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Corresponding author
Jongha Park, MD, PhD
Department of Internal Medicine,
Inje University Haeundae Paik Hospital,
875 Haeundae-ro, Haeundae-gu,
Busan 48108, Korea
E-mail: neakker@gmail.com

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# Comparison of Endoscopic Submucosal Dissection With Endoscopic Mucosal Resection After Circumferential Precutting to Treat Gastric Adenomas ≤15 mm

Jin Lee, Junghwan Lee, Ji Eun Na, Yong Eun Park, Joon Hyuk Choi, Nae-Yun Heo, Seung Ha Park, Tae Oh Kim, and Jongha Park

Department of Internal Medicine, Inje University Haeundae Paik Hospital, Inje University College of Medicine, Busan, Korea

**Objectives:** Endoscopic submucosal dissection (ESD) is a widely used approach for the resection of superficial gastric neoplastic lesions. Endoscopic mucosal resection (EMR) is acceptable for lesions <10–15 mm in size. Herein, we compared the clinical outcomes of ESD with those of EMR after circumferential precutting (EMR-P) for gastric adenomas ≤15 mm. **Methods:** We retrospectively analyzed the data of 213 patients with 228 gastric adenomas ≤15 mm in size who were treated endoscopically at a single tertiary hospital in Korea between November 2018 and October 2022. We evaluated the complete endoscopic resection rate, recurrence rate, procedure-related complications, and procedure time according to the procedure used. **Results:** Among the 228 gastric adenomas, 49 were treated with EMR-P and 179 with ESD. The histological complete resection rate was higher in the ESD group than in the EMR-P group (87% vs. 57%, $p<0.001$). No significant between-group differences were observed in endoscopic en bloc resection rates (ESD vs. EMR-P, 96% vs. 90%; $p=0.081$). The procedure time was significantly shorter in the EMR-P group than in the ESD group (28.9±19.7 min vs. 8.8±5.9 min, $p<0.001$). The local recurrence rate in patients with histologically incomplete resection did not differ between the two groups (ESD vs. EMR-P, 8.7% vs. 9.5%; $p=0.924$). **Conclusions:** For gastric adenomas ≤15 mm, EMR-P may be the preferable treatment method considering the en bloc resection rate, procedure time, and local recurrence rate. However, considering the complete resection rate, ESD is recommended as the treatment of choice for high-grade adenomas and early gastric cancer lesions.

**Keywords** Adenoma; Stomach neoplasms; Endoscopic mucosal resection.

## INTRODUCTION

Gastric adenomas are benign lesions that arise from the inner lining of the stomach. If left untreated, gastric adenomas can progress into gastric cancer, emphasizing the importance of early detection and treatment of such adenomas. Endoscopic resection is widely used to treat superficial gastric neoplastic lesions. Current guidelines recommend endoscopic resection for the treatment of gastric superficial neoplastic lesions, such as gastric adenomas or early gastric cancers (EGCs).[1-4] While endoscopic submucosal dissection (ESD) is the recommended treatment of choice for gastric superficial neoplastic lesions,[4,5] endoscopic mucosal resection (EMR) is preferred for lesions smaller than 10−15 mm that are not likely to show advanced histological findings. Modified EMR procedures facilitate the safe and rapid removal of small gastric lesions; these procedures include EMR after circumferential precutting (EMR-P), cap-assisted EMR (EMR-C), and EMR using a ligation device

 

(EMR-L). For low-grade dysplasia, argon plasma coagulation (APC) can be used to remove lesions faster, more conveniently, and with fewer complications compared to mucosal or submucosal dissection.[6]

EMR-P is the preferred treatment approach for gastric adenomas. In EMR-P, adenoma removal involves the creation of a circular incision around the adenoma, followed by lifting and resection of the lesion. Contrastingly, in ESD, en bloc resection of the lesion is performed by dissecting and removing the submucosal layer. Both EMR-P and ESD have proven to be effective for treating gastric neoplastic lesions.[7,8] However, the debate regarding the most effective technique for adenomas, especially those with a diameter of ≤15 mm, is still ongoing. This cutoff diameter is important because it represents a clinically relevant size threshold for the management of gastric adenomas. Selecting between EMR-P and ESD for small gastric adenoma treatment is challenging, as it necessitates the identification of the technique yielding superior outcomes in terms of complete resection, safety, and recurrence rate. Understanding the advantages and disadvantages of each technique would facilitate selection of the optimal treatment approach for each patient. While previous studies have compared EMR-P and ESD for EGC,[7] no consensus has been reached on the optimal treatment approach for smaller gastric adenomas. A comprehensive evaluation of the treatment of adenomas ≤15 mm is required to guide clinical decision-making. Thus, this study aimed to compare the outcomes of EMR-P and ESD for gastric adenomas ≤15 mm in size.

## METHODS

### Patients

We retrospectively analyzed the findings of 228 gastric adenomas in 213 patients who were endoscopically treated at a single tertiary hospital in Korea between November 2018 and October 2022. We analyzed the baseline characteristics of the patients and gastric adenomas. The clinical outcomes of endoscopic resection, including the endoscopic en bloc resection rate, histological complete resection rate, recurrence rate, and procedure time were also analyzed. Patients aged ≥18 years, with gastric adenomas confirmed by endoscopic resection, and with a maximum adenoma diameter of ≤15 mm in the final pathological results were included. Patients with a history of surgery for gastric lesions or carcinomas were excluded. This study was approved by the Institutional Review Board of Inje University Haeundae Paik Hospital (HPIRB 2023-06-006). Informed consent was not obtained because this was a retrospective study.

### Endoscopic resection methods

The endoscopic resection procedures were performed by experienced endoscopists proficient in both the EMR-P and ESD techniques. For low-grade adenomas (LGDs) ≤15 mm in size that were not associated with risk factors, the treatment approach employed followed the endoscopist's preference. Risk factors for the development of high-grade adenomas (HGDs) or malignancy were a lesion size of >2 cm or the presence of a depression, rough or reddish surface, or spontaneous bleeding. ESD was performed in patients with HGDs or LGDs associated with risk factors. Even if the gastric adenoma was <15 mm in size, ESD was performed in case the patient desired it or when the tumor was initially estimated to be >15 mm prior to resection but was ultimately confirmed to be <15 mm. Patients in the ESD group underwent a second-look endoscopy the subsequent day, while those in the EMR-P group were discharged without a second-look endoscopy.

Herein, EMR-P was performed as follows. A 15-mm snare with a 0.47-mm wire diameter (SD-210U-15; Olympus, Tokyo, Japan) was used for the procedure. Once the lesion size and location were confirmed, a snare tip was used to mark the circumference approximately 2–5 mm outside the margin of the lesion. Subsequently, a saline solution containing a mixture of epinephrine and indigo carmine was injected submucosally around the lesion to lift it. Initial and circumferential mucosal incisions were then taken using the snare tip. The saline solution containing a mixture of epinephrine and indigo carmine was then submucosally injected under the lesion. Finally, the lesion was ensnared using a snare and resected as per conventional EMR.

The ESD procedures were performed using a dual knife (KD-650L; Olympus, Tokyo, Japan). Once the lesion was confirmed, a needle knife was used to mark the circumference approximately 2–5 mm outside the lesion margin. A saline solution containing a mixture of epinephrine and indigo carmine was the injected submucosally around the lesion to lift it. Subsequently, a circumferential incision was taken and submucosal dissection was performed using a needle knife.

### Follow-up

Follow-up endoscopy was performed at 6 months or 1 year after endoscopic resection. Gastric adenomas carry a low risk of malignancy development even in cases of incomplete resection, and false positive tumor margins can be caused by the cautery effect. Therefore, no additional treatment was performed, and follow-up endoscopy was then planned.

### Outcome measures

The primary outcome measures were the complete resec-

tion rate, en bloc resection rate, and procedure time. Complete resection was defined as the absence of residual adenoma tissue upon histopathological examination of the resected specimen. En bloc resection was defined as removal of the lesion in a single piece without fragmentation. Procedure time was measured from the start of the procedure to the end of the resection. Furthermore, the secondary outcome measures included the perforation, bleeding, and recurrence rates. Perforation was defined as the presence of an iatrogenic full-thickness hole in the gastric wall that required endoscopic or surgical intervention, or free air on a post-procedure chest radiograph without the presence of a definite gastric wall defect during the procedure. Bleeding was defined as any massive intraprocedural or postprocedural bleeding that necessitated blood transfusion. Recurrence was defined as the presence of a recurrent adenoma at the resection site during follow-up endoscopy.

### Statistical analysis

Data are presented as mean±standard deviation for numerical variables and as frequencies and percentages for categorical variables. Numerical data were analyzed using the independent t-test or Mann–Whitney U test, and categorical data were analyzed using the chi-square or Fisher's exact test. Factors related to incomplete histological resection were analyzed using univariate and multivariate logistic regression analyses. All statistical analyses were performed using IBM SPSS software version 25.0 (IBM Corp., Armonk, NY, USA). Statistical significance was set at $p<0.05$.

## RESULTS

### Patients and tumors

A total of 213 patients with 228 gastric adenomas were treated endoscopically. Among the 228 gastric adenomas ≤15 mm in size, 49 were treated with EMR-P and 179 with ESD. The mean age of the enrolled patients was 68 years (range, 40–85 years), and the study population included 127 (59.6%) men and 86 (40.4%) women. Overall, 204 lesions (89.5%) were LGDs and 24 (10.5%) were HGDs. The final pathological results revealed 23 HGDs in the ESD group (12.8%), which was significantly higher than the number of HGDs in the EMR group (n=1; 2.0%). The EMR-P and ESD groups showed no significant differences in age, sex, endoscopic tumor appearance, or tumor location. However, the tumor size was significantly smaller in the EMR-P group than in the ESD group (6.9 mm vs. 8.5 mm, $p<0.05$). The patient and lesion characteristics are shown in Table 1.

**Table 1.** Baseline characteristics of patients and tumors

| Characteristics | EMR-P (n=49) | ESD (n=179) | *p*-value |
|---|---|---|---|
| Age (yr) | 67.6±10.7 | 66.4±8.9 | 0.101 |
| Male sex | 27 (55.1) | 111 (62.0) | 0.381 |
| Tumor size (mm) | 6.9±3.1 | 8.5±3.5 | 0.003 |
| Type of adenoma | | | 0.029 |
| Low-grade dysplasia | 48 (98.0) | 156 (87.2) | |
| High-grade dysplasia | 1 (2.0) | 23 (12.8) | |
| Macroscopic appearance | | | 0.489 |
| Elevated | 29 (59.2) | 96 (53.6) | |
| Flat or depressed | 20 (40.8) | 83 (46.4) | |
| Tumor location | | | 0.802 |
| Antrum | 28 (57.1) | 90 (50.3) | |
| Angle | 3 (6.1) | 30 (16.8) | |
| Body | 17 (34.7) | 54 (30.2) | |
| Cardia | 1 (2.0) | 5 (2.8) | |

Values are presented as mean±standard deviation or n (%).
EMR-P, endoscopic mucosal resection after circumferential precutting; ESD, endoscopic submucosal dissection.

### Clinical outcomes

The outcomes of EMR-P and ESD are shown in Table 2. Overall, the complete histological resection rate in both groups was 80.7% and the en bloc resection rate was 94.7%. The histological complete resection rate was significantly higher in the ESD group than in the EMR-P group (87% vs. 57%, $p<0.001$). The ESD group showed a trend toward superior en bloc resection rates. While the difference was not statistically significant (96% vs. 90%, $p=0.081$), this indicated that ESD may be more effective in removing gastric adenomas with a diameter of ≤15 mm. The procedure time was significantly shorter in the EMR-P group than in the ESD group (28.9±19.7 min vs. 8.8±5.9 min, $p<0.001$). No significant between-group differences in bleeding rates were observed, and no perforations were observed in either group.

### Follow-up and recurrence

The mean follow-up period was 12 months in the EMR-P group and 14 months in the ESD group, with no significant intergroup differences. Over a median follow-up period of 12 (range: 2.6–44.7) months, low-grade gastric adenomas recurred in four patients, all of whom were in the histological incomplete resection group. Two patients who relapsed after EMR-P underwent additional ESD, while two patients who relapsed after ESD underwent EMR and APC, respectively. The local recurrence rates did not differ significantly between the two groups (ESD vs. EMR-P, 1.1% vs. 4.1%; $p=0.162$). Thus, both EMR-P and ESD were effective in preventing the recurrence of gastric adenomas ≤15 mm. There were no surgical interventions or

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deaths, and there were no significant between-group differences in the long-term prognoses.

### Factors influencing histologic incomplete resection of gastric adenomas ≤15 mm

In the univariate and multivariate analyses, non-antral tumor location and the EMR-P method were associated with incomplete histological resection (Table 3). For non-antral tumor location (vs. antral location), the odds ratios (ORs) were 2.7 (95% confidence interval [CI], 1.38–5.59; $p$=0.004) in the univariate analysis and 3.7 (95% CI, 1.73–8.16; $p$<0.001) in the multivariate analysis. For the EMR-P method (vs. ESD method), the ORs were 5.4 (95% CI, 2.48–10.40; $p$<0.001) in the univariate analysis and 6.8 (95% CI, 3.07–15.09; $p$<0.001) in the multivariate analysis. Tumor size and macroscopic appearance were not associated with incomplete histological resection in the univariate and multivariate analyses.

## DISCUSSION

Gastric adenomas are precancerous lesions. Appropriate diagnosis and treatment of these lesions are crucial for the early detection and prevention of gastric cancer. While consensus regarding the treatment of HGDs has been achieved, the treatment of LGDs remains controversial. LGDs have a low probability of progressing to cancer (<10%), and some spontaneously disappear during follow-up.[9,10] Therefore, a previous version of the revised Vienna classification[11] recommended endoscopic treatment or follow-up for LGDs and endoscopic treatment for HGDs. However, the most recent guidelines recommend endoscopic treatment for HGDs and endoscopic resection for accurate pathological diagnosis for most LGDs. The most recent British Society of Gastroenterology (BSG) guidelines recommend complete endoscopic resection of both LGDs and HGDs.[3] Furthermore, the American Society for Gastrointestinal Endoscopy guidelines also recommend endoscopic resection of adenomas of any grade or size.[2]

Considering the histologic discrepancy between forceps biopsy and endoscopic resection, ESD is an effective treatment approach for HGDs or lesions that are highly likely to progress to cancer after endoscopic resection. Risk factors that indicate a high risk of high-grade dysplasia or malignancy development are a lesion size of >2 cm and the presence of a depression, a rough or reddish surface, and spontaneous bleeding. Although several previous studies have reported that ESD is more effective than EMR for endoscopic resection of superficial gastric neoplastic lesions,[7,12-14] ESD is associated with a high frequency of complications, such as bleeding and perforation. It requires more time and is costlier than EMR. In Korea, the cost of an ESD knife is approximately 210000 KRW (158 USD), and

**Table 2.** Clinical outcomes of EMR-P and ESD for gastric adenomas ≤15 mm

| Outcomes | Overall (n=228) | EMR-P (n=49) | ESD (n=179) | *p*-value |
|---|---|---|---|---|
| En bloc resection | 216 (94.7) | 44 (89.8) | 172 (96.1) | 0.081 |
| Histologic complete resection | 184 (80.7) | 28 (57.1) | 156 (87.2) | <0.001 |
| Procedure time (min) | 24.6±19.5 | 8.8±5.9 | 28.9±19.7 | <0.001 |
| Bleeding | 0 | 0 | 0 | |
| Perforation | 0 | 0 | 0 | |
| Local recurrence | 4 (1.8) | 2 (4.1) | 2 (1.1) | 0.162 |

Values are presented as mean±standard deviation or n (%).
EMR-P, endoscopic mucosal resection after circumferential precutting; ESD, endoscopic submucosal dissection.

**Table 3.** Risk factors for incomplete histologic resection

| Risk factors | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | OR (95% CI) | *p*-value | OR (95% CI) | *p*-value |
| Tumor size ≥10 mm (vs. <10 mm) | 1.1 (0.59–2.32) | 0.631 | 1.6 (0.75–3.43) | 0.215 |
| EMR-P (vs. ESD) | 5.4 (2.48–10.40) | <0.001 | 6.8 (3.07–15.09) | <0.001 |
| Location | | | | |
| Antrum | 1 (reference) | | | |
| Non-antrum | 2.7 (1.38–5.59) | 0.004 | 3.7 (1.73–8.16) | <0.001 |
| Macroscopic appearance | | | | |
| Elevated | 1 (reference) | | | |
| Non-elevated (flat/depressed) | 0.8 (0.41–1.57) | 0.527 | 0.7 (3.37–1.61) | 0.498 |

EMR-P, endoscopic mucosal resection after circumferential precutting; ESD, endoscopic submucosal dissection; OR, odds ratio; CI, confidence interval.

additional costs are incurred if additional knives are used. In EMR-P, the cost of the snare is approximately 64000 KRW (48 USD), which is the same as that of conventional EMR because the snare tip is used for precutting. Socioeconomically, differences in the scope of medical expense coverage based on the medical insurance system of each country may affect the choice of treatment method. Another limitation of ESD is that the success of the procedure depends on operator proficiency.

EMR is a widely used treatment method because it requires less time than ESD and is relatively less affected by the operator's skill level. EMR is an acceptable option for LGDs smaller than 10–15 mm that are not associated with risk factors. Modified EMR technique, including EMR-P, EMR-C, and EMR-L, were developed to safely and rapidly remove small gastric lesions. However, compared with ESD, EMR has a lower rate of en bloc and complete resection. In particular, en bloc and complete resection rates decrease significantly when the lesion is >2 cm in size or has an unfavorable location. Therefore, EMR may be a good method for treating small LGDs with no associated risk factors. Nevertheless, no clear cutoff for lesion size is currently available to determine treatment methods. The BSG guidelines recommend EMR for gastric adenomas ≤10 mm in size and EGC and ESD for lesions >10 mm in size. Japanese studies have reported that en bloc resection rates are significantly lower with EMR than with ESD for tumors >1 cm in size.[15-17] In Korea, ESD for LGDs <15 mm without fibrosis is not covered by medical care and EMR or APC are widely used to treat such lesions in clinical practice. Compared with endoscopic resection, APC offers advantages such as shorter operative time, lower risk of bleeding or perforation, no requirement for hospitalization, lower operative cost, and reduced reliance on operator skill. However, APC for large or sunken lesions is associated with a low treatment efficacy and high recurrence rate. In addition, a biopsy of the entire lesion cannot be performed. Therefore, EMR is preferred for small LGDs, with EMR-P recommended as a good approach in such cases.

Although previous studies have compared the effectiveness of ESD and modified EMR for EGC resection,[7] few studies have analyzed the effects of ESD and modified EMR on small gastric adenomas. Our study provides important insights by comparing the effectiveness of EMR-P and ESD for gastric adenomas ≤15 mm. Our findings indicate that ESD is more effective than EMR-P in achieving complete resection of smaller adenomas, which is consistent with the results of previous studies, which demonstrated the superiority of ESD for larger lesions. As ESD facilitates accurate dissection and removal of the submucosal layer, thereby ensuring the complete removal of the lesion, it leads to higher complete and en bloc resection rates. In contrast, EMR-P involves lesion resection without dissection of the submucosal layer, potentially increasing the risk of incomplete resection and residual adenoma tissue. However, the longer procedure times associated with ESD requires consideration, as this may increase patient discomfort and potentially limit the applicability of this technique. Thus, endoscopists should consider the trade-off between effectiveness and efficiency when choosing the appropriate resection technique. Notably, our findings indicate that both EMR-P and ESD are safe in terms of perforation and bleeding rates, suggesting that both techniques can be performed safely with the appropriate expertise and caution. Endoscopists should carefully consider their own experience and skills when deciding which technique to use.

In the present study, while the histological complete resection rate differed significantly between the two groups, the local recurrence rate did not. This may be due to the securing additional margins by tissue ablation during the pre-cut process and the interpretation of false-positive tumor margins in the pathology results owing to the effects of cautery during the procedure. The similar recurrence rates between the two groups indicate that both techniques are effective in preventing the recurrence of gastric adenomas ≤15 mm. However, long-term follow-up studies are required to evaluate the durability of resection and assess the long-term risk of recurrence.

Furthermore, herein, the tumor size was significantly smaller in the EMR-P group than in the ESD group (6.9 mm vs. 8.5 mm, $p<0.05$). This difference is thought to be because EMR-P was preferred for the resection of slightly smaller adenomas, as the procedure was chosen per the operator's discretion. As the complete resection rate in ESD is higher than that in EMR for small adenomas, ESD may be the most effective resection method. Our study demonstrated that a non-antral tumor location was significantly associated with incomplete histological resection. Thus, herein, consistent with the results of previous studies,[18,19] the lesion location was an important factor that affected curative endoscopic resection.

This study has several limitations that require consideration. First, because the procedures were performed at a single hospital, the sample size was relatively small, which may limit the generalizability of our findings. Second, the basic characteristics of the EMR-P and ESD groups differed because this was a retrospective rather than a randomized study. There were more patients in the ESD group than in the EMR-P group. In addition, the tumor size was significantly smaller and the proportion of HGDs was lower in the EMR-P group. Finally, the follow-up period was relatively short, with five patients having a follow-up period of <3 months and 42 patients having a follow-up period of <6 months. This may have affected our analysis of recurrence rates. Therefore, it would be beneficial to

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report the long-term results of these data in a follow-up study.

In conclusion, our study suggests that in terms of complete resection, ESD is more effective than EMR-P for gastric adenomas ≤15 mm in size. However, ESD is a challenging procedure in terms of skill, and it involves a long operative time and high cost. For gastric adenomas ≤15 mm, EMR-P may be preferred considering the en bloc resection rate, procedure time, and local recurrence rate. Nevertheless, considering the complete resection rate, ESD is recommended as the treatment of choice for HGDs and EGC. The choice between the two techniques should be based on individual patient factors and operator expertise. Further studies are required to validate our findings and evaluate long-term outcomes.

### Authors' Contribution

Conceptualization: Jin Lee. Data curation: Jin Lee, Ji Eun Na, Yong Eun Park. Formal analysis: Jin Lee. Investigation: Junghwan Lee, Joon Hyuk Choi, Nae-Yun Heo. Methodology: Seung Ha Park, Jongha Park. Writing—original draft: Jin Lee. Writing—review & editing: Jin Lee, Tae Oh Kim, Jongha Park. Approval of final manuscript: all authors.

### ORCID iDs

Jin Lee https://orcid.org/0000-0003-2404-385X
Junghwan Lee https://orcid.org/0000-0002-2910-479X
Ji Eun Na https://orcid.org/0000-0003-3092-9630
Yong Eun Park https://orcid.org/0000-0003-4274-8204
Joon Hyuk Choi https://orcid.org/0000-0001-5014-6436
Nae-Yun Heo https://orcid.org/0000-0001-6571-8935
Seung Ha Park https://orcid.org/0000-0002-5950-2713
Tae Oh Kim https://orcid.org/0000-0002-7359-1599
Jongha Park https://orcid.org/0000-0002-5241-1747

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