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**Endoscopic submucosal dissection for early gastric cancer: It is time to consider the quality of its outcomes**

Kim GH. Quality indicators of ESD

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**Abstract**

Endoscopic resection, particularly endoscopic submucosal dissection (ESD), is widely used as a standard treatment modality for early gastric cancer (EGC) when the risk of lymph node metastasis is negligible. Compared with surgical gastrectomy, ESD is a minimally invasive procedure with additional advantages, such as preservation of the entire stomach and maintenance of the patient’s quality of life. However, not all patients achieve curative resection after ESD of EGC. Several patients require surgical gastrectomy after ESD to achieve a curative treatment. Additional surgery after ESD, owing to non-curative resection, places considerable emotional and financial burdens on patients. Recently, as the number of endoscopists performing ESD has increased, the rate of non-curative resection after ESD has increased correspondingly. In order to decrease the non-curative resection rate, as well as determine the ideal rate of non-curative resection after ESD, it is time to consider quality indicators for the outcomes of ESD for EGC.

**Key Words:** Early gastric cancer; Endoscopic resection; Quality indicator

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**Core Tip:** Endoscopic resection, particularly endoscopic submucosal dissection (ESD), is widely used as a standard treatment modality for early gastric cancer (EGC) when the risk of lymph node metastasis is negligible. Recently, the policy of “diagnostic ESD” has been commonly implemented, especially when accurate prediction of the depth of EGC invasion before ESD is impossible; however, it is neither ideal nor scientific. Therefore, it is time to consider quality indicators for the outcomes of ESD for EGC.

**INTRODUCTION**

Gastric cancer (GC) is the fifth most common malignant tumor and the fourth leading cause of cancer-related deaths worldwide[1]. The diagnosis rate of early GC (EGC) has been increasing owing to the widespread use of endoscopy, especially during health checkups, and the development of advanced endoscopy techniques, such as high-definition endoscopy and virtual chromoendoscopy[2-4]. Endoscopic resection, particularly endoscopic submucosal dissection (ESD), is widely used as a standard modality for the curative treatment of EGC when the risk of lymph node metastasis is negligible[5,6]. Compared with surgical gastrectomy, ESD is a minimally invasive procedure with additional advantages, such as preservation of the entire stomach and maintenance of the patient’s quality of life. Curative resection after ESD is confirmed based on the following lesion characteristics: (1) Differentiated-type mucosal cancer without ulceration, irrespective of tumor size; (2) Differentiated-type mucosal cancer measuring ≤ 3 cm with ulceration; (3) Differentiated-type cancer measuring ≤ 3 cm with minimal submucosal invasion (depth of invasion into the submucosa < 500 μm); and (4) Undifferentiated-type mucosal cancer measuring ≤ 2 cm without ulceration[5,7]. Although ESD achieves *en bloc*/R0 resection in > 90% of cases, it is not curative in up to 20% of cases. This may be due to previously unsuspected submucosal invasion or horizontal extension, changes in histopathological type (especially to the undifferentiated-predominant mixed type), or lymphovascular invasion on histopathological examination[8]. Therefore, accurate evaluation of the size, invasion depth, horizontal extent, and histopathological type of EGC is essential to improve patient selection for curative ESD.

Advances in ESD techniques and devices, as well as increased opportunities to learn ESD (*e.g.,* visiting ESD training centers, participating in *ex vivo* ESD courses, or watching online or offline videos), have enabled more endoscopists to safely and completely perform ESD in clinical practice, especially in Asian countries. However, not all patients achieve curative resection after ESD of EGC. The main risk factors for non-curative resection are as follows: Tumor location in the upper body, large tumor size (≥ 2 cm), presence of an ulcer, presence of undifferentiated-type component tumor, submucosal invasion, and an inexperienced endoscopist[9-11]. Several patients require surgical gastrectomy after ESD to achieve a curative treatment. Although ESD has merits (*e.g.,* preservation of the stomach and maintenance of quality of life), additional surgery after ESD, owing to non-curative resection, places considerable emotional and financial burdens on patients. Recently, as the number of endoscopists performing ESD has increased, the rate of non-curative resection after ESD has increased correspondingly. In order to decrease the non-curative resection rate, as well as determine the ideal rate of non-curative resection after ESD, we return to the basics.

**Tips for successful ESD of EGC**

Successful ESD of EGC requires accurate prediction of the invasion depth, horizontal extent, and histopathological type of the tumor[2]. To accurately predict the depth of EGC invasion, the macroscopic morphology of the tumor is first considered. Macroscopic findings such as tumor size > 30 mm, remarkable redness, uneven surface, subepithelial tumor-like margin elevation, and mucosal fold convergence are useful for determining the depth of tumor invasion, with a reported accuracy of 83%-97%[12]. However, endoscopic prediction of the invasion depth is subjective and influenced by the endoscopist’s level of experience. Endoscopic ultrasonography (EUS) can also be used for determining the depth of EGC invasion, and its overall accuracy with a high-frequency (20 MHz) catheter probe is 81%[13]. EUS is an operator-dependent procedure. In addition, in a retrospective study comparing the accuracy of EUS and conventional endoscopy (based on macroscopic findings) in determining the depth of EGC invasion, EUS was not superior to conventional endoscopy[14]. An integrated diagnostic strategy combining conventional endoscopy and EUS has shown an accuracy of > 85%[15].

The horizontal extent of EGC is mainly determined using conventional endoscopy; however, making accurate prediction becomes challenging when the height and color of the tumor are similar to those of the surrounding normal mucosa. In this situation, chromoendoscopy with indigo carmine alone or indigo carmine and acetic acid, and magnifying endoscopy with narrow-band imaging (ME-NBI) can increase the accuracy of horizontal extent prediction to 90% approximately[16,17]. However, in undifferentiated-type EGC, predicting the horizontal extent using these modalities is challenging. Therefore, during endoscopic examination, biopsy specimens should be obtained from the surrounding tissues and examined histopathologically prior to ESD[12].

The histopathological type of EGC is usually determined based on the results of endoscopic forceps biopsies. However, because these results often do not correctly reflect the final histopathology, histological discrepancies may occur between endoscopic biopsy and ESD-resected specimens. Although the macroscopic morphology and color of lesions have been shown to help predict the histopathological type of EGC, adequate evidence is lacking. Several studies have reported that microsurface and microvascular patterns on ME-NBI can predict the histopathological type of EGC[2,18]. However, systematic ME classification systems, such as those for colorectal polyps and esophageal lesions, have not yet been developed for EGC.

Hence, other methods to accurately predict the depth of invasion and horizontal extent of EGC are required. Recent studies have reported the use of artificial intelligence (AI) systems for this purpose. Two recent meta-analyses reported that the pooled sensitivity and specificity of AI for predicting deep submucosal invasion were 72%-82% and 79%-90%, respectively[19,20]. In the future, endoscopist-AI cooperation can improve the predictive rates of the depth of invasion, horizontal extent, and histopathological type of EGC before ESD.

**CONCLUSION**

Recently, the policy of “diagnostic ESD” has been commonly implemented, especially when accurate prediction of the depth of EGC invasion before ESD is impossible. Many young endoscopists have adopted this approach. However, despite its value as diagnostic ESD, it is neither ideal nor scientific. The standard endoscopic process for EGC consists of the following steps: Presence diagnosis (determination of the presence or absence of cancer), qualitative diagnosis (determination of histopathological type), and quantitative diagnosis (determination of depth of invasion and horizontal extent)[2]. Although this process is not perfect, it is recommended for all endoscopists as a basis for every effort to avoid non-curative resection after ESD. Performing ESD without such efforts is likely to increase the non-curative resection rate after ESD for EGC, leading to emotional and economic burdens on patients. Based on the accuracy of endoscopic prediction of the depth of tumor invasion (about 80%) and horizontal tumor extent (about 90%), the ideal non-curative resection rate after ESD is < 15%-20%. According to a recent meta-analysis, *en bloc*, complete, and curative resection rates in Eastern studies were 95% [95% confidence interval (CI): 94%-96%], 89% (95%CI: 88%-91%), and 82% (95%CI: 81%-84%), respectively[21]. EGC cases in which ESD is performed beyond the current ESD indications, considering patient factors such as comorbidities, life expectancy, and the ability to tolerate surgery, should be excluded from this calculation. Furthermore, the main adverse events of ESD, such as post-ESD bleeding and perforation, should be considered when evaluating the quality of ESD outcomes. The overall rates of delayed bleeding and perforation are reported to be 2.6%-8.5% and 2.3%-3.9%, respectively[22-24]. Based on previous reports, I suggest quality indicators for the outcomes of ESD for EGC in Table 1.

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**Table 1 Suggested quality indicators for outcomes of endoscopic submucosal dissection for early gastric cancer**

|  |  |
| --- | --- |
| **Quality indicator** | **Performance target** |
| *En bloc* resection rate | > 95% |
| Complete resection rate | > 90% |
| Curative resection rate | > 80% |
| Adverse events |  |
| Post-ESD bleeding | < 10% |
| Perforation | < 5% |

ESD: Endoscopic submucosal dissection.



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