



## Recurrence Rate and Short-Term Outcomes of Endoscopic Submucosal Dissection (ESD) Using Pocket Creation Method vs. Laparoscopic Surgery in Management of Colonic Lateral Spreading Tumor from Surgeons' Prospective

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### Abstract

**Background:** We aimed to compare the clinical outcomes of ESD using PCM versus laparoscopic surgery in management of colonic LST.

**Method:** We conducted a retrospective comparative study of the management of colonic LST not able to be removed by standard endoscopic methods. They either have undergone ESD with PCM or laparoscopic surgeries including colectomy or colotomy and polypectomy. Patient's demographics, perioperative data were retrieved from a database. Patients with other concomitant procedures were excluded.

**Results:** From 2008 to 2018, 42 and 41 patients have undergone ESD and laparoscopic surgeries respectively. The demographic data and mean sizes of the LST in the two groups were similar. Although ESD had significantly longer procedure time ( $141 \pm 43$  min vs.  $115 \pm 44$  min,  $p=0.008$ ), but it had shorter hospital stay ( $4.7 \pm 1.4$  days vs.  $8.9 \pm 5.4$  days,  $p<0.005$ ). The ESD group had a trend of lower complication rate ( $2/42$  vs.  $7/41$ ,  $p=0.071$ ) than laparoscopic group. The en-bloc resection rate of ESD was 90.5% and the R0 resection rate was 83.3%. There was one postoperative mortality in the laparoscopic group with no mortality in the ESD group ( $p=0.31$ ).

**Conclusion:** In management of colonic LST, ESD with PCM due to its less invasiveness results in less morbidities, shorter hospital stay than laparoscopic surgeries, even in a unit with low volume of ESD.

**Keywords:** Endoscopic Submucosal Dissection (ESD); Pocket creation method; Laparoscopic surgery; Lateral spreading tumor

### Introduction

Due to increasing surveillance programs for colon cancer, early colonic neoplasm is becoming more commonly detected. Lateral spreading tumor is difficult to be removed en-bloc by ordinary endoscopic treatment due to its sessile nature. Endoscopic Submucosal Dissection (ESD) has been proven to be superior in the en-bloc resection rate than EMR in treating sessile early colorectal lesions to allow detailed pathological examination, resulting in a lower recurrence rate in the long-term [1-7]. Before the introduction of ESD, large lateral spreading tumors were resected by surgical method if not able to be removed by endoscopic method; however, complication rates can be as high as 11.8% to 15% [8-9].

There were few reports comparing ESD and surgeries in the literature, showing better short-term outcomes for ESD [10-13]. New Techniques like the Pocket Creation Method (PCM) further improved the results of ESD [15-18]. In most parts of the world, ESD is done by gastroenterologist, usually in centre with large volume, mostly in Asia [19,20]. The aim of this study is to assess both short-term outcomes and long-term recurrence rate of ESD using PCM vs. laparoscopic surgery in management of colonic lateral spreading tumor in a surgical unit, in which the case load of ESD is relatively small.

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## Methods

### Patient selection and pre-operative data

From August, 2008 to February, 2018, data of consecutive patients diagnosed with colonic lateral spreading tumor larger than 2 cm deemed not able to be removed by ordinary endoscopic methods in our unit were retrieved in a prospectively maintained database. Lesions are assessed by Narrow Band Imaging (NBI) according to Narrow-Band Imaging International Colorectal Endoscopic (NICE) classification. Only lesions of NICE type 2, which is compatible with adenoma or of benign histology in biopsy, are recruited. Lesions of NICE type 3, which is compatible with invasive cancer or proven to be malignant by initial endoscopic biopsies, were excluded. Rectal lesions were excluded. They either have undergone ESD or laparoscopic surgeries including colectomy or colotomy and polypectomy. Informed consents were obtained for both procedures.

### Surgical procedure and technique

Patients in both groups were admitted on the day before procedures and mechanical bowel preparation of polyethylene glycol solution was given. A prophylactic antibiotic in form of a single dose of 1.2 g intravenous amoxicillin and clavulanic acid was given upon anesthetic induction. All the ESD and laparoscopic surgeries were performed by the same team of colorectal specialist surgeons. Surgeons who performed ESD had undergone training in expert centers of ESD in Japan.

### ESD

All ESD were performed under Monitored Anesthesia Care (MAC). We used GIF 190 (OLYMPUS, Tokyo, Japan) as the endoscope, and ST Hood (DH-15GR; Fujifilm, Tokyo, Japan) as the endoscopic hood to allow easy insertion into the submucosal space. Flush knives (Fujifilm), Dual knife (OLYMPUS) are our preferred main dissection instruments as they allowed water jet function. IT knife nano (OLYMPUS) was used if retraction of the lesions was suboptimal. Coagrasper (OLYMPUS) was used as hemostatic forceps. The solution to be injected was a mixture of to a 1% sodium hyaluronate solution (Hyruan; LG Life Science, Korea), gelofusin, a small amount of methylene blue and adrenaline. VIO300 D (ERBE Elektromedizin Ltd, Tübingen, Germany) was used as the high-frequency electrical generator. We insufflate Carbon Dioxide (CO<sub>2</sub>) to reduce patients' discomfort. We used "Pocket Creation Method" (PCM) as our strategy in which a wide submucosal pocket is created under the lesion after a minimal mucosal incision. A circumferential mucosal incision including an oral side incision was made only in the final steps of the procedure. Hemostasis was achieved by using hemostatic forceps for the exposed blood vessels on the muscle surface after resection. Mucosal defects were closed with endoclips. Once perforation happened, the muscle layer was closed with endoclips if possible. Salvage surgery was needed if the conservative management failed. If the patient recovered well, fluid diet would be resumed on day 1 after the procedure.

### Laparoscopic surgeries

The operations were all performed under general anesthesia. For colectomy, surgeries were done in medial approach; vascular pedicle was ligated followed by mobilization of the colon laparoscopic laparoscopically. For lesions in the left sided colon, a mini-laparotomy incision was made in the suprapubic area for specimen retrieval and anvil insertion colorectal anastomosis was performed intracorporeally. For lesions in the right-sided colon, a mini-

laparotomy incision was made in the left upper quadrant, and then the anastomosis was performed extracorporeally. If the lesions were in the redundant part of colon, e.g. the sigmoid colon, laparoscopy was used to identify the lesions and mobilized the colon if necessarily. Similar mini-laparotomy incision was made and the colon delivered out. A longitudinal colostomy was made and the lesions were excised. The mucosal defects were closed. Colostomy was transversely by interruptedly. Diet was resumed if the bowel function returned.

### Post-operative management and follow-up

Patient would be discharged if they tolerated diet and were ambulatory with normal white cell count. Patient demographics, perioperative data like procedure time, length of stay, complications, mortality and local recurrence rate were retrieved from a database for comparison. Patients with other concomitant procedures were excluded.

### Statistical analysis

Data were analyzed with an intention-to-treat principle. Statistical analysis was performed using the Statistical Package for the Social Sciences for Windows version 19.0 (IBM SPSS Statistics, IBM Corporation, New York, USA). The difference in the continuous variables between the two groups was correlated by Student's t-test, while Chi-squared test was used for categorical variables. A P-value of less than 0.05 was regarded as statistically significant.

## Results

From August, 2008 to February, 2018, 42 patients have undergone ESD and 41 patients have undergone laparoscopic surgeries. The demographic data and mean sizes of the lateral spreading tumors in the two groups were similar. For laparoscopic surgery group, there were 26 laparoscopic right hemicolectomies, 1 laparoscopic left hemicolectomy, 6 laparoscopic anterior resections, 9 laparoscopy and colotomy. The mean procedure time was significantly longer in the ESD group when compared with laparoscopic surgical group ( $141 \pm 43$  min vs.  $115 \pm 44$  min,  $p=0.008$ ). However, ESD had shorter total hospital stay than that of laparoscopic group ( $4.7 \pm 1.4$  days vs.  $8.9 \pm 5.4$  days,  $p<0.005$ ) reflecting faster recovery. The blood loss in ESD was negligible, while the mean blood loss in laparoscopic group was  $23.1 \pm 19$  ml. The en-bloc resection rate of ESD was 90.5%. The R0 resection rate was 83.3%. ESD had lower complication rate that of laparoscopic group, (2/42 vs. 7/41,  $p=0.071$ ) which was not statistically significant. There were two perforations in ESD group (4.8%). One is managed by endoscopic clipping. Another perforation required surgical repair and was operated laparoscopically by the same surgeon who did the ESD. The patient was discharged on D7 uneventfully after the surgery. There was no delayed bleeding in the ESD group. There was one postoperative mortality in the laparoscopic group due to anastomotic leakage and postoperative pulmonary embolism while there was no mortality in the ESD group ( $p=0.31$ ).

For long-term results, there was one local recurrence in the ESD group (2.4%) which required colectomy and there was 2 local recurrence after colotomy in the laparoscopic group (4.9%), one of which was managed by ESD ( $p=0.309$ ).

## Discussion

As ESD can be done under MAC, the complications secondary to general anesthesia like myocardial infarction, cerebral vascular accident, chest infection, can be avoided. As there is no wound over the abdominal wall after ESD, complications related to wound as well

as those related to pain are therefore entirely abolished. Therefore, speedy recovery is the beauty of ESD, which is reflected in the 4 days shorter in the mean hospital stay in the ESD group in our study. All these benefits are of paramount importance to our patients, especially elderly. Although ESD is expected to have lower complication rate than that of laparoscopic surgeries, however, the difference was not statistically significant in this study, probably due to the small sample size.

Good clinical outcomes of colorectal ESD have been reported by high-volume centers, especially in Japan and Asia [19-23] and most of the colorectal ESD were done by gastroenterologists in Japan. Studies also reported that the en bloc resection rate was significantly higher with lower complication rates in high-volume centers especially in Asia than that in low-volume centers [19,23].

Literature showed that there were superior benefits of ESD in terms of complete resection and tumor recurrence as compared to EMR or conventional endoscopic methods [1-7]. This paper is one of the few studies on the results of ESD from a surgical unit. Despite the relative small case load of ESD in a surgical unit and surgeons need to distribute their time on both surgeries and ESD, our morbidity rate; en-bloc resection rate and R0 resection rate were comparable with high-volume centers in the world. A recent multicentre study showed the en bloc and R0 resection rates 12 institutions in Japan were 92.6% and 83.7%, respectively [23]. This showed that ESD can be done by surgeons after proper training and the pocket creation methods, resulting in promising results. Surgeons have the advantage of providing continual care for patients and arrange timely repair once perforation arose.

Our promising results were partly attributed by the advancement of techniques and technology in ESD with the use of Pocket Recreation Method (PCM). Hayashi first reported the pocket creation method in 2014, in which a wide submucosal pocket is created under the lesion after a minimal mucosal incision [15]. Circumferential incision was not made until the submucosal dissection has been completed. PCM has the beauty of maintenance of the thick submucosal layer with a minimal mucosal incision, provision of optimal traction and the tangential approach to the muscle layer to avoid injury even at a fold or a flexure [16]. When compared with conventional ESD, PCM has been proved to have higher rates of en bloc resection and curative endoscopic resection [14,17]. In cases with severe fibrosis, the PCM improved en bloc resection rates and shortened the procedure time and reduced the discontinuation rate compared to the conventional non-PCM [18]. Saito et al. reported that the complication rate was as high as 17.6% at units in which the number of ESDs performed was less than 50 [21]. Our promising results despite relatively low volume indicate that PCM may shorten the learning curve of ESD. It is especially useful for surgeons, who may not be able to contribute a lot of time in ESD apart from surgeries, to start ESD.

ESD had been compared with laparoscopic colectomy for early colorectal cancer in two Japanese studies [10,11] which showed that ESD had shorter length of hospital stay and time to oral intake after the procedures, fewer complications, better quality of life. However, the indications for ESD and LAC are quite different (ESD for noninvasive tumors; LC for invasive cancers). Also Hon et al. has also reported the short-term benefits of ESD over laparoscopic resection for early colorectal neoplasia by surgeons [12]. Apart from short-term outcomes, our study also assessed the long-term recurrence rate. For early rectal neoplasms, ESD offers better short-term clinical

outcomes in terms of faster recovery and possibly lower morbidity than local excision [13].

The weakness in this study is that the numbers of both arms are relatively small. The cases in these studies included the cases in the initial learning curve of our surgeons and we were able to achieved results comparable with the literature. With further mastering of the skills and improvement in technique, strategy, the difference in the procedure time between ESD and laparoscopic surgeries can be further shortened.

## Conclusion

In management of colonic lateral spreading tumor, ESD with pocket creation method, although with longer procedure time, has shorter hospital stay than laparoscopic surgeries, probably due its less invasiveness, resulting in less morbidity and mortality, even in a unit with low volume of ESD. The long-term local recurrence rates are comparable.

## Author Contributions

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

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