Endoscopic Treatment for Esophageal Squamous Cell Carcinoma

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Contents

1 Introduction

Esophageal endoscopic mucosal resection (EMR) was developed in the late 1980s (Makuuchi 1996; Yoshida T 2004; Inoue et al. 1993; Pech et al. 2004). And EMR was widely accepted as the treatment for superficial esophageal squamous cell carcinoma (SCC). However, there was limitation in size, and precise resection was

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impossible. Piecemeal resection was performed for big lesions, and local recurrence after piece meal EMR was high (Momma 2007). Therefore, a novel endoscopic treatment, endoscopic submucosal dissection (ESD) was developed to resolve such disadvantage of EMR (Oyama and Kikuchi 2002; Oyama et al. 2005; Fujishiro et al. 2006; Ishihara et al. 2008; Hiroaki et al. 2010).

The other endoscopic treatment is ablation method such as radio frequent ablation. However, pathological findings, such as invasion depth, histological type, and lymphatic or venous permeation, could not be learned by ablation therapy. Therefore, the first choice endoscopic treatment is EMR/ESD rather than ablation therapy.

2 Indications of Endoscopic Resection for Esophageal SCC

2.1 Absolute Indication

The indication of endoscopic resection is esophageal cancer without lymph node metastasis. According to Japanese criteria, the invasion depth of mucosal SCC (T1a) was divided into three groups, as follows:
T1a EP: SCC those remaining in the mucosal epithelium (EP).
T1a LPM: SCC those remaining in the lamina propria mucosae (LPM).
T1a MM: SCC those contact or invade muscularis mucosae (MM).

And, the invasion depth of submucosal SCC was divided into two groups, as follows:
T1b SM1: SCC those invaded submucosal layer 200 micrometer or less.
T1b SM2: SCC those invaded submucosal layer 201 micrometer or deep.

The incidence of lymph node metastasis of T1a EP and LPM is extremely rarely (Oyama Oyama 2011). Therefore, T1a EP or LPM SCC was defined as the indications for endoscopic resection by the guidelines of Japan Esophageal Society (Kuwano et al. 2008).

2.2 Relative Indications

The incidence of lymph node metastasis of T1a MM, T1b SM1, and T1b SM2 reported as 9.3, 19.30, and 40 %, respectively (Oyama et al. 2002). The standard treatment for T1a MM or T1b SM is esophagectomy with lymph node dissection. However, the quality of life (QOL) after esophagectomy is not good. Therefore, T1a MM or T1b SM1 with clinical N0 (no lymph node swelling by CT and EUS) was defined as relative indications of endoscopic resection.

In addition, lymphatic or venous involvement and infiltrative growth have been reported as the risk factors. However, precise pathological diagnosis is impossible by the piecemeal resected specimen. Therefore, an en bloc resection is necessary for the treatment of superficial esophageal SCC.

3 Endoscopic Mucosal Resection

3.1 Procedures

Many EMR methods have been reported. Especially, EMRC method has been widely accepted. At first, a transparent hood was attached at the tip of the scope and saline was injected into the submucosal layer to separate mucosal cancer from the proper muscular layer. After that, a snare was inserted from the working channel of the scope and opened on the cancer. The cancer was sucked into the transparent hood and snared. Finally, the cancer could be resected using a high frequency generator.

3.2 Advantage and Disadvantage of EMR

The skill of EMR is easy, and the procedure duration is short. However, the size of resected specimens was small, 10–20 mm or less, and piecemeal resection was performed for larger lesions. A precise pathological examination of piecemeal-resected specimens was impossible. And local recurrent rate has been reportedly high after piecemeal resection.

According to the report by Ishihara et al. (Fujishiro et al. 2006), since the results of EMR and ESD were comparable in achieving en bloc complete resection of lesions less than 15 mm diameter, they recommended the easier EMR method in this situation.

4 Endoscopic Submucosal Dissection (ESD)

The risk of perforation in esophageal ESD is higher than gastric ESD, because the esophageal proper mucosal layer is thinner than that of stomach. The maneuverability of scope is more difficult, because the space of esophagus is narrow, and bended by compression with heart, aorta, and vertebra. Therefore, ESD should be performed carefully.

4.1 Procedure

Many endo knives have been developed for ESD. Usually, the hook knife (KD-620LR, Olympus, Tokyo) has been selected for esophageal ESD, because it is the safest knife. The tip of the knife is bent at right angle. The length of hook part is 1.3 mm and that of the arm part is 4.5 mm (Fig. 1). The hook knife has a handle on the proximal side and the direction of hook can be controlled with the handle rotation. It is a useful device to cut mucosa, submucosal fibers, vessels, and to stop minor bleeding (Oyama et al. 2006). The direction of the hook knife should be controlled, and kept parallel with the muscular layer to prevent perforation during ESD. A therapeutic scope that has water jet system is useful for ESD. We usually use GIFQ260 J, Olympus, Tokyo, Japan, and a high-frequency generator (VIO 300D; ERBE Elektromedizin, Tübingen, Germany).

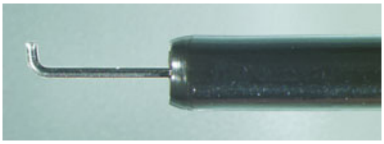

Fig. 1 A hook knife. The tip of the knife is bent at a right angle. The length of hook part is 1.3 mm and that of the arm part is 4.5 mm. The knife is hosted within an outer sheath. The tip of the sheath has a hood like shape that allows the hook of the knife to be retracted within it

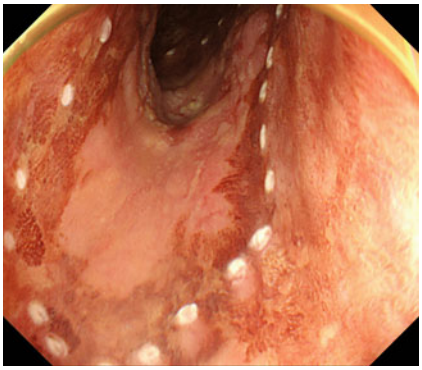

Fig. 2 Marks should be placed 2 or 3 mm away from the edge of the lateral extension of the cancer. The hook knife is a useful device to place the marks safely. The tip of hook knife can be retracted within the sheath, and a sharp mark can be placed when the tip of hook knife makes contact with the mucosa. We use soft coagulation (effect 4, 20 W) for the esophagus

4.2 Marking and Submucosal Injection

The lateral extension of SCC could be diagnosed easily after 0.75–1 % iodine dying. Marks should be placed 2 or 3 mm away from the edge of the unstained area that represents the cancer. The esophageal wall is thinner than that of stomach. Therefore, perforation can occur during marking if a needle knife is used. The hook knife is a useful device to place the marks safely. The tip of hook knife could be retracted within the sheath, and a sharp mark could be placed when the tip of hook knife was contacted with the mucosa, and coagulated by soft coagulation (effect 4, 20 W) (Fig. 2). Next, Glyceol® (CHUGAI Pharmaceutical Co., LTD., Tokyo, Japan) was injected into the submucosal layer to separate the mucosa from the proper muscular layer. This solution includes 10 % glycerin.

4.3 Mucosal incision

Basically, the mucosal incision is performed from oral side. At first, the backside of the hook knife was contacted with the mucosa, and a hole was made by Endo

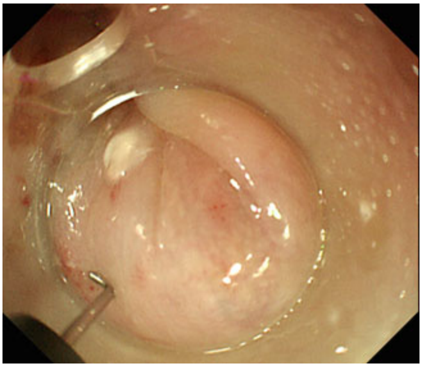

Fig. 3 We initially place the backside of the hook knife in contact with the mucosa after submucosal injection, and then make a mucosal defect using Endo cut I mode (Effect 3)

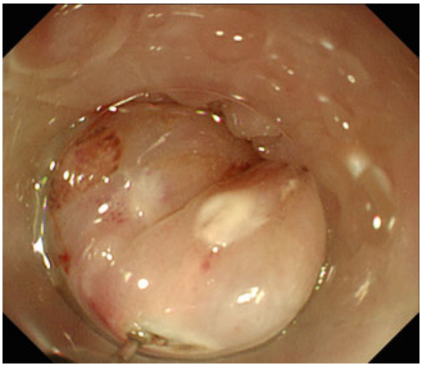

Fig. 4 After that, we insert the tip of hook knife into submucosal layer, and hook and cut the mucosa with the hook part of the knife

cut I mode (Effect 3) (Fig. 3). After that, the tip of hook knife was inserted into submucosal layer, and mucosa was hooked and cut with the hook part of the knife (Fig. 4). It is an important point to prevent perforation.

The arm part of the hook knife is used for longitudinal mucosal incision. The direction of the hook knife is turned to the esophageal lumen, and the knife was inserted into the submucosal layer by sliding the back side. Then the mucosa is captured by the arm part of the knife (Fig. 5); finally, the mucosa was cut by the combination of Spray coagulation (Effect 2, 60 W) and Endo cut mode (Effect 3, duration 2, and interval 2). It is important procedure to prevent bleeding during mucosal incision. The submucosal vessels could not be observed by endoscopy. Sometimes they are cut unexpected, and bleeding occurs during mucosal incision. The initial spray coagulation can coagulate submucosal vessel; therefore, such unexpected bleeding could be prevent with initial spray coagulation.

Deeper cut of submucosal fibers was performed after mucosal incision. The hook knife was inserted into submucosal layer, and submucosal fibers were hooked and cut. Then the lesion shrank by the contraction of muscularis mucosa (Fig. 6). After that, the mucosal incision and deeper cut of the other side was performed and a circumferential incision was completed.

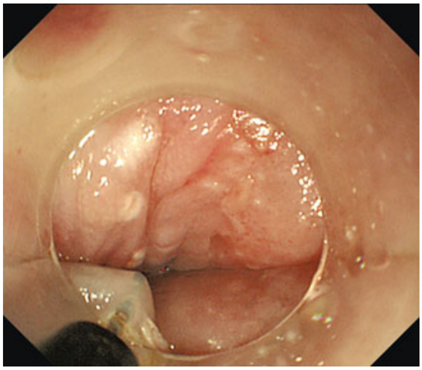

Fig. 5 The arm part of the hook knife is used for longitudinal mucosal incision. We then direct the hook knife to the lumen, and insert it into the submucosal layer by sliding the back of the knife. Then the mucosa is elevated to the lumen by the arm part of the knife

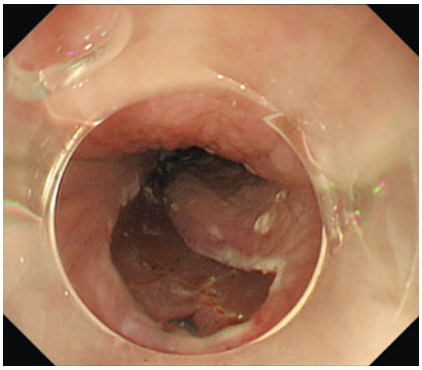

Fig. 6 Deeper cut of submucosal fibers is performed following mucosal incision. We insert the hook knife into the submucosal layer, and move it to the lumen side in order to hook the submucosal fibers

4.4 Submucosal Dissection

Submucosal dissection was performed from oral to anal side. There are two strategies for submucosal dissection. In one strategy, dissection of the submucosal layer is performed sequentially from the oral side to the anal side. The hook knife should be held parallel with the proper muscle, and submucosal fibers could be cut with spray coagulation mode (effect 2, 60 W) (Fig. 7).

The resected part may cause gradual inversion of the lesion, leading to insufficient counter traction of the submucosal layer, that can make residual dissection difficult. Therefore, if the circumference is half or more, a tunnel method is better (Oyama et al. 2006). A local injection is added after a circumferential incision followed by a tunnel-shaped dissection of the center of the lesion, Tunnel-shaped dissection of the central part enables counter traction using a transparent hood, providing more efficient dissection. Finally, the fibers on both sides are dissected.

Sometimes the dissected part was turned to anal side, and enough counter traction could not be gained in this situation. "Clip with line" method is useful in this situation (Oyama et al. 2002; Oyama 2011). This method utilizes a modified clip with a line. A clip with a line is loaded to the clip placement device. The attached string is kept outside of the scope and inserted with the scope into the

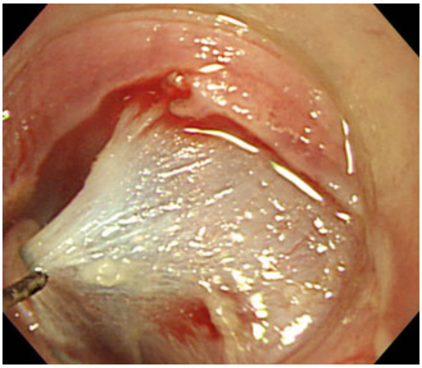

Fig. 7 Submucosal fibers was hooked using the hook part of the knife, and cut by spray coagulation (effect 2, 60 W)

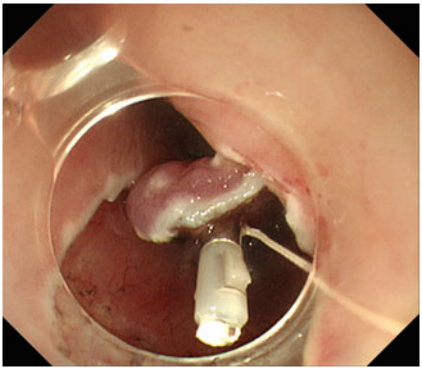

Fig. 8 Clip with line method. The clip is released to grasp the lesion for intended counter traction

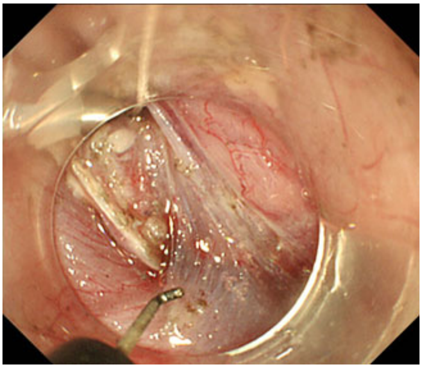

Fig. 9 The clipped site is gently pulled with a traction line to provide counter traction to facilitate submucosal dissection

esophageal lumen. The clip is released to grasp the lesion to make counter traction (Fig. 8). The clipped site is gently pulled with a traction line to provide counter traction to facilitate submucosal dissection (Fig. 9).

The most severe complication during submucosal dissection is perforation. Therefore, the operator should check the upper level of the proper muscular layer, and take care not to injure the proper muscular layer.

4.5 Hemostasis

Bleeding makes the visual field worse; therefore hemostasis should be performed as soon as possible. When bleeding occurs during mucosal incision or dissection, the area should be flushed using a water jet system to find the origin of bleeding. Minor bleeding could be stopped using knife. However, a hemostatic forceps (coagrasper, FD-410LR, Olympus, Tokyo) should be selected for more severe bleeding.

4.5.1 Hemostasis Using Knife

Hemostasis using the endo knife is useful for controlling oozing bleeds. The tip of knife is brought close to the origin, and electrical discharge is done with Spray mode to obtain hemostasis (effect 2, 60 W). Since prolonged electrical discharge may cause perforation, electrical discharge should be performed momentarily. Therefore, it is important to maintain optimal distance using a transparent hood (Oyama et al. 2006).

A water jet system must be used to confirm the precise origin of the bleeding. A scope equipped with a water jet should be selected for esophageal ESD.

4.5.2 Hemostatic Procedures Using a Hemostatic Forceps

A hemostatic forceps FD-410LR (Olympus, Tokyo, Japan) is useful in cases of more active or spurting bleeding. After flushing with a water jet to clear the origin of bleeding, the origin is grasped accurately with the hemostatic forceps. After that, re-flushing with a water jet enables us to determine whether the origin is grasped accurately. Then, the forceps are elevated a little to separate forceps from the proper muscular layer followed by electrical discharge with soft coagulation (effect 5, 40 W) momentarily to obtain hemostasis.

For hemostatic procedures using hemostatic forceps, an accurate grasp is the most important factor. An accurate grasp of the bleeding point may provide reliable hemostasis, while an inaccurate grasp will not provide hemostasis by electrical discharge. Unnecessary electrical discharge may cause delayed perforation, so an accurate grasp should be ensured. Since the wall of the esophagus is thinner than that of the stomach, to prevent delayed and other types of perforation, care should be taken.

4.6 Prevention of Bleeding

Bleeding may worsen the visual field, leading to a higher risk of accidents. Inadvertent coagulation may cause coagulation of the blood, which creates an impaired field of vision. Incision and dissection with preventing bleeding are more desirable than hastily attempting hemostasis after bleeding starts. There are many vessels in the deep submucosal layer. A small vessel 1 mm or less could be cut using the hook knife without bleeding, when spray coagulation mode was used (effect 2, 60 W) (Figs. 10, 11). However, if the size of the vessel was 1 mm or larger, pre cut coagulation should be performed to prevent bleeding (Fig. 12). The large vessel was grasped by the hemostatic forceps, and was coagulated by soft

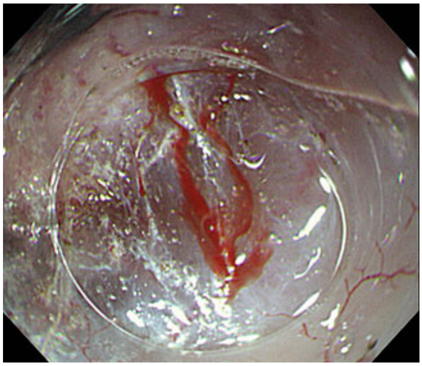

Fig. 10 Oozing was found during submucosal dissection

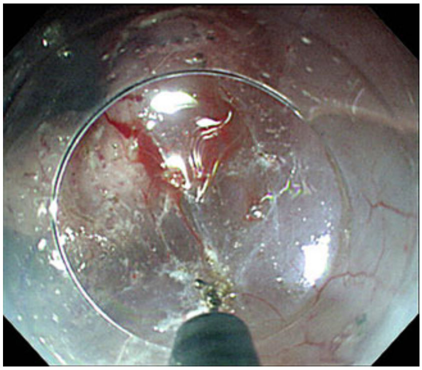

Fig. 11 Such minor bleeding could be stopped by spray coagulation (effect 2, 60 W) using the back side of the hook knife

coagulation effect 5, 60 W. After that, the vessel could be cut using the hook knife and spray coagulation (effect 2, 60 W) without bleeding.

En-bloc resection for this large lesion was completed (Fig. 13). The patient could eat soft food 2 days after ESD. The resected specimen was 72 × 47 mm and the cancer was 54 × 38 mm in area (Fig. 14). Pathological diagnosis was squamous cell carcinoma, 0-IIc type, invasion depth was proper mucosal layer (T1a LPM), without lymphatic and venous involvement, and the lateral and vertical margin was negative.

5 Complications of Esophageal EMR/ESD

The major complication of EMR/ESD is perforation, bleeding, and aspiration pneumonia. Perforations may cause mediastinal emphysema, which increases the mediastinal pressure crushing the esophageal lumen, leading to difficulty in securing the visual field. Severe mediastinal emphysema may be complicated by pneumothorax, leading to shock; therefore, electrocardiography, arterial oxygen saturation, and blood pressure (using automated sphygmomanometer) monitoring should be conducted during ESD, as well as periodic observation for subcutaneous emphysema through palpation.

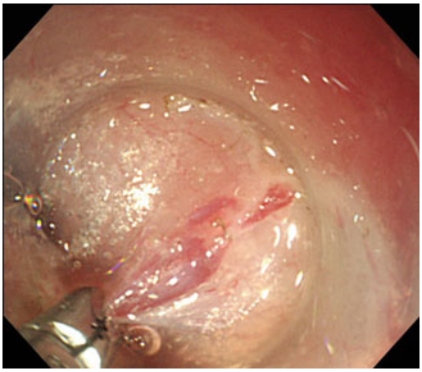

Fig. 12 When the size of vessel was 1 mm or thicker, pre-cut coagulation is useful. The vessel was grasped by hemostatic forceps, and coagulated using soft coagulation (effect 3, 60 W)

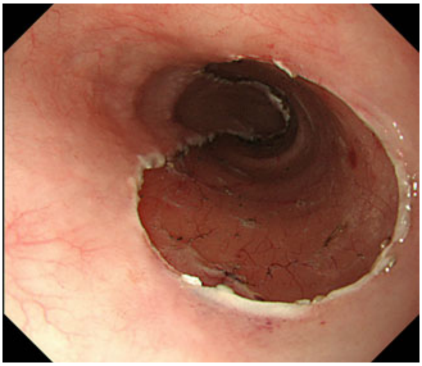

Fig. 13 En bloc resection was completed. There were no perforation and bleeding

Since the esophagus has no serous membrane and the intramediastinal pressure is lower than that of the esophageal lumen, mediastinal emphysema may appear without perforation. Dissection immediately above the proper muscular layer may damage the proper muscular layer during electrical discharge, which often causes mediastinal emphysema. Therefore, it is important to dissect the submucosal layer leaving the lowest one-third without exposure of the proper muscular layer.

Under intubation general anesthesia, the mediastinal pressure is higher than the intraesophageal pressure, enabling prevention of mediastinal emphysema and/or subcutaneous emphysema. Therefore, intubation general anesthesia is preferable for the large lesion that is expected to take two or more hours to complete the resection of the lesion.

Perforation rate caused by esophageal EMR has been reported as 0–2.4 % (Makuuchi 1996; Yoshida T 2004; Inoue et al. 1993; Pech et al. 2004) and that of ESD has been reported as 0–6.4 % (Oyama et al. 2005; Fujishiro et al. 2006; Ishihara et al. 2008; Hiroaki et al. 2010). The shape and size of perforation caused by EMR is different from that caused by ESD. 1 cm or larger proper muscle was removed by EMR and sometimes closure by clips is difficult. On the other hand, the shape of perforation caused by ESD is linier without defect of proper muscle. Therefore, usually closure by clips is easier than that of EMR. However,

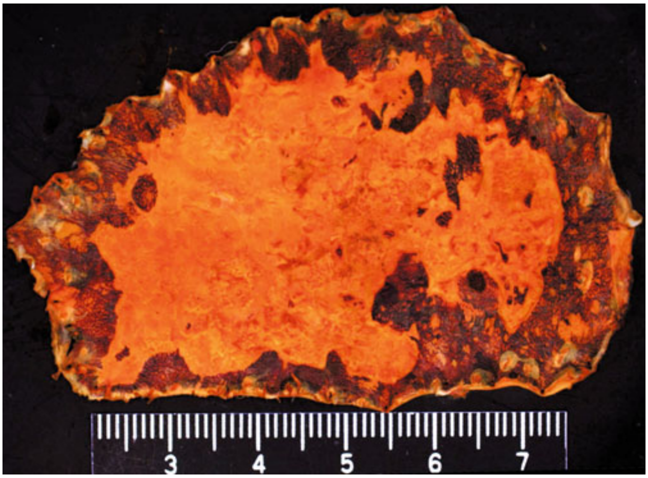

Fig. 14 The resected specimen showed a well demarcated iodine unstained lesion with enough cut margin

sometimes the clip may injure remaining proper muscle and make the perforation larger. Therefore, the operator should be skilled clipping.

Usually, such perforation can be treated by fast, insertion of nasoesophageal tube and intravenous antibiotics without surgical operation.

The water jet is useful for the detection of bleeding point. However, sometimes water reflex cases aspiration pneumonia. A flexible overtube® (Sumitomo Bakelite, Akita, Japan) is a useful device to prevent aspiration pneumonia. General anesthesia with tracheal intubation is necessary for the cervical esophageal ESD, because the risk of aspiration pneumonia is high.

References

Fujishiro M, Yahagi N, Kakushima N, Kodashima S, Muraki Y, Ono S et al (2006) Endoscopic submucosal dissection of esophageal squamous cell neoplasms. Clin Gastroenterol Hepatol 4:688–694

Hiroaki T, Yoshiaki A, Hosokawa M et al (2010) Endoscopic submucosal dissection is superior to conventional endoscopic resection as a curative treatment for early squamous cell carcinoma, of the esophagus. Gastrointest Endosc 71:255–264

Inoue H, Takeshita K, Hori H, Muraoka Y, Yoneshima H, Endo M (1993) Endoscopic mucosal resection with a cap-fitted panendoscope for esophagus, stomach and colon mucosal lesions. Gastrointest Endosc 39:58–62

Ishihara R, Iishi H, Uedo N, Takeuchi Y, Yamamoto S, Yamada T (2008) Comparison of EMR and endoscopic submucosal dissection for en bloc resection of early esophageal cancers in Japan. Gastrointest Endosc 68:1066–1072

Kuwano H, Nishimura Y, Ohtsu A, Kato H, Kitagawa Y, Tamai S, Toh Y, Matsubara H (2008) Guidelines for diagnosis and treatment of carcinoma of the esophagus April 2007 edn, edited by the Japan Esophageal Society, Esophagus 5: 61–73

Makuuchi H (1996) Endoscopic mucosal resection for early esophageal cancer indication and techniques. Dig Endosc 8:175–179

Momma K (2007) Endoscopic treatment of esophageal mucosal carcinomas: indications and outcomes. Esophagus 4:93–98

Oyama T (2011) Endoscopic submucosal dissection using a hook knife. Tech Gastrointest Endosc 13:70–73

Oyama T, Kikuchi Y (2002) Aggressive endoscopic mucosal resection in the upper GI tract—hook knife EMR method. Min Invas Ther Alied Technol 11:291–295

Oyama T, Miyata Y, Shimatani S, Tomori A, Hotta K, Yoshida M (2002a) Lymph nodal metastasis of m3, sm1 esophageal cancer (in Japanese with English abstract). Stomach Intest (Tokyo) 37:71–74

Oyama T, Yuichi Kikuchi, Shimaya S, Tomori A, Hotta K, Miyata Y, Yamada S (2002) Endoscopic Mucosal Resection using a Hooking Knife—Intra gastric lesion lifting method. Stomach Intestine 37: 1155–1161. Japanese with English summary

Oyama T, Tomori A, Hotta K, Morita S, Kominato K, Tanaka M et al (2005) Endoscopic submucosal dissection of early esophageal cancer. Clin Gastroenterol Hepatol 3:S67–S70

Oyama T, Tomori A, Hotta K, Morita S, Tanaka M, Furutachi S et al. (2006) ESD with a Hook knife for Early Esophageal Cancer. Stomach Intestine 41:491-97. Japanese with English summary

Oyama T, Akihisa T, Hotta K, Miyata Y (2006b) Hemostasis with hook knife during endoscopic submucosal dissection. Dig Endosc 18:S128–S130

Pech O, Gossner L, May A, Stolte M, Ell C (2004) Endoscopic resection of superficial esophageal squamous-cell carcinomas: western experience. Am J Gastroenterol 99:1226–1232

Kodama M, Kakegawa T (1998) Treatment of superficial cancer of the esophagus: a summary of responses to a questionnaire on superficial cancer of the esophagus in Japan. Surgery (St. Louis) 123:432–9

Makuuchi H, Yoshida T, EII C (2004) Four-Step endoscopic esophageal mucosal resection tube method of resection for early esophageal cancer. Endoscopy 36:1013–1018