Endoscopic submucosal multi-tunnel dissection for large early esophageal cancer lesions

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Abstract

Objective : **To evaluate the safety and efficacy of endoscopic submucosal multi-tunnel dissection (ESMTD) for early esophageal cancer lesions larger than 3 cm in diameter or cumulatively greater than 1/2 lumen size.**

Method : **Early esophageal cancer lesions in 15 patients were detected by endoscopy and endoscopic ultrasonography in our endoscopy center from December 2012 to June 2015. All lesions were successfully resected by ESMTD and diagnosed by pathology, and therapeutic efficiency and safety were followed after surgery.**

Results : **All 15 of the early esophageal cancer lesions were resected by ESMTD. The pathological results showed 9 moderately differentiated and 6 highly differentiated squamous cell carcinomas. En bloc resection was achieved in 13 lesions, with negative lateral and basal margins on pathology, whereas the other 2 required additional surgery. The average diameter of the resected lesions was 4.2±0.9 cm. The mean procedure time was 94.7±52.9 min. Esophageal stenosis was observed in 7 patients for whom esophageal water balloon dilatation was performed. No residual or recurrent lesion was found during the 6-36-month follow-up period.**

Conclusion : **ESMTD is a safe and efficient technique for treating large early esophageal cancer lesions. Grasping the key techniques of this procedure can reduce operating difficulty and shorten the operating time.** (Acta gastroenterol. belg., **2019**, 82, **355-358**).

Keywords : Endoscopy, Endoscopic submucosal dissection, Esophageal cancers

Background

With the development of endoscopic diagnostic technology and the wide application of endoscopic ultrasound, endoscopic treatment of early esophageal cancer has become a trend. In recent years, tunnel technology has been devised as a new operation in the treatment of esophageal lesions. Compared with endoscopic submucosal dissection (ESD), endoscopic submucosal tunnel dissection (ESTD) benefits from a shorter operation time, quick stripping speed, and high tumor resection rate (1, 2). However, when we perform the same surgical procedure for large esophageal lesions, the use of single-tunnel technology during the dissecting process can result in mucosal congestion in the lumen after partial stripping that affects the surgical field and can easily lead to bleeding and perforation. To solve these problems, we performed endoscopic multi-tunnel submucosal dissection (ESMTD) in 15 patients treated for early esophageal cancer larger than 3 cm in diameter to investigate its value and safety and optimization of related techniques.

Methods

Patients

From December 2012 to June 2015, patients diagnosed as having early esophageal cancer in our digestive endoscopy center were included in this study. The inclusion criteria were patients with an early esophageal cancer lesion larger than 3 cm in diameter or cumulatively greater than 1/2 lumen size, and no ulcer in the esophageal lesion. Patients were diagnosed as having esophageal cancer by gastroscopy and biopsy. Endoscopic ultrasonography was used to ensure that the lesion did not invade beyond the muscularis mucosa, and computed tomography (CT) or positron emission tomography-CT scans were performed to exclude peripheral lymph node and distant metastases. We excluded patients with severe cardiac and pulmonary insufficiency and blood coagulation abnormalities. We enrolled 15 patients including 10 men and 5 women aged between 51-69 (average, 60.3±6.6) years old. Lesion diameters ranged from 3.0-6.0 (average, 4.2±0.9) cm in size. The distance from the incisors to the lateral edge of the lesions ranged between 23.0-33.0 (average 27.4±2.9) cm.

Instruments

The instruments used in this technique included the Pentax EG-2990i EPKi digital high-definition endoscope and endoscopic host EG-3830UT ; endoscopic ultrasound EPM-3500 host, EUB-5500 color Doppler ultrasound and APC2 host device ; Argon plasma coagulation and ERBE ICC200 electroincision devices ; Olympus NM-4L-1 injection needle ; KD-640L knife, KD-650L Dualknife and KD-611L IT2 electric knife ; SD-230U-20 or SD-230U-30 snare ; and ND-201-11802 FG-8U-1 Coagrasper transparent cap.

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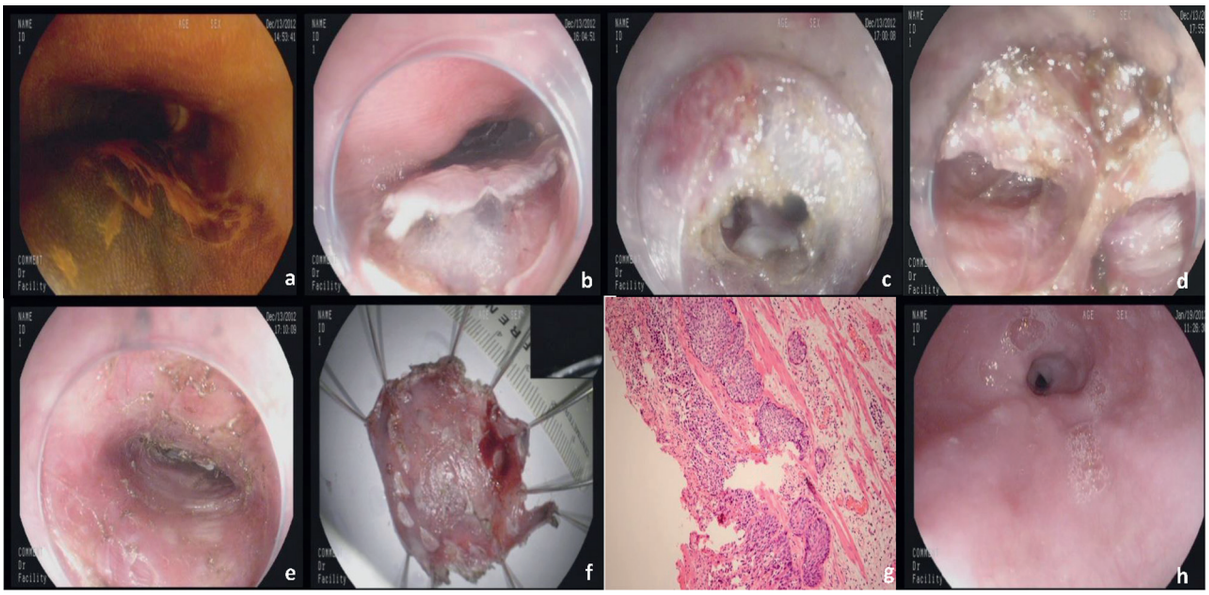

Figure 1. — Operative procedure of endoscopic submucosal multi-tunnel dissection (ESMTD). a. Lugol staining ; b. Anal incision and lateral incision ; c. Establishment of esophageal tunnel ; d. Incision between the two tunnels in the submucosa ; e. Through-tunnel establishment ; f. Measuring and confirming the lesion ; g. Pathology result showing highly differentiated squamous cell carcinoma ; h. Endoscopy confirming no recurrence.

Operative method

The procedure required that the patient be in the left decubitus position, tracheally intubated and administered intravenous propofol combined anesthesia. CO_2 insufflation was also required during the operation (3). The operative method included the following steps (Figure 1). (1) Staining with 3% Lugol is performed to determine the range of the lesions, which are marked by the argon knife 0.5 cm from the lesion edge at a marker spacing of 0.5 cm. (2) An indigo carmine-saline mixture (100 mL saline + 2 mL indigo carmine + 1 mL epinephrine) is injected submucosally at the anal side of the lesion, and an incision the width of the lesion is made at the anal-side marker point with the KD-640L knife to open it to the mucosal layer. (3) Injections at multiple points around the lesion are made to lift the lesion, and a transverse incision 2-3 cm above the oral-side edge marker is made to form a tunnel opening according to the lesion width. With reasonable planning, 2 or 3 tunnels of about 1.5-2.0 cm in width can be established. (4) The two tunnels are stripped open between the submucosa, thus forming a large tunnel ; (5) A triangle knife is used bilaterally in an alternating synchronous manner along the tunnel marking line to open the submucosa from the inside until the entire lesion is resected. After the lesion is removed, staining with 3% Lugol solution is performed again to confirm no residual lesion. (6) Hemostasis and cleansing of the submucosal tissue are achieved with argon spray coagulation and electrocoagulation forceps to prevent bleeding and residue. (7) The specimen is observed to determine whether its edge contains all of the measurement points, its size is measured, and it is then sent for pathological examination.

Postoperative treatment and follow-up

All patients were fasted for three days after the operation and were observed for complications such as bleeding and perforation. CT scans or endoscopy were performed as necessary. Gastroscopy and biopsy for pathological examination were performed during follow-up at 1, 3, 6 and 12 months to observe wound healing and check for residual recurrence and postoperative complications.

Results

Treatment outcome (Table 1)

Early esophageal cancers were successfully removed by ESMTD in the 15 patients in whom we established 2 tunnels in 14 and 3 tunnels in 1 patient. The en bloc resection rate was 100% (15/15), and the cancers were diagnosed in 9 patients as moderately differentiated and in 6 patients as highly differentiated squamous cell carcinoma. Cancers were confined to the mucosal epithelial layer (M1) in 7 patients and invaded the mucous lamina (M2) in 8 patients. The one-time radical resection rate was 86.7% (13/15), and the other 2 patients were found to have residual tumor tissue and required additional surgical procedures. The lesion diameters ranged from 3-6 (average 4.2±0.9) cm, and the operation time was 50-270 (average 94.7±52.9) min.

Table 1. — **Characteristics of the 15 patients with large early esophageal cancer**

No.	Sex	Age (Y)	Size (cm)	Distance from incisors (cm)	Number of tunnels	Operation time (min)	Radical resection	Penetration depth	Pathology	Postoperative complications	Follow-up time (m)
1	M	67	4.5	33	2	270	Y	m2	Moderately	Stenosis	36
2	M	55	4.2	27	2	96	N	m2	Well	–	–
3	M	53	6.0	26	3	115	Y	m2	Moderately	Stenosis	19
4	F	59	3.5	23	2	64	Y	m2	Moderately	No	28
5	M	69	3.8	26	2	58	Y	m1	Well	No	11
6	M	58	4.0	24	2	72	Y	m1	Moderately	No	15
7	F	62	4.5	28	2	90	Y	m2	Moderately	Stenosis	20
8	F	65	5.2	30	2	105	Y	m2	Moderately	Stenosis	18
9	M	56	3.5	25	2	83	Y	m1	Well	No	12
10	M	68	3.8	26	2	60	Y	m2	Moderately	No	10
11	F	57	4.2	29	2	97	Y	m1	Moderately	Stenosis	8
12	M	60	5.5	25	2	95	Y	m1	Well	Stenosis	14
13	M	51	3.2	32	2	55	Y	m1	Moderately	Stenosis	6
14	F	66	5.0	30	2	110	N	m2	Well	–	–
15	M	59	3.0	27	2	50	Y	m1	Well	No	16

Complications

In this study, ESMTD caused no delayed hemorrhage, and the perforation rate was 0% (0/15). Excluding the 2 patients who required additional surgery, 13 patients were followed up for 6 to 36 months, with a median follow-up time of 15 months. No residual carcinoma or recurrence was found after gastroscopy and pathological biopsy. However, 7 patients (53.8%) were complicated by esophageal stenosis. After multiple balloon dilatation was performed, the gastroscope could be passed smoothly through the stenotic esophageal segment, and dysphagia and other obstructive symptoms were relieved.

Discussion

With the rise of the minimally invasive endoscopic treatment of early esophageal cancer, treatment of large early esophageal cancer by endoscopy has become a common requirement (3). A variety of endoscope treatments are currently being explored. Yamashina et al. (4) reported that ESD can be used for the treatment of large esophageal cancer of at least 50 mm in diameter. Zhai et al. (5) first presented the double-tunnel ESTD technique for esophageal lesions, and Gan et al. (6) reported the benefit of faster stripping with double-tunnel technology when treating circumferential superficial esophageal lesions. Inspired by the experience with STER (submucosal tunnel endoscopic resection) and POEM (peroral endoscopic myotomy) in our department, we treated 15 cases of large early carcinoma of the esophagus using ESMTD with 2 or 3 tunnels from December 2012 to June 2015. The en bloc resection rate was 100% in these patients, and the radical resection rate was 86.7%. No patients experienced perforation or bleeding. These results suggested that ESMTD can safely and effectively remove large areas of esophageal early cancer.

Compared with using a single tunnel, ESMTD can divide a large lesion into 2 or 3 parts. In our experience, in stripping the esophageal lesions, less work is required in each tunnel, and traction applied from both sides of the tunnel provides a better operating space and surgical view. This solves the problem with the single-tunnel treatment that stripping large areas causes mucosal collapse and obstructs the surgical field, and reduces the risks of bleeding and perforation (6,7). To ensure the successful performance of ESMTD, we have realized the following points : (1) The opening of the tunnel should be marked 2-3 cm away from the edge of the lesion to prevent residual cancer tissue. (2) Because there are few vessels in the SM3 layer and it is far from the cancerous tissue, we create the tunnel in the SM3 layer to reduce bleeding and residue. Because the SM3 layer is adjacent to the fascia, by peeling to the muscle with reference to the fascia, a good grasp of the depth of tumor invasion can be had. (3) Points at which abundant blood vessels on the mucosal side are reduced or the tunnel clearance decreases often indirectly suggest tumor invasion and indicate where the tumor should be peeled off closely to the intrinsic muscle fascia layer to prevent bleeding and residue. (4) Using the method of placing alternate incisions on both sides of the mucosa instead of on one side can avoid loss of support at the tumor site and its collapse in the esophageal cavity, thus hindering the operation.

Esophageal stenosis is the most common complication after endoscopic resection of the lesions. The greater the resection area, the higher the rate of postoperative stenosis (2%-100%) (2, 7, 8), especially in circumferential lesions. At present, the methods for treating postoperative stenosis are endoscopic balloon dilation, oral and local injection of hormone and esophageal stents, but the efficacy of these modalities requires further study (9). Postoperative

stenosis occurred in 7 (58.3%) patients in this study, and most (6/7) were found in the first month of follow-up. We proved that repeated endoscopic balloon dilatation can solve the problem of symptoms of dysphagia, but it may result in economic and health burdens. The experiments of Linghu et al. (2), Zhai et al. (5) and Pioche et al. (7) also confirmed this point. The stenosis is less severe when there is more residual mucosa intraoperatively, and this may be due to the appearance of fibrous connective tissue in hyperplastic scarring after the mucous layer is peeled away. Thus, retaining the mucosal tissue plays an important role in later repair. Therefore, it is important to prevent the occurrence of stenosis as much as possible in conjunction with completely removing the lesion. Especially in the near circumferential lesion, retention of an island of normal mucosal between the two tunnels is particularly important. We also assume that if the esophageal lesions cover a large area, transplantation of esophageal mucosal tissue may be an effective method to prevent stenosis, but more evidence is needed to confirm this assumption.

In conclusion, ESMTD is an effective treatment for early esophageal cancer. Grasping the key techniques of this procedure can reduce operating difficulty and shorten the operating time. However, because of the short development time and small number of cases accumulated so far, the value and limitations of this procedure will need to be confirmed in the future.

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Author contributions : L. Li and W. Yang contributed equally to this study. L. Li and W. Yang designed the study and wrote the manuscript ; Y. Ou, B. Wang collected the data and performed the majority of analyses ; S. Deng and Q. Peng provided technical support ; S. Deng and H. Yue revised the manuscript and made the decision to submit.

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