Original Article

Sharing Single Surgeon Experience of Learning Endoscopic Submucosal Dissection for Colorectal Lesions

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Key Words

ESD; Endoscopic submucosal dissection; Colorectal polyps; Learning curve **Background.** Endoscopic submucosal dissection (ESD) is used for removing colorectal lesions. It is a very technically demanding but less widespread therapy. We try to demonstrate our single-surgeon experience in learning this operation.

Method. We reviewed patient from October 2015 to December 2018 who received the operation. 18 patients were enrolled. Patient profiles, lesion size, location, pathology report, en bloc resection, margin involvement, operating time, and complications were analyzed.

Results. The lateral spreading tumors treated with endoscopic submucosal dissection located at the cecum (n = 4), ascending colon (n = 3), transverse colon (n = 2), descending colon (n = 1), sigmoid colon (n = 5) and rectum (n = 3). The average size of the tumors was 2.46 cm (range, 1 to 3.7 cm). The en bloc resection rate was 83.33%, and the complete resection rate was 61.1%. Only one patients experienced micro-perforation, and the overall complication rate was 5.56%. Positive correlation was noted between lesion size and operation time (co-efficient value = 0.33).

Conclusion. ESD is a difficult procedure. Small lesions can decreased operative duration. Cecum is more challenging because of nearby structure. Through experience accumulation, improving en bloc and R0 resection rate can be seen.

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E ndoscopic submucosal dissection (ESD) for colorectal tumors was initially introduced by Japanese endoscopists.^{1,2} Lower recurrence rate and better en bloc and R0 resections, interpreted as one-piece resection and negative margin involvement, when comparing ESD with endoscopic mucosal resection (EMR).^{2,3} Proper application of ESD is usually costeffective and beneficial for certain patients who wish to avoid invasive surgical treatment.^{4,5} The procedure has a similar 5-year mortality rate as conventional surgery for lateral spreading tumors in the large intestine.⁶ ESD has been gradually accepted and performed world-

wide, but it is used in a limited number of cases in Taiwan.⁷⁻⁹ It is because the procedure is technique demanded and not covered by insurance. Also, it needs special device for endoscopic management. Therefore, we share our experience and learning curve and wish to find a better way for beginners.

Methods

The standard equipment for ESD in our facility is the ERBE system and Olympus endoscope. The endo-

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scopic cutting system includes an I-type and O-type hybrid knife and VIO 300D electrocoagulation. For submucosal injection, a solution consisting of glycerol, hyaluronic acid, and methylene blue is used. The endoscope used for ESD is labeled as CF-H290ECI.

Before the operation, abdominal computed tomography (CT) was performed to confirm the malignant character of the lesion. The lesion was reevaluated under colonoscopy and classified using the system of Kudo's pit pattern classification and JNET classification.

We selected patients who underwent ESD from October 2015 to December 2018. Data collected included age, gender, operation duration (minutes), lesion location, and size (long axis, cm). Patient demographics are shown in Table 1. We also recorded the pathology report to pursue tumor/polyp type, involved depth, margin, en bloc rate, and complications. We also differentiated the data by year, lesion size, and location to determine whether a difference or relation existed between these factors. The correlation coefficient value was also used and calculated by Excel software to evaluate the trends of our grouping.

Results

The average age of the patients was 65.6 years

Table	1.	Patient	demogra	phics
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Characteristics, n(%)	Overall number $(n = 18)$
Mean age in years	65.6 (51-83) ^a
Male	10
Female	8
Cecum	4
Ascending	3
Transverse	2
Descending	1
Sigmoid	5
Rectum	3
Tumor size, cm ²	$2.46(1-3.7)^{a}$
Procedure time/procedure time per unit, min	192.8/47.84
Enbloc rate (%)	15 (83.33%)
R0 resection (%)	7 (61.1%)
Complication (%)	1 (5.56%)

^a Range.

(Table 1). The male-to-female ratio was 5:4 (10 men, 8 women). Lesion locations were as follows: 4 cases at the cecum, 3 at the ascending colon, 2 at the transverse colon, 1 at the descending colon, 5 at the sigmoid colon, and 3 at the rectum. The average tumor size was 2.46 cm and ranged from 1 to 3.7 cm in the long axis. The average procedure duration was 192.8 minutes and 47.84 minutes per 1 cm². R0 resection was achieved in 61.1% of cases, whereas 7 cases had a positive horizontal margin. The en bloc resection rate was 83.33%. Fifteen lesions were sent as 1-piece specimens for final pathological study. There was one case had micro-perforation after the procedure. The total complication rate was 5.56%.

The trend graph in Fig. 1 shows the recorded lesion size (cm²) and operation time (minutes), for which a modestly positive correlation (correlation coefficient value as 0.33) can be observed. This confirms our hypothesis that a larger lesion would require a longer operation time.

To determine the learning curve in Fig. 2, we divided our cases equally into 3 groups based on procedure date (6 patients in each group). We evaluated the included items as minutes/cm², en bloc resection, and

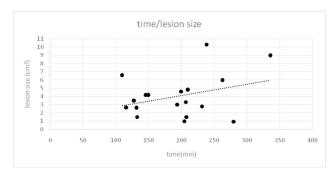


Fig. 1. Size, operation time correlation.

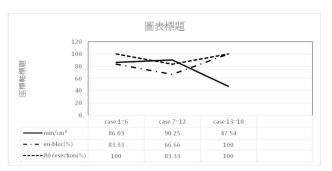


Fig. 2. Learning curve.

margin status to determine if a tendency toward improvement could be identified. We noted a shortened operative duration per 1-cm² dissection in the third stage. The en bloc resection rate and R0 resection rate revealed an improving trend in the second and third stages. We also demonstrate difference between different locations in Table 3 and which showed the complication developed in cecal group. Because of uneven distribution of case number, the difference is less significant.

After the procedure, we reviewed the pathology report for margin evaluation and polyp classification. In Table 2, there were 11 cases of high-grade dysplastic adenoma and 4 cases of low-grade dysplastic adenoma. One case of adenoma was not classified. Narrow-band imaging and pit pattern classification were also recorded to determine the pre-ESD evaluation and its feasibility. Through the review, no highrisk invasion was seen in either vascular or neural invasion. The invasion depth was less than 1000 μ m.

Table 2.	Pathology	and	endosco	pic	finding	category

	Number
Pathology	
Adenoma with high-grade dysplasia	11
Adenoma with low-grade dysplasia	4
Adenoma	1
Adenocarcinoma	1
Hyperplastic polyp	1
Invasion	
Vascular invasion	0
Neural invasion	0
Submucosal invasion > 1000 µm	0
Gross finding	
Sessile	2
LST-G	12
LST-NG	4
Kudo pit pattern	
II	1
IIIL	6
IIIS	4
IV	6
VL	1
JNET	
Ι	1
IIA	5
IIB	11
III	1

Grossly, granular-type lateral spreading tumor occurred in most of the 12 cases, whereas 2 cases were sessile-type and 4 non-granular-type lesions.

To demonstrate the feasibility of ESD, we used the Kudo pit pattern and JNET classification to identify the proper lesion. Both systems presented similar results and percentages.

All 18 cases maintained regular follow-up after the operation, including the patient with adenocarcinoma, and no focal recurrence was developed at 1year follow-up.

Discussion

Micro-perforation developed in one case after the operation. The granular-type lesion with type IIA JNET classification appearance occurred at the cecum next to the appendix orifice with a size of 9 cm^2 (Figs. 3-5). ESD was performed, and en bloc resection was completed. The vertical margin was free of adenoma. The horizontal margin was involved. No perforation was noted after the polyp was removed. Multiple hemoclips was applied after the specimen was removed. No peritonitis was developed, but minimal pneumoperitoneum was noted by abdominal radiography taken after abdominal pain developed. Empiric antibiotics were given, and symptoms of abdominal pain subsided at 2 days. Hospital length of stay was prolonged as the NPO status was maintained until the patient's clinical condition improved. After 2-year follow-up, there were no signs of recurrence on endoscopy. No other complication developed, such as postoperative bleeding. R0 resection rate at the cecum group was

Table 3. Subgroup in locations

Location	R0 resection (%)	En bloc resection (%)	Complication (n)
Cecum $(n = 4)$	50%	100%	1
Ascending colon $(n = 3)$	33.33%	100%	0
Transverse colon $(n = 2)$	50%	50%	0
Descending colon $(n = 1)$	100%	100%	0
Sigmoid colon $(n = 5)$	80%	60%	0
Rectum $(n = 3)$	66.67%	100%	0

50% (Table 3) and our only complication came from the lesion sit at the cecum. There are some studies reported the difficulty and feasibility of resecting cecal lesions, when the procedure is performed by experienced surgeons using advanced tools, this site has no influence on the R0 resection or en bloc resection rate, even though the ileocecal valve and appendix orifice may increase the difficulty of the operation.¹⁰⁻¹²

One adenocarcinoma occurred after ESD. The le-

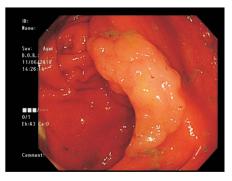


Fig. 3. Operation picture of case developed micro-perforation (initial).



Fig. 4. Operation picture of case developed micro-perforation (NBI image).

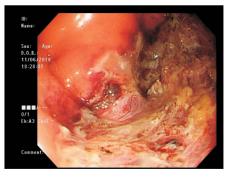


Fig. 5. Operation picture of case developed micro-perforation (removal completion).

sion was located at the descending colon with size of $2.2 \times 1.2 \times 0.5$ cm. Kudo pit pattern was type VL. JNET type was IIB (Figs. 6-9). The lesion was completely removed in one piece with both free horizontal and vertical margin. There was no lymphovascular or neural invasion. The invasion depth was about 700 µm beneath the muscularis mucosae. No immediate complication developed. During 2-year follow-up, which included 3 colonoscopies and an abdominal CT scan, there was no evidence of recurrence, malignant change, or lymph node metastasis.

We attempted to determine the type of lesion more suitable for a ESD beginners. Location and lesion size have long been discussed as the main challenges in this operation.^{13,14} Emmanuel et al. recommended that



Fig. 6. Operation picture of case with final diagnosis of adenocarcinoma (initial).



Fig. 7. Operation picture of case with final diagnosis of adenocarcinoma (NBI).

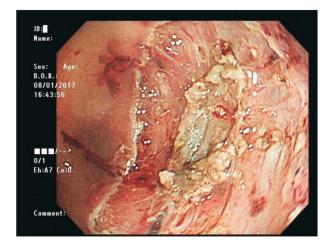


Fig. 8. Operation picture of case with final diagnosis of adenocarcinoma (removal completion).

granular lesions larger than 3 cm and nongranular lateral spreading tumors larger than 2 cm are better treated with ESD.¹⁴ A prospective study conducted by Sakamoto et al. suggested that a lesion smaller than 4 cm is better for beginning ESD training.¹³ In our short-term experience, the difficulty and risk of perforation is increased for lesions that are larger in size and located at the cecum, because of its redundancy and its thin bowel wall. In addition, lesions that sit at an angulation site or behind a valve will also increase the difficulty of the procedure. Through the trend graph in Fig. 1, which displays the lesion size and operation time, we can observe a trend line with a moderately positive correlation (correlation coefficient = 0.33). This low correlation may be affected by the location, as we redistributed and grouped our data by lesion location and year of surgery.

The learning curve for colorectal ESD has been analyzed and presented in several studies. Mainly, European and Japanese guidelines mention 2 aspects of a qualified ESD: margin status and en bloc resection.^{2,15} It is suggested in some studies that as many as 80 cases might need to be completed before obtaining excellent results (promising en bloc and R0 resection).^{16,17} Despite the fact that we collected only 18 cases, the en bloc resection rate in our records was 83.33%. Respectively, it was 66.6% in the first year, 100% in the second year, and 70% in the third year. A trend in improvement was seen through accumulating experience. In Hong Kong, a low-volume center demonstrated a

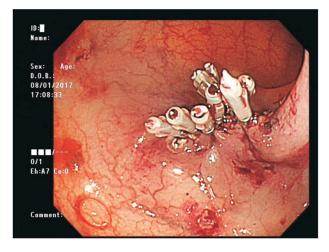


Fig. 9. Operation picture of case with final diagnosis of adenocarcinoma (after hemo-clipping).

similar pattern, with a learning curve of more than70 operations.¹⁸ Iacopini et al. demonstrated a nonacademic learning curve in which the rectal ESD en bloc resection rate was 80% after 5 procedures and the operating time per square centimeter decreased significantly after 20 procedures, whereas the colonic ESD learning curve showed an en bloc resection rate of 80% after 20 procedures. In that study, the operating time per square centimeter decreased significantly after 20 procedures.¹⁹ Both studies hint at a training curve similar to our result. Although ESD is a technique-dependent operation, through proper training and experience, the result can still be improved and acceptable. Among these three unsuccessful en bloc resection lesions, no tumor recurrence was observed on follow-up colonoscopy. Some studies have demonstrated that EMR or piecemeal EMR had a similar low recurrence rate and could adequately manage most early colonic tumors.^{20,21} This result can intercede for the initial experience and unsatisfied en bloc resection.

Based on the European ESD guidelines published in 2015, the involvement of the is classified as horizontal resection margin and vertical one. High-risk resection is defined when positive vertical margin is present or margin less than 1000 μ m or lymphvascular invasion is yielded or poorly differentiation. Surgical treatment with or without adjuvant therapy is recommended because of the risk of lymph node metastasis in early cancer.^{2,22,23} As a result, positive lateral margins would suggest endoscopic follow-up rather than adjuvant therapy or surgical intervention.^{2,19,23} In our series, most of the R1 resection margins were involved in the horizontal plane but not the vertical plane. That does not contribute to high-risk resection because no features such as neural invasion or lym-

The limitation of our study mainly comes from the case selection method and the fact that the lesion location could not be categorized because of the small sample size. For example, only one descending colon lesion was obtained.

phovascular invasion were yielded in such lesions.

Conclusion

ESD remains a difficult procedure but it is efficient and less invasive. A smaller lesion size can significantly decrease the perforation rate and shortened operative duration. Cecal lesion may increase intervention difficulty because of its adjacent structure. En bloc and R0 resection can improved under experience accumulation.

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References

- Puli SR, et al. Successful complete cure en-bloc resection of large nonpedunculated colonic polyps by endoscopic submucosal dissection: a meta-analysis and systematic review. *Ann Surg Oncol* 2009;16(8):2147-51.
- Pimentel-Nunes P, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2015;47(9):829-54.
- Saito Y, et al. A prospective, multicenter study of 1111 colorectal endoscopic submucosal dissections (with video). *Gastrointest Endosc* 2010;72(6):1217-25.

- Niimi K, et al. Long-term outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms. *Endo*scopy 2010;42(9):723-9.
- Fukami N. Surgery versus endoscopic mucosal resection versus endoscopic submucosal dissection for large polyps: making sense of when to use which approach. *Gastrointest Endosc Clin N Am* 2019;29(4):675-85.
- Oka S, et al. Local recurrence after endoscopic resection for large colorectal neoplasia: a multicenter prospective study in Japan. *Am J Gastroenterol* 2015;110(5):697-707.
- Chiu HM, et al. Current status and future perspective of endoscopic diagnosis and treatment for colorectal neoplasia - situation in Taiwan. *Dig Endosc* 2009;21 Suppl 1:S17-21.
- Yoda Y, et al. A large-scale multicenter study of long-term outcomes after endoscopic resection for submucosal invasive colorectal cancer. *Endoscopy* 2013;45(9):718-24.
- Choo CH, et al. Short-term outcomes of endoscopic submucosal dissection for colorectal neoplasms in a single medical center. *Advances in Digestive Medicine* 2015;2(2):54-60.
- Song EM, et al. Endoscopic resection of cecal polyps involving the appendiceal orifice: a KASID Multicenter Study. *Dig Dis Sci* 2017;62(11):3138-48.
- Ge PS, Thompson CC, Aihara H. Endoscopic submucosal dissection of a large cecal polyp using a scissor-type knife: implications for training in ESD. *VideoGIE* 2018;3(10):313-5.
- Suzuki T, et al. Feasibility of endoscopic submucosal dissection for cecal lesions. *Scand J Gastroenterol* 2018;53(3): 359-64.
- Sakamoto T, et al. Short-term outcomes of colorectal endoscopic submucosal dissection performed by trainees. *Digestion* 2014;89(1):37-42.
- Emmanuel A, et al. Colorectal endoscopic submucosal dissection: patient selection and special considerations. *Clin Exp Gastroenterol* 2017;10:121-31.
- Tanaka S, et al. Japan Gastroenterological Endoscopy Society guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. *Dig Endosc* 2020;32(2): 219-39.
- Hotta K, et al. Learning curve for endoscopic submucosal dissection of large colorectal tumors. *Dig Endosc* 2010;22(4): 302-6.
- 17. Herreros de Tejada A. ESD training: a challenging path to excellence. *World J Gastrointest Endosc* 2014;6(4):112-20.
- Chong DH, Poon CM, Leong HT. Colorectal endoscopic submucosal dissection at a low-volume centre: tips and tricks, and learning curve in a district hospital in Hong Kong. *Hong Kong Med J* 2016;22(3):256-62.
- Iacopini F, et al. Stepwise training in rectal and colonic endoscopic submucosal dissection with differentiated learning curves. *Gastrointest Endosc* 2012;76(6):1188-96.
- Nakajima T, et al. Current status of endoscopic resection strategy for large, early colorectal neoplasia in Japan. Surg Endosc 2013;27(9):3262-70.

- Pearson RK, Endoscopic mucosal resection outcomes and prediction of submucosal cancer from advanced colonic mucosal neoplasia. *Yearbook of Gastroenterology* 2011;2011: 128-9.
- 22. Beaton C, et al. Systematic review and meta-analysis of histopathological factors influencing the risk of lymph node

metastasis in early colorectal cancer. *Colorectal Dis* 2013; 15(7):788-97.

23. Butte JM, et al. Rate of residual disease after complete endoscopic resection of malignant colonic polyp. *Dis Colon Rectum* 2012;55(2):122-7.

<u>原 著</u>

單一醫師、內視鏡黏膜下切除之經驗分享

黃暐聖 楊靖國 林秉緯 孫文俊 陳建勳 賴正大 蔡伯立 梁偉雄 許希賢 陳明仁 劉建國

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背景 大腸鏡黏膜下切除可用於較大的大腸直腸瘜肉,執行難度高而且比較不普及,本 篇多個案分析研究希望藉由單一外科醫師手術經驗提供初學者參考。

方法 收集 2015 年至 2018 年共 18 個案例,針對個案分類,瘜肉的病理分析,以及術後追蹤,整合出學習曲線以及手術成果的進步。

成果 本研究的病灶位置位在盲腸 (4 例)、升結腸 (3 例)、橫結腸 (2 例)、降結腸 (1 例)、乙狀結腸 (5 例) 及直腸 (3 例)。平均大小為 2.46 公分。完整切除比例為 83.33%。 邊緣陰性率為 61.1%。僅一例於術後有輕微腸穿孔之併發症,併發症發生率為 5.56%。 病灶大小與手術時間為正相關,相關係數為 0.33。

結論 黏膜下切除雖然是一個難度高的手術。較小的病灶可以縮短手術時間。盲腸因為 鄰近的構造,會增加手術的難度。藉由經驗的累積,在完整切除以及邊緣侵犯的比例都 能進步。

關鍵詞 黏膜下切除、大腸直腸瘜肉、學習曲線。