basic study using *an ex vivo* porcine animal model. One limitation of this model is that the mucosal layer of the upper third of the porcine stomach is too thick to perform ESD procedures comparable, which might be attributed to the anatomical features of the porcine stomach that differ from those of the human stomach. This is the reason as to why the lesions assessed in this study were limited to the middle or lower part of the stomach. In contrast, we agree with you that the number of cases conducted in this study was small. However, unlike in a clinical study, which usually involves a variation in size, morphology, and location, considering that *ex vivo* porcine animal models could be generated quite stably, we considered

that the sample size of this study was acceptable. Following your suggestion, we mentioned these limitations in the discussion of the revised manuscript. Therefore, we have revised the manuscript as follows:

Revised Manuscript (page17, lines 385-387)

This study has several limitations. First, this study limited target lesions to 30 mm in size in the middle or lower thirds of the stomach because the mucosal layers in the upper third of the porcine stomach are too thick to perform the ESD-C procedure.

2. The description of complications was not detailed, such as postoperative bleeding and emptying, which need to be further improved.

Response: Thank you very much for your valuable comment. We agree with you. This was a basic study using *ex vivo* porcine models. The excised porcine stomach possesses neither motility nor blood flow. Therefore, we could not assess complications such as postoperative bleeding and emptying as you suggested. That is one of the limitations of this study. We have mentioned this limitation in the discussion of the revised manuscript. Further studies on live animals or humans are desired in the future. Therefore, we have revised the manuscript as follows:

Revised Manuscript (page 17-18, lines 388–396)

Second, this was an *ex vivo* study using a porcine animal model without any blood flow. The ESD procedure-related complications, including intra/postoperative bleeding other than intraoperative perforation, could not be evaluated. Hemostasis in ESD-C can depend on the assistant skill level because the bleeding point must be properly grasped by the CC. We assume that the importance of the assistant skill in ESD-C found in this study would be more significant in clinical practice when performed on humans. Further studies in live animals or humans are required to assess such complications in the future.

3. The language still needs some polishing.

Response: Thank you very much for your valuable comments. We submitted the manuscript for English proofreading again and revised the whole manuscript. Certification of English proofreading was attached to the supplemental file.

5 Issues raised:

(1) Original figures using PowerPoint

Original figures using Power Point was added.

(2) PubMed numbers and DOI citation numbers. Reference list and list all authors of references.

The reference list was revised with PubMed numbers, DOI citation numbers, and all authors of the references.

(3) I found the authors did not write the “article highlight” section.

Article highlight has been added to the manuscript.

(4) For statistical significance, please use superscript letters. Statistical significance is expressed as aP < 0.05, bP < 0.01 (P > 0.05 usually does not need to be denoted). If there are other series of P values, cP < 0.05 and dP < 0.01 are used, and a third series of P values is expressed as eP < 0.05 and fP < 0.01

Statistical significance was expressed as mentioned above in tables.

(5) “Conclusion” section at the end of the main text

“Conclusion” section was added at the end of the main text.

(6) Please provide the signed Conflict-of-Interest Disclosure Form and the Copyright License Agreement.

Conflict-of-Interest Disclosure Form and Copyright License Agreement were added.

(7) Please provide the audio core tip file where the content of the core tip is recorded.

Audio core tip was added.

ARTICLE HIGHLIGHT

Research background

A Clutch Cutter is used as a scissor-type endoscopic knife in endoscopic submucosal dissection (ESD) of gastrointestinal tract tumors. Assistant staff support operators to manipulate the endoscopic devices during the ESD procedure. ESD with the Clutch Cutter (ESD-C) requires technical skills for assistant staff to rotate the device and grasp the target tissue.

Research motivation

It is unclear whether the skills of the assistant staff affect the technical outcomes of ESD-C.

Research objectives

The aim of this study was to investigate how the skills of the assistant staff may affect the technical outcomes of ESD-C.

Research methods

A total of 32 ESD-Cs on mock lesions in an ex vivo porcine stomach model were performed by trainees; 16 ESD-Cs were assisted by an expert (ESD-C-E) and the other 16 ESD-Cs were assisted by a non-expert (ESD-C-NE). Technical outcomes were compared between the two groups.

Research results

ESD-C-E achieved significantly shorter procedure time, with high curability and low perforation rate compared to ESD-C-NE. Assistant skill was significantly associated with the difficulty of ESD on multivariate analysis.

Research conclusions

Assistant skill is an important factor when trainees perform ESD-C procedures.

Research perspectives

This was an ex vivo porcine model study with small sample size. Validation study in human with large sample size is desired in the future.