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Resection of Mucosal and Submucosal Gastrointestinal Lesions and a Double Endoscope Experience

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ABSTRACT

Aim: The patients who underwent endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) for mucosal and submucosal lesions of the esophagus, stomach, and duodenum and the advantages of the double endoscope method we used for traction during ESD were evaluated.

Material and Methods: The patients who underwent ESD and EMR due to upper gastrointestinal lesions were evaluated retrospectively between January 2014 and April 2018 in our endoscopy unit.

Result: The mean age of 10 patients with esophageal lesions was 53 years. ESD was performed for 7 lesions and EMR for 3 lesions. The most common lesion was leiomyoma and the median size of the lesions was 1.4 cm (range, 0.6–2.5 cm).

The median age of 26 patients with gastric lesions was 61 years. EMR were performed for 11 lesions and ESD for 15 lesions. Double endoscope was used in 6 patients. One patient had intramucosal carcinoma, while the other lesions were benign and dysplasia was the most common lesion. The median size of lesions was 1.8 cm (range, 1–3 cm).

All lesions were evaluated with endoscopic ultrasonography. Bleeding was seen in 4 patients and perforation in 1 patient during ESD and defect was closed with endoscopic clips.

Conclusion: The advantages of endoscopic resections; short hospitalization, low complication rates, patient comfort, and doesn't require the general anesthesia. For endoscopic resection, we think that the second endoscope shortens the duration of the procedure, reduces the complication rate, and increases the comfort of the endoscopist.

Keywords: Endoscopic mucosal resection, Endoscopic submucosal dissection, Double endoscope experience.

INTRODUCTION

The mucosal and submucosal lesions of the esophagus, stomach, and duodenum are benign, premalignant, or malignant lesions depending on the cell type in the layers of these organs and have specific features.

These lesions were mostly detected in diagnostic endoscopy but were occasionally detected incidentally during the other diagnostic procedures. The Paris and Kudo classification were used to define the superficial lesions of the mucosa and the depth of lesions were determined by endoscopic ultrasonography (EUS).[1,2] Considering the potential for malignancy, forceps biopsy was performed from superficial lesions before endoscopic resection. The echogenicity of the submucosal lesions and the layer of origin were evaluated by EUS.

The patients were informed of the detailed about the lesions and the procedures to be performed, and detailed informed consent was obtained from all of patients included in this study. The comorbidities of the patients were evaluated. The treatment of patients receiving anticoagulant medication was regulated to prevent bleeding related to the procedure.

According to the scores determined by the American Society of Anesthesiologists, patients with an American Society of Anesthesiologists score higher than three, the procedures were performed under the management of the anesthesiologist.

Endoscopic mucosal resection (EMR) was performed following submucosal injection in mucosal lesions up to 2 cm in diameter. On the other hand, endoscopic submu-

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cosal dissection (ESD) was performed in order to perform complete resection for larger than 2 cm and submucosal localized lesions. ESD procedures, submucosal injection materials with longer duration of absorption were used, and some procedures were performed using a double endoscope.

PATIENTS AND METHODS

We retrospectively reviewed the 36 patients who underwent ESD and EMR due to mucosal and submucosal lesion of upper gastrointestinal tract between January 2014 and April 2018.

Esophageal Lesions

The median age of 10 patients (4 female/6 male) with esophageal lesions was 53 years (range, 20–66 years). Four of the lesions were located in the middle and 6 in the distal esophagus (**Table 1**).

When two lesions that originated from the mucosal layer were evaluated by EUS, it was seen that they extended to the muscularis propria. In these patients, EMR was performed. In the other 8 patients, the lesions were submucosal layer. The echogenicity and location of the lesions were assessed with EUS and ESD was performed.

In esophageal lesions, submucosal injection was not used for the prevention of narrowing the luminal area. The upper mucosa of 5 submucosal lesions was opened with a needle knife and reached the lesion. Submucosal dissection was performed with an insulated tipped knife to complete the en block resection of the lesion. In 2 patients with mucosal lesions, the free margin was identified with electrocautery and submucosal dissection was performed with insulated tipped knife and the procedure was completed. In a patient who underwent ESD for submucosal lesion, esophagus variceal band was used for the up traction of the lesion and the submucosal dissection area was better demonstrated. There was no serious complication in the patient. Hemostasis was achieved with endoscopic clips in 2 patients whom hemostasis was not controlled by electrocautery. The most common lesion in the pathological examination was leiomyoma and the median size was 1.4 cm (range, 0.6–2.5 cm).

In one of the patients with ESD, the surgical margin was positive. In other cases, a free surgical margin was obtained. Due to the submucosal location of this lesion, no additional intervention was performed and followed. Patients who underwent EMR were discharged from the endoscopy unit while ESD patients were hospitalized 1 day for followup.

Table 1.
Characteristics of Esophageal Lesions

Average age of patients (years)	53 (20–66)		
Gender	4 Female/6 Male		
Localization of the lesions & Procedures	ESD	EMR	Total
Proximal	—	—	—
Middle	2	2	4
Distal esophagus	6	—	6
Pathology of Lesions		Surgical margin ±	
Leiomyom	4	1 patient (+)	
Lipom	2	—	
Granulosa celular tumor	1	—	
High grade dysplasia	1	—	
Hyperplastic polyp	1	—	
Adenomatous polyp	1	—	
Complications	Perforation	Bleeding	
EMR	—	—	
ESD	—	2	

EMR, Endscopic Mucosal Resection; ESD, Endoscopic Submucosal Disection.

Gastric Lesions

The median age of 26 patients (13 women/13 men) with gastric lesions was 61 years (range, 40–80 years). ESD and EMR were performed in 15 and 11 patients, respectively (**Table 2**).

The lesions originated from the mucosal layer in 21 patients and biopsy was performed before the procedure. Five of the lesions were localized in the submucosal layer. The layer from which these lesions originated in the stomach wall was identified by EUS before the procedure.

According to the Paris classification, the appearance of the lesions was between 0 and IIb. The depth of these lesions were determined by EUS and it was decided whether EMR or ESD was appropriate. The lesions were located in the antrum, corpus, pylorus, cardia, and fundus according to their frequency. EMR was performed by injecting saline and diluted adrenaline into the submucosal area. A submucosal injection and variceal band were used to raise the lesion of three patients.

Considering the duration of ESD, sodium hyaluronate and diluted adrenaline was injected into the sumbucosal area for 8 patients, while saline and diluted adrenaline was injected into the other 7 patients.

Perforation occurred in a patient who underwent ESD for Gastrointestinal stromal tumor (GIST) during the procedure. Perforation was detected during the procedure and the perforation area was closed using two endoscopic clips. This patient was hospitalized. Antibiotic treatment was started and oral intake was discontinued for 3 days. The patient was discharged on the sixth day without any problems. In other ESD procedures, patients were hospitalized for 1 to 3 days according to lesion size and the mean duration of hospitalization was 1.6 days. Two patients who underwent endoscopic clip for bleeding were

Table 2.
Characteristics of Gastric Lesions

Average age of patients (years)	61 (40–80)		
Gender	13 Female/13 Male		
Localization of the lesions & procedures	ESD	EMR	Total
Cardia	1	1	2
Fundus	—	1	1
Corpus	3	2	5
Antrum	10	6	16
Pylor	1	1	2
Pathology of lesions		Surgical margin ±	
Leiomyom	2	—	
Lipom	1	—	
Metaplasia/hyperplasia/dysplasia	1/1/5	—	
Hyperplastic polyp	3	—	
Inflammatory fibrinoid polyp	4	1 patient (+)	
Neuroendocrin tumor	2	1 patient (+)	
Gastrointestinal stromal tumor	2	—	
GastriC duplication cyst	1	—	
Intramucosal carsinoma	1	—	
Submucosal fibrosis	2	—	
Submucosal ectopic pancreas tissue	1	—	
Complications	Perforation	Bleeding	
EMR	—	—	
ESD	1	4	

EMR, Endoscopic Mucosal Resection; ESD, Endoscopic Submucosal Disection; GastriC, Gastric duplication cyst.

admitted to hospital for observation 1 and 3 days, while other patients were discharged from the endoscopy unit.

Double endoscopes were used for 6 patients during the ESD procedure; In antrum, 4; in cardia, 1; and in the fundus, 1. Because the location and size of the lesions made dissection difficult, a second endoscope was used for traction purposes (**Figures 1 and 2**). There was no differences between the duration of the procedure, who were used the double endoscope and those who were not, and the median duration of the procedure was 54 minutes (range, 45–75 min). The median duration of the procedure in patients who underwent EMR was 26 minutes (range, 18–45 min).

One of the patients had an intramucosal carcinoma with free surgical margins. Of the other lesions, 11 were premalignant and 14 were benign. The mean size of the lesions was 1.8 (1–3) cm. Secondary EMR was performed for a patient who received a neuroendocrine tumor diagnosed with a positive surgical margin. Since neuroendocrine hyperplasia maintained at the surgical margin in this patient, we decided to follow up by EUS. The other patients diagnosed submucosal localized inflammatory fibroid polyp and was followed up with EUS.

Duodenal Lesion

A 74 years old male patient was treated with EMR at different times for different localized lesions of duodenum. The lesions were evaluated with EUS and it was seen that the sessile polyp derived from the mucosal layer. Both lesions were pathologically compatible with hyperplastic polyps and sizes 1.5 and 1.8 cm.

The median follow-up period of the patients was 18 months (range, 2–51 months). Malignancy was detected in one patient and free surgical margin was obtained. This patient was followed closely with the first year, every 3 months after the first year, every 6 months with endoscopy and abdominal computed tomography. Premalign lesions were detected in 12 of the patients. The first endoscopic control was performed after 6 months and annually endoscopic controls were performed in these patients. The surgical margin was positive in three patients. The free surgical margin was obtained in 20 (91%) of 22 patients who underwent ESD and 14 (93.3%) of 15 patients who underwent EMR.

DISCUSSION

Minimally invasive interventions are progressing with the possibilities of technology. The obtained data support the safe implementation of these procedures. Today, endoscopy is used as part of surgical practice as a diagnostic, therapeutic, and follow-up method.

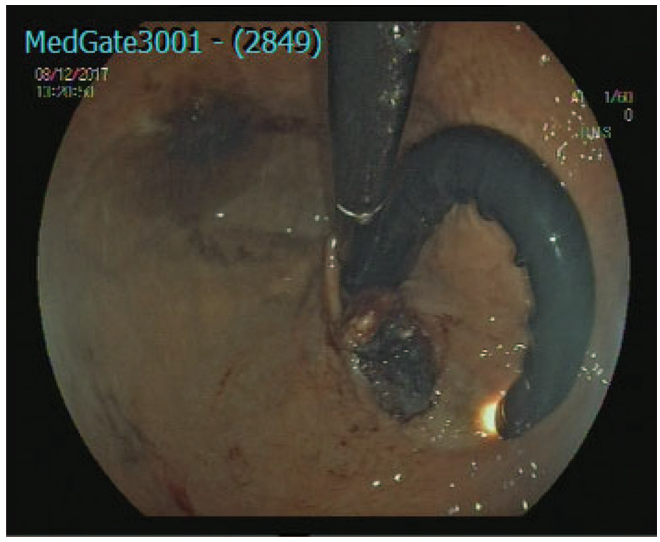

Figure 1. Double endoscope images for the submucosal lesion of cardia.

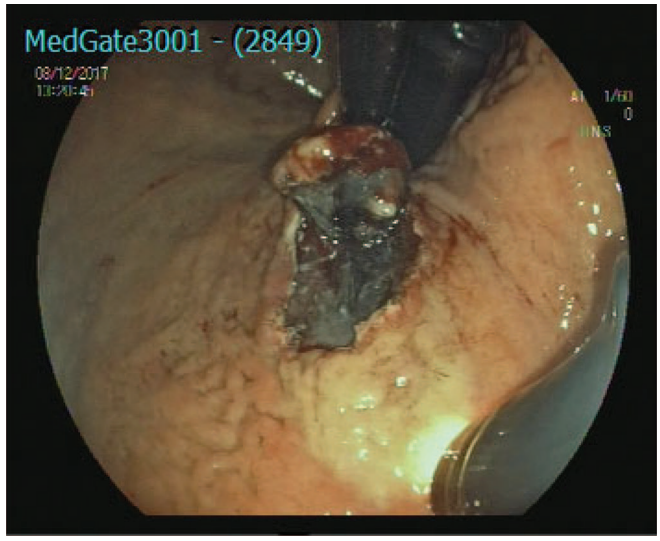

Figure 2. Double endoscope and submucosal dissection of lesion located in cardia.

The most important component of early-stage esophageal, gastric, and duodenal lesions is to evaluate the surface characteristics, size, and depth of the lesion in a comprehensive way.[3] For this purpose, an endoscopic examination of the lesion is first performed and the type of lesion, as well as the pit pattern is determined according to Paris classification.[1,2] Narrow-band imaging, magnification en-

doscopy, indigo carmine and chromoendoscopy, high-resolution Endoscopy, and endoscopic ultrasonography (EUS) can be combined with each other for detailed examination of the lesion and for a clean surgical margin.[3] Guideline states that performing two diagnostic biopsies prior to ESD and EMR for mucosal and submucosal lesions makes endoscopic resection difficult due to fibrosis. Besides, EUS-guided fine-needle biopsy for diagnostic purposes can be performed from submucosal lesions.[4,5] The accuracy rate of EUS-guided fine-needle biopsy varies between 52% and 71%.[6]EMR has been used since 1973. Deyhle and his colleagues,[7] who used EMR for the first time, based this technique on the following principle. Because of the fact that only biopsies from proximal colon polyps can cause inadequate, false, and negative diagnosis for carcinoma, the lesions should be removed completely for correct diagnosis. However, in stalked polyps, polypectomy is performed with the help of cautery in the middle of the stalk. The polypectomy for sessile polyps, with a liquid cushion by creating a safe space for prevent the damage of intestinal wall is safer.

EMR has a high success rate in en bloc resection of mucosal lesions smaller than 10 mm. However, complete resection of lesions up to 20 mm in diameter with EMR can also be achieved.[8] Peacemeal resection is common in larger lesions but free surgical margin cannot be achieved. However, EMR still provides diagnostic and prognostic information, even with incomplete resections.[1] ESD is recommended for large lesions requiring en bloc resection and larger than 20 mm.[9]

The ESD technique was first described by Gotoda et al[11] in 1999 for large, flat, rectum lesions and then used for early gastric cancer. Asian countries such as Japan and Korea are endemic regions for stomach cancer, and the mortality and morbidity rate of this disease is very high. These countries also established stomach cancer screening protocols. Thus, early diagnosis of gastric cancer increased and this allowed these cancers to be treated with ESD.[10,11]

The success rate of ESD in early gastric cancer or recurrence after EMR ranged from 81% to 93% and this indicating a safe rate.[12,13] There is a difficulty in recognizing the location of the lesion in the treatment of submucosal lesions.[6]

Advantages of EMR

The learning curve is short, easy to apply, safe, and able to obtain larger tissue samples compared to biopsies. Limitations of EMR are that it has a higher recurrence rate because of the low rate of en bloc resection in large lesions and obtaining free surgical margin is difficult compared to ESD. In ESD, the learning curve is long, its application is partly more difficult, and bleeding and perforation rates are high.[14,15] Some solutions are used to raise the lesion and reduce the complication rate in ESD and EMR. These are normal and hypertonic saline solution, dextroz water, hyaluronic acid, fibrinogen mixture, glycerol, hydroxypropyl methylcellulose.[16,17] Normal saline was the most commonly used solution. The advantages of saline is cheap and easy to obtain, the disadvantage is that it is not suited for long-term procedures due to its rapid absorption. We used saline mostly in EMR. We used hyaluronic acid in 8 patients who we considered to be long procedure time. The advantage of this fluid is that it provides a long working time whereas the disadvantage is that it is expensive and its availability is limited.[18,19]

Inoue et al[20,21] treated early esophageal cancer using EMR without complication and leaving the intact muscularis propria. They used a transparent tube attached to the endoscope tip.[20,21] Then Oyama et al[22] reported using a hook knife for ESD to treat 102 patients with superficial esophageal squamous cell tumor that lateral size ranging from 4 to 64 mm. They reported successful en bloc resection rate was 95% and a median follow-up period was 21 months (range, 3–54 mo) without the local recurrence.[22]

Kang et al[23] performed ESD for 647 patients due to early gastric cancer. Most of the lesions (77%) were located in the antrum. The mean size of the lesions was 15.0 ± 9.3 mm and the rate of en bloc resection was 96.4%. They stated that early gastric cancers with gastric antrum and small curvature could be resected by ESD and the rate of submucosal invasion was increased in proximal tumors.[23]

Endoscopic resection of early-stage squamous cell carcinoma is the standard in esophagus; however, endoscopic resection and ablation therapy is recommended for high-grade dysplasia, intra-mucosal carcinoma and barret esophagus.[24] Recently, new traction methods have been used to simplfy the ESD procedure such as clip with line method, external forceps method, clip and snare method, prelooping technique, internal traction method and double scope method.[25] Traction methods are used to facilitate better visualization of the submucosal layer, to ensure correct identification of the incision line and submucosal vessels. Therefore, traction methods are promising approaches to shorten the duration of ESD and to help reduce complication rates. This may lead to more widespread use of ESD.[26]

Uraoka et al[27] used the double endoscope method for endoscopic submucosal dissection of large colorectal tumor in 2007. Subsequently, Morita et al[28] used double endoscopy in

early gastric cancer in 2010. In recent years, a wide range of ESD series has been published for early-stage cancers in the stomach and esophagus with intraluminal operation of the double endoscope (DEILO). Sohda et al[29] performed ESD with DEILO in 26 patients with early esophageal cancer. This method is very useful for early esophageal cancer and the progress in the procedure will increase the indications of DEILO for lesions of esophagus.[29] Toyomasu and colleagues[30] performed ESD with DEILO for 101 patients because of early gastric cancer and performed en bloc resection in 97% of the patients and histologically curative resection achieved 84% of patients. It is reported that the operation time of ESD with DEILO is short and effective and the complication rate is comparable to open surgery.[30] In our study, we used double endoscopy for the purpose of traction due to the location and size of the lesions in six patients for ESD. In this method, a second endoscopy device and a second endoscopist required. We think that the number of patients is extremely limited and it is not correct to compare patients with and without double endoscopy because of the location of the lesions. However, we think that the endoscopist provides much comfort.

Most bleedings during EMR are self controlled without any additional intervention. However, some meta-analyses for early stomach cancer show that the bleeding rates during the procedure are the same for ESD and EMR.[31] Although perforation is not uncommon for EMR, it ranges from 0.8% to 2.9%.[32] There are publications indicating that the risk of bleeding is up to 7% for ESD.[33] Delayed bleeding ranges from 0% to 15.6%, defined at various intervals, and this risk is increased for proximal lesions.[34] The perforation rate ranges from 1.2% to 5.2%.[35] Meta-analysis of early esophageal cancers revealed no statistically significant difference between ESD and EMR in terms of bleeding, and this ratio is between 1.1% and 2.7%. The perforation rate in ESD was slightly higher than EMR and was reported as 2.3% to 4% in the literature.[24,36] Another complication of esophageal lesions is stenosis. The incidence of this complication ranges from 1% to 4.6%.[37] If radiofrequency ablation therapy is added to EMR, the rate of stenosis increases by 7.6%.[38] If the circumferential EMR is performed as in Barrett's esophagus and radiofrequency ablation is applied, the stenosis rate increases to 37%.[39]

In our study, ESD and EMR were performed in 36 patients and hemorrhage occurred in 4 patients during operation, but bleeding was controlled using endoclips. We did not have any bleeding in the late period. While perforation was seen in one out of 22 ESD patients (4.5%), perforation was not observed in patients with EMR. This rate was evaluated within normal limits and the patient was discharged with conservative treatment.

CONCLUSION

The use of EMR and ESD is increasingly accepted in the treatment of mucosal and submucosal lesions of the esophagus, stomach, and duodenum. The general advantages of ESD and EMR are short recovery period, high en bloc resection rate in early-stage tumors and benign lesions, minimally surgical trauma with few recurrences in follow-up, and don't required the general anesthesia. On the other hand, EMR and ESD are advanced endoscopic procedures and require serious endoscopy experience. If the lesion is difficult to resect and the lesion is large, it is important to use double endoscopes at the same time to reduce the complication rate and ease the endoscopic procedure. Although the number of our cases is insufficient, we think that double endoscope use in EMR and ESD procedures gives confidence in patient and endoscopist.

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