Introduction

Endoscopic resection (ER) for esophageal squamous cell neoplasms (ESCN) includes endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), with ESD has enabled en bloc resection for large tumors. ESD for ESCN is technically difficult and requires advanced endoscopic skills because of the narrow space and peristalsis of the esophagus. This technical difficulty may result in incomplete tumor resection, increasing the likelihood of recurrence. Different risk factors associated with local recurrence have been reported, including the size of lesion, piecemeal resection, and EMR as compared with ESD. Although ESD enabled to overcome these factors, effort should be made to achieve en bloc curative resection of ESCN.

Endoscopic treatment

1. Indications for endoscopic resection

ESD is currently indicated for lesions that do not exceed the mucosal layer (T1a), particularly for those confined to the lamina propria mucosa, because of their negligible risk of lymph node metastasis.1,2 Although some reports showed favorable outcomes, ESD for tumors invading the muscularis mucosa or the submucosa (T1b) remains controversial and is considered relative to the indications.3,4 There have been attempts to expand the indications of ESD for superficial ESCN. However, the long-term risk of metastasis after endoscopic resection was associated with the tumor invasion depth, and the 5-year overall survival rates of patients with tumors invading the muscularis mucosa or submucosa were significantly lower than those of patients with tumors confined to the lamina propria mucosa in a previous report.5 More evidence regarding the risk of lymph node and distant metastasis in patients with tumors invading the muscularis mucosa or submucosa is warranted to justify the use of ESD for these lesions.

2. Complications related to endoscopic resection

Complications associated with ER for ESCN include bleeding, perforation, and stricture. Bleeding during the procedure can be successfully treated with coagulation forceps or hemoclips. Delayed bleeding may require emergency endoscopy and can be managed endoscopically. Perforation during ER can be treated by endoscopic
closure with endoclips followed by conservative medical treatment. Stricture is a well-known complication in patients who undergo ESD for circumferential tumors in the esophagus, and the risk of stricture was reportedly as high as 17%. Several risk factors for stricture formation were reported, including a mucosal defect occupying more than three-fourths of the circumference, longitudinal mucosal defects > 30 mm, and EMR compared to ESD. Endoscopic balloon dilatation is effective in controlling post-ESD stricture, and various innovative prevention methods including intraluminal injection or oral administration of steroid and endoscopic transplantation of cell sheets can be beneficial in case of anticipated risk of stricture formation.

**Recurrence after endoscopic resection**

There have been few reports about local recurrence after ER for superficial ESCN. The prevalence of local recurrence was reported variously, from 2.0% to 21%, and the rate of recurrence after ER was higher in patients with squamous cell carcinoma than in patients with adenocarcinoma of the esophagus. The local recurrence after ER usually occurs within 1 year after index ER, however, may develop after 2-3 years. Therefore, rigorous endoscopic follow-up is necessary after ER in patients with superficial ESCN for early detection and treatment of recurrence. Follow-up endoscopic examinations are usually performed at 6-months intervals or at 3-months intervals for up to 6 months to 1 year after ER. Various risk factors for local recurrence have been investigated, including the size of lesion, piecemeal resection, multiple lugol-voiding lesions, and EMR compared with ESD. Accurate pre-procedural assessment and en bloc curative resection with enough tumor-free safety margins are important, and the application of narrow band imaging and chromoendoscopy with lugol’s solution could provide information for ensuring safety margins before and during ER.

ESCN invading the MM or deeper layer is associated with increased risks of lymph node metastasis and distant metastasis. Lymph node metastasis and organ metastasis were detected in 1.9% and 1.0% of patients after EMR for MM cancer. Lymph node metastasis and distant metastasis are usually detected within 2 years after ER, but can occur after 4 years. However, there is no established follow-up protocol after ER in patients with a high risk of lymph node metastasis or distant metastasis. Further studies are needed to define protocols for follow-up in patients with superficial esophageal squamous cell carcinoma after ER.

**Additional treatment after endoscopic resection**

Additional treatment after endoscopic resection should be based on the risks of lymph node and distant metastasis as well as patients’ medical fitness. Surgery has been a mainstay of the definite treatment for non-metastatic esophageal cancer and non-curative resection after endoscopic resection. However, perioperative mortality and morbidity remain higher than other procedures despite advances in surgical techniques. In this study, five of six patients with non-curative resection after ESD underwent additional treatment, including concurrent chemoradiotherapy, radiotherapy, and surgery. The remaining patient with submucosal invasion refused additional treatment. During the follow-up period, all patients but one had no local or distant recurrence. Considering that esophageal cancer is diagnosed in old age in most patients and additional treatments such as surgery may affect patients’ quality of life, the decision to perform additional treatment should be made carefully. Concurrent chemoradiotherapy or radiotherapy may be an effective and relatively safe alternative treatment modality compared to surgery, and watchful waiting may be an option for selected patients.
Conclusions

ER has been accepted as an effective, minimally invasive treatment for ESCN with favorable long-term outcomes. Indications for ER should be adopted based on the risks of lymph node metastasis and distant metastasis. Various complications including bleeding, perforation, and stricture can occur, while most complications are managed successfully with endoscopic treatment. The decision to undergo additional treatment after non-curative resection should be made on considering the risks of metastasis as well as medical fitness of the patients. Long-term follow-up endoscopic examination after ER is necessary to detect and treat recurrent cancer at an early stage.

References