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EDITORIAL

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

Gwang Ha Kim

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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

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.

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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.

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.

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.

FOOTNOTES

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REFERENCES

1 **Sung H**, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021; **71**: 209-249 [PMID: 33538338 DOI: 10.3322/caac.21660]

2 **Kim GH**. Systematic Endoscopic Approach to Early Gastric Cancer in Clinical Practice. *Gut Liver* 2021; **15**: 811-817 [PMID: 33790057 DOI: 10.5009/gnl20318]

3 **Lee SP**. Role of linked color imaging for upper gastrointestinal disease: present and future. *Clin Endosc* 2023; **56**: 546-552 [PMID: 37430400 DOI: 10.5946/ce.2023.015]

4 **Lee W**. Application of Current Image-Enhanced Endoscopy in Gastric Diseases. *Clin Endosc* 2021; **54**: 477-487 [PMID: 34315196 DOI: 10.5946/ce.2021.160]

5 **Park CH**, Yang DH, Kim JW, Kim JH, Min YW, Lee SH, Bae JH, Chung H, Choi KD, Park JC, Lee H, Kwak MS, Kim B, Lee HJ, Lee HS, Choi M, Park DA, Lee JY, Byeon JS, Park CG, Cho JY, Lee ST, Chun HJ. Clinical Practice Guideline for Endoscopic Resection of Early Gastrointestinal Cancer. *Clin Endosc* 2020; **53**: 142-166 [PMID: 32252507 DOI: 10.5946/ce.2020.032]

6 **Palacios-Salas F**, Benites-Goñi H, Marin-Calderón L, Bardalez-Cruz P, Vásquez-Quiroga J, Alva-Alva E, Medina-Morales B, Asencios-Cusihuallpa J. Efficacy and Safety of Endoscopic Submucosal Dissection for Superficial Gastric Neoplasms: A Latin American Cohort Study. *Clin Endosc* 2022; **55**: 248-255 [PMID: 34763382 DOI: 10.5946/ce.2021.192]

7 **Japanese Gastric Cancer Association**. Japanese Gastric Cancer Treatment Guidelines 2021 (6th edition). *Gastric Cancer* 2023; **26**: 1-25 [PMID: 36342574 DOI: 10.1007/s10120-022-01331-8]

8 **Park YM**, Cho E, Kang HY, Kim JM. The effectiveness and safety of endoscopic submucosal dissection compared with endoscopic mucosal resection for early gastric cancer: a systematic review and metaanalysis. *Surg Endosc* 2011; **25**: 2666-2677 [PMID: 21424201 DOI: 10.1007/s00464-011-1627-z]

9 **Lee SH**, Kim MC, Jeon SW, Lee KN, Park JJ, Hong SJ. Risk Factors and Clinical Outcomes of Non-Curative Resection in Patients with Early Gastric Cancer Treated with Endoscopic Submucosal Dissection: A Retrospective Multicenter Study in Korea. *Clin Endosc* 2020; **53**: 196-205 [PMID: 31648421 DOI: 10.5946/ce.2019.123]

10 **Toyokawa T**, Inaba T, Omote S, Okamoto A, Miyasaka R, Watanabe K, Izumikawa K, Fujita I, Horii J, Ishikawa S, Morikawa T, Murakami T, Tomoda J. Risk factors for non-curative resection of early gastric neoplasms with endoscopic submucosal dissection: Analysis of 1,123 lesions. *Exp Ther Med* 2015; **9**: 1209-1214 [PMID: 25780411 DOI: 10.3892/etm.2015.2265]

11 **Horiuchi Y**, Fujisaki J, Yamamoto N, Ishizuka N, Omae M, Ishiyama A, Yoshio T, Hirasawa T, Yamamoto Y, Nagahama M, Takahashi H, Tsuchida T. Undifferentiated-type component mixed with differentiated-type early gastric cancer is a significant risk factor for endoscopic non-curative resection. *Dig Endosc* 2018; **30**: 624-632 [PMID: 29570860 DOI: 10.1111/den.13059]

12 **Hisada H**, Sakaguchi Y, Oshio K, Mizutani S, Nakagawa H, Sato J, Kubota D, Obata M, Cho R, Nagao S, Miura Y, Mizutani H, Ohki D, Yakabi S, Takahashi Y, Kakushima N, Tsuji Y, Yamamichi N, Fujishiro M. Endoscopic Treatment of Superficial Gastric Cancer: Present Status and Future. *Curr Oncol* 2022; **29**: 4678-4688 [PMID: 35877231 DOI: 10.3390/curroncol29070371]

13 **Kim GH**, Park DY, Kida M, Kim DH, Jeon TY, Kang HJ, Kim DU, Choi CW, Lee BE, Heo J, Song GA. Accuracy of high-frequency catheter-based endoscopic ultrasonography according to the indications for endoscopic treatment of early gastric cancer. *J Gastroenterol Hepatol* 2010; **25**: 506-511 [PMID: 20074167 DOI: 10.1111/j.1440-1746.2009.06111.x]

14 **Choi J**, Kim SG, Im JP, Kim JS, Jung HC, Song IS. Comparison of endoscopic ultrasonography and conventional endoscopy for prediction of depth of tumor invasion in early gastric cancer. *Endoscopy* 2010; **42**: 705-713 [PMID: 20652857 DOI: 10.1055/s-0030-1255617]

15 **Tsujii Y**, Kato M, Inoue T, Yoshii S, Nagai K, Fujinaga T, Maekawa A, Hayashi Y, Akasaka T, Shinzaki S, Watabe K, Nishida T, Iijima H, Tsujii M, Takehara T. Integrated diagnostic strategy for the invasion depth of early gastric cancer by conventional endoscopy and EUS. *Gastrointest Endosc* 2015; **82**: 452-459 [PMID: 25841580 DOI: 10.1016/j.gie.2015.01.022]

16 **Nagahama T**, Yao K, Maki S, Yasaka M, Takaki Y, Matsui T, Tanabe H, Iwashita A, Ota A. Usefulness of magnifying endoscopy with narrow-band imaging for determining the horizontal extent of early gastric cancer when there is an unclear margin by chromoendoscopy (with video). *Gastrointest Endosc* 2011; **74**: 1259-1267 [PMID: 22136775 DOI: 10.1016/j.gie.2011.09.005]

17 **Lee BE**, Kim GH, Park DY, Kim DH, Jeon TY, Park SB, You HS, Ryu DY, Kim DU, Song GA. Acetic acid-indigo carmine chromoendoscopy for delineating early gastric cancers: its usefulness according to histological type. *BMC Gastroenterol* 2010; **10**: 97 [PMID: 20731830 DOI: 10.1186/1471-230X-10-97]

18 **Ok KS**, Kim GH, Park do Y, Lee HJ, Jeon HK, Baek DH, Lee BE, Song GA. Magnifying Endoscopy with Narrow Band Imaging of Early Gastric Cancer: Correlation with Histopathology and Mucin Phenotype. *Gut Liver* 2016; **10**: 532-541 [PMID: 27021504 DOI: 10.5009/gnl15364]

19 **Xie F**, Zhang K, Li F, Ma G, Ni Y, Zhang W, Wang J, Li Y. Diagnostic accuracy of convolutional neural network-based endoscopic image analysis in diagnosing gastric cancer and predicting its invasion depth: a systematic review and meta-analysis. *Gastrointest Endosc* 2022; **95**: 599-609.e7 [PMID: 34979114 DOI: 10.1016/j.gie.2021.12.021]

20 **Jiang K**, Jiang X, Pan J, Wen Y, Huang Y, Weng S, Lan S, Nie K, Zheng Z, Ji S, Liu P, Li P, Liu F. Current Evidence and Future Perspective of Accuracy of Artificial Intelligence Application for Early Gastric Cancer Diagnosis With Endoscopy: A Systematic and Meta-Analysis. *Front Med (Lausanne)* 2021; **8**: 629080 [PMID: 33791323 DOI: 10.3389/fmed.2021.629080]

21 **Daoud DC**, Suter N, Durand M, Bouin M, Faulques B, von Renteln D. Comparing outcomes for endoscopic submucosal dissection between Eastern and Western countries: A systematic review and meta-analysis. *World J Gastroenterol* 2018; **24**: 2518-2536 [PMID: 29930473 DOI: 10.3748/wjg.v24.i23.2518]

22 **Uozumi T**, Abe S, Makiguchi ME, Nonaka S, Suzuki H, Yoshinaga S, Saito Y. Complications of endoscopic resection in the upper gastrointestinal tract. *Clin Endosc* 2023; **56**: 409-422 [PMID: 37430401 DOI: 10.5946/ce.2023.024]

23 **Hatta W**, Koike T, Abe H, Ogata Y, Saito M, Jin X, Kanno T, Uno K, Asano N, Imatani A, Masamune A. Recent approach for preventing complications in upper gastrointestinal endoscopic submucosal dissection. *DEN Open* 2022; **2**: e60 [PMID: 35310735 DOI: 10.1002/deo2.60]

24 **Peng LJ**, Tian SN, Lu L, Chen H, Ouyang YY, Wu YJ. Outcome of endoscopic submucosal dissection for early gastric cancer of conventional and expanded indications: systematic review and meta-analysis. *J Dig Dis* 2015; **16**: 67-74 [PMID: 25421172 DOI: 10.1111/1751-2980.12217]

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