



PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 78391

Title: Endoscopic submucosal tunnel dissection for early esophageal squamous cell carcinoma in patients with cirrhosis: a propensity score analysis

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05429162

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Academic Fellow, Chief Doctor, Doctor, Research Fellow, Research Scientist

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2022-06-24

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2022-08-08 16:59

Reviewer performed review: 2022-08-16 15:40

Review time: 7 Days and 22 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection



Re-review	[<input checked="" type="checkbox"/>] Yes [<input type="checkbox"/>] No
Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

Summary Zhu et al. analyzed the significance of endoscopic submucosal tunnel dissection for early esophageal squamous cell carcinoma in patients with liver cirrhosis. Although the authors showed the benefits of endoscopic submucosal tunnel dissection for patients with liver cirrhosis, there are some major points to be revised. Major points 2. Patients and methods 2.2 Pre-ESTD evaluation 1) The endoscopy used for evaluation is not clear. There are several types of endoscopes for evaluation of early esophageal cancer. Also, the NBI (narrow-band imaging) and LCI (linked color imaging) certain benefits for detecting esophageal cancer. Please describe the specific method for evaluating esophageal cancer by endoscope (Gruner et al. Endoscopy. 2021 Jul;53(7):674-682; Nakamura et al. Esophagus. 2021 Jan;18(1):118-124). 2.3 ESTD procedure 1) The definition of “experienced endoscopists” is not clear. Please specify this point. 2.6 Statistical analysis 1) The authors performed the propensity score matching in the results section. The matching method (Caliper width, matching ratio) should be described (Reiffel et al. Am J Med. 2020 Feb;133(2):178-181). 3. Results 1) In the table 1, some background data is missing. The data of the knife and hemostatic forceps used in the procedure should be described (Although the authors described in the 2.3 ESTD procedure section, it is not reasonable that 2 knives and 2 hemostatic forceps were used during the one ESTD procedure). 2) The background data of the cirrhotic patients should be clearly described. The data of the Child-Pugh score (Median and distribution), serum albumin and other factors associated to the grading of the Child-Pugh score, or MELD scores should be described. These data is essential to discuss



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whether decreased overall survival is reasonable in this cirrhotic patients cohort. 3) “p=0.000” is not commonly used for expressing “Statistically significant.” The “p=0.000” seems that the statistics is not performed for the comparison of 2 groups. The authors should describe $p < 0.01$ or actual p-value for describing “Statistically significant.” 4) The overall survival data must be described as median overall survival (months or days). It is not clear that time point evaluated the percentage of overall survival in the main text. 5) The authors stated that the costs and duration of hospitalization were statistically longer in the cirrhotic patients group. However, the more costs should be offered when the patients stayed longer in the hospital. The authors should perform multivariate analysis to exclude that the costs and duration of hospitalization is independently associated with liver cirrhosis. 4. Discussion 1) From figure 4, decrease survival in the cirrhotic patients were observed in relatively early days after the ESTD (between 0-40 months). From this point of view, it is questionable whether the cirrhotic patients should be received ESTD. The medial overall survival received chemoradiation therapy in the stage I esophageal cancer was around 80 (Kato et al. Jpn J Clin Oncol. 2009 Oct;39(10):638-43). 2) This study is retrospective study, and the certain bias could no be excluded. For reaching conclusion that the esophageal ESTD can be safely and effectively performed in patients with liver cirrhosis, the comparison between ESTD and ESD in the cirrhotic patient’s cohort should be performed. Please consider to discuss this point. Minor points 2. Patients and methods 2.5 Outcome measurements 1) The hemoglobin unit should be described as g/dl, according to the original article (Kim et al. Eur J Gastroenterol Hepatol. 2007 May;19(5):409-15). 2.6 Statistical analysis 1) The authors used SPSS for statistical analysis. Please describe manufacturer and originated country of the SPSS. 3. Results 1) The method used for evaluating gastroesophageal varices should be described in the “Patients and methods” section.



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Reviewer's code: 02536339

Position: Editorial Board

Academic degree: PhD

Professional title: Associate Professor

Reviewer's Country/Territory: India

Author's Country/Territory: China

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Reviewer chosen by: Dong-Mei Wang

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [] Onymous Conflicts-of-Interest: [] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

This article requires minor language polishing rest is fine



RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Manuscript NO: 78391

Title: Endoscopic submucosal tunnel dissection for early esophageal squamous cell carcinoma in patients with cirrhosis: a propensity score analysis

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Reviewer's code: 05429162

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Academic Fellow, Chief Doctor, Doctor, Research Fellow, Research Scientist

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

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Scientific quality	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
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SPECIFIC COMMENTS TO AUTHORS

The manuscript has been revised well. I agree that the manuscript described the significance of ESTD for hepatic cirrhosis patients. I think this manuscript will be potentially acceptable after some correction have been done. I hope my comments would help to improve the quality of this article.

7. The overall survival data must be described as median overall survival (months or days). It is not clear that time point evaluated the percentage of overall survival in the main text. Answer: Dear professor, thank you for your kind proposal. Since there were fewer deaths during follow-up in both groups, we were unable to calculate the median overall survival. In addition, limited by the small sample size and the number of deaths, we were also unable to correctly calculate the survival at a specific time point. Therefore, we hope you can agree with our current expression of survival rate. The authors stated that median overall survival (OS) could not be calculated because of the fewer deaths during follow-up period. However, the median OS estimation should be performed using Kaplan-Meier method and if less than 50% of the patients did not reach the endpoint, the authors should clearly state that point.

9. From figure 4, decrease survival in the cirrhotic patients were observed in relatively early days after the ESTD (between 0-40 months). From this point of view, it is questionable whether the cirrhotic patients should be received ESTD. The medial overall survival received chemoradiation therapy in the stage I esophageal cancer was around 80 (Kato et al. Jpn J Clin Oncol. 2009 Oct;39(10):638-43). Answer: Dear professor, thank you for your suggestion. We believe that patients with early esophageal cancer coexisting with cirrhosis should undergo ESTD based on the following viewpoints: ①EEC usually has a good prognosis after



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endoscopic resection, with a reported 5-year survival rate of more than 90%, thus, it is worth exerting effort for endoscopists to try it. ②The most predominant cause of death during follow-up in our study was not due to ESTD or esophageal cancer but rather cirrhosis-related complications, such as hepatic encephalopathy. ③If esophageal cancer patients with liver cirrhosis receive chemoradiation therapy, cirrhosis-related complications will also happen. In addition, patients with liver cirrhosis often have a poor liver function, which affects the implementation of radiotherapy and chemotherapy, and are prone to cause complications related to liver cirrhosis or radiotherapy and chemotherapy. Therefore, we hope you can agree with us. The authors stated that the predominant cause of death during follow-up was not due to esophageal cancer or ESTD. Again, the authors should describe why the ESTD should be performed in these patients. If most of the esophageal cancer patients with cirrhosis will not die due to the esophageal cancer, there is less priority to perform ESTD in these patients. 10. This study is retrospective study, and the certain bias could not be excluded. For reaching conclusion that the esophageal ESTD can be safely and effectively performed in patients with liver cirrhosis, the comparison between ESTD and ESD in the cirrhotic patient's cohort should be performed. Please consider to discuss this point. Answer: Dear professor, thanks for your suggestion. In our center, ESTD is a preferred endoscopic resection method for the treatment of early esophageal cancer; thus, we have little data on ESD for esophageal cancer patients with cirrhosis. Therefore, the comparison between ESTD and ESD in the cirrhotic patient's cohort cannot be performed in our study. The authors answered that the ESTD were preferred to perform in the author's affiliation. However, the comparison between ESTD and ESD is essential to evaluate the usefulness of ESTD. If the authors could not collect the ESD cases for early esophageal cancer with cirrhosis, this point should be described as limitation of the study in the discussion section.



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