

Peer Review File

Article information: <https://dx.doi.org/10.21037/tcr-21-1545>

Major comments:

Comment 1: As the author mentioned at the limitation in discussion, the number of cases is not sufficient to conclude in this study. It is hopefully to investigate about the prognosis for more many cases at several facilities. And also, the period of the observation after ESD is not sufficient. The duration (the period of the observation) is necessary to add in both group in Table 1.

Reply 1: For the problem that the number of cases is not sufficient to conclude in this study, we adjusted the conclusion of the study (see Page3, line 47-51 and Page14, line 289-291). Of course, it's a great idea to investigate about the prognosis for more many cases at several facilities. We added it at the limitation in discussion (see Page13, line 277-278). As for the period of the observation after ESD, we added it in both group in Table 1 as Reviewer suggested (see Table 1).

Changes in the text: The main conclusion was adjusted (see Page3, line 47-51 and Page14, line 289-291). The content at the limitation in discussion was added (see Page13, line 277-278). The period of the observation after ESD was added (see Table 1).

Comment 2: Therefore, it should be change to conclude in this manuscript. For example, high risk patients suffered from severe heart disease, pulmonary disease and so on for surgical operation are suitable for the observation, carefully.

Reply 2: It is really true as Reviewer suggested that it should be change to conclude in this manuscript. We adjusted the conclusion of the study (see Page3, line 47-51 and Page14, line 289-291).

Changes in the text: The main conclusion was adjusted (see Page3, line 47-51 and Page14, line 289-291).

Comment 3: If authors wish to strongly state the unnecessary to do the additional surgical resection for T1 Ca. after ESD, another good study is recommended to use as the reference including 6 to 9. (Journal of gastroenterol. Yasue c., et al 27; 2019 DOI 10.1007/s00535-019-01564-y)

Reply 3: Considering the Reviewer's suggestion, we have adjusted the conclusion of the study (see Page3, line 47-51 and Page14, line 289-291).

Changes in the text: The main conclusion was adjusted (see Page3, line 47-51 and Page14, line 289-291).

Comment 4: In this study, all cases are treated by ESD. But it is necessary to describe about the reason to select the only cases resected by ESD except for EMR or polypectomy.

Reply 4: As we mentioned in the text, ESD enables en bloc resection of early CRC without LN metastasis, resulting in very low rates of local recurrence, high-quality pathologic specimens for accurate histopathologic diagnosis and potentially curative treatment of early adenocarcinoma without resorting to major surgical resection (see Page7, line 142-145). In addition, we added some reasons for selecting ESD instead of EMR or polypectomy in the introduction (see Page4 line 79-84).

Changes in the text: We added some reasons for selecting ESD instead of EMR or polypectomy in the introduction (see Page4 line 79-84).

Minor comment:

Comment 1: Please write with one decimal point or less in manuscript.

Reply 1: Now write with one decimal point in manuscript.

Changes in the text: See Page2 line 41-43 and Page9 line 177-198

Comment 2: Please replace the total case number "60" to "65" in high-risk factors (>3) of Table 1.

Reply 2: We have replaced the total case number "60" to "65" in high-risk factors (>3) of Table 1.

Changes in the text: See Table 1.

Comment 3: Concerning about the pathological findings. How was it to evaluate for lymphatic and venous permeation by immunohistochemical staining (D2-40, EVG...)? And how to evaluate for budding. Is it means "positive" is grade 2 or 3?

Reply 3: As we mentioned in the part of Histopathological examination in the text (see Page6), The early CRC pathological features examination was performed using 3 methods, i.e. hematoxylin and eosin (H&E) staining for identifying perineuronal invasion, D2-40 immunostaining for lymphatic invasion, and Victoria blue staining for venous invasion. As Reviewer suggested, we added that Lymphatic

invasion was defined as the invasion of at least one tumor cell into a lymphatic vessel in D2-40 stained slides. Venous invasion was defined as a tumor deposit in a space surrounded by a rim of smooth muscle and/or containing red blood corpuscles, Budding was defined as “cancer cell clusters made up of one-to-four constituent cells present at the stroma of invasive front,” and evaluated on H&E stained slides (See Page6-7 line 129-134). The budding “positive” contains all grades including grade 2 and grade 3.

Changes in the text: See Page6-7 line 129-134.