ORIGINAL ARTICLE

Technical feasibility and oncologic safety of diagnostic endoscopic resection for superficial esophageal cancer

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Background and Aims: Active use of endoscopic resection (ER) for cM3-SM2 esophageal cancer may enable sufficient extent of esophageal resection and help determine the need for lymph node dissection based on histopathologic findings. However, ER preceding esophagectomy may have an adverse impact on outcomes. This study was designed to determine the technical feasibility and oncologic safety of diagnostic ER.

Methods: A single-institution retrospective cohort study was performed between July 2008 and June 2014. During this period, 135 consecutive patients with clinical T1a-M3N0M0, T1b-SM1N0M0, and T1b-SM2N0M0 primary esophageal cancer were referred to our division. Eight patients who underwent chemoradiotherapy as primary treatment were excluded because of inadequate pathologic findings. Based on oncologic and physical factors, we categorized the remaining 127 patients into 2 groups: primary esophagectomy (n = 54) and primary ER (n = 73).

Results: In all 127 patients, the 3-year overall survival (OS) and disease-free survival (DFS) rates were 95.7% and 87.6%, respectively. No adverse event requiring surgical intervention was observed after ER. Diagnostic ER had no negative impact on surgical outcomes, DFS, and OS after esophagectomy. Fourteen patients (19.2%) of those who received primary ER underwent curative resection, whereas 11 (20.4%) who had pT1a disease, no lymphovascular invasion, and no pathologic lymph node metastasis underwent primary esophagectomy.

Conclusions: Diagnostic ER for cM3-SM2 esophageal cancer with or without subsequent esophagectomy was feasible and safe, not only from a surgical perspective but also an oncologic perspective. Approximately 20% of cM3-SM2N0M0 patients can potentially avoid undergoing additional treatment including esophagectomy using diagnostic ER. (Gastrointest Endosc 2018;■:1-10.)

Although esophagectomy with 3-field lymph node dissection is the standard therapy for clinical T1a/T1b (cM3-cSM2) N0M0 esophageal cancer,[1] it has high risk of postoperative mortality and morbidity because of its complexity.[2] The procedure is associated with other long-term postoperative problems, such as aspiration pneumonia caused by dysphagia and malnutrition.

Endoscopic resection (ER) is the standard treatment for clinical T1a-M1/M2 N0M0 disease with cancerous involvement of no more than three fourths of the esophageal circumference; it is a safe, less-invasive procedure that preserves esophageal function. ER for pathologic T1a-M1 and T1a-M2 is sufficiently radical because pathologic lymph node metastasis is rarely observed. According to the

Abbreviations: ASA, American Society of Anesthesiologists; CRT, chemoradiotherapy; DSF, disease-free survival; ER, endoscopic resection; M-NBI, magnifying endoscopy with narrow-band imaging; OS, overall survival; PPV, positive predictive value.

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Japanese Esophageal Society guidelines, ER may be indicated in patients with pathologic T1a-M3 and T1b-SM1 lesions not accompanied by clinical evidence of lymph node metastasis.[3] However, performing unnecessary esophagectomy in patients with cT1a-M3/cT1b-SM1/cT1b-SM2 disease is possible because tumor depth assessment accuracy is limited even after using magnifying endoscopy with narrow-band imaging (M-NBI), EUS, and esophagography. Moreover, because of technical advances, ER can be safely applied for cT1a-M3/cT1b-SM1/cT1b-SM2 disease and for involvement of more than three-fourths of the esophageal circumference. Therefore, active use of ER and its subsequent pathologic findings (also referred to as diagnostic ER) can help determine the appropriate esophageal resection extent when necessary, combined with radical lymph node dissection, provided that ER preceding esophagectomy does not have any negative impact on outcomes. This study was designed to determine technical feasibility and oncologic safety of diagnostic ER for clinical T1a-M3, T1b-SM1, and T1b-SM2 esophageal cancer.

METHODS

Patients

A single-institution retrospective cohort study was performed between July 2008 and June 2014, wherein 135 patients with clinical T1a-M3N0M0, T1b-SM1N0M0, and T1b-SM2N0M0 primary esophageal cancer were referred to our division. Of these, 127 patients were enrolled after excluding 8 patients who underwent chemoradiotherapy (CRT) as primary treatment because of inadequate pathologic findings.

Based on oncologic and physical factor assessments, 127 patients were categorized into 2 groups: primary esophagectomy and primary ER groups. Fifty-four patients with tumor length ≥5 cm and/or distinct clinical T1b-SM2 underwent primary esophagectomy, whereas the remaining 73 patients underwent primary ER. After ER, patients with no more than pM3, negative resection margins and negative lymphovascular invasion (n = 14) were recognized as curatively treated and observed with strict endoscopic surveillance. Of the remaining 59 patients, 32 received curative treatment, including radical esophagectomy (n = 19) and definitive CRT (n = 13) (Fig. 1).

From hospital records, patient clinical information, including age, sex, American Society of Anesthesiologists (ASA) classification, performance status, Charlson comorbidity index score, pathologic findings, and prognosis, were retrospectively evaluated. Baseline characteristics and outcomes were compared between the primary esophagectomy and primary ER groups. The incidence of postoperative adverse events was considered when clinically significant adverse events requiring surgical, endoscopic, or radiologic intervention appeared that corresponded to the Clavien-Dindo classification of more than grade IIIa ≤30 days after treatment.[4] Among patients who underwent CRT/radiotherapy or those who received no additional treatment after ER, relapse in regional lymph nodes within 1 year after ER was considered as indicative of pre-existing lymph node metastasis.

Disease-free survival (DFS) and overall survival (OS) were also calculated from the primary treatment date. The presence of residual tumors was classified as R0, no residual tumor; R1, microscopic; and R2, macroscopic residual tumor.

Pretreatment patient workup included laboratory investigations, upper GI endoscopy, esophagography, thoracoabdominal contrast-enhanced CT, and positron emission tomography. Esophageal cancer was diagnosed based on histopathologic examination of endoscopic biopsy specimens. Clinical cancer stage was determined according to International Union Against Cancer, seventh edition.[5] Tumor invasion depth was determined by 6 experienced endoscopists based on both macroscopic findings and advanced imaging, including M-NBI[6] according to the Japanese Esophageal Society classification, which is based on degree of microvascular irregularity observed by M-NBI.[7] On identifying type B1, B2, and B3 vessels in the tumor, the histologic tumor invasion depth was predicted as T1a-M1/M2, T1a-M3/T1b-SM1, and T1b-SM2 or greater, respectively.[7,8] B1 is defined as type B vessels with a loop-like formation, B2 is defined as type B vessels without a loop-like formation that have a stretched and markedly elongated transformation, and B3 is defined as highly widened abnormal vessels.[7] The avascular area was also defined as a low or no vascularity area surrounded by stretched irregular vessels. Large avascular areas were those ≥3 mm and were suggestive of T1b-SM2 or greater.

Moreover, we also used chromoendoscopy in combination with M-NBI. The presence of pink-color sign in the Lugol-voiding lesions evaluated a few minutes after spraying with a Lugol dye solution was regarded as diagnosis of esophageal cancer.[9] EUS was also used according to the endoscopist's preference. Tumor depth was determined using EUS as follows: the second, third, fourth, and fifth layers in a 9-layered image corresponded to the superficial epithelium plus the interface echo, deep epithelium, lamina propria plus interface echo, muscularis mucosae minus interface echo, and submucosa, respectively.[10] Initial endoscopic diagnosis regarding invasion depth was confirmed based on the agreement by expert endoscopists at the medical conference before therapy. This study was approved by the Ethics Committee of the Keio University School of Medicine.

ER and esophagectomy procedures

Endoscopic submucosal dissection was conducted as reported by us according to the following steps: the tumor margin was demarcated using NBI and sprayed iodine. A peritumoral cutting margin of ≥10 mm was demarcated